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Deanship of Graduate Studies

Faculty of Education

Faculty of Nursing

Assessment of Tramadol Abuse Among Clients Who Are Attending Private Psychiatric Clinics –KAP Study

Submitted By

Mohammed Rafeq Hassan Tafesh

BSc. of Nursing Islamic University of Gaza- Palestine

Supervised By

Dr.Jehad Hammad

Assistant professor

Faculty of Medicine

Pharmacological Department

Islamic University- Gaza

Dr.Abed alfatah Alhams

Associated professor

Faculty of Education

Islamic University -Gaza

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Dedication

I dedicate this work to the soul of my father who generously dedicated his life for us.

To my dear mother that the secret of my success is her du'aa.

To my wife and my beautiful children's "Hala, Tala , Qusai" who are the joy of my life for their patience and support .

To my brothers, sisters and all my relatives who encouraged and inspired me.

To my friends for their support and endless help.

To the Palestinian people especially for martyrs and prisoners .

Thank you and may Allah bless you

Mohammed Rafeq Hassan Tafesh

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Abstract

Tramadol hydrochloride is centrally acting analgesic. It is used for the management of moderate to severe pain. There are increasing concerns worldwide regarding the addiction potential of tramadol. The overall aim of this study is to assess the abuse of tramadol among clients who attend private psychiatric clinics, by assessing the level of knowledge, attitude, and practice. The study also evaluated the psychological status, and the presence of side effects related to abuse of tramadol.

The design of the study is a descriptive, analytical cross sectional one. 100 clients were selected from two private psychiatric clinics in Gaza city over one month by taking 4 clients every day, the response rate was 83.3. The questionnaire was developed to reflect the study domains. Data were collected utilizing the self-administered questionnaire approach and the reliability coefficient (Cronbach's Alpha was high 0.8633 the result ensures the reliability of the questionnaire).

The results of this study showed that 84% of the sample was male and 14% was female. They started with 100 mg tramadol capsule daily and increased the dose progressively with time until they ended up with around 1800 mg daily, which is four times the therapeutic maximum daily dose (400-600 mg daily). This study showed that there is clear awareness among the tramadol abusers toward the size of problem as 96.4% of the sample believe that the abuse of tramadol is problem in Gaza strip, and 94.4% ensured that abuse of tramadol caused addiction. This study showed strong association between smoking and tramadol abuse as around 80% of our sample was smokers. There were various motivations for tramadol abuse but the most two common causes were to get euphoria 92.4% and to help them to delay ejaculation 79.4%. The insistent efforts to secure the drug led around two thirty (63.4%) of the sample to do illegal action to get the drug. Around 76.24% of the sample complained of psychological problem . Around 90% of the sample complain of withdrawal symptoms. Among the various side effects convulsion was represented by 71.8% of the sample. There is a significant difference at $\alpha \leq 0.05$ among the respondents' answers due to profession .

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List of Abbreviations

APNA	American psychiatric nurses association
ARCI-CV	Addiction Research Center Inventory-Chinese Version
ACMD	Advisory Council on the Misuse of Drugs
APA	American Psychiatric Association
CPK	Creatinine phospho kinase
DSM-IV	Diagnostic and Statistical Manual DSM-IV
DEA	The Drug Enforcement Agency
DAAC	Drug Abuse Advisory Committee
ECG	Electrocardiogram
FDA	Food and Drug Administration
GABA	Gamma amino butyric acid
GNP	Gross National Product
ICD-10	International classification of disease -10 revision
IELT	Intravaginal ejaculatory latency time
KAP	Knowledge attitude and practice
K-S Test	Kolmogorov-Smirnov Test
LHHPC	Loghman-Hakim Hospital Poisoning Center
LSD	Lysergic acid diethylamide
NCCMH	National Collaborating Centre for Mental Health
MOF	Ministry Of Finance
NDTMS	National Drug Treatment Monitoring System
NIDA	National Institute on Drug Abuse
NTA	National Treatment Agency for Substance Misuse
NTORS	National Treatment Outcomes Research Study
NIS	New Israeli Shekel
ANOVA	One way Analysis of Variance
OWS	Opiate withdrawal scale
ODT	orally disintegrating tablet
PCBS	Palestinian Central Bureau of Statistics
PE	premature ejaculation
RCICV	Research Center Inventory-Chinese Version
RCP	Royal college of psychiatrists

Sq. Km	Square Kilometer
SPSS	Statistical Package of Social Science
SW EDIS	Swedish Drug Information System
OCHA	UN office of coordination humanitarian affairs
US	United states
VAS	visual analogue scale
WHO	World Health Organization

Chapter one

- **Introduction**
- **Study Goal**
- **Research Question**
- **Operational definition**

Chapter (One)

1.1 Introduction

There is no doubt that the strength of any society derives from the power of his sons, they work as a first line of defense against any breach of the social fabric, by maintaining values and morals, religion and heritage. From this standpoint, if spread phenomenon of drug and substance abuse among members of the community, especially young people, this threatens catastrophe will occur in the community.

Substance abuse and addictive behavior are universal phenomena and are regarded in the twentieth century as a major public health problem . Historical evidence suggest that since ancient times living with psychoactive substance seems to be part of the fabric of our lives (Gossop,1993). The desire to experience some altered state of unconsciousness seems to be an intrinsic part of the human condition .

The health and social costs of the abuse of these psychoactive substances unfortunately reflect most disturbing morbidity and mortality (Rassool & Gafor, 1997).

The squealer of the harm physical ,social, psychological and economic derived from the abuse of psychoactive substance not only affect the individual user but also the family. Following the December 2008 Israeli criminal war, a United Nations survey of Gaza residents found increases in risk taking behavior, including a significant rise in cases of drug addiction(Hammami, 2009). One drug associated with this trend is Tramadol, first developed in Germany during the 1970s and introduced in the 1990s as a centrally acting analgesic with properties similar to codeine and morphine and which is widely prescribed as a pain killer(Lewis & Han,1997). Although illegal without a prescription in some regions, Tramadol is relatively easy to obtain in Gaza, either with fake prescriptions from pharmacies or on the black market. News reports prior to the 2008

offensive suggested that up to 30 percent of males between the ages of 14 and 30 had already been using Tramadol on a regular basis, with some15,000 showing signs of addiction(O'Loughlin, 2008),idly or significant others and the whole community .

Under the broad ranging and comprehensive Israeli blockade of the Gaza Strip, which has been in place since 2007, Gaza society has come to rely heavily on a vast network of cross border tunnels, some as much as 18 meters underground, which have become crucial supply routes for Palestinians who are cut off from the outside world. Around the clock shifts of tunnel workers transport a wide variety of items, from food and clothing to household goods and even furniture. Recently, illicit pharmaceuticals and other drugs have become hot commodities in the burgeoning tunnel trade.

The last criminal war against Gaza strip produced a very high degree of comorbidity between war-related trauma and depression, along with drug abuse, among Gaza people who, have also been psychologically affected by the ongoing war(Bleich, 1997). The tunnels are the main entry point for Tramadol and other substances into Gaza missed an important opportunity to explore drug trafficking as a transnational crime(Chawla S& Pietschmann , 2005). Although Tramadol is known as Tramal in Gaza and Tramadex in Israel, the Palestinian police in Gaza displayed boxes labeled Tramajack, which is the name under which tramadol is manufactured in India. The police also showed packets of green capsules labeled Tramadol, but which appear to have originated in the European Union. Other drugs on display were Proxam, a compound including dextropropoxyphene hydrochloride, which is a weak opioid, and Amirol, which is the Australian name for amitriptyline hydrochloride, a powerful antidepressant with sedative properties.

In addition to this phenomena the researcher will concentrate to assess the abuse of tramadol to identifying the level of knowledge ,attitudes ,and practice ,psychological state , and presence of side effects of tramadol abusers. The researcher will take the target population of this study from persons who already abuse tramadol and who are attending private psychiatric clinics .

1.2 Statement of the problem

Drug abuse and addiction has become one of the most important public health problems in recent years. Information providing role of lay theories is undeniable in preventive and rehabilitative works related to drug addiction. Several studies investigated lay beliefs and attitudes related to different kinds of drugs. For instance,(Furnham &Thomson, 1996) found that the participants' political views were the most important determinant of lay beliefs about heroin addiction.

Research also indicated that certain variables increase the risk of drug abuse. Younger people are more prone to drug abuse (Royo-Bordonada *et al*,1997)**.**

The increase in abuse of marketed medications in recent years has highlighted the need for abuse-liability assessment (Samhsa, 2003).

The abuse of tramadol among people in the Gaza strip, News reports prior to the 2008 offensive suggested that up to 30 percent of males between the ages of 14 and 30 had Despite consistent border seizures of the smuggled drugs, thousands of boxes of Tramadol still make their way to Gaza's who are increasingly dependent on the drug, some having become seriously addicted.

1.3 Significance of the study

Psychoactive substance abuse problems are prevalent and widespread worldwide, and are associated with significant morbidity and mortality. The World Health Organization (WHO) has identified alcohol, tobacco, and illicit drugs as among the top 20 risk factors for ill-health (World Health Organization, 2002) and has adopted as public health approach to screening for alcohol and drug abuse, and early intervention for such problems (WHO Assist Working Group, 2002).

This study shows the importance of the fact located in the Gaza Strip, about abuse of the tramadol.

Because of the spread of tramadol abuse, and the lack of studies around it, and the lack of incidence, this is encouraged the researcher to study the phenomena. And also this is the first study of its kind to address the issue of tramadol abuse . This study will assess the extent of the phenomenon of abuse of the tramadol on persons who are have tramadol abuse in Gaza strip.

1.4General objective

This study aims to assess the abuse of Tramadol among persons who have tramadol abuse by examining the level of knowledge, attitude, and practice about the drug.

1.5 Specific objectives:

1-To identify the knowledge ,practice , and attitude of tramadol, among persons who abuse tramadol.

2-To assess the effect of socio demographic factors (age, sex, economic status, level of education) on Tramadol abuse.

3-To assess the effect of psychological stress on abuse of Tramadol .

4-To assess the side effects of tramadol among Tramadol abusers .

5-To suggest recommendations for policy and decision makers regarding the opportunity to stop tramadol abuse .

1.6 Research questions

1- Do the people who abuse Tramadol have any knowledge about Tramadol ?

2- What is the attitude of persons who have abused Tramadol ?

3- How do the persons abused Tramadol ?

4-Does age factor effect on abuse of Tramadol ?

5-Does the sex factor effect on the abuse of Tramadol ?

6-Does the marital status factor effect on abused of tramadol ?

7-Does the kind of occupation factor affect on abused of tramadol ?

8-Does the economic status factor effect on tramadol abuse ?

9-Does the abusers complain of any psychological stress ?

10-Does the abusers complain of any side effects related to abuse of tramadol ?

1.7 Context of the study

The researcher provides an overview about the context where the study was performed and variables that influence the topic under the study. The context involves socio-demographic variables, economic, and political situation.

1.7.1 Demographic Context

Palestine is an Arabic Country, relatively small one. The total surface area of the historical Palestine is about 27.000 Km² (Palestine, MOH, 2006). Palestine has been occupied in 1948 by Israel and the two remaining parts are separated geographically (West Bank and Gaza Strip) after the war in 1967 (Palestine, MOH, 2006). Palestine is surrounded by Lebanon, Syria, Jordon, Egypt, and the Mediterranean Sea. The total area of the Gaza Strip(GS) and West Bank is about 6020 Sq. Km with total population living in is about 4,108,631 individuals (1,561,906 in GS and 2,546,725 in West Bank) with a population density of 682 capita per sq. Km (Palestinian Central Bureau of Statistics-PCBS, 2011).

GS is a narrow piece of land lying on the coast of Mediterranean Sea. The total area of the GS is about 365 square kilometer (PCBS, 2011). GS is overcrowded area with total population about 1.561.906 with population density of 4279 inhabitants/ Km² and about 69% of them are refugees as estimated in 2010 (PCBS, 2011).

GS is divided into five governorates: Gaza Governorates, North Governorates, Mid-zone Governorate, Khan-Younis Governorate, and Rafah Governorate.

1.7.2 Socio-economic and Political Context

The GS undergone a restriction, political and economic closure after the Palestinian election in 2006, the conflict between the two main parties Fateh and Hamas resulted in a division of control between Palestinian Authority and Hamas government which has been complicated by the Israeli closure have had a profoundly negative impact on the public health.

The Israeli war on Gaza in December 2008 through January 2009 resulted in hundreds of fatalities and thousands of injuries; and further badly affected the already weakened status of the water, sanitation and power sectors in the GS (WB, 2009). The ongoing deteriorating economic situations in the GS lead to the rise in the unemployment rate to 40% in 2008 and 80% of households were living under the poverty line in 2007 household survey (International Monetary Fund - IMF, 2009).

1.8 Operational definitions:

1.8.1 Tramadol

Is an effective analgesic in the opioid family that has somewhat lesser narcotic associated side effects.

Tramadol hydrochloride is a widely prescribed, centrally acting analgesic marketed in over 90 countries. Before being released in the U.S. in 1995, the drug had been available in Europe for almost two decades. Thus, the pharmacokinetic and pharmacodynamics properties of tramadol have been extensively investigated.

Tramadol is a novel centrally acting analgesic used for the treatment of mild to severe pain (Clarot F *et al*,2003).

Tramadol is an oral analgesic, which stems from both norepinephrine and serotonin reuptake inhibition and direct-receptor agonism(C. Hernandez-Lopez *et al*,2006).

1.8.2 Substance abuse:

Refers to the harmful or hazardous use of psychoactive substances, including alcohol and illicit drugs*(*WHO, 2006).

The DSM defines substance abuse as a pattern of maladaptive substance use that is associated with recurrent and significant adverse consequences(DSM-IV).

1.8.3 Drug misuse

Drug misuse is defined as the use of a substance for a purpose not consistent with legal or medical guidelines (WHO, 2006).

1.8.4 Dependence

Is defined as a strong desire or sense of compulsion to take a substance, a difficulty in controlling its use, the presence of a physiological withdrawal state, tolerance of the use of the drug, neglect of alternative pleasures and interests and persistent use of the drug, despite harm to oneself and others (WHO, 2006).

A compulsive pattern of substance use characterized by a loss of control over substance use and continued use despite the significant substance-related problems(DSM-IV).

1.8.5 Drug tolerance

Repeated use of a drug in which increased doses of the drug are required to produce the same effect.

1.8.6 Depressants

Are sedatives which act on the nervous system. Artificial relaxation and relief from anxiety and mental stress tend to produce psychological dependence and withdrawal from heavy use is severe.

1.8.7 Stimulants

are agents that activate, enhance, or increase neural activity. They include amphetamines and synthetic appetite suppressants such as phenmetrazine or methylphenidate. They can give rise to symptoms suggestive of intoxication, including tachycardia, pupillary dilation, elevated blood pressure, nausea or vomiting and abnormal behavior such as fighting. agitation and impaired judgment. A full-blown delusional psychosis may occur .

1.8.8 Hallucinogens

Are a chemically divers group which produce profound mental changes such as euphoria, anxiety, sensory distortion, hallucination, delusion, paranoia and depression. They include mescaline and LSD.

1.8.9 Tramadol abuse

From the view point of the researcher tramadol abuse can be defined as use of tramadol without medical reasons ,and the daily dose excess 400-600 mg.

Chapter two

- **Theoretical Framework**
  - **Drug Abuse**
  - **Tramadol**
- **Previous Studies**

Chapter (Two)

2.1Drug abuse

2.1.1Introduction

The term opioids refers to a class of psychoactive substances derived from the poppy plan including opium, morphine and codeine, as well as semi-synthetic forms including heroin and synthetic compounds including methadone and buprenorphine with similar properties (WHO, 2006). Illicit use of opioids generally involves injecting, or inhaling the fumes produced by heating the drug. The term opiate refers strictly to the subset of opioids that are naturally occurring or semi-synthetic, and therefore includes heroin and morphine but excludes methadone and buprenorphine.

Stimulants refer broadly to any substance that activates, enhances or increases neural activity (WHO,2006) . Illicit stimulants include cocaine, crack cocaine and amphetamines. Cocaine is one of the most commonly abused illicit stimulants in the Europe (Roe & Man, 2006). It is extracted from the leaf of the coca plant and generally sniffed in powder form. Crack cocaine is usually smoked but sometimes injected. Amphetamines are a group of synthetic substances with different chemical structures but broadly similar stimulant properties to cocaine, and include dexamphetamine sulphate a prescription drug licensed for the treatment of narcolepsy and attention-deficit hyperactivity disorder but which has misuse potential) and methamphetamine.

Cannabis is a generic term denoting the various preparations of the cannabis sativa plant, including cannabis leaves the most common form, which is smoked, hashish resin and the rarely used cannabis oil. Tetrahydrocannabinol is the key constituent of cannabis that produces the psychoactive effect sought by most users, and the different forms of cannabis vary in their tetrahydrocannabinol content (WHO, 2006).

Drug misuse is defined as the use of a substance for a purpose not consistent with legal or medical guidelines (WHO, 2006). It has a negative impact on health or functioning and may take the form of drug dependence, or be part of a wider spectrum of problematic or harmful behavior (DH, 2006).

The Advisory Council on the Misuse of Drugs (ACMD) characterizes problem drug use as a condition that may cause an individual to experience social, psychological, physical or legal problems related to intoxication and regular excessive consumption, and dependence (ACMD, 1998).

2.1.2 Drug dependence

Dependence is diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) when three or more of the following criteria are present in a 12-month period: tolerance; withdrawal; increasing use over time; persistent or unsuccessful attempts to reduce use; preoccupation or excessive time spent on use or recovery from use; negative impact on social, occupational or recreational activity; and continued use despite evidence of its causing psychological or physical problems (American Psychiatric Association [APA], 1994).

The diagnosis of dependence is clearest with opioids. The WHO states that:

'opioid dependence develops after a period of regular use of opioids, with the time required varying according to the quantity, frequency and route of administration, as well as factors of individual vulnerability and the context in which drug use occurs. Opioid dependence is not just a heavy use of the drug but a complex health connotation that has social, psychological and biological determinants and consequences, including changes in the brain. It is not a weakness of character or will (WHO, 2006).

However, dependence, as characterized by the above definition, can also occur with stimulants and cannabis.

2.1.3Tolerance

Repeated use of a drug can lead to the development of tolerance in which increased doses of the drug are required to produce the same effect. Tolerance develops to opioids, stimulants and cannabis. Cessation of use leads to reduced tolerance and this may present significant risks for individuals who return to drug doses at a level to which they had previously developed tolerance. This can result in accidental overdoses and, in the case of opioid misuse, could lead to respiratory depression and death.

2.1.4Withdrawal

Withdrawal syndromes have clearly been identified after cessation or reduction of opioid and stimulant use. DSM-IV criteria for a withdrawal disorder include the development of a substance-specific syndrome due to cessation or reduction in use; the syndrome causing clinically significant distress; and symptoms not due to a general medical condition or better explained by another mental disorder (APA, 1994). While withdrawal effects have been associated with cessation of heavy opioid use, their clinical significance is uncertain at present (Budney *et al.*, 2004).

People who abuse drugs may present with a range of health and social problems other than dependence, which may include (particularly with opioid abusers):

- physical health problems (for example, thrombosis, abscesses, overdose, hepatitis B and C, HIV, and respiratory and cardiac problems).
- mental health problems (for example, depression, anxiety, paranoia and suicidal thoughts).
- social difficulties (for example, relationship problems, financial difficulties, unemployment and homelessness).
- criminal justice problems.

Many people who abuse drugs use a range of substances concurrently and regularly known as polydrug abuse. The use of opioids alongside cocaine or crack cocaine is common, with the National Drug Treatment Monitoring System (NDTMS), which collects, collates and analyses information from those involved in the drug treatment system, reporting an increase in the use of both drugs, from 18% of those presenting for drug treatment in 1998 to 24% in 2001 National Treatment Agency for Substance Misuse (NTA, 2005). Alcohol abuse is also common in all types of people who misuse drugs; data from the National Treatment Outcomes Research Study (NTORS) on drug misuse suggested that 22% of participants also drank alcohol frequently, 17% drank extremely heavily and 8% drank an excessive amount on a daily basis (Gossop *et al.*, 2000). People who misuse opioids in particular may often take a cocktail of substances, including alcohol, cannabis and prescribed drugs such as benzodiazepines, which can have especially dangerous effects in comparison with one of the drugs taken individually.

The association between drug misuse and crime also applies in the younger population., The Home Office 2004 Offending Crime and Justice Survey (The Information Centre, Lifestyle Statistics, 2006) found that young people who had used drugs in the past year were over twice as likely to have committed an offence compared with those who reported not having used drugs (52% versus 19%). In addition, young offenders who had taken a Class A drug in the past year were more likely to be frequent offenders than those who reported using other types of drugs. However, in contrast to figures for the general population, Class A drug users comprise a very small proportion (1% testing

positive for heroin and 4% for cocaine) of arrestees aged below 18 years (Matrix Research and Consultancy & Institute for Criminal Policy Research, 2007).

2.1.5Etiology and maintenance of drug abuse

Drug abuse is increasingly portrayed in the field as a medical disorder known as the disease model of drug misuse or abuse, in part due to advances in our understanding of the neurobiology underlying dependence (Volkow & Li, 2005). There is also no question that numerous socioeconomic and psychological factors all play an important part in the etiology of drug abuse. These conceptualizations are not mutually exclusive; rather they are facets of the multifactorial a etiology of drug abuse .

The most robust evidence highlights peer drug use, availability of drugs and also elements of family interaction, including parental discipline and family cohesion, as significant risk factors for drug misuse (Frischer *et al.*, 2005). In particular, traumatic family experiences such as childhood neglect, homelessness or abuse increase the likelihood that the individual will develop problems with drugs later on in life (Kumpfer & Bluth, 2004). Recent studies of twins, families and people who have been adopted suggest that vulnerability to drug abuse may also have a genetic component (Prescott *et al.*, 2006), although it is unclear whether repeated use is primarily determined by genetic predisposition, or socioeconomic and psychological factors lead an individual to try and then later to use drugs compulsively. Risk factors for heavy, dependent drug use are much more significant when they occur together rather than individually.

A defining characteristic of drug dependence is that drug use begins as a voluntary action to seek a rewarding stimulus, but continued use results in loss of control over the use, despite its negative consequences (Dackis & O'Brien, 2005). The effects of many illicit drugs are mediated via various brain circuits, in particular the mesolimbic systems, which have evolved to respond to basic rewards such as food and sex to ensure survival. A diverse range of substances, including opioids, stimulants and cannabis, as well as alcohol and nicotine, all appear to produce euphoric effects via increasing levels of dopamine a neurotransmitter in the nucleus accumbens (Dackis & O'Brien, 2005).

This has been well demonstrated in human brain-imaging studies (Volkow *et al.*, 1999). Euphoria resulting from use then potentiates further use, particularly for those with a genetic vulnerability.

Chronic drug use may produce long-lasting changes in the reward circuits, including reductions in dopamine receptor levels (Volkow *et al.*, 1999), and these contribute to the clinical course of drug dependence, including craving, tolerance and withdrawal (Lingford-Hughes & Nutt, 2003).

In addition, other types of neurotransmitter systems for example, opioids, glutamates and cannabinoids are implicated in the abuse of specific drugs.

Although initiation into drug use does not lead inevitably to regular and problematic use for many people (Anthony *et al.*, 1994), it is clear that when use begins, it often escalates to abuse and sometimes to dependence tolerance, withdrawal symptoms and compulsive drug taking. Once dependence is established, particularly with opioids, there may be repeated cycles of cessation and relapse extending over decades (National Consensus Development Panel on Effective Medical Treatment of Opiate Addiction, 1998). Vulnerability to use is highest among young people, with most problem drug users initiating by the age of 20.

Individuals dependent on drugs often become so in their early twenties and may remain intermittently dependent for many years.

With cannabis and cocaine, recreational use is more common and it is likely that there are different patterns of use, with those taking cocaine being divided between those who take the drug on an episodic basis and those who take it daily; in contrast, usually only a small number of people taking cannabis move to repeated daily increasingly heavy use, with many taking the drug intermittently. A general US population survey of 8,098 individuals (Anthony *et al.*, 1994) found that among those who had used cocaine or cannabis in their lifetime, 16.7% and 9.1% subsequently became dependent on the respective drugs; for heroin, Such differences may relate to the different intensities of action different drugs produce within the neural reward sites (Stimmel & Kreek, 2000).

The neurobiological account of fundamental reward systems implicated in drug abuse may parallel the sociocultural–behavioral–cognitive model presented by Orford (2001). He conceptualized drug abuse as an excessive appetite , belonging to the same class of disorders as gambling, eating disorders and sex addiction. All involve activities that form strong attachment, and were once rewarding, but with excessive consumption result in compulsion and negative consequences. Orford argued that the emotional regulation of such appetitive behaviors in their respective social contexts for example,

the excitement associated with gambling or the anticipation of the next 'fix' of heroin, well characterized within the principles of operant conditioning, is a primary factor driving excessive use. Secondary factors such as internal conflict knowing that the behavior is harmful yet being unable to disengage from it potentiate these emotions and thus excessive use, but an alternative result is that the individual alters behavior in order to resolve such conflict. This crucially suggests that recovery is not impossible, but also that successful treatment attempts are likely to operate against a background of powerful natural processes (Orford, 2001).

2.1.6The sequence of drug abuse

Drug abuse is a relapsing and remitting condition often involving numerous treatment episodes over several years (Marsden *et al.*, 2004). While the initiation of drug use does not lead inevitably to dependence over the long term (Anthony & Petronis, 1995), a number of factors can potentiate this developmental course. Earlier initiation of drug use increases the likelihood of daily use, which in turn results in a greater likelihood of dependence (Kandel *et al.*, 1986).

Among people who misuse opioids, who form the predominant in-treatment population, most individuals develop dependence in their late teens or early twenties, several years after first using heroin, and continue using over the next 10–30 years. In a long-term outcome study up to 33 years of 581 male opioid users in the US, 30% had positiveor refused urine tests for opioids, 14% were in prison and 49% were dead (Hser *et al.*, 2001). Longitudinal data from the US also showed that the average time from first to last opioid use was 9.9 years, with 40% dependent for over 12 years (Joe *et al.*, 1990). Although it is the case that problem drug users can cease drug use without any formal treatment (Biernacki , 1986), particularly for individuals with primary cocaine or cannabis misuse, for many it is treatment that alters the course of opioid dependence.

Most initiation of cocaine use occurs around the age of 20, with the risk of cocaine dependence occurring early and explosively after first use, and persisting for an average of 10 years (Anthony *et al.*, 1994).

Cannabis use typically begins in early adolescence with heaviest use in the 15–24 age group (Harkin *et al.*, 1997), which may in part be explained by strong peer influences (Frischer *et al.*, 2005). Most use tends to decline steadily from the mid-20s to the early

30s (Bachman *et al.*, 1997). Cannabis dependence persisting through adulthood is the most prevalent among those with sustained frequent use, as high as 40% among those who have used almost daily (Kandel & Davies, 1992).

Although drug abuse can affect all socioeconomic groups, deprivation and social exclusion are likely to make a significant contribution to the maintenance of drug abuse (ACMD,1998) . That said, an association has been found between income in adolescence and early adulthood and cannabis use (Makkai & McAllister, 1997), which may reflect the recreational nature of the majority of cannabis use.

Factors that influence the cessation of drug use in adulthood are similar to those associated with lack of drug use in adolescence. For example, transitions into social roles with greater conventionality, responsibility and contexts that are not favorable to using drugs such as employment, marriage and pregnancy; for example, (Bachman *et al.*, 1997) and good health are not associated with long-term use. Peer pressure is a major influence on experimental use and is also likely to affect a move towards regular use. The level of drug use is again a clear predictor of continued use.

Once an individual is dependent, drug use is generally a chronic condition, interspersed with periods of relapse and remission (Marsden *et al.*, 2004). Repeated interaction with the criminal justice system, long-term unemployment and increasing social isolation serve to further entrench drug use.

2.1.7 THEORETICAL REVIEW ON SUBSTANCE ABUSE

2.1.7.1 Expectancy Model

This theory evolved from cognitive-behavioral and social learning perspectives (Dimeff & Marlatt, 1998). According to this model, people with alcohol dependence develop problematic beliefs about substances use relatively early in life can occur through a combination of reinforcement and observational learning

Another concept of expectancy model is that of self- efficacy and coping. Self-expectancy refers to an individual's perception that he or she has the ability to meet the challenges of a difficult situation while coping refers to the strategies that an individual uses to reduce the perception of a threat or danger.

Based on Dimeff and Marlatt's (1988) expectancy model, a series of reactions can occur when a drug-dependent individual attempts to remain abstinent. There will be a

contrasting scene when two persons try to remain abstinent in high-risk situations. For example, Persons A and B encountered high-risk situations, such as parties where people are consuming alcohol. "A" is able to abstain from drinking at the party because he or she has learned how to cope with such situations, and he or she feels capable of carrying through with his or her intention not to drink alcohol. Each successful episode of abstinence reinforces his or her sense of self-efficacy, causing him or her to feel more capable of abstaining in subsequent situations. "B" lacks a satisfactory coping response. The actual consumption of alcohol is not what leads to a relapse, but, rather, his or her interpretation of the act of drinking as a sign of loss of self-control.

Thus, when "B" enters a high-risk situation, he or she feels incapable of staying away from alcohol because of his or her low sense of self-efficacy. A compelling expectation that alcohol will have a positive mood-altering effect adds to his or her low sense of self-efficacy and leads him or her to take the first drink.

The positive sensations that the drug produces further undermine 'B's resolve, but cognitive factors enter at this point in the process as well. Having violated the self-imposed rule of remaining abstinent, "B" now is subject to the abstinence violation effect, a sense of loss of control over one's behavior that has an overwhelming and demoralizing effect. Thus, 'B's self-efficacy is further eroded, initiating a down-ward spiral trend, which eventually ends in renew drug dependence.

2.1.7.2 Eysenck's Personality Theory

Hans Eysenck, a trait theorist (1916-1997), defined personality as the sum total of the actual or potential behaviour pattern of the organism, as determined by hereditary and environment and traits as enduring characteristics within individual that determines his or her behaviour. Employing factor analysis he concluded that, traits can be subsumed under three basic types:

(1) Introversion-Extraversion .

(2) Neuroticism .

(3) Psychoticism.

2.1.7.2.1 Personality and Substance abuse

Personality variables help to explain why certain people are drawn to substance abuse. In this regard, researchers have studied high levels of negative affect and an enduring desire for arousal and increased positive affect. In one study (Davison & Neale, 2001),

kindergarten children were rated by their teachers on several personality traits and were followed up several years later. Anxiety (e.g., worries about things, fear of new things or situations) and novelty seeking (e.g., restlessness, forgetting) predicted the onset of getting drunk, using drugs, and smoking (Killen *et al*, 1997). Drug use in general has been found to correlate with anti-social personality disorder (Ball, Carroll, & Rounsaville, 1994). Rebelliousness and high levels of aggression have been found to be related to substance abuse (Anderson *et al*, 1997; Davison & Neale, 2001). (Lavelle, Hammersley, & Forsyth, 1991) showed that drug user were shrewd, tough-minded, anxious, streetwise and experience-seeking. Further, Ekstrand (1985) reported that drug users seemed to be immature, compulsive and possess low self-esteem and are incapable of managing failure. Also Shedler & Block (1990) indicate that frequent drug users were maladjusted, socially alienated, and deficient in impulse control and manifestly distressed. Conversely, abstainers were observed to be anxious, emotionally constricted and lacking in social skills.

With respect to extraversion, findings on its relationship with substance abuse have been mixed. Eysenck's (1967) arousal theory categorized it on the bases of stimulation, excitement and gregariousness and these are potent factors in predicting drug use. Furthermore, Oluwatelure (1995) found a positive relationship between extraversion and alcohol abuse. However, Ifeagwazi's (2005) study failed to find a positive relationship between extraversion and drug use. The researcher explained the result by suggesting that extraversion is not a pronounced personality trait that distinguishes drug users from non-users. However, it seems that extraversion is a more positively valued personality trait (than introversion) and thus is not likely to be higher among drug users than in the general population.

With respect to neuroticism, studies have found a strong relationship between it and substance abuse. Neuroticism reflects individual differences in the extent to which a person perceives and experiences the world as problematic, threatening and distressing. High scorers on this scale experience various negative emotions such as anxiety, guilt, sadness, and hostility. They tend to feel inadequate and inferior and report elevated level of stress and indicate that they cope poorly with stress, causing pronounced emotional liability (Watson, Clark, & Harkness, 1994).

The experience of negative unpleasant states, has been linked with alcohol and drug use (Ifeagwazi; 2005). Pharmacological evidence indicates that opiates and tranquilizers are used more frequently by anxious and neurotic persons to reduce their emotional distress. In fact, emotional instability including frustration, anxiety, depression and unhappiness has become crucial in etiological explanations of substance abuse (Kuna & Bande, 1993) for instance; anger or unhappiness is related to cigarette smoking and alcohol use. With reference to psychoticism, studies have repeatedly shown a positive relationship between psychoticism and substance abuse. High scorers on the psychoticism scale exhibit some personality and behavioral traits e.g., aggressiveness, impulsivity, egocentrism; and impersonal feelings and anti-social tendencies (Carey & dilalla, 1994); these are linked with the initiation and maintenance of drug use (Anderson *et al*, 1997).

2.2 The Pharmacological Effects Of Drug Abuse

2.2.1 Opioids

Opioids have many effects on the brain, mediated through specific receptors (μ, κ, or δ). The key opioid receptor subtype is μ, which mediates 'euphoria', as well as respiratory depression, and is the main target for opioids (Lingford-Hughes & Nutt, 2003), while the κ receptor is involved in mood regulation. Drugs such as heroin and methadone are agonists, which stimulate the receptor. Buprenorphine is a partial agonist; that is, it occupies the receptor in the same way but only partially activates it. In addition, it is an antagonist at the κ receptor and therefore is less likely to lower mood compared with μ agonists.

Soon after injection or inhalation, heroin metabolizes into morphine and binds to opioid receptors. This is subjectively experienced as a euphoric rush, normally accompanied by a warm flush, dry mouth, and sometimes nausea, vomiting and severe itching. As the rush wears off, drowsiness, and slowing of cardiac function and breathing (sometimes to the point of death in an overdose), persist for several hours (National Institute on Drug Abuse [NIDA], 2005). The effects of methadone are similar but more drawn out and therefore less intense lasting up to 24 hours when taken orally as prescribed; however, this may be circumvented by illicit users who inject the drug.

The most obvious consequence of long-term opioid use is the development of opioid dependence itself, and the associated harms. Repeated injection will also have medical

consequences, such as scarring, infection of blood vessels, abscesses, and compromised functioning of the kidney, liver and lungs (with increased vulnerability to infections).

2.2.2 Stimulants

As central nervous system stimulants, cocaine and amphetamine affect a number of neurotransmitter systems in the brain but exert their effects primarily via dopamine, which mediates reward. Cocaine blocks the presynaptic reuptake of dopamine, such that it is not removed from the intracellular space and leads to extended firing of postsynaptic neurons, resulting in physiological arousal. Amphetamines also increase the availability of dopamine but are thought to do so by triggering a presynaptic leakage.

The acute subjective effects of cocaine are euphoria, increased energy, heightened alertness, sexual arousal, increased sociability and talkativeness. Physiologically there can be acute adverse effects on breathing, and the cardiovascular and central nervous systems: increased heart rate, blood pressure and body temperature, and pupil dilation. All these effects have near-immediate onset but also diminish quickly (after roughly 15–30 minutes if the drug is snorted and 5–10 minutes if smoked), as cocaine is metabolized rapidly by the body (NIDA, 2004). As acute effects wear off, users experience a rebound period crash, which may include restlessness, anxiety, agitation and insomnia. This can lead to the user bingeing on cocaine in an attempt to displace these negative effects. Chronic misuse of cocaine may lead to increased paranoia, inability to concentrate, sexual dysfunction and cognitive deficits.

For amphetamines, the acute effects are broadly similar except that they are long lasting (normally 4–8 hours), due to slower metabolism. Overdoses may lead to dangerously elevated body temperature, convulsions or even death. Chronic misuse may cause long-term damage to the brain's ability to manufacture dopamine, possibly resulting in amphetamine psychosis.

2.2.3 Cannabis

Cannabis affects almost every body system, via cannabinoid receptors in the brain, which regulate a range of cognitive and motor functions (NIDA, 2005b). Within minutes of smoking cannabis, the heart rate increases and the bronchial passages relax. Often the individual experiences intoxication, mild euphoria and increased sociability. However, anxiety or paranoia may sometimes occur, particularly among first-time or

psychologically vulnerable users (Johns, 2001). Distorted perceptions are common, for example colors may appear more intense and time may seem to slow down. The euphoria reaches a plateau lasting 2 hours or more, depending on the dose, after which the individual may feel sleepy or depressed.

Cannabis use also impairs memory, attention and motor coordination, with especially dangerous consequences on driving performance. Such effects may last for many hours after administration of the drug; the numerous metabolites of a single moderate dose of cannabis may require up to 4 weeks to be completely eliminated from the body (Maykut, 1985). The smoke from cannabis contains the same constituents as tobacco smoke; hence chronic cannabis smoking is associated with a range of respiratory tract disorders, including bronchitis, emphysema and cancers (Hashibe *et al.*, 2005; Tashkin, 1990).

2.3DSM-IV Substance Abuse Criteria

Substance abuse is defined as a maladaptive pattern of substance use leading to clinically significant impairment or distress as manifested by one (or more) of the following, occurring within a 12-month period:

1. Recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home (such as repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; or neglect of children or household).
2. Recurrent substance use in situations in which it is physically hazardous (such as driving an automobile or operating a machine when impaired by substance use)
3. Recurrent substance-related legal problems (such as arrests for substance related disorderly conduct)
4. Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (for example, arguments with spouse about consequences of intoxication and physical fights).

Note: The symptoms for abuse have never met the criteria for dependence for this class of substance. According to the DSM-IV, a person can be abusing a substance or dependent on a substance but not both at the same time.

2.4 DSM-IV Substance Dependence Criteria

Substance dependence is defined as a maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring any time in the same 12-month period:

1. Tolerance, as defined by either of the following: (a) A need for markedly increased amounts of the substance to achieve intoxication or the desired effect or (b) Markedly diminished effect with continued use of the same amount of the substance.
2. Withdrawal, as manifested by either of the following: (a) The characteristic withdrawal syndrome for the substance or (b) The same (or closely related) substance is taken to relieve or avoid withdrawal symptoms.
3. The substance is often taken in larger amounts or over a longer period than intended.
4. There is a persistent desire or unsuccessful efforts to cut down or control substance use.
5. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects.
6. Important social, occupational, or recreational activities are given up or reduced because of substance use.
7. The substance use is continued despite knowledge of having a persistent physical or psychological problem that is likely to have been caused or exacerbated by the substance (for example, current cocaine use despite recognition of cocaine-induced depression or continued drinking despite recognition that an ulcer was made worse by alcohol consumption).

2.5 ICD-10 Clinical description

A cluster of physiological, behavioral, and cognitive phenomena in which the use of a substance or a class of substances takes on a much higher priority for a given individual than other behaviors that once had greater value. A central descriptive characteristic of the dependence syndrome is the desire (often strong, sometimes overpowering) to take psychoactive drugs (which may or may not have been medically prescribed), alcohol, or tobacco. There may be evidence that return to substance use after a period of abstinence

leads to a more rapid reappearance of other features of the syndrome than occurs with nondependent individuals.

2.5.1 ICD-10 Diagnostic guidelines

A definite diagnosis of dependence should usually be made only if three or more of the following have been present together at some time during the previous year:

- A strong desire or sense of compulsion to take the substance;
- Difficulties in controlling substance-taking behavior in terms of its onset, termination, or levels of use;
- A physiological withdrawal state when substance use has ceased or have been reduced, as evidenced by: the characteristic withdrawal syndrome for the substance; or use of the same (or closely related) substance with the intention of relieving or avoiding withdrawal symptoms;
- Evidence of tolerance, such that increased doses of the psychoactive substance are required in order to achieve effects originally produced by lower doses (clear examples of this are found in alcohol- and opiate-dependent individuals who may take daily doses sufficient to incapacitate or kill non tolerant users);
- Progressive neglect of alternative pleasures or interests because of psychoactive substance use, increased amount of time necessary to obtain or take the substance or to recover from its effects;
- Persisting with substance use despite clear evidence of overtly harmful consequences, such as harm to the liver through excessive drinking, depressive mood states consequent to periods of heavy substance use, or drug-related impairment of cognitive functioning; efforts should be made to determine that the user was actually, or could be expected to be, aware of the nature and extent of the harm.

2.5.2 ICD-10 Diagnostic criteria for research

Three or more of the following manifestations should have occurred together for at least 1 month or, if persisting for periods of less than 1 month, should have occurred together repeatedly within a 12-month period:

- A strong desire or sense of compulsion to take the substance;
- Impaired capacity to control substance-taking behavior in terms of its onset, termination, or levels of use, as evidenced by the substance being often taken in

larger amounts or over a longer period than intended, or by a persistent desire or unsuccessful efforts to reduce or control substance use.

- A physiological withdrawal state when substance use is reduced or ceased, as evidenced by the characteristic withdrawal syndrome for the substance, or by use of the same (or closely related) substance with the intention of relieving or avoiding withdrawal symptoms.
- Evidence of tolerance to the effects of the substance, such that there is a need for significantly increased amounts of the substance to achieve intoxication or the desired effect, or a markedly diminished effect with continued use of the same amount of the substance.
- Preoccupation with substance use, as manifested by important alternative pleasures or interests being given up or reduced because of substance use; or a great deal of time being spent in activities necessary to obtain, take or recover from the effects of the substance.
- Persistent substance use despite clear evidence of harmful consequences as evidenced by continued use when the individual is actually aware, or may be expected to be aware, of the nature and extent of harm.

2.6 The public health impact of drug abuse

The harms associated with illicit drugs use include increased mortality from overdose and from other directly or indirectly associated harms such as increased risk of infection with blood-borne viruses HIV, hepatitis B and hepatitis C; high levels of depression and anxiety disorders; social problems such as disrupted parenting, employment and accommodation; and increased participation in income-generating crime.

(Oppenheimer *et al.*, 1994) and 22 times (Frischer *et al.*, 1997) that of the general population. In England and Wales, there were 1,382 drug-related deaths in 2005 (National Programme on Substance Abuse Deaths, 2005). The majority (59%) were cases of accidental poisoning, although a sizeable proportion (16%) was a result of intentional self-poisoning. Opioids alone or in combination with other drugs accounted for some 70% of the deaths, and cocaine 13%. Many of the deaths appear to be due to multiple drug toxicity, especially the presence of central nervous system depressants for example, alcohol and benzodiazepines, rather than simply an overdose of an opioid. This is supported by research that shows those whose deaths were attributed to overdose

have opioid levels no higher than those who survive, or than heroin users who die from other causes (Darke & Zador, 1996). Recent cohort studies have shown that mortality rates from methadone-related death are decreasing (Brugal *et al.*, 2005).

Psychiatric comorbidity is common in drug abuse populations, with anxiety and depression generally common, and antisocial and other personality disorders in opioid-using populations (Regier *et al.*, 1990, 1998). The national US Epidemiological Catchment Area study of the prevalence of mental health disorders reported a 47% lifetime prevalence rate of substance abuse drugs and alcohol among people with schizophrenia compared with 16% in the general population, and found that more than 60% of people with a diagnosis of bipolar I disorder had a lifetime diagnosis of substance misuse disorder. Around one in five of the people in the NTORS sample had previously received treatment for a psychiatric health problem other than substance misuse (Marsden *et al.*, 2000). Drug misuse disorders complicated by other comorbid mental disorders have been recognized as having a poorer prognosis and being more difficult to treat than those without comorbid disorders; comorbid disorders are more likely to be chronic and disabling, and result in greater service utilization.

Lost productivity and unemployment increase with the severity and duration of drug misuse, and personal relationships are placed under considerable strain by dependent drug use. Problems with accommodation are also common in such groups. For example, prior to intake in the NTORS, 7% of the study group were homeless and living on the street, 5% were living in squats and 8% were living in temporary hostel accommodation (Gossop *et al.*, 1998).

Drug abuse may also have a negative impact on children and families (ACMD, 2003).

In Gaza there is no prevalence or incidence data of drug abuse in general ,and tramadol abuse particularly .

2.7 The aims of treatment of drug abuse

The clinical management of drug abuse may be categorized into three broad approaches: harm reduction, maintenance-oriented treatments and abstinence-oriented treatments. All treatments aim to prevent or reduce the harms resulting from use of drugs. Care planning and key working should form a core part of subsequent treatment and care.

2.7.1Harm reduction

Aims to prevent or reduce negative health or other consequences associated with drug abuse, whether to the drug-using individual or, more widely, to society. With such approaches, it is not essential for there to be a reduction in the drug use itself although, of course, this may be one of the methods of reducing harm. For instance, needle and syringe exchange services aim to reduce transmission of blood-borne viruses through the promotion of safer drug injecting behavior.

2.7.2Maintenance

In the who context primarily refer to the pharmacological maintenance of people who are opioid dependent, through the prescription of opioid substitutes (methadone or buprenorphine). This therapy aims to reduce or end their illicit drug use and the consequential harms.

2.7.3 Abstinence

Aim to reduce an individual's level of drug use, with the ultimate goal of abstinence. The NTORS found that approximately one third of those entering treatment services were abstinent 5 years later (Gossop *et al.*, 2003). However, these treatments may be associated with an increased risk of death from overdose in the event of relapse after a period of abstinence, during which time drug tolerance is lost (Verger *et al.*, 2003). Consequently, it is particularly important for abstinence oriented treatment to include education on post-detoxification vulnerability to relapse (Gossop *et al.*, 1989) and to overdose, and for wider psychosocial rehabilitation support to be provided.

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2.7.4 Care planning

Should consider the following when any treatment or management plan is developed:

- type and pattern of use
- level of dependence

- comorbid mental and physical health problems
- setting
- age and gender
- service user's aspirations and expectations.

The general principles of treatment are that no single treatment is appropriate for all individuals, treatments should be readily available and begin when the service user presents, and there should be the capacity to address multiple needs. It is also accepted that treatments will change over time. It appears that treatment does not need to be voluntary to be successful – comparisons of voluntary and legally coerced drug treatment have been reviewed recently elsewhere (NCCMH, 2008). For most people in long-term treatment, that is those with opioid dependence, substitute medications, such as methadone and buprenorphine, are important elements of care. However, services also need to address coexisting problems, such as mental health and physical health problems, alongside the drug misuse.

2.7.5Continous practice

Only a minority entering treatment initially chooses abstinence and enforced abstinence appears ineffective. However, approximately one third entering treatment services generally are abstinent 5 years later at least for a period of time (Gossop *et al.*, 1998).

The most common types of psychosocial interventions programmed specifically targeting drug-use behaviors might be based on one of a number of models, including cognitive-behavioral for example, motivational interviewing and relapse prevention, humanistic and 12-step approaches (Wanigaratne *et al.* 2005). Often this is unfocused, and therapist and client may not have a clear understanding of the therapeutic goals or therapeutic method. In addition, there exist formal psychological therapies delivered within adult mental health settings, aiming to address drug users coexisting mental health problems (NTA, 2006).

Brief interventions, typically empathic in nature and lasting up to two sessions, have a variety of potential advantages in the treatment of drug misuse, including ease of delivery and retention of drug users. These interventions can be conducted in a variety of settings, opportunistically to people not in formal drug treatment and as an adjunct to formal, structured drug treatment (Ashton, 2005). Although brief interventions are

considered to be an important component of psychosocial treatment in open-access drug services (NTA, 2002., NTA, 2006).

2.8 Drug Abuse And The Family

In the literature, drug abuse is seen as both a problem of the family and a problem for the family' (Bancroft *et al.*, 2002). The evidence that points to traumatic family experiences, such as childhood neglect, homelessness, abuse, loss and bereavement, increasing the likelihood that a person will go on to have drug problems (Kumpfer & Bluth, 2004) can be seen as a problem of the family.

As 60–80% of people who abuse drugs live or are in regular contact with their family (Stanton & Heath, 2005), and approximately 2–3% of all children under the age of 16 years have parents with a drug problem (ACMD, 2003), drug abuse can also be said to be a problem for the family. The impact may be psychological for example, depression and anxiety, physical raised blood pressure and ulcers (Velleman *et al.*, 1993), social feelings of isolation and work, family and social difficulties (Hudson *et al.*, 2002) and financial.

Appropriate involvement of family members and careers in the assessment and treatment process may also support the family member/career and facilitate a more successful outcome for the user. There is evidence that families including parents, children and siblings have a role to play in effective treatments.

2.9Tramadol

2.9.1Introduction

Tramadol is a novel centrally acting analgesic used for the treatment of mild to severe pain (Clarot F *et al*., 2003). It has been approved in some countries since 1980 and become the most prescribed opioid worldwide(Loughrey *et al*.,2003).

Selecting Committee in 2002 as an analgesic. During this period, it has been abused especially by the younger population. Tramadol binds weakly to the μ-opioid receptor and also inhibits reuptake of monoamines such as serotonin and norepinephrine (Shadnia *et al*, 2008). Most of the analgesic effect of tramadol may be secondary to non-opioid properties, via the central monoaminergic pathways. The most common route of administration of tramadol is oral. Opioid dependency, overdose, and related

complications are common in Iran in various age groups and gender (Koushesh *et al*,2009). In recent years, tramadol overdose has become one of the most common causes of poisoning admissions to emergency departments in this country (Talaie *et al*,2009). An increased rate of seizure due to tramadol poisoning has also been observed It is reported that 15% to 35% of patients with tramadol overdose experience seizure (Kroenke e*t al*.2009). Research indicates that in high concern tractions tramadol exerts an inhibitory effect on gamma aminobutyric acid (GABA) receptors. In addition, GABA receptor inhibition induced by tramadol can be secondary to its opioid receptor agonist activity (Rehni *et al*, 2008), and continuing this agonist activity on opioid receptor has been proven to precipitate seizure due to inhibition of GABA pathways In addition to overdose, seizures have been reported in patients receiving tramadol at recommended doses (Kahn *et al*,1997).

Tramadol may also increase the seizure risk in patients receiving other medications such as tricyclic antidepressants, phenothiazine's, and selective serotonin reuptake inhibitors. While tramadol-related seizures can be controlled by diazepam, they are not responsive to naloxone, and tramadol-induced seizures can be precipitated by administration of naloxone, at high tramadol doses (Raffa &Stone,2008). The analgesic effect of tramadol is dose dependent. The relation between serum concentrations and analgesia varies between individuals. It is estimated that serum concentrations of 100 to 300 ng/mL are needed for analgesia (Shadnia *et al* b, 2008). In medical literature, no study in regard to blood concentrations of tramadol-induced seizures is available.

2.9.2Description of Tramadol

Tramadol is an analgesic medication that is a synthetic analogue of codeine. In comparison with other opiates, tramadol is renowned for having less abuse potential and less respiratory depression. In terms of specific neurotransmitter effects, at the central level, tramadol is a mu-opioid receptor agonist. The affinity of tramadol for mu-opioid receptors (analgesic effect) is 10-fold less than codeine. However, the active metabolite of tramadol, o-desmethyltramadol, has a far greater affinity (up to 200-fold) than the parent compound. In addition to its central effects on mu receptors, at the peripheral level, tramadol inhibits serotonin and norepinephrine reuptake. These latter effects are

likely to be an important element in analgesia, but may also account for some of the adverse properties of the drug(Gold S, 2008).

2.9.3Tramadol poisonings main features and toxicity

Originally it was claimed that tramadol is rather safe and has low potential for abuse. However, contradicting evidence has emerged in later stages. Food and Drug Administration has issued safety alert on this drug, including special cautions for patients who are simultaneously taking tranquilizers or antidepressants as well as individuals who consume alcohol excessively, or for those who suffer from emotional disturbances or depression. Potential misuse abuse and diversion were also stressed. Consistently, it has been recently suggested to place tramadol into the Schedule of the Controlled Substances Act Complications in tramadol overdose are disproportionately higher(Fass J, 2010).

Much of the toxicity in tramadol overdose appears to be attributable to the monoamine uptake inhibition rather than its opioid effects(Spiller HA *et al* ,1997). Frequency of theamadol induced complications is on the rise. Prescription on the Internet, initial marketing on safety, low potential for abuse and diversion as well as dextropropoxyphene withdrawal in hospital settings have been contributive on this(Bäckstrom*etal*,2010).

Reported tramadol overdoses are dominantly intentional acute ingestions. The majority of cases become symptomatic within the first 4 hours of ingestion.

2.9.4Adverse effects

The most commonly reported adverse drug reactions are nausea, vomiting, sweating, itching and constipation. Drowsiness is reported, although it is less of an issue than for non-synthetic opioids. Patients prescribed tramadol for general pain relief with or without other agents have reported withdrawal symptoms including uncontrollable nervous tremors, muscle contracture, and thrashing in bed similar to restless leg syndrome if weaning off the medication happens too quickly. Anxiety, buzzing, 'electrical shock' and other sensations may also be present, similar to those noted in Effexor withdrawal. Respiratory depression, a common side-effect of most opioids, is not clinically significant in normal doses. By itself, it can decrease the seizure threshold.

When combined with SSRIs, tricyclic antidepressants, or in patients with epilepsy, the seizure threshold is further decreased. Seizures have been reported in humans receiving excessive single oral doses (700 mg) or large intravenous doses (300 mg). However, there have been several rare cases of people having grand-mal seizures at doses as low as 100–400 mg orally(Pseudome,2009). An Australian study found that of 97 confirmed new-onset seizures, eight were associated with tramadol, and that in the authors First Seizure Clinic, tramadol is the most frequently suspected cause of provoked seizures (Labate, 2005). There appears to be growing evidence that tramadol use may have serious risks in some individuals and it is contra-indicated in patients with uncontrolled epilepsy (BNF 59). Seizures caused by tramadol are most often tonic-clonic seizures, more commonly known in the past as grand mal seizures. Also when taken with SSRIs, there is an increased risk of serotonin toxicity, which can be fatal. Fewer than 1% of users have a presumed incident seizure claim after their first tramadol prescription. Risk of seizure claim increases two- to six-fold among users adjusted for selected comorbidities and concomitant drugs. Risk of seizure is highest among those aged 25–54 years, those with more than four tramadol prescriptions, and those with a history of alcohol abuse, stroke, or head injury(Gardner,2000) . Dosages of warfarin may need to be reduced for anticoagulated patients to avoid bleeding complications. Constipation can be severe especially in the elderly requiring manual evacuation of the bowel. Furthermore, there are suggestions that chronic opioid administration may induce a state of immune tolerance, although tramadol, in contrast to typical opioids may enhance immune function. Some have also stressed the negative effects of opioids on cognitive Seizure functioning and personality.

2.9.5 Physical dependence and withdrawal

Tramadol is associated with the development of physical dependence and a severe withdrawal syndrome(Barsotti *et al* .,2003) . Tramadol causes typical opiate-like withdrawal symptoms as well as atypical withdrawal symptoms including seizures. The atypical withdrawal symptoms are probably related to tramadol's effect on serotonin and norepinephrine re-uptake. Symptoms may include those of SSRI discontinuation syndrome, such as anxiety, depression, anguish, severe mood swings, aggressiveness, brain, electric-shock-like sensations throughout the body, paresthesias, sweating,

palpitations, restless legs syndrome, sneezing, insomnia, vivid dreams or nightmares, nonsense and weird thoughts, micropsia and/or macropsia, tremors, and headache among others. In most cases, tramadol withdrawal will set in 12–20 hours after the last dose, but this can vary. Tramadol withdrawal lasts longer than that of other opioids; seven days or more of acute withdrawal symptoms can occur as opposed to typically three or four days for other codeine analogues. It is recommended that patients physically dependent on pain killers take their medication regularly to prevent onset of withdrawal symptoms and this is particularly relevant to tramadol because of its SSRI and SNRI properties, and, when the time comes to discontinue their tramadol, to do so gradually over a period of time that will vary according to the individual patient and dose and length of time on the drug.(Choong *et al*, 2008).

2.9.6 Psychological dependence and recreational use

Some controversy regarding the abuse potential of tramadol exists. Grünenthal has promoted it as an opioid with a lower risk of opioid dependence than that of traditional opioids, claiming little evidence of such dependence in clinical trials which is true; Grünenthal never claimed it to be non-addictive. They offer the theory that, since the M1 metabolite is the principal agonist at μ-opioid receptors, the delayed agonist activity reduces abuse liability. The norepinephrine reuptake inhibitor effects may also play a role in reducing dependence.

It is apparent in community practice that dependence to this agent may occur after as little as three months of use at the maximum dose generally depicted at 400 mg per day. However, this dependence liability is considered relatively low by health authorities, such that tramadol is classified as a Schedule 4 Prescription Only Medicine in Australia, and been rescheduled in Sweden rather than as a Schedule 8 Controlled Drug like opioids. Similarly, tramadol is not currently scheduled by the U.S. DEA, unlike opioid analgesics. It is, however, scheduled in certain states. Nevertheless, the prescribing information for Ultram warns that tramadol may induce psychological and physical dependence of the morphine-type. Using tramadol as recreational drug may be preferred also because at this time, tramadol is the only opioid, that cannot be detected by the standard urinal drug-tests, due to its atypical binding to μ-opioid receptors. Dependence on tramadol has been reported to be a major social problem in the Gaza Strip. The

Hamas government has attempted to cut off supplies of the drug, and in April 2010 burnt 2 million tablets which had been intercepted while being smuggled into the territory.

Because of the possibility of convulsions at high doses for some users, recreational use can be very dangerous(Jovanović *et al*.,2006). Tramadol can, however, via agonist of μ opioid receptors, produce effects similar to those of other opioids (codeine and other weak opioids), although not nearly as intense due to tramadol's much lower affinity for this receptor. Tramadol can cause a higher incidence of nausea, dizziness, loss of appetite compared with opiates which could deter abuse to some extent(Rodriguez *et al*,2007) . Tramadol can help alleviate withdrawal symptoms from opiates, and it is much easier to control the quantity of its usage than street drugs(Adams *et al* ,2006) . It may also have large effect on sleeping patterns and high doses may cause insomnia. Especially for those on methadone, both for maintenance and recreation. Though there is no scientific proof tramadol lessens effects or is a mixed agonist-antagonist, some people get the impression it is, while someone else might benefit being prescribed both for pain and breakthrough pain(Vorsanger *et al*.,2008) .

2.9.7 Tramadol and Serotonin syndrome

Serotonin syndrome (SS) has been reported with tramadol overdose-induced SS remains unknown; however, it probably does not exceed 5 % in hospital settings(Tashakori A,& Afshari,2010). SS may occur during single tramadol use, but it appears to be more common following either excessive use or overdose or with the co-administration of other medications, particularly antidepressants. No association was found between the frequency of SS and the alleged dose of tramadol overdose. Tramadol could have a synergistic effect on other drug induced SS. It may occur with tramadol monotherapy, but SS has been documented in combinations of tramadol and the following medications, (Mahlberg *et al*,2004) citalopram, fluoxetine, fluvoxamine, moclobemide-clomipramine, mirtazapine, paroxetine, sertraline and venlafaxine. Interestingly, we are convinced that true rate of tramadol-induced SS might be even higher than currently reported, if agitation, tachycardia, confusion, and hypertension were considered as possible mild SS symptoms, which easily could be missed in clinical settings(Houlihan DJ ,2004).

SS may develop via.(Sun-Edelstein *et al*.,2008):

(i) excessive serotonergic agonism of serotonin receptors in the central and peripheral nervous systems .

(ii) as a result of increased serotonin synthesis.

(iii) decreased serotonin metabolism.

(iv) increased serotonin release.

(v) inhibition of serotonin reuptake (e.g. SSRIs).

(vi) direct agonism of serotonin receptors.

Tramadol, in addition to affecting μ-opioid receptors, stimulates pre-synaptic release of serotonin and inhibits serotonin reuptake(Kitson R, Carr .,2005). Otherwise, SSRIs can inhibit the CYP2D6 isoenzyme metabolising tramadol, resulting in therapeutic overdose of tramadol and, in susceptible individuals, idiosyncratic induction of SS.overdoses.

2.9.8 Biological features

Tramadol overdose may induce a rise of creatinine phospho kinase (CPK). Although CPK rise could be independent from seizure, in cases with seizure, CPK rise is more dramatic and may be associated to acute renal failure(Boyd ,2005).

Increase in white blood cell count has been reported(Tashakori & Afshari, 2010). Bleeding risks due to tramadol interaction with oral anticoagulants has also been stated(Hersh EV*et al*.,2007).

2.9.9 Availability of tramadol

Tramadol is classified as a central nervous system drug usually marketed as the hydrochloride salt (tramadol hydrochloride); the tartrate is seen on rare occasions, and rarely (in the US at least) tramadol is available for both injection (intravenous and/or intramuscular) and oral administration. The most well-known dosing unit is the 50 mg generic tablet made by several manufacturers. It is also commonly available in conjunction with APAP (paracetamol, acetaminophen) as Ultracet, in the form of a smaller dose of 37.5 mg tramadol and 325 mg of APAP. The solutions suitable for injection are used in patient-controlled analgesia pumps under some circumstances, either as the sole agent or along with another agent such as morphine.

Tramadol comes in many forms, including:

- capsules (regular and extended release).
- tablets (regular, extended release, chewable, low-residue and/or uncoated tablets that can be taken by the sublingual and buccal routes).
- suppositories.
- effervescent tablets and powders.
- ampules of sterile solution for SC, IM, and IV injection.
- preservative-free solutions for injection by the various spinal routes (epidural, intrathecal, caudal, and others).
- powders for compounding.
- liquids both with and without alcohol for oral and sub-lingual administration, available in regular phials and bottles, dropper bottles, bottles with a pump similar to those used with liquid soap and phials with droppers built into the cap.
- tablets and capsules containing (acetaminophen/APAP), aspirin and other agents.

2.10 Previous studies

Study of (Emamhadi M *et al* .,2012)

Electrocardiographic manifestations of tramadol toxicity with special reference to their ability for prediction of seizures.

The aims of this study are to determine the electrocardiographic (ECG) manifestations of the symptomatic patients with isolated tramadol toxicity and to predict seizures based on ECG parameters.

Medical charts of a total of 479 patients with isolated tramadol toxicity were retrospectively evaluated. Their clinical manifestations were recorded, and their ECG parameters including rate, PR interval, QRS duration, corrected Q T interval, terminal 40-millisecond frontal plane QRS axis, and the height of R wave and R/S ratio in the lead aVR were measured. The data were analyzed using Kolmogorov-Smirnov test, Mann-Whitney U test, Pearson $\chi(2)$, Pearson correlation coefficient (r), and the Student t test.

Electrocardiographic heart rate more than 100 beats per minute in 30.6%, QRS 120 milliseconds or more in 7.5%, corrected QT interval more than 440 milliseconds in 24.6%, height of R wave more than 1 mm in lead aVR in 22.1%, R/S ratio more than 0 in lead aVR in 23.5%, terminal 40-millisecond frontal plane QRS axis greater than 120° in 31.7%, and complete or incomplete right bundle-branch block in 4.6% of the patients were detected. There were no statistically significant differences between the patients who had not convulsed and those who had convulsed after admission regarding age, sex, vital signs, and ECG findings at presentation (all P values were >.05).

Tramadol toxicity shows ECG changes consistent with sodium channel blockade and potassium channel blockage effects. The risk of development of seizures cannot be predicted based on the changes of ECG parameters at presentation.

Study of (Kaynar M *et al* .,2012)

On-demand tramadol hydrochloride use in premature ejaculation treatment.

The purpose of this study is To determine the efficacy of tramadol in premature ejaculation (PE) treatment compared with placebo.

A single-blind, placebo-controlled, crossover study was conducted with 60 lifelong (primary) patients with PE. The patients were randomized into 2 groups, each consisting of 30 patients, who took tramadol or placebo on demand. PE was defined as an

intravaginal ejaculation latency time of ≤60 seconds in 90% of intercourse episodes. The efficacy of the drugs was assessed using the intravaginal ejaculation latency time, ability of ejaculation control, and sexual satisfaction scores after an 8-week treatment period.

All participants completed the study voluntarily. Two groups were similar in terms of the patient demographics. Increases in the intravaginal ejaculation latency time, ability of ejaculation control, and sexual satisfaction score between the placebo and tramadol groups were compared with the baseline values in both groups. At the end of study period, the tramadol group had significantly (P<.001) greater values for all 3 parameters compared with those in the placebo group.

On-demand use of low-dose tramadol is effective for lifelong PE.

Study of (Xiong GG *et al* .,2011)

Safety and efficacy of tramadol hydrochloride with behavioral modification in the treatment of premature ejaculation.

To evaluate the efficacy and safety of tramadol hydrochloride with behavioral modification in delaying ejaculation in patients with premature ejaculation.

Seventy-two potent men with premature ejaculation were equally and randomly assigned to a treatment group and control group, the former received 50 mg tramadol hydrochloride with behavioral modification approximately 2 hours before planned sexual activity, while the latter underwent behavioral therapy only, both treated for 8 weeks. Intravaginal ejaculatory latency time (IELT), intercourse satisfaction of the partners, total therapeutic effectiveness, adverse reactions, and hepatic and renal function of the patients were recorded and compared before and after the treatment.

Both the treatment and the control groups showed significant differences from pretreatment in the mean IELT and intercourse satisfaction domain values ($P < 0.01$). The total rate of effectiveness was 72.2% in the treatment group and 47.2% in the control. The former exhibited even more significant improvement than the latter in the mean IELT, intercourse satisfaction domain values and total rate of effectiveness ($P < 0.05$). Adverse reactions occurred in 10 cases (27.8%), and no statistically significant differences were found in hepatic and renal function before and after treatment ($P > 0.05$). Tramadol hydrochloride with behavioral modification showed positive effects in prolonging IELT and improving partners' intercourse satisfaction.

Study of (Bar-Or D *et al*.,2011)

A Randomized Double-Blind, Placebo-Controlled Multicenter Study to Evaluate the Efficacy and Safety of Two Doses of the Tramadol Orally Disintegrating Tablet for the Treatment of Premature Ejaculation Within Less Than 2 Minutes.

To assess the safety of tramadol orally disintegrating tablet (ODT) (Zertane) and its efficacy in prolonging intravaginal ejaculation latency time (IELT) and improving Premature Ejaculation Profile (PEP) scores.

He conducted an integrated analysis of two identical 12-wk randomized double-blind, placebo-controlled phase 3 trials across 62 sites in Europe. Healthy men 18-65 yr of age with a history of lifelong PE according to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition.

Subjects were randomized to receive 1:1:1 placebo (n=200), 62mg tramadol ODT (n=206), or 89mg tramadol ODT (n=198).

We measured overall change and fold increase in median IELT and the mean change in all four measures of the PEP. Differences across treatment groups were analyzed using Wilcoxon rank-sum tests, analysis of variance, and chi-square analyses.

Tramadol ODT resulted in significant increases in median IELT compared with placebo; increases were 0.6min (1.6 fold), 1.2min (2.4 fold), and 1.5min (2.5 fold) for placebo, 62mg tramadol ODT, and 89mg tramadol ODT, respectively ($p<0.001$ for all comparisons). Men saw significantly greater improvement in all four measures of the PEP in both doses compared with placebo ($p<0.05$ for all comparisons). Tramadol ODT was well tolerated; study discontinuation occurred in 0%, 1.0%, and 1.6% of subjects in placebo, 62mg, and 89mg tramadol ODT groups, respectively. Limitations include study inclusion for men with IELT up to 120s.

On-demand 62mg tramadol ODT is an effective treatment for PE in a low and safe therapeutic dose and provides anew option for managing mild to severe PE.

Study of (Yarkan *et al*.,2011)

Epileptic seizure following IV tramadol in a patient with mental retardation and cerebellar ataxia.

To present a case of an epileptic seizure related to intravenous (IV) tramadol for pain control following a total abdominal hysterectomy operation on a patient with mental retardation and cerebellar ataxia.

A 42-year-old female with mental retardation and cerebellar ataxia presented with an epileptic seizure after administration of IV tramadol for postoperative pain. Magnetic resonance imaging scans were normal, but laboratory tests showed hypocalcemia. Next, calcium replacement was administered. Postoperative pain treatment with tramadol was discontinued because tramadol was felt to be a possible cause of the seizure observed in this patient. In order to treat the epileptic seizure, IV phenytoin sodium infusion was started. On the second postoperative day, calcium levels were found to be normal, and the IV antiepileptic medication was changed to an oral form. The patient had no subsequent seizures during the clinical follow-up. She was discharged on the fourth postoperative day without any other complications.

Even in recommended doses ,IV tramadol may cause epileptic seizures on predisposed patients.

Study of(Lanier Rk *et al* .,2010)

Physical dependence potential of daily tramadol dosing in humans.

The current study assessed the level of physical dependence and opioid blockade efficacy produced by daily maintenance on oral tramadol.

Nine residential opioid-dependent adults were maintained on two doses of daily oral tramadol (200 and 800 mg) for approximately 4-week intervals in a randomized, double-blind, crossover design. The acute effects of intramuscular placebo, naloxone (0.25, 0.5, and 1.0 mg), and hydromorphone (1.5, 3.0, and 6.0 mg) were tested under double-blind, randomized conditions. Outcomes included observer- and subject-rated measures and physiologic indices.

Challenge doses of naloxone resulted in significantly higher mean peak withdrawal scores compared to placebo. Withdrawal intensity from naloxone was generally greater during 800 versus 200 mg/day tramadol maintenance. Mean peak ratings of agonist effects were elevated at higher hydromorphone challenge doses, but did not differ significantly between tramadol doses. Physiologic measures were generally affected by challenge conditions in a dose-dependent manner, with few differences between tramadol maintenance dose conditions.

Chronic tramadol administration produces dose-related opioid physical dependence without producing dose-related attenuation of agonist challenge effects. Tramadol, may be a useful treatment for patients with low levels of opioid dependence or as a treatment

for withdrawal during opioid detoxification, but does not appear to be effective as maintenance medication due to a lack of opioid cross tolerance .

Study of (Tashakori & Afshari,2010)

Tramadol overdose as a cause of serotonin syndrome: a case series.

Tramadol overdose impairs consciousness and may induce ECG changes and convulsions. These effects may be opioid and/or serotonin related. This study describes clinical manifestations, electrophysiological and hemodynamic findings, and the frequency of potential serotonin syndrome in tramadol overdose in a case series. It also focuses on potential factors by which convulsions could be predicted.

This is a prospective observational case series. All cases admitted with suspected tramadol overdose from September 1, 2006 to August 31, 2007 were included.

Tramadol overdose accounted for 1.2% of all poisonings (n = 158), of which 65% were tramadol only. It was predominantly male (63%). Mean age was 22.6 (7.4) years. Among these cases, 24 (15%) experienced seizure and in 10 (6%) cases creatine phosphokinase increased. Death occurred in one patient. Seizure occurred more frequently in patients with tramadol use only (odds ratio 3.0, 95% confidence interval 1.1, 8.4) and mydriasis (odds ratio 8.9, 95% confidence interval 1.9, 42.4) on admission. Eight cases were treated for potential serotonin syndrome. Concurrent intoxication with central nervous system depressants, age, alleged dose, consciousness level, respiratory rate, history of drug abuse, and naloxone administration was not associated with the occurrence of seizures.

Study of (Rehni *et al* .,2010)

Tramadol-induced seizurogenic effect: a possible role of opioid-dependent histamine H1 receptor activation-linked mechanism.

The present study has been designed to investigate the role of opioid receptors, mast cells, and histamine receptors (H(1) subtype) in the seizurogenic effect of tramadol on pentylenetetrazole-treated mice. A single injection of pentylenetetrazole (80 mg kg(-1)) was used to elicit seizure activity in mice. Seizures were assessed in terms of the time latency of the onset of Straub-like tail, onset of jerky movements of whole body, convulsions, and death. Tramadol administration (50 mg kg (-1)) caused a marked increase in seizurogenic activity of pentylenetetrazole as measured in terms of a significant decrease in the time latency of the onset of Straub-like tail, jerky movements of whole body, convulsions, and death. Moreover, prior administration of naloxone (2

mg kg(-1)), fexofenadine (100 mg kg(-1)), cetrizine, sodium cromoglycate, and ketotifen (10 mg kg(-1)), respectively, attenuated the seizurogenic activity that tramadol exerted on pentylenetetrazole-treated mice. Therefore, it may be suggested that tramadol exerts a seizurogenic effect on mice via an H(1) receptor activation-linked pathway possibly through an opioid receptor-dependent release of histamine from the mast cells .

Study of (Afshari R& Ghooshkhanehee H, 2009)

Tramadol overdose induced seizure, dramatic rise of CPK and acute renal failure.

Tramadol, an analgesic with a low affinity to opioid receptors, inhibits the reuptake of norepinephrin and serotonin. It is also abused by opioid addicts. Tramadol overdose can induce CNS and respiratory depression, tachycardia, and seizures. In this report, a 19 years male was admitted due to suicidal attempt of ingestion of 4000 mg of Tramadol. He experienced frequent seizures, confusion, myosis, and dramatic rise of CPK, LDH and Creatinine. Improvement was had in the following days by administering fluids, NaHCO3 and chlordiasopoxide and routine management. He was discharged with no further sequelae.

Study of (Talaie H *et al* .,2009)

Dose-independent occurrence of seizure with tramadol.

In this study the researcher assessed the incidence of seizure, as it is one of the most important adverse effects.

In a cross-sectional study, 215 cases of tramadol users or abusers who were admitted to Loghman-Hakim Hospital Poisoning Center (LHHPC) in Tehran during a 5-month period, from April 2007 to September 2007, were assessed to evaluate the occurrence of seizure. Patients with positive history of co-ingestion of other drugs, addiction, convulsive disorders, renal diseases, or head trauma with abnormal electroencephalography (EEG) or computerized tomography (CT) scan of the brain were excluded, thus 132 patients were included in the study. For patients who had seizure, CT scan of the brain and EEG were performed, and frequency and type of seizure were identified. Mean tramadol dose was compared between patients with and without seizure.

Among the patients, 97 (73.5%) were male. Seizure occurred in 61 patients (46.2%) within 24 hours after tramadol ingestion. The majority of patients who had seizure were male (male, 83.6% vs. female, 16.4%). Mean tramadol dose was lower among females

than males (males, 2413 mg vs. females, 1706 mg), but the difference was not statistically significant. Of 35 patients with documented seizure type, all showed generalized tonic-clonic seizure and 12 patients had abnormal EEG (35.3%). No statistically significant difference was observed in mean tramadol intake between patients with or without seizure. Analysis of patients with seizure, according to tramadol intake, indicated that most patients used tramadol in the dose range of 500-1000 mg followed in occurrence by 1500-2000 mg, then 100-500 mg, 2500-3000 mg, and 3500-4000 mg.

Mean tramadol intake does not differ between patients with and without seizure, and the most common dose range in those with seizure is 500-1000 mg. We thus conclude that the incidence of seizure with tramadol is not dose dependent .

Study of (Sansone RA *et al*., 2009)

Tramadol: seizures, serotonin syndrome, and coadministered antidepressants.

This ongoing study is dedicated to the challenging clinical interface between psychiatry and primary care-two fields that are inexorably linked. Tramadol (Ultram) is a commonly prescribed analgesic because of its relatively lower risk of addiction and better safety profile in comparison with other opiates. However, two significant adverse reactions are known to potentially occur with tramadol-seizures and serotonin syndrome. These two adverse reactions may develop during tramadol monotherapy, but appear much more likely to emerge during misuse/overdose as well as with the coadministration of other drugs, particularly antidepressants. In this article, we review the data relating to tramadol, seizures, and serotonin syndrome. This pharmacologic intersection is of clear relevance to both psychiatrists and primary care clinicians.

Study of (Tjäderborn M *et al* .,2009).

Tramadol dependence: a survey of spontaneously reported cases in Sweden.

The aim of this study was to investigate occurrence of tramadol dependence and associated risk factors using spontaneously reported adverse drug reactions.

The Swedish database for spontaneously reported adverse drug reactions, Swedish Drug Information System (SweDIS), was searched for reports on tramadol dependence from 1 January 1995 until 31 December 2006. Selection was conducted based on the DSM-IV definition of dependence. Available information was scrutinized and registered and then presented descriptively.

A total of 104 reports of tramadol dependence were identified, of which 60 (58%) concerned women. The median age (range) was 45 (15-84) years. Information on a history of substance abuse was present in 31 patients (30%) and 41 patients (39%) had a documented past or current use of a drug of abuse. Prescribed doses of tramadol ranged between 50-800 mg/day, and ingested doses between 50-4000 mg/day. Time of onset ranged from some weeks up to 4 years. In 72 (69%) cases the reaction was classified as serious, mainly due to hospitalizations for detoxification or discontinuation of tramadol. There is an occurrence of tramadol dependence in association with analgesic treatment within the recommended dose range. In susceptible patients a severe and serious dependence syndrome may develop. A history of abuse or use of a drug of abuse seems to be an important risk factor.

Study of (Pollice R *et al*.,2008)

Severe tramadol addiction in a 61 year-old woman without a history of substance abuse.

This study describe the first case of Tramadol addiction and withdrawal in an elderly female patient in apparently good physical health. We report successful treatment with mirtazapine and clonidine. We believe that patients must be advised to take Tramadol regularly and to stop gradually especially after long treatment periods; moreover physicians must consider the potential physical dependence when they prescribe Tramadol for pain. Hence, we are observing some patients who continue to take Tramadol in order to achieve a feeling of well-being, even though their pain is controlled after disease regression. Finally, the establishing of an evidence-based tramadol detoxification protocol would be highly desirable.

Study of (Shadnia S *et al* .,2008)

Tramadol intoxication: a review of 114 cases.

Tramadol as a centrally acting analgesic is extensively used in the management of moderate to severe pain. It slightly affects opioid receptors and inhibits the reuptake of norepinephrin and serotonin in the CNS. There are reports about toxicity and abuse of tramadol. The objective of the present study was to evaluate epidemiology of intentional tramadol intoxications. All poisoning cases that admitted to Loghman-Hakim Hospital Poison Center from April to May 2007 were studied. A total of 114 cases (82 men and 32 women) of intentional tramadol intoxications with the median age of 23.66 +/- 6.87

years (range 16-54 years) were identified. Other illicit drugs were found to be used in combination with tramadol in some of the cases, which among them benzodiazepines were the most common. Tramadol overdose has been one of the most frequent causes of drug poisoning in the country in the recent years, especially in male young adults with history of substance abuse and mental disorders. Nausea, vomiting, Central Nervous System (CNS) depression, tachycardia, and seizure are the most common findings in this kind of poisoning. Cardiopulmonary arrest was found as the cause of death in cases who had ingested more than 5000 mg tramadol.

Study of (Salem EA *et al*.,2008)

Tramadol HCL has promise in on-demand use to treat premature ejaculation.

Premature ejaculation (PE) is a worldwide problem without an approved treatment. Selective serotonin reuptake inhibitors (SSRIs) are widely used "off label" as pharmacotherapeutic agents in the treatment of PE.

This study investigates Tramadol efficacy for on-demand treatment of PE.

Intravaginal ejaculation latency time (IELT) was used as an objective tool to assess the efficacy of the investigated treatments.

Single-blind, placebo-controlled, crossover, stopwatch monitored two-period study was conducted, on 60 patients with lifelong PE. PE was defined as IELT of <2 minutes in 80% of intercourse episodes. A total of 25 mg of Tramadol hydrochloride was given to one group (30) prior to intercourse and placebo was supplied for the other group (30) for 8 weeks. Drugs were taken 1-2 hours before sexual activity and sexual intercourse was required at least once per week. After the initial treatment period, the two groups took the alternate medication for another 2 months. The two 8-week treatment periods were separated by 1 week washout period. IELT was timed by a stopwatch at each intercourse and was reported by patients or partners.

The baseline (mean +/- SD) IELT for patients before treatment was 1.17 +/- 0.39 minutes. At the end of the treatment period utilizing the active drug, the mean IELT was increased significantly in patients on Tramadol treatment to 7.37 +/- 2.53 minutes. The same patients on placebo medication had mean IELT of only 2.01 +/- 0.71 minutes. Patients uniformly reported satisfaction with their resulting control over ejaculation.

Study of (Jovanović-Cupić V *et al* .,2006)

Seizures associated with intoxication and abuse of tramadol.

The purpose of this study is to assess the frequency of seizures and patient characteristics associated with tramadol intoxication and abuse in young addicts.

Patients with history of tramadol abuse and intoxication were prospectively studied during a 3-year period. The characterstics of patients with seizures and those without seizures were compared.

Fifty-seven patients (mean age 22.3 years [range 16-43 years], 47 males) were included. Tonic/clonic seizures occurred in 31 (54.4%) patients, (26 males and 5 females): single in 14 (45%), multiple in 17 (55%) patients after a tramadol dose ranging from 250-2500 mg. Seizures occurred within 24 h after tramadol intoxication in 26 (84%) patients, and later in 5 (16%) patients. Compared to addicts without seizures, the abusers with seizures were younger ($p < 0.05$). Both epileptiform and nonepileptiform electroencephalographic patterns were more common in patients with seizures than in patients without seizures, but the differences did not reach statistical significance.

The neurotoxicity of tramadol commonly manifests as generalized tonic-clonic seizures occurring most frequently within 24 h after tramadol intake. Seizures were more common in younger abusers with a longer duration of exposure to tramadol and with the combined use of tramadol with alcohol.

Study of (Alafifi *et al* .,2005)

Drug Misuse Among University Students In the Gaza Strip

This study was aimed to assess the prevalence of drug misuse among university students in Gaza strip , it consist of two phase. The first phase of the project entailed surveying the high schools in the Gaza Strip and was carried out in 2002-2003. The second phase was carried out in 2004 in the universities of the Gaza Strip.

A sample of 491 students (248 males and 243 females) were randomly selected from five universities in the Gaza Strip in the second and fourth year, during the second phase of the project. The survey revealed a prevalence of use of a drug one or more times: Marijuana (4.6% of male students and 1.2% of female students); consumption of beer and other alcoholic products (7.1% among males, 2.6% among females); tried

powder (heroin or cocaine) (2.8% of males and 1.6% of females); use of CNS stimulant tablets (5.4% of males, 1.3% of females); use of inhalants (9.1% of males and 1.6% of females); and use of other narcotics including ecstasy and locally made materials (1.6% of males and 0.8% of females) **.**

Study of (Näslund S& Dahlqvist R,2003).

Treatment with tramadol can give rise to dependence and abuse.

Tramadol is a centrally acting opioid analgesic which is increasingly used in Sweden. Dependence, abuse and withdrawal has been reported in patients treated with tramadol. The incidence of these adverse effects is considered to be low. Patients with a history of substance abuse might be at higher risk than others to develop dependence. The number of forged tramadol prescriptions uncovered in Swedish pharmacies was relatively low in 2001, compared to those of prophoxyphene and codien ,but increasing .

Study of (Senay EC *et al*., 2003) .

Physical dependence on Ultram (tramadol hydrochloride): both opioid-like and atypical withdrawal symptoms occur.

In 1994, the Drug Abuse Advisory Committee (DAAC) of the Food and Drug Administration (FDA) concluded that Ultram (tramadol hydrochloride) could be marketed as an analgesic drug without scheduling under the Controlled Substances Act based upon extensive pre-clinical, clinical and European epidemiological data. However, to guard against unexpectedly high levels of abuse in the United States, the DAAC recommended that an independent steering committee (ISC) be appointed to proactively monitor abuse/dependence. In the event that high rates of abuse were found, this ISC was given the authority to immediately recommend to the FDA that Ultram be scheduled. In the course of the surveillance project, the ISC received reports of withdrawal following abrupt discontinuation of Ultram and in some instances, following dose reductions. In most cases, the withdrawal symptoms consisted of classical opioid withdrawal, but in some cases were accompanied by withdrawal symptoms not normally observed in opiate withdrawal, such as hallucinations, paranoia, extreme anxiety, panic attacks, confusion and unusual sensory experiences such as numbness and tingling in one or more extremities. Withdrawal symptoms of either type were one of the more prevalent adverse events associated with chronic Ultram use, comprising nearly 40% of all adverse events reported with Ultram. Most of these consisted of

typical opiate withdrawal symptoms, but 1 in 8 cases presented as atypical. These results indicate that physicians and other healthcare professionals need to be aware of the potential of Ultram to induce withdrawal of the classical opioid type, and that atypical withdrawal may also occur.

Study of (Liu ZM,1999).

Drug dependence and abuse potential of tramadol.

This study aimed to assess the drug dependence and abuse liability of tramadol.

Subjects of opiate addicts with history of tramadol abuse were 219. Physical dependence of tramadol was assessed using opiate withdrawal scale (OWS), psychic dependence was assessed by association test of Addiction Research Center Inventory-Chinese Version (ARCI-CV); the degrees of craving experienced for tramadol was self-reported on visual analogue scale (VAS).

The scores of OWS of tramadol were 0.05-1.07; 3 scores on scales in particular being used the identify euphoric effects--MBG, sedative effects--PCAG, and psychotomimetic effects--LSD of ARCI were 7.3, 6.1, and 3.4, respectively ($F = 38.1$, $P < 0.01$); 57.1% of tramadol abuse subjects had craving for tramadol (chi $2 = 75.86$, $P < 0.01$).

Tramadol produced high abuse potential among opiate addicts.

Study of (Tobias JD,1997)

Seizure after overdose of tramadol.

Tramadol (Ultram) is a new analgesic agent with a dual mechanism of action that includes weak agonistic effects at the mu-opioid receptor as well as inhibition of neurotransmitter (serotonin, norepinephrine) re-uptake. Although it has proven to be a safe and effective agent for the control of pain, adverse effects can occur with its use. He report the occurrence of seizure activity after the inadvertent administration of 4 mg/kg of tramadol to a child. Previous reports of seizure activity after tramadol administration.

2.10.1 Comment about previous studies

According to the literature review that mentioned by the researcher there are a few of studies about the tramadol abuse but the mentioned studies clarified the following :

1-The relationship between tramadol and its effect on premature ejaculation.

2- The relation between the use of tramadol and the potential of dependence .

3- The relation between the misuse of tramadol and potential of addiction and dependence .

4- The effect of tramadol as anti-depressant .

5- The effect of tramadol on changing of ECG .

6- The toxicity of tramadol abuse .

7- Convulsions that caused by abuse of tramadol .

8- Abusing of tramadol and serotonin syndrome .

The Kaynar M *et al* (2012) confirm that using of tramadol with low dose can help in treatment of premature ejaculation , they use the comparison between two groups of people complain of premature ejaculation one group was giving placebo and the another group was giving low dose of tramadol , the result observed that the group of people who take tramadol succeed on delayed ejaculation .

The Xiong GG *et al* (2011) confirm that using of 50mg of tramadol and behavioral modification have an effect of treatment of premature ejaculation , on this study the researcher assigned two group one of them are control group , and the researchers apply the treatment of tramadol on one group and behavioral modification on control group with closed monitoring of kidney and hepatic functions , the result show that efficacy of tramadol for treatment of premature ejaculation with behavioral modification without effect on kidney and hepatic function.

The Bar-Or D *et al*(2011) confirm that using of oral administer tramadol with low dose 62mg can help people who are suffer from premature ejaculation .

All of Kaynar M *et al* (2012) , Xiong GG *et al* (2011) ,and Bar-Or D *et al*(2011) are agree that tramadol with low dose can help in treatment of premature ejaculation, without any effect on renal and hepatic function .

The Emamhadi M *et al* (2012) confirm that tramadol toxicity can cause seizures by making disturbance in calcium & sodium channels .

The Yarkan *et al*(2011) show that tramadol administration have an incidence to cause epileptic fit even in recommended dose that tramadol exerts a seizurogenic effect on mice via an H(1) receptor activation-linked pathway possibly through an opioid receptor-dependent release of histamine from the mast cells .

The Afshari R& Ghooshkhanehee H (2009) was write a report about addict person who take large dose of tramadol the result was that person complain of delirium and convulsions .

The Talaie H *et al* (2009) confirm that tramadol intake does not differ between patients with and without seizure, and the most common dose range in those with seizure is 500-1000 mg. We thus conclude that the incidence of seizure with tramadol is not dose dependent .

The Sansone RA *et al*(2009) show that the use and abuse of tramadol can be cause seizures and serotonin syndrome .

The Shadnia S *et al* (2008) show that tramadol have high incidence of intoxication after abused and occurrence of seizures and the fatal dose is 5000mg .

The Jovanović-Cupić V *et al* (2006) confirm that The neurotoxicity of tramadol commonly manifests as generalized tonic-clonic seizures occurring most frequently within 24 h after tramadol intake. Seizures were more common in younger abusers with a longer duration of exposure to tramadol and with the combined use of tramadol with alcohol the dose range between 250- 2500mg.

The Tobias JD (1997) confirm that tramadol intoxication cause tonic clonic convulsions

All of The Emamhadi M *et al* (2012) , Yarkan et al(2011, Afshari R& Ghooshkhanehee H (2009), Talaie H *et al* (2009), Sansone RA et al(2009) , Shadnia S et al (2008) , Jovanović-Cupić V *et al* (2006) , and Tobias JD (1997) agree that intoxication of tramadol due to misuse can cause tonic clonic seizures .

The Lanier RK *et al* (2010) show that Chronic tramadol administration produces dose-related opioid physical dependence without producing dose-related attenuation of agonist challenge effects.

The Tjäderborn M *et al* (2009) show that There is an occurrence of tramadol dependence in association with analgesic treatment within the recommended dose range. In susceptible patients a severe and serious dependence syndrome may develop. A history of abuse or use of a drug of abuse seems to be an important risk factor.

The Pollice R *et al*(2008) have a report about tramadol addiction in old woman without a history of substance abuse.

The Näslund S& Dahlqvist R(2003) show that persons who are treated with tramadol has high percentage tramadol abuse , and there are has already substance abuse .

The Senay EC *et al*(2003) show that tramadol has potential to induce withdrawal of the classical opioid type, and that atypical withdrawal may also occur.

The Liu ZM(1999) confirm that tramadol produced high abuse potential among opiate addicts.

All of the Lanier RK *et al* (2010), Tjäderborn M et al (2009) , Pollice R *et al*(2008) , Näslund S& Dahlqvist R(2003) , Senay EC *et al*(2003) ,and Liu ZM(1999) agree that tramadol has high potential of abuse and dependence .

Chapter three

- **Methodology**
- **Study Design**
- **Study Population**
- **Study Sample**
- **Study Tools**
- **Pilot Study**
- **Statistical Method**

3.1Methodology

This chapter describes the methodology that was used in this research. The adopted methodology to accomplish this study uses the following techniques: the information about the research design, research population, questionnaire design, statistical data analysis, content validity, place of the study , illegibility criteria , ethical considerations, and pilot study.

3.1.1Study Design

The design of this study is descriptive, analytical, cross sectional study as it assesses the Knowledge, attitude, practice, psychological state , and presence of side effects of tramadol abusers .Cross sectional study was chosen because it appropriate for describing the status of phenomena or for describing relationships among phenomena at fixed point in time.

The first phase of the research thesis proposal included identifying and defining the problems and establishment objective of the study and development research plan.

The second phase of the research included a summary of the comprehensive literature review. Literatures on claim management was reviewed.

The third phase of the research included a field survey which was conducted with **the study of** " assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice "

The fourth phase of the research focused on the modification of the questionnaire design, through distributing the questionnaire to pilot study, The purpose of the pilot study was to test and prove that the questionnaire questions are clear to be answered in a way that help to achieve the target of the study. The questionnaire was modified based on the results of the pilot study.

The fifth phase of the research focused on distributing questionnaire. This questionnaire was used to collect the required data in order to achieve the research objective.

The sixth phase of the research was data analysis and discussion. Statistical Package for the Social Sciences, (SPSS) was used to perform the required analysis. The final phase includes the conclusions and recommendations.

A one hundred and twenty questionnaires were distributed to the research population and **one hundred** questionnaires are received.

Figure (1) shows the methodology flowchart, which leads to achieve the research objective.

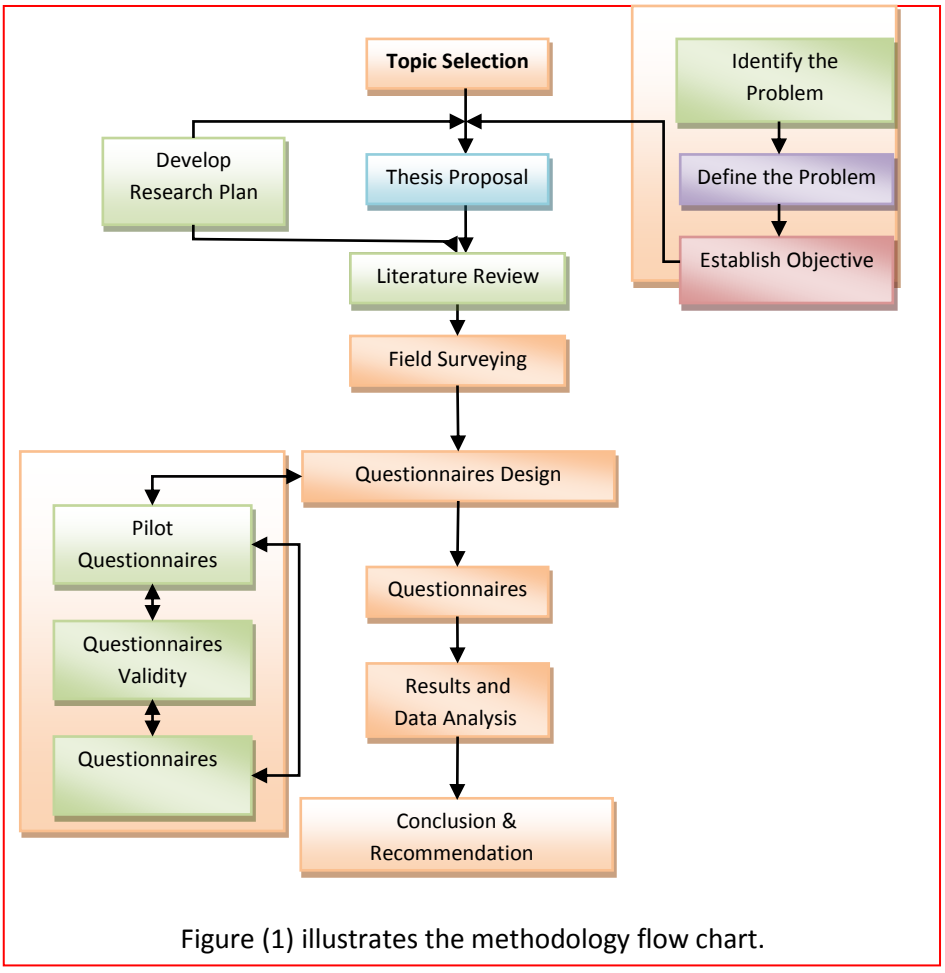

Figure (1) illustrates the methodology flow chart.

Research methodology

3.1.2 Data Collection Methodology

In order to collect the needed data for this research , we use the secondary resources in collecting data such as books, journals, statistics and web pages , in addition to preliminary resources that not available in secondary resources through distribute questionnaires on study population in order to get their opinions about the " assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice ". Research methodology depend on the analysis of

data on the use of descriptive analysis, which depends on the poll and use the main program (SPSS).

3.1.3Study Population

The study population of this study in not defined , and there is no statistical report about the number of tramadol abusers , the researcher select two famous private psychiatric clinics to take the study sample.

The study population of the present work is all males and females they recorded and treated as tramadol abusers on the two private psychiatric clinics in Gaza city .

3.1.4Sample size and sampling procedure

The researcher have an approval from the directors of the two private psychiatric clinics to apply the study in their clinics ,and by assessment about the number of clients who are attend the clinics to recover from tramadol every day , there is 4-6 client attend clinics daily .

From the viewpoint of the researcher The sample size of the present study will be calculated by collecting the sample on one month in the two private psychiatric clinics as 4 cases in every day during the month, and questionnaires were distributed to the convenient sample and 100 questionnaires are received .

3.1.5 Place of study:

This study was carried out in the two private psychiatric clinics in Gaza city with sample size relatively compatible, as much as possible, with the population size of each clinic.

The two psychiatric clinics are following to the Dr ayesh samour and Dr mohammed abu sebah .The two doctors are working on Palestinian ministry of health on general directory of mental health , and eternally their consent to apply the study in their clinics.

3.1.6 Period of study:

The study started when the researcher have approval from seminar committee and expected to be completed by the end of 2012.

3.1.7 Eligibility criteria:

3.1.7.1 Inclusion criteria:

All males and females they recorded and treated as tramadol abusers , and age from 16-50 years old ,and they are abused tramadol daily.

3.1.7.2 Exclusion criteria:

Any client who treated for other psychiatric disorders.

3.1.8 Ethical consideration :

Approval from each person who will participate in the study.

Approval from Islamic university about the study .

Approval from Dr.Ayesh samuor(Annex1).

Approval from Dr.Mohammed abu sebah(Annex 2).

3.2 Questionnaire content

One questionnaire was provided with a covering letter explaining the purpose of the study, the way of responding, the aim of the research and the security of the information in order to encourage a high response. The questionnaire included multiple choice question: which used widely in the questionnaire, The variety in these questions aims first to meet the research objectives, and to collect all the necessary data that can support the discussion, results and recommendations in the research.

The sections in the questionnaires will verify the objectives in this research related to measure the " assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice as follows

First section : personal data consist from 8 Sentences.

second section: Knowledge of tramadol abusers consist from 13 Sentences.

third section : Practices of tramadol abusers consist from 24 Sentences.

forth section : Attitudes of tramadol abusers consist from 17 Sentences.

fifth section : The psychological state of the abusers before abused tramadol consist from 5 Sentences.

Sixth section : The presence of side effects of the abuse of tramadol consist from 9 Sentences.

and the Instruments of the study consist as follow:

Level	**Strongly disagree**	**Disagree**	**Hesitant**	**Agree**	**Strongly agree**
Scale	1	2	3	4	5

3.3 Pilot Study

A pilot study for the questionnaire was conducted before collecting the results of the sample. It provides a trial run for the questionnaire, which involves testing the wordings of question, identifying ambiguous questions, testing the techniques that used to collect data, and measuring the effectiveness of standard invitation to respondents .

Twenty five of questionnaires were distributed for this goal and the result of pilot study have few modifications don on the questionnaire and the pilot study sample were excluded from the study sample .

3.4Validity of the Tool

We can define the validity of an instrument as a determination of the extent to which the instrument actually reflects the abstract construct being examined. "Validity refers to the degree to which an instrument measures what it is supposed to be measuring". High validity is the absence of systematic errors in the measuring instrument. When an instrument is valid; it truly reflects the concept it is supposed to measure. Achieving good validity required the care in the research design and sample selection . The amended questionnaire was by the supervisors and five expertise in the tendering and bidding environments to evaluate the procedure of questions and the method of analyzing the results. The expertise agreed that the questionnaire was valid and suitable enough to measure the purpose that the questionnaire designed for.

3.4.1Content Validity of the Questionnaire

Content validity test was conducted by consulting one groups of experts. They was requested to evaluate and identify whether the questions agreed with the scope of the items and the extent to which these items reflect the concept of the research problem. The other was requested to evaluate that the instrument used is valid statistically and

that the questionnaire was designed well enough to provide relations and tests between variables. The group of experts did agree that the questionnaire was valid and suitable enough to measure the concept of interest with some amendments.

3.4.2 Statistical Validity of the Questionnaire

To insure the validity of the questionnaire, two statistical tests should be applied. The first test is Criterion-related validity test (Pearson test) which measure the correlation coefficient between each item in the field and the whole field. The second test is structure validity test (Pearson test) that used to test the validity of the questionnaire structure by testing the validity of each field and the validity of the whole questionnaire. It measures the correlation coefficient between one filed and all the fields of the questionnaire that have the same level of similar scale.

3.4.2.1 Criterion Related Validity :

3.4.2.1.1 Internal consistency:

Internal consistency of the questionnaire is measured by a scouting sample, which consisted of **twenty five** questionnaires, through measuring the correlation coefficients between each paragraph in one field and the whole filed. Tables No. (1) below shows the correlation coefficient and p-value for each field items. As show in the table the p-Values are less than 0.05 or 0.01,so the correlation coefficients of this field are significant at $\alpha = 0.01$ or $\alpha = 0.05$, so it can be said that the paragraphs of this field are consistent and valid to be measure what it was set for.

Table(1)
The correlation coefficient between each paragraph in the field and the whole field (Knowledge of tramadol abusers)

No.	Statement	Pearson coefficient	p-value
1	DO you Know tramadol	0.449	0.015
2	Do you Believe that the abuse of tramadol, is a problem in the Gaza Strip	0.529	0.004
3	Do you Believe that there is a certain group abuse tramadol.	0.466	0.011
4	Do you Believe that, taking tramadol affects the persons daily life	0.623	0.000
5	Do you Know that the tramadol is a pain reliever.	0.546	0.002
6	Do you Believe that the widespread misuse tramadol is an impact of the siege.	0.476	0.009
7	Do you Believe that taking tramadol, affects the sexual life.	0.571	0.001
8	Were you aware of this drug doses when you take it .	0.518	0.004

9	Do you Believe that the misuse of tramadol causes addiction.	0.636	0.000
10	Did your work was affected due to using tramadol negatively .	0.642	0.000
11	Did your work was affected due to using tramadol positively .	0.724	0.000
12	Do you Believe that the misusing tramadol is religiously for bidden.	0.684	0.000
13	Do you Believe that the smoking is religiously for bidden.	0.694	0.000

Table(2)
The correlation coefficient between each paragraph in the field and the whole field (Practices of tramadol abusers)

No.	Statement	p-value	Pearson coefficient
1	Can you get tramadol from pharmacies easily .	0.743	0.000
2	Can you get tramadol from drug dealers .	0.628	0.000
3	Can you get tramadol from friends .	0.556	0.002
4	Can you get tramadol from those who work in the tunnels .	0.635	0.000
5	Did you use tramadol to treat premature ejaculation .	0.707	0.000
6	Did tramadol help you to delay ejaculation.	0.760	0.000
7	Did tramadol help you to take your time in delaying ejaculation.	0.693	0.000
8	Did you use tramadol while you did not suffer from premature ejaculation.	0.562	0.002
9	Did you use tramadol in order to stay late .	0.646	0.000
10	Did you start taking pills of 100mg.	0.680	0.000
11	Did you increase taking the number of pills from time to time .	0.682	0.000
12	Did you use tramadol to reach the state of euphoria	0.695	0.000

13	Did you use tramadol to help you in your work .	0.663	0.000
14	Did you take tramadol at the same time of the last dose.	0.684	0.000
15	Did you do any illegal action to get tramadol .	0.717	0.000
16	Did the effect of tramadol was affected with the amount and the number of pills	0.575	0.001
17	Did you use tramadol to help in your study.	0.431	0.020
18	Did you use tramadol to help you in increasing your physical efforts in parties .	0.622	0.000
19	Did you take tramadol during pregnancy.	0.621	0.000
20	Are you smoking .	0.530	0.003
21	Are you a heavy smoker .	0.486	0.008
22	Did the use of tramadol affect in increasing the number of cigarettes and change the euphoria of smoking.	0.678	0.000
23	Do you take alcoholic drinks	0.680	0.000
24	Did you abuse another drug with tramadol.	0.598	0.001

Table(3)
The correlation coefficient between each paragraph in the field and the whole field (Attitudes of tramadol abusers)

No.	Statement	p-value	Pearson coefficient
1	Do you Support the measures of concerned people to stop the spread of this phenomenon.	0.719	0.000
2	Do you support programs of mass media to stop the spared of this phenomena.	0.651	0.000
3	Did you try to stop the using tramadol due to some circumstances.	0.554	0.004

4	Did you try stop using tramadol due to the hardness of getting it.	0.645	0.001
5	Did you feel of the stigma because of taking tramadol .	0.673	0.000
6	Was there any one who expected that you were taking tramadol .	0.574	0.003
7	Did anyone around you suffer from your taking tramadol .	0.746	0.000
8	Did you neglect your family because of using tramadol .	0.566	0.003
9	Were you exposed to confrontation or embarrassments due to taking tramadol .	0.736	0.000
10	Did you Try to stop on your own.	0.659	0.000
11	Were you engaged in a treatment program.	0.700	0.000
12	Were you Committed to the instructions of the treatment program.	0.706	0.000
13	Were you able to get rid of the using tramadol for more than a month.	0.771	0.000
14	Were you able to stop taking tramadol.	0.646	0.000
15	Are the reasons behind stopping the use of tramadol, religious.	0.745	0.000
16	Are the reasons behind stopping the use of tramadol social .	0.618	0.001
17	Are the reasons behind stopping the use of tramadol economic .	0.604	0.001
18	Are the reasons behind stopping the use of tramadol healthy .	0.634	0.001

Table(4)
The correlation coefficient between each paragraph in the field and the whole field
(The psychological state of the tramadol abusers)

No.	Statement	p-value	Pearson coefficient
1	Did you take this drug while you were suffering from psychological stress.	0.534	0.015
2	Were you suffering from anxiety.	0.812	0.000
3	Were you suffering from a sleep disorder.	0.557	0.004
4	Did you deal with tramadol to escape from reality	0.556	0.004
5	Did you use tramadol to avoid social problems .	0.649	0.000

Table(5)
The correlation coefficient between each paragraph in the field and the whole field
(The presence of side effects related to abuse of tramadol)

No.	Statement	p-value	Pearson coefficient
1	Did you suffered from gastrointestinal disorders that caused by abuse of tramadol .	0.537	0.006
2	Did you suffer from convulsions or coma that caused by the abuse of tramadol .	0.616	0.001
3	Did you Suffer from itching feeling in the feet or electrical waves during the misusing tramadol.	0.533	0.006
4	Did you Suffer from a rise in body temperature during the abuse of tramadol .	0.571	0.003
5	Did you Suffer from tremor when you did not use tramadol .	0.495	0.012
6	Did you feel dizzy while you were taking tramadol .	0.649	0.000

7	Did you have physical symptoms when you stop using tramadol.	0.483	0.014
8	Did you have high blood pressure when you stop using tramadol .	0.537	0.006
9	Did you have excessive sweating when you stop using tramadol.	0.616	0.001

3.6.1.2 Structure Validity of the Questionnaire

Structure validity is the second statistical test that used to test the validity of the questionnaire structure by testing the validity of each field and the validity of the whole questionnaire. It measures the correlation coefficient between one filed and all the fields of the questionnaire that have the same level of likert scale.

As shown in table No. (6), the significance values are less than 0.05 or 0.01, so the correlation coefficients of all the fields are significant at $\alpha = 0.01$ or $\alpha = 0.05$, so it can be said that the fields are valid to be measured what it was set for to achieve the main aim of the study .

Table No. (6)
Structure Validity of the Questionnaire

Number	**Section**	Pearson **correlation coefficient**	**p-value**
1	Knowledge of tramadol abusers	0.701	0.000
2	Practices of tramadol abusers	0.805	0.000
3	Attitudes of tramadol abusers	0.687	0.000
4	The psychological state of the abusers of tramadol	0.742	0.000
5	The presence of side effects related to tramadol abuse .	0.651	0.000

3.7 Reliability of the Tool

Reliability of an instrument is the degree of consistency with which it measures the attribute it is supposed to be measuring . The test is repeated to the same sample of people on two occasions and then compares the scores obtained by computing a reliability coefficient. For the most purposes reliability coefficient above 0.7 are considered satisfactory. Period of two weeks to a month is recommended between two tests Due to complicated conditions that the contractors is facing at the time being, it was too difficult to ask them to responds to our questionnaire twice within short period. The researcher explained that, overcoming the distribution of the questionnaire twice to measure the reliability can be achieved by using cronbach Alpha coefficients and Half Split Method through the SPSS software.

3.7.1 Half Split Method

This method depends on finding Pearson correlation coefficient between the means of odd rank questions and even rank questions of each field of the questionnaire. Then, correcting the Pearson correlation coefficients can be done by using Spearman Brown correlation coefficient of correction. The corrected correlation coefficient (consistency coefficient) is computed according to the following equation :

Consistency coefficient = 2r/(r+1), where r is the Pearson correlation coefficient. The normal range of corrected correlation coefficient 2r/(r+1) is between 0.0 and + 1.0 As shown in Table No.(7), all the corrected correlation coefficients values are between 0.8085 and 0.8785 and the general reliability for all items equal 0.8408 , and the significant (α) is less than 0.05 so all the corrected correlation coefficients are significance at α = 0.05. It can be said that according to the Half Split method, the dispute causes group are reliable.

Table (7)
Split-Half Coefficient method

Number	Section	person-correlation	Spearman-Brown Coefficient	Sig. (2-(Tailed
1	Knowledge of tramadol abusers.	0.7424	0.8521	0.000
2	Practices of tramadol abusers.	0.6926	0.8184	0.000

Number	Section	person-correlation	Spearman-Brown Coefficient	Sig. (2-(Tailed
3	Attitudes of tramadol abusers.	0.6785	0.8085	0.000
4	The psychological state of the tramadol abusers .	0.7832	0.8785	0.000
5	The presence of side effects related to tramadol abuse.	0.7143	0.8333	0.000
	Total	0.7254	0.8408	0.000

3.7.2 Cronbach's Coefficient Alpha

This method is used to measure the reliability of the questionnaire between each field and the mean of the whole fields of the questionnaire. The normal range of Cronbach's coefficient alpha value between 0.0 and + 1.0, and the higher values reflects a higher degree of internal consistency. As shown in Table No. (8) the Cronbach's coefficient alpha was calculated for the first field of the causes of claims, the second field of common procedures and the third field of the Particular claims. The results were in the range from 0.8267and 0.8925, and the general reliability for all items equal 0.8633. This range is considered high; the result ensures the reliability of the questionnaire.

Table (8)
Cronbach's Alpha for Reliability

Number	Section	No. of Items	Cronbach's Alpha
1	Knowledge of tramadol abusers.	13	0.8364
2	Practices of tramadol abusers.	24	0.8456
3	Attitudes of tramadol abusers.	18	0.8267

Number	Section	No. of Items	Cronbach's Alpha
4	The psychological state of the tramadol .abusers	5	0.8925
5	The presence of side effects related to tramadol abuse .	9	0.8513
	Total	69	0.8633

Statistical Manipulation

To achieve the research goal, researcher used the statistical package for the Social Science (SPSS) for Manipulating and analyzing the data.

Statistical methods are as follows

1- Frequencies and Percentile

2- Alpha- Cronbach Test for measuring reliability of the items of the questionnaires

3- Person correlation coefficients for measuring validity of the items of the questionnaires.

4- spearman –Brown Coefficient

5- one sample t test

6-independent samples T test

7- one way ANOVA test

8- one sample K-S test

Chapter four

Data Analysis and Discussion

4.1 One Sample K-S Test

One Sample K-S test will be used to identify if the data follow normal distribution or not, this test is considered necessary in case testing hypotheses as most parametric Test stipulate data to be normality distributed and this test used when the size of the sample are greater than 50. Results test as shown in table (9) , clarifies that the calculated p-value is greater than the significant level which is equal 0.05 (p-value. > 0.05), this in turn denotes that data follows normal distribution, and so parametric Tests must be used.

Table (9)
One Sample K-S

	Section		Statistic	P-value
1	Knowledge of tramadol abusers	13	0.940	0.340
2	Practices of tramadol abusers	24	0.919	0.367
3	Attitudes of tramadol abusers	18	0.767	0.598
4	The psychological state of the abusers of tramadol	5	1.083	0.191
5	The presence of side effects related to abuse of tramadol.	9	1.052	0.218
	All sections	69	1.248	0.089

4.2 Discussion of Research Question

We use a one sample t test to test if the opinion of the respondent in the content of the sentences are positive (weight mean greater than "60%" and the p-value less than 0.05) or the opinion of the respondent in the content of the sentences are neutral (p- value is greater than 0.05) or the opinion of the respondent in the content of the sentences are negative (weight mean less than "60%" and the p-value less than 0.05) .

4.2.1Section one: Personal information

1-Age

Table No.(10) show that 42.0% from the samples age " less than 25years " , and 38.0% from the samples age " from 25-30 year " , and 20.0 % from the samples age " more than 30 years ".

Table No.(10)

Age

Age	**Frequency**	**Percentages**
less than 25 years	42	42.0
from 25-30 year	38	38.0
more than 30 years	20	20.0
Total	100	100.0

2-Sex :

Table No.(11) show that 89.0% from the samples are " male" , and **14.0**% from the samples are " female" **,** this attributed to the seriousness of this phenomenon, as the abuse of Tramadol is not limited to men, but that there are ladies slating tramadol , and this attributed to the to the psychological reality of the situation in which citizens live in Gaza .

Table No.(11)

Sex

Sex	**Frequency**	**Percentages**
Male	86	86.0
Female	14	14.0
Total	100	100.0

3- Address :

Table No.(12) show that 18.0% from the samples from " North governorate ", and 52.0% from the samples from " Gaza governorate ", and 18.0% from the samples from " Middle governorate ", and 9.0% from the samples from " Khan yunis governorate ", and 3.0% from the samples from " Rafah governorate ".

Table No.(12)

Address	**Frequency**	**Percentages**
North governorate	18	18.0
Gaza governorate	52	52.0

Middle governorate	18	18.0
Khan yunis governorate	9	9.0
Rafah governorate	3	3.0
Total	100	100.0

4- Marital Status

Table No.(13) show that 38.0% from the sample are " Single " , and 57.0% from the sample are " Married " , and 5.0% from the sample are " Divorce " .

Table No.(13)
Marital Status

Marital Status	**Frequency**	**Percentages**
Single	38	38.0
Married	57	57.0
Widowed	0	0.0
Divorce	5	5.0
Total	100	100.0

5- Number of family members who live with you in the same house

Table No.(14) show that 25.0% from the sample Number of family members who live with you in the same house " Less than 5 **members** " , and **63.0**% from the sample Number of family members who live with you in the same house "5-10 members " , and 12.0% from the sample Number of family members who live with you in the same house " **More than 10 members** ".

Table No.(14)
Number of family members who live with you in the same house

Number of family members who live with you in the same house	**Frequency**	**Percentages**
Less than 5 **members**	25	25.0
5-10 members	63	63.0
More than 10 members	12	12.0
Total	100	100.0

6-Monthly income of NIS:

Table No.(15) show that 51.0% from the sample the Monthly income of NIS " Less than1000 NIS " **, and 35.0**% from the sample the Monthly income of NIS " 1000-2000 NIS" **, and 12.0** % from the sample the Monthly income of NIS " 2100- 3000 NIS " **, and**

2.0% from the sample the Monthly income of NIS " 3100 NIS and above " **.**

Table No.(15)
Monthly income of NIS

Monthly income of NIS	**Frequency**	**Percentages**
Less than 1000 NIS	51	51.0
1000-2000 NIS	35	35.0
2100- 3000 NIS	12	12.0
3100 and above	2	2.0
Total	100	100.0

7- Scientific level:

Table No.(16) show that 22.0% from the sample the Scientific level are " Less than High School " , and 25.0% from the sample the Scientific level are " High School " , and 17.0% from the sample the Scientific level are " Diploma of two years " , and 36.0% from the sample the Scientific level are " Bachelor " .

Table No(16)
Scientific level

Scientific level	**Frequency**	**Percentages**
Less than High School	22	22.0
High School	25	25.0
Diploma of two years	17	17.0
Bachelor	36	36.0
Up Graduate	0	0.0
Total	100	100.0

8-Profession :

Table No.(17) show that 25.0% from the sample's Profession are " Employee " , and **25.0**% from the sample's Profession are " Worker " , and 22.0% from the sample's Profession are " Student " , and 23.0% from the sample's Profession are " Unemployed " , and 5.0% from the sample's Profession are " Others " .

Table No.(17)
Profession

Profession	**Frequency**	**Percentages**
Employee	25	25.0
Worker	25	25.0
Student	22	22.0
Unemployed	23	23.0
Others	5	5.0
Total	100	100.0

4.2.2Section two: Knowledge of tramadol abusers

We use a one sample t test to test if the opinion of the respondent about **Knowledge of tramadol abusers** and the results shown in Table No. (18) as follows:

The three highest statements according to weight mean as follows:

1. In item No. (2) the weight mean equal " 96.40%" and p-value equal " 0.000" which is less than 0.05, that means (the sample Believe that the using of tramadol, is a problem in the Gaza Strip), this result can be explained that there is a spread of this phenomenon in the Gaza Strip, and this is consistent with a study (Afifi et al, 2005), where the study explain the prevalence rates of drug abuse among universities students in the Gaza Strip.
2. In item No. (1) the weight mean equal " 94.80%" and p-value equal " 0.000" which is less than 0.05, that means (the sample Know tramadol).
3. In item No. (9) the weight mean equal " 94.40%" and p-value equal " 0.000" which is less than 0.05, that means (the sample Believe that the abuse of tramadol cause addiction), this result confirm that abuse of tramadol has high potential to

cause dependence , and this consistent with a study of (Liu ZM;1999) where the study confirm that tramadol has high potential abuse among addicts persons .and also this result consistent with the study of (Tjäderborn M et al ;2009) where the study explain the result of tramadol dependence in Sweden and explain the dependence dose that cause adverse drug reactions .

And the three lowest statements according to weight mean as follows

1- In item No. (11) the weight mean equal " 66.00%" and p-value equal "0.078 " which is greater than 0.05, that means (the sample Believe that work was affected due to using tramadol positively moderately).
2- In item No. (10) the weight mean equal " 62.60%" and p-value equal " 0.431" which is greater than 0.05, that means (the sample Believe that work was affected due to using tramadol negatively moderately).
3- In item No.(12) the weight mean equal " 62.40%" and p-value equal "0.790" which is greater than 0.05, that means (the sample Believe that the misusing tramadol is religiously for bidden moderately) this result can be explained that there is lack of .

For general the results for all items of the field show that the average mean equal 4.09 and the weight mean equal 81.86 % which is greater than " 60%" and the value of t test equal 26.482 which is greater than the critical value which is equal 1.98 and the p- value equal 0.000 which is less than 0.05, that means the sample has good knowledge about tramadol at significant level $\alpha = 0.05$.

Table No.(18)
Knowledge of tramadol abusers

No.	Sentence	Mean	standard deviation	Weight mean	t-value	P-value
1	DO you Know tramadol	4.74	0.613	94.80	28.370	0.000
2	Do you Believe that the abusing of tramadol, is a problem in the Gaza Strip	4.82	0.575	96.40	31.639	0.000
3	Do you Believe that there is a certain groupmisuses tramadol.	4.19	1.070	83.80	11.119	0.000
4	Do you Believe that, taking tramadol affects the persons daily life	4.29	0.891	85.80	14.479	0.000

6	Do you Believe that the widespread misuse tramadol is an impact of the siege.	4.48	0.979	89.60	15.112	0.000
7	Do you Believe that taking tramadol, affects the sexual life.	4.41	0.911	88.20	15.475	0.000
8	Were you aware of this drug doses when you take it .	4.25	0.999	85.00	12.516	0.000
9	Do you Believe that the misuse of tramadol causes addiction.	4.72	0.668	94.40	25.753	0.000
10	Did your work was affected due to using tramadol negatively .	3.13	1.643	62.60	0.791	0.431
11	Did your work was affected due to using tramadol positively .	3.30	1.685	66.00	1.781	0.078
12	Do you Believe that the misusing tramadol is religiously for bidden.	3.12	1.731	62.40	0.693	0.490
13	Do you Believe that the smoking is religiously for bidden.	3.69	1.316	73.80	5.244	0.000
	All items	4.09	0.413	81.86	26.482	0.000

Critical value of **t** at df "99" and significance level 0.05 equal 1.98

4.2.3 Section three : Practices of tramadol abusers

We use a one sample t test to test if the opinion of the respondent about Practices of tramadol abusers and the results shown in Table No. (19) as follows:

The three highest statements according to weight mean as follows:

1. In item No. (3) the weight mean equal " 94.80%" and p-value equal " 0.000" which is less than 0.05, that means (the sample get tramadol from friends) this result can be confirm that the get of tramadol is easily accessible to everyone.
2. In item No. (12) the weight mean equal " 92.60%" and p-value equal " 0.000" which is less than 0.05, that means (the sample use tramadol to reach the state of euphoria) this result can be explained that tramadol has an effect on CNS Produces a state of euphoria and this consistent with study of(Liu ZM;1999) that confirm that abuse of tramadol produce euphoria .
3. In item No. (11) the weight mean equal " 92.40%" and p-value equal " 0.000" which is less than 0.05, that means (the sample increase taking the number of pills

from time to time) this result can be explained that tramadol cause drug tolerance , Which is evident by the increase the number of pills from time to time to get the same result of the first dose .

Also the results show that the weight mean of item No(6) equal "79.40" that mean the tramadol help the sample to in delaying ejaculation , this mean that tramadol has an effect of delaying ejaculation , and this result consistent with the study of (Kaynar M *et al* ;2012) that confirm the On-demand use of low-dose tramadol is effective for lifelong PE , (Xiong GG *et al* ;2011) that confirm the Tramadol hydrochloride with behavioral modification showed positive effects in prolonging and improving partners' intercourse satisfaction , (Bar-Or D *et al*;2011) that confirm the On-demand 62mg tramadol ODT is an effective treatment for PE in a low and safe therapeutic dose and provides anew option for managing mild to severe PE .

In item No (20) the weight mean equal "79.20" mean that sample is smoke cigarettes , this explain the close association between smoking and abuse of tramadol , were the smoking is kind of addiction .

In item No"15" the weight mean equal "63.40" has illegal action to get tramadol , the researcher observe that the main illegal action is stealing .

And the three lowest statements according to weight mean as follows

1. In item No. (17) the weight mean equal " 51.60%" and p-value equal "0.008 " which is less than 0.05, that means (tramadol not help in your study).
2. In item No. (24) the weight mean equal " 45.20%" and p-value equal "0.000 " which is less than 0.05, that means (not abuse another drug with tramadol).
3. In item No.(23) the weight mean equal " 33.00%" and p-value equal " 0.000" which is less than 0.05, that means (the sample not take alcoholic drinks) this result can be explained that the Palestinian community is Conservative society ,and muslim community and the Islamic religion prohibits drinking alcohol.

For general the results for all items of the field show that the average mean equal 3.65 and the weight mean equal 72.98% which is greater than " 60%" and the value of t test equal 11.938 which is greater than the critical value which is equal 1.98 and the p- value equal 0.000 which is less than 0.05, that means that the samples used tramadol misusers with wrong Practices at significant level $\alpha = 0.05$

Table No.(19)
Practices of tramadol abusers

No.	Sentence	Mean	standard deviation	Weight mean	t-value	P-value
1	Can you get tramadol from pharmacies easily .	2.91	1.342	58.20	-0.671	0.504
2	Can you get tramadol from drug dealers .	4.41	1.055	88.20	13.365	0.000
3	Can you get tramadol from friends .	4.74	0.525	94.80	33.171	0.000
4	Can you get tramadol from those who work in the tunnels .	3.64	1.360	72.80	4.707	0.000
5	Did you use tramadol to treat premature ejaculation .	3.42	1.485	68.40	2.828	0.006
6	Did tramadol help you to delay ejaculation.	3.97	1.306	79.40	7.426	0.000
7	Did tramadol help you to take your time in delaying ejaculation.	3.71	1.320	74.20	5.377	0.000
8	Did you use tramadol while you did not suffer from premature ejaculation.	2.63	1.426	52.60	-2.595	0.011
9	Did you use tramadol in order to stay late .	4.07	1.112	81.40	9.619	0.000
10	Did you start taking pills of 100mg.	4.31	1.032	86.20	12.697	0.000
11	Did you increase taking the number of pills from time to time .	4.62	0.749	92.40	21.625	0.000
12	Did you use tramadol to reach the state of euphoria .	4.63	0.906	92.60	17.986	0.000
13	Did you use tramadol to help you in your work .	3.72	1.356	74.40	5.308	0.000
14	Did you take tramadol at the same time of the last dose.	4.17	1.111	83.40	10.535	0.000
15	Did you do any illegal action to get tramadol .	3.17	1.484	63.40	1.145	0.255
16	Did the effect of tramadol was affected with the amount and the number of pills	4.58	0.806	91.60	19.596	0.000
17	Did you use tramadol to help in your study.	2.58	1.552	51.60	-2.707	0.008

18	Did you use tramadol to help you in increasing your physical efforts in parties .	3.92	1.323	78.40	6.952	0.000
19	Did you take tramadol during pregnancy.	2.94	0.722	58.80	-0.831	0.408
20	Are you smoking .	3.96	1.435	79.20	6.690	0.000
21	Are you a heavy smoker .	3.66	1.565	73.20	4.218	0.000
22	Did the use of tramadol affect in increasing the number of cigarettes and change the euphoria of smoking.	3.91	1.615	78.20	5.635	0.000
23	Do you take alcoholic drinks	1.65	1.209	33.00	-11.165	0.000
24	Did you abuse another drug with tramadol.	2.26	1.411	45.20	-5.243	0.000
	All items	3.65	0.544	72.98	11.938	0.000

Critical value of **t** at df "99" and significance level 0.05 equal 1.98

4.2.4 Section four : Attitudes of tramadol abusers

We use a one sample t test to test if the opinion of the respondent about Attitudes of tramadol misusers and the results shown in Table No. (20) as follows:

The three highest statements according to weight mean as follows:

1. In item No. (18) the weight mean equal " 89.00%" and p-value equal " 0.000" which is less than 0.05, that means (the reasons behind stopping the use of tramadol healthy) this result can be explained that abusers complain of medical problem as related to abuse a high amount of tramadol , and this result consistent with study of (Shadnia S, et al 2008) that explain the common effect of tramadol intoxication .
2. In item No. (2) the weight mean equal " 87.60%" and p-value equal " 0.000" which is less than 0.05, that means (the sample support programs of mass media to stop the spared of this phenomena).
3. In item No. (11) the weight mean equal " 85.40%" and p-value equal " 0.000" which is less than 0.05, that means (the sample engaged in a treatment program).

And the three lowest statements according to weight mean as follows

1. In item No. (9) the weight mean equal " 69.60%" and p-value equal " 0.001" which is less than 0.05, that means (the sample exposed to confrontation or embarrassments due to taking tramadol).
2. In item No. (5) the weight mean equal " 67.20%" and p-value equal "0.020 " which is less than 0.05, that means (the sample feels of the stigma because of taking tramadol).
3. In item No.(4) the weight mean equal " 65.40%" and p-value equal "0.070 "
4. which is greater than 0.05, that means (the sample try moderately stop using tramadol due to the hardness of getting it).

For general the results for all items of the field show that the average mean equal 3.87 **and the weight mean equal** 77.47**% which is greater than " 60%" and the value of t test equal** 12.568 **which is greater than the critical value which is equal 1.98 and the p- value equal 0.000 which is less than 0.05, that means reasons behind stopping the use of tramadol, social , economic, and healthy at significant level** $\alpha = 0.05$

Table No.(20)

Attitudes of tramadol abusers

No.	Sentence	Mean	standard deviation	Weight mean	t-value	P-value
1	Do you Support the measures of concerned people to stop the spread of this phenomenon.	4.11	1.442	82.20	7.699	0.000
2	Do you support programs of mass media to stop the spared of this phenomena.	4.38	1.187	87.60	11.623	0.000
3	Did you try to stop the using tramadol due to some circumstances.	3.90	1.210	78.00	7.437	0.000
4	Did you try stop using tramadol due to the hardness of getting it.	3.27	1.476	65.40	1.829	0.070
5	Did you feel of the stigma because of taking tramadol .	3.36	1.528	67.20	2.357	0.020

6	Was there any one who expected that you were taking tramadol .	3.51	1.219	70.20	4.185	0.000
7	Did anyone around you suffer from your taking tramadol .	3.68	1.302	73.60	5.224	0.000
8	Did you neglect your family because of using tramadol .	3.53	1.494	70.60	3.548	0.001
9	Were you exposed to confrontation or embarrassments due to taking tramadol .	3.48	1.337	69.60	3.590	0.001
10	Did you Try to stop on your own.	4.15	0.978	83.00	11.755	0.000
11	Were you engaged in a treatment program.	4.27	1.033	85.40	12.290	0.000
12	Were you Committed to the instructions of the treatment program.	4.13	1.152	82.60	9.812	0.000
13	Were you able to get rid of the using tramadol for more than a month.	4.09	1.303	81.80	8.363	0.000
14	Were you able to stop taking tramadol.	3.77	1.448	75.40	5.316	0.000
15	Are the reasons behind stopping the use of tramadol, religious.	3.49	1.630	69.80	3.006	0.003
16	Are the reasons behind stopping the use of tramadol social .	4.04	1.406	80.80	7.394	0.000
17	Are the reasons behind stopping the use of tramadol economic .	4.11	1.348	82.20	8.237	0.000
18	Are the reasons behind stopping the use of tramadol healthy .	4.45	1.104	89.00	13.129	0.000
	All sentences	3.87	0.695	77.47	12.568	0.000

Critical value of t at df "99" and significance level 0.05 equal 1.98

4.2.5 Section five : The psychological state of the abusers of tramadol

We use a one sample t test to test if the opinion of the respondent about **The psychological state of the abusers of tramadol** and the results shown in Table No. (21) according to weight mean from highest to lowest as follows:

1. In item No. (1) the weight mean equal " 82.80%" and p-value equal " 0.000" which is less than 0.05, that means (the sample takes this drug while you were suffering from psychological stress).
2. In item No. (2) the weight mean equal " 80.60%" and p-value equal " 0.000" which is less than 0.05, that means (the sample suffering from anxiety).
3. In item No. (4) the weight mean equal " 78.40%" and p-value equal " 0.000" which is less than 0.05, that means (the sample deals with tramadol to escape from reality).
4. In item No. (5) the weight mean equal " 77.20%" and p-value equal " 0.000" which is less than 0.05, that means (the sample use tramadol to avoid social problems).
5. In item No. (3) the weight mean equal " 62.20%" and p-value equal " 0.441" which is greater than 0.05, that means (the sample suffering moderately from a sleep disorder).

For general the results for all items of the field show that the average mean equal 3.81 and the weight mean equal 76.24% which is greater than " 60%" and the value of t test equal 7.972 which is greater than the critical value which is equal 1.98 and the p- value equal 0.000 which is less than 0.05, that means The psychological state of the misusers of tramadol unstable at significant level $\alpha = 0.05$, and this can be explained that unstable psychological state for persons may increase the risk of substance abuse .

Table No.(21)

The psychological state of the abusers of tramadol

No.	Sentence	Mean	standard deviation	Weight mean	t-value	P-value
1	Did you take this drug while you were suffering from psychological stress.	4.14	1.271	82.80	8.966	0.000
2	Were you suffering from anxiety.	4.03	1.275	80.60	8.079	0.000
3	Were you suffering from a sleep disorder.	3.11	1.421	62.20	0.774	0.441

4	Did you deal with tramadol to escape from reality .	3.92	1.323	78.40	6.952	0.000
5	Did you use tramadol to avoid social problems .	3.86	1.271	77.20	6.764	0.000
	All items	3.81	1.019	76.24	7.972	0.000

Critical value of **t** at df "99" and significance level 0.05 equal 1.98

4.2.6 Section sixth : The presence of side effects of the abuse of tramadol.

We use a one sample t test to test if the opinion of the respondent about **The presence of side effects of the misuse of tramadol** and the results shown in Table No. (22) as follows:

The three highest statements according to weight mean as follows:

1. In item No. (7) the weight mean equal " 90.00%" and p-value equal " 0.000" which is less than 0.05, that means (the sample have physical symptoms when you stop using tramadol), this result can explained that tramadol cause addiction , and the interruptions cause the presence of withdrawal symptoms ,and this result consistent with study of (Senay EC et al;2003) that confirm the tramadol has withdrawal symptom like opiates. In most cases, the withdrawal symptoms consisted of classical opioid withdrawal, but in some cases were accompanied by withdrawal symptoms not normally observed in opiate withdrawal, such as hallucinations, paranoia, extreme anxiety, panic attacks, confusion and unusual sensory experiences such as numbness and tingling in one or more extremities.
2. In item No. (3) the weight mean equal 85.60" %" and p-value equal " 0.000" which is less than 0.05, that means (the sample Suffer from itching feeling in the feet or electrical waves during the misusing tramadol).
3. In item No. (1) the weight mean equal " 85.40%" and p-value equal " 0.000" which is less than 0.05, that means (the sample suffered from gastrointestinal disorders that caused by abuse of tramadol) this can be explained that intoxication of tramadol affect many centers on the brain , this result consistent with study of(Shadnia S et al 2008) that confirm the Tramadol overdose has been one of the most frequent causes of drug poisoning in his country in the recent years, especially in male young adults with history of substance abuse and mental disorders. Nausea, vomiting, Central Nervous System (CNS) depression, tachycardia, and seizure are the most common findings in this kind of poisoning. Cardiopulmonary arrest was

found as the cause of death in cases who had ingested more than 5000 mg tramadol.

And the three lowest statements according to weight mean as follows

1. In item No. (2) the weight mean equal " 71.80%" and p-value equal " 0.000" which is less than 0.05, that means (the sample suffer from convulsions or coma that caused by the misuse of tramadol) this result can be explained that tramadol has an effect on CNS and abuse it may cause epileptic fits , and this attributed to ingestion of large amount of tramadol , this result consistent with study of (Jovanović-Cupić V et al ;2006) which confirm that The neurotoxicity of tramadol commonly manifests as generalized tonic-clonic seizures occurring most frequently within 24 h after tramadol intake. Seizures were more common in younger abusers with a longer duration of exposure to tramadol and with the combined use of tramadol , also study of(Talaie H et al ;2009) which confirm that incidence of seizures not depend on dose dependent , also(Tobias JD ;1997) report the occurrence of seizure activity after the inadvertent administration of 4 mg/kg of tramadol to a child. Previous reports of seizure activity after tramadol administration .
2. In item No. (4) the weight mean equal " 67.00%" and p-value equal " 0.018" which is less than 0.05, that means (the sample Suffer from a rise in body temperature during the abuse of tramadol).
3. In item No.(8) the weight mean equal " 60.60%" and p-value equal 0.834" " which is greater than 0.05, that means (the sample have high blood pressure when you stop using tramadol moderately).

For general the results for all items of the field show that the average mean equal 3.84 **and the weight mean equal** 76.80**% which is greater than " 60%" and the value of t test equal** 12.276**which is greater than the critical value which is equal 1.98 and the p- value equal 0.000 which is less than 0.05, that means there are side of effects of the abuse of tramadol at significant level** $\alpha = 0.05$

Table No.(22)
The presence of side effects of the abuse of tramadol

No.	Sentence	Mean	standard deviation	Weight mean	t-value	P-value
1	Did you suffered from gastrointestinal disorders that caused by abuse of tramadol .	4.27	1.004	85.40	12.655	0.000

2	Did you suffer from convulsions or coma that caused by the abuse of tramadol .	3.59	1.609	71.80	3.668	0.000
3	Did you Suffer from itching feeling in the feet or electrical waves during the abusing tramadol.	4.28	1.138	85.60	11.250	0.000
4	Did you Suffer from a rise in body temperature during the abuse of tramadol .	3.35	1.452	67.00	2.410	0.018
5	Did you Suffer from tremor when you did not use tramadol .	3.84	1.339	76.80	6.274	0.000
6	Did you feel dizzy while you were taking tramadol .	3.84	1.277	76.80	6.578	0.000
7	Did you have physical symptoms when you stop using tramadol.	4.50	0.937	90.00	16.001	0.000
8	Did you have high blood pressure when you stop using tramadol .	3.03	1.425	60.60	0.211	0.834
9	Did you have excessive sweating when you stop using tramadol.	3.86	1.206	77.20	7.130	0.000
	All items	3.84	0.684	76.80	12.276	0.000

Critical value of **t** at df "99" and significance level 0.05 equal 1.98

All the items

We use a one sample **t** test to test the opinion of the respondent about the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of **knowledge, attitude, and practice and the results shown in Table No. (23) which show that the average mean for all dimensions equal 3.83 and the weight mean equal 76.56% which is higher than " 60%" and the absolute value of t test equal 24.291which is greater than the critical value which is equal 1.98 and the p-value equal 0.000 which is less than 0.05, that mean the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice this means that the sample had good knowledge about tramadol ,were the sample aware that tramadol is an analgesic medication .Also the sample had used tramadol in bad practice ,were the statistical result show that the sample were abused tramadol for un therapeutic way .Also the sample had attitude to stop abused tramadol and the main reason for this is healthy , and socially aspects .**

Table(23)
All the items symptom dimensions

No.	symptom dimensions	Mean	standard deviation	Weight mean	t-value	P-value
1	Knowledge of tramadol abusers	4.09	0.413	81.86	26.482	0.000
2	Practices of tramadol abuse	3.65	0.544	72.98	11.938	0.000
3	Attitudes of tramadol abuse	3.87	0.695	77.47	12.568	0.000
4	The psychological state of the abusers of tramadol	3.81	1.019	76.24	7.972	0.000
5	The presence of side effects of the abuse of tramadol.	3.84	0.684	76.80	12.276	0.000
	All sections	3.83	0.341	76.56	24.291	0.000

Critical value of **t** at df "99" and significance level 0.05 equal 1.98

Q1. Is there a significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding in (assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to demographic data (sex, Age, Address, Marital Status, Number of family members who live with you in the same house, Monthly income of NIS , Scientific level, Profession).

And this question divided into sub questions as follows:

1.1 **Is there a significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding in (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to sex.**

To test the question we use the Independent Samples Test and the result illustrated in table no.(24) which shows the following results: the p-value equal 0.569 which is greater than 0.05 and the absolute value of T test equal 0.572 which is less than the value of critical value which is equal 1.98, that's means there is no significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding in (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to sex . This attribute that problem is very dangerous and affect all society members .

Table No.(24)
Independent Samples Test for difference among the respondents' answers regarding the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice due to sex

Research problem	sex	N	Mean	Std. Deviation	T	P-value
the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice	Male	86	3.836	0.346	0.572	0.569
	female	14	3.780	0.315		

Critical value of **t** at df "98" and significance level 0.05 equal 1.98

1.2-Is there a significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding (assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Age.

To test the question we use the one way ANOVA test and the result illustrated in table no.(25) which shows the following results: the p-value equal 0.744 which is greater than 0.05 and the value of **F** test equal 0.297 which is less than the value of critical value which is equal 3.09 , that's means There is no significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding (assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Age. This attribute that the abusers from young people .

Table No.(25)
One way ANOVA test for difference among the respondents' answers regarding among the (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Age

Research problem	Source	Sum of Squares	df	Mean Square	F value	Sig.(P-Value)
the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice	Between Groups	0.070	2	0.035	0.297	0.744
	Within Groups	11.432	97	0.118		
	Total	11.502	99			

Critical value of F at df "2,97" and significance level 0.05 equal **3.09**

1.3-Is there a significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding in (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Address.

To test the question we use the one way ANOVA test and the result illustrated in table no.(26) which shows the following results: the p-value equal 0.309 which is greater

than 0.05 and the value of **F** test equal 1.215 which is less than the value of critical value which is equal 2.47 , that's means There is no significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Address . This attribute that the problem is speared on all Gaza strip governorates

Table No.(26)

One way ANOVA test for difference among the respondents' answers regarding among the (assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Address

Research problem	Source	Sum of Squares	df	Mean Square	F value	Sig.(P-Value)
the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice	Between Groups	0.560	4	0.140	1.215	0.309
	Within Groups	10.942	95	0.115		
	Total	11.502	99			

Critical value of F at df "4,95" and significance level 0.05 equal **2.47**

1.4-Is there a significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding in (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Marital Status.

To test the question we use the one way ANOVA test and the result illustrated in table no.(27) which shows the following results: the p-value equal 0.632 which is greater than 0.05 and the value of F test equal 0.461 which is less than the value of critical value which is equal 3.09 , that's means There is no significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Marital Status

Table No.(27)

One way ANOVA test for difference among the respondents' answers regarding among the (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Marital Status.

Research problem	Source	Sum of Squares	df	Mean Square	F value	Sig.(P-Value)
the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice	Between Groups	0.108	2	0.054	0.461	0.632
	Within Groups	11.394	97	0.117		
	Total	11.502	99			

Critical value of F at df "2,97" and significance level 0.05 equal **3.09**

1.5-Is there a significant difference at α ≤ 0.05 among the respondents' answers regarding in (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Number of family members who live with you in the same house.

To test the question we use the one way ANOVA test and the result illustrated in table no.(28) which shows the following results: the p-value equal 06.03 which is greater than 0.05 and the value of **F** test equal 0.508 which is less than the value of critical value which is equal 3.09 , that's means There is no significant difference at α ≤ 0.05 among the respondents' answers regarding (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to **Number of family members who live with you in the same house.**

Table No.(28)

One way ANOVA test for difference among the respondents' answers regarding among the (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Number of family members who live with you in the same house.

Research problem	Source	Sum of Squares	df	Mean Square	F value	Sig.(P-Value)
the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice	Between Groups	0.119	2	0.060	0.508	0.603
	Within Groups	11.383	97	0.117		
	Total	11.502	99			

Critical value of F at df "2,97" and significance level 0.05 equal **3.09**

1.6-Is there a significant difference at α ≤ 0.05 among the respondents' answers regarding in (assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Monthly income of NIS.

To test the question we use the one way ANOVA test and the result illustrated in table no.(29) which shows the following results: the p-value equal 0.401which is greater than 0.05 and the value of F test equal 0.990 which is less than the value of critical value which is equal 2.70 , that's means There is no significant difference at α ≤ 0.05 among the respondents' answers regarding (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Monthly income of NIS

Table No.(29)

One way ANOVA test for difference among the respondents' answers regarding among the (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Monthly income of NIS

Research problem	Source	Sum of Squares	df	Mean Square	F value	Sig.(P-Value)
the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice	Between Groups	0.345	3	0.115	0.990	0.401
	Within Groups	11.157	96	0.116		
	Total	11.502	99			

Critical value of F at df "3,96" and significance level 0.05 equal **2.70**

1.7-Is there a significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding in (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Scientific level.

To test the question we use the one way ANOVA test and the result illustrated in table no.(30) which shows the following results: the p-value equal 0.088 which is greater than 0.05 and the value of F test equal 2.246 which is less than the value of critical value which is equal 2.70 , that's means There is no significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Scientific level.

Table No.(30)

One way ANOVA test for difference among the respondents' answers regarding among the (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Scientific level

Research problem	Source	Sum of Squares	df	Mean Square	F value	Sig.(P-Value)
the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice	Between Groups	0.754	3	0.251	2.246	0.088
	Within Groups	10.748	96	0.112		
	Total	11.502	99			

Critical value of F at df "3,96" and significance level 0.05 equal **2.70**

1.8-Is there a significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding in (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Profession.

To test the question we use the one way ANOVA test and the result illustrated in table no.(31) which shows the following results: the p-value equal 0.014 which is greater than 0.05 and the value of F test equal 3.305 which is less than the value of critical value which is equal 2.47 , that's means There is a significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Profession, and Scheffe Multiple Comparisons test table no.(32) show that there in a difference between " Worker " , and " other Profession " , and the difference in favor of " Worker "

Table No.(31)
One way ANOVA test for difference among the respondents' answers regarding among the (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Profession

Research problem	Source	Sum of Squares	df	Mean Square	F value	Sig.(P-Value)
assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice	Between Groups	1.405	4	0.351	3.305	0.014
	Within Groups	10.097	95	0.106		
	Total	11.502	99			

Critical value of F at df "4,95" and significance level 0.05 equal 2.47

Table No.(32)
Scheffe Multiple Comparisons test

Mean Difference	**Profession**				
	Employee	Worker	Student	Unemployed	Others
Employee		-0.278	-0.111	-0.069	0.161
Worker	0.278		0.167	0.209	0.439*
Student	0.111	-0.167		0.042	0.272
Unemployed	0.069	-0.209	-0.042		0.230
Others	-0.161	-0.439*	-0.272	-0.230	

* The mean difference is significant at the .05 level

4.3 Daily Dose of tramadol

Table No(33) explain the daily average dose of tramadol ,which abused by the study sample , it is different between person to person , the below table identify the mean of daily dose of tramadol which is 8 tablets from 225 mg .

Table No.(33)

"No" of Persons	"No" of tablet that abused daily	"No" of tablet according to persons
2	5	10
3	3	9
4	12	48
6	4	24
7	13	91
9	8	72
13	9	117
15	6	90
19	7	133
22	10	220

Chapter five

Conclusion and Recommendations

Chapter (Five): Conclusion and Recommendation

5.1Conclusion

This study aims to assess the tramadol abuse among clients who are attending private psychiatric clinics in Gaza city by assessing the level of knowledge , attitude , and practice of abusers. It was descriptive, analytical and cross sectional study. Two private clinics were selected for the study . The target population of this study is all clients who are treated as tramadol abusers. The study excludes clients who are treated for other psychiatric disorders .The sample of this study was 100 clients were selected by taking 4 clients from two clinics every day during one month . The response rate was 83%.The study tool was a self-administer questionnaire which has six categories (knowledge , attitude , practice , psychological state , and the presence of side effects related to abuse of tramadol) .

Male were more dominant in the study , the researcher attributed this dominance to the fact that women in Palestinian society are afraid of the stigma, especially knowing that the community is considered a conservative community. 42% of the sample were less than twenty five years old. These results come with the fact that the percentage of young people in Palestinian society is high, according to the Palestinian Center for Statistic. 57% of the sample were married, this can be explained by the finding that tramadol has an effect of prolong the time of sexual intercourse. 51% of the sample were has low monthly income the researcher attributed that to the bad economic status in Gaza strip people . 36% of respondents hold a Bachelor degree which might be attributed to the low level of stigma associated with tramadol abuse compared to other substances such as cannabises and alcohol in Gaza Strip. Additionally tramadol abuse might provide a window for educated youth to escape from tough reality.

5.1.1Knowledge

96.40% of the sample believe that the abuse of tramadol, is a problem in the Gaza Strip

94.8 % of the sample known that tramadol is medical drug use for analgesia .

94.40% of the sample believe that abusing of tramadol cause addiction ,researcher attributed that the using of tramadol not for treatment but to at chive other goals.

66% of the sample believe that work was affected due to using tramadol positively moderately.62.60% of the sample believe that work was affected due to using tramadol

negatively moderately . Researcher attributed that difference of doses between abusers. 62.40% of the sample Believe that the abusing of tramadol is not religiously forbidden moderately , this attributed there is no religious guidance about tramadol .

In general the results for all items of the field show that the average mean equal 4.09 and the weight mean equal 81.86 % which is greater than " 60%" and the value of t test equal 26.482 which is greater than the critical value which is equal 1.98 and the p-value equal 0.000 which is less than 0.05, that means the sample Believe that taking tramadol, affects the sexual life and the misusing tramadol is not religiously forbidden at significant level $\alpha = 0.05$.

5.1.2Practices

The result show that 94.80% of the sample get tramadol from friends , 92.60% of the sample use tramadol to reach the state of euphoria ,92.4% and to help them to delay ejaculation . 92.40% of the sample increase taking the number of pills from time to time this approve that abuse of tramadol cause addiction . Our study showed a strong association between smoking and tramadol abuse as around 80% of our sample was smokers.

In general the results for all items of the field show that the average mean equal 3.65 and the weight mean equal 72.98% which is greater than " 60%" and the value of t test equal 11.938 which is greater than the critical value which is equal 1.98 and the p-value equal 0.000 which is less than 0.05, that means that the samples abused tramadol with wrong Practices at a significant level $\alpha = 0.05$.

5.1.3Attitude

The result show that 89.00% of the sample reasons behind stopping the use of tramadol healthy ,researcher attributed that for high doses of tramadol ,and taken tramadol for non-medical cause . 87.60% of the sample support programs of mass media to stop the spared of this phenomena ,this attributed that may few media programs have constructed to explore the dangerous result of abuse tramadol The abuser haven't felt any embarrassment or stigma about abusing tramadol, this attributed the fast of speared of this problem .

5.1.4 Psychological state

The most of sample have psychological stress ,anxiety , sleeping disorder , and abused tramadol to escape from there reality , this attributed that Israel occupation and siege and speared of unemployment have the main effect of abusing tramadol .

5.1.5 Presence of side effects

Tramadol has side effect, most of the sample have complained about side effect , and it has varied between person to person and it depend on the volume of the dose .The more side effect is convulsion this attributed that the abuser has toxic dose, also the abuser has another side effect such as gastrointestinal disturbance ,irritability , physical symptom especially when the abuser stop taking tramadol .

There is no significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding in (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to sex. There is no significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Age. There is no significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Address. There is no significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Marital Status. There is no significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Number of family members who live with you in the same house. There is no significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Monthly income of NIS. There is no significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and

practice) due to Scientific level. There is a significant difference at $\alpha \leq 0.05$ among the respondents' answers regarding (the assess the abuse of tramadol among persons who have tramadol abuse by examine the level of knowledge, attitude, and practice) due to Profession, and Scheffe Multiple Comparisons test show that there in a difference between " Worker " , and " other Profession " , and the difference in favor of " Worker ".

5.2 Recommendations

1-Decision makers should tighten controls on tunnels.

2- All authorities including political, social, academic and religious authorities should be engaged to know the reasons for the spread of this phenomenon.

3- Legal bodies should enforce strict laws against drug dealers .

4- Encourage media programs across various media, to educate people about the dangers of abuse of Tramadol.

5-Organizing awareness campaigns against tramadol abuse at schools and universities

6- Only licensed pharmaceutical companies should be allowed for importing narcotic drugs.

7- Development of well-trained psychiatric clinics to deal with addicted people .

8- Publication of books, brochures, flyers that address the problem of addiction.

9- Dissemination of legal awareness and clear warning against tramadol use and marketing

10- Dissemination of religious consciousness, and religious culture, and the consolidation of the social and educational values to the members of the community.

5.3 Recommendations for Further Research

- Further Studies to chemically analyze the substance of tramadol that enter through the tunnels .

- Further Studies for the work of rehabilitation programs for addicts.

- Further Studies to know the prevalence of addiction in Palestine .

- More objective studies to show the impact of tramadol abuse on personal health .

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Annexes

Annex 1

بسم الله الرحمن الرحيم

الجامعة الإسلامية – غزة
The Islamic University - Gaza

كلية التمريض
Faculty of Nursing
هاتف داخلي: 2700

الرقم Ref .....

التاريخ Date 08 صفر 1433هـ
03 يناير 2012م

الأخ الدكتور/ محمد أبو السبح حفظه الله،،،

السلام عليكم ورحمة الله وبركاته،

الموضوع: تسهيل مهمة بحثية لباحث ماجستير

نرجو التكرم بتسهيل مهمة **الباحث/ محمد رفيق حسن طافش** برقم جامعي 120093469 حيث أنه مسجل لدرجة الماجستير في قسم تمريض الصحة النفسية المجتمعية، وهو أحد موظفي وزارة الصحة الفلسطينية، ويحتاج لبعض الإحصاءات والمعلومات، لذا نرجو مساعدته حسب ما تسمح به اللوائح والأنظمة المعمول بها.

وبارك الله فيك،،،

رئيس المجلس الأكاديمي
لبرنامج ماجستير الصحة النفسية المجتمعية
د. يوسف الجيش

د. محمد أحمد أبو السبح
Dr. Mohamed Abusalbah
Lic.6365 Psychiatrist

صورة لـ/الملف.

P.O. Box 108, Rimal, Gaza, Palestine fax: +970 (8) 286 0800 فاكس Tel: +970 (8) 286 0700 هاتف ص.ب. 108 الرمال. غزة. فلسطين
public@iugaza.edu.ps www.iugaza.edu.ps

Annex 2

بسم الله الرحمن الرحيم

الجامعة الإسلامية – غزة
The Islamic University - Gaza

كلية التمريض
Faculty of Nursing
هاتف داخلي: 2700

الرقم Ref .....

التاريخ 08 صفر 1433هـ Date .....
03 يناير 2012م

الأخ الدكتور/ عايش سمور حفظه الله،،،
مدير عام الصحة النفسية بوزارة الصحة
السلام عليكم ورحمة الله وبركاته،

الموضوع: تسهيل مهمة بحثية لباحث ماجستير

نرجو التكرم بتسهيل مهمة الباحث/ **محمد رفيق حسن طافش** برقم جامعي 120093469 حيث أنه مسجل لدرجة الماجستير في قسم تمريض الصحة النفسية المجتمعية، وهو أحد موظفي وزارة الصحة الفلسطينية، ويحتاج لبعض الإحصاءات والمعلومات، لذا نرجو مساعدته حسب ما تسمح به اللوائح والأنظمة المعمول بها.

وبارك الله فيك،،،

رئيس المجلس الأكاديمي
لبرنامج ماجستير الصحة النفسية المجتمعية
د. يوسف الجيش

صورة لـ/الملف.

P.O. Box 108, Rimal, Gaza, Palestine fax: +970 (8) 286 0800 فاكس Tel: +970 (8) 286 0700 ص.ب. 108 الرمال، غزة، فلسطين هاتف
public@iugaza.edu.ps www.iugaza.edu.ps

Annex 3

Questionnaire

" **Assessment of tramadol abuse among clients who are attending private psychiatric clinics-KAP study.**

Brothers and sisters who are participating in the study.

This study carried out by the researcher as a requirement for a master's degree in community mental health - the Islamic University.

Researcher thanks for your participation in this study by answering the questionnaire, which does not take more than 20 minutes of your valuable time and your participation contribute to the success of the study aimed to identify the knowledge, attitudes and practices of people who are misused and abuse tramadol.

Researcher would like to emphasize that the information will remain confidential and for the purpose of scientific research that does not need to mention names.
Note that the right to refrain from participating answer any question or refused to participate.

Thank you for participating.

Researcher
Mohammed Rafiq Tafesh
0598-910907

بسم الله الرحمن الرحيم

Questionnaire NO ☐ Date: / /

personal data

Please tick × in the appropriate box for you

1-Age……

2-Sex : male ☐ female ☐

3- Address :

North governorate ☐ Gaza governorate ☐

Middle governorate ☐ Khan yunis governorate ☐

Rafah governorate ☐

4- Marital Status:

Single ☐ Married ☐ Widowed ☐ Divorce ☐

5- Number of family members who live with you in the same house :…….

6- Monthly income of NIS:

Less than 1000 NIS ☐ NIS 1000-2000 ☐

NIS 2100-3000 ☐ 3100 and above ☐

7- Scientific level:

Less than High School ☐ High School ☐

Diploma of two years ☐ Bachelor ☐ up Graduate ☐

8- Profession :

Employee ☐ Worker ☐ Student ☐ Unemployed ☐

Others ……..

Knowledge of tramadol abusers

N.O	Sentence	strongly agree	agree	Hesitant	disagree	Strongly disagree
9	DO you Know tramadol.					
10	Do you Believe that the using of tramadol, is a problem in the Gaza Strip					
11	Do you Believe that there is a certain group misuses tramadol.					
12	Do you Believe that, taking tramadol affects the persons daily life					
13	Do you Know that the tramadol is a pain reliever.					
14	Do you Believe that the widespread misuse tramadol is an impact of the siege.					
15	Do you Believe that taking tramadol, affects the sexual life.					
16	Were you aware of this drug doses when you take it .					
17	Do you Believe that the misuse of tramadol causes addiction.					
18	Did your work was affected due to using tramadol negatively .					
19	Did your work was affected due to using tramadol positively .					
20	Do you Believe that the misusing tramadol is religiously for bidden.					
21	Do you Believe that the smoking is religiously for bidden.					

Practices of tramadol abusers.

N.o	Sentence	Strongly agree	Agree	Hesitant	Disagree	Strongly disagree
22	Can you get tramadol from pharmacies easily .					
23	Can you get tramadol from drug dealers .					
24	Can you get tramadol from friends .					
25	Can you get tramadol from those who work in the tunnels .					
26	Did you use tramadol to treat premature ejaculation .					
27	Did tramadol help you to delay ejaculation.					
28	Did tramadol help you to take your time in delaying ejaculation.					
29	Did you use tramadol while you did not suffer from premature ejaculation.					
30	Did you use tramadol in order to stay late .					
31	Did you start taking pills of 100mg.					
32	Did you increase taking the number of pills from time to time .					
33	Did you use tramadol to reach the state of euphoria .					
34	Did you use tramadol to help you in your work .					
35	Did you take tramadol at the same time of the last dose.					

N.o	Sentence	Strongly agree	Agree	Hesitant	Disagree	Strongly disagree
36	Did you do any illegal action to get tramadol .					
37	Did the effect of tramadol was affected with the amount and the number of pills .					
38	Did you use tramadol to help in your study.					
39	Did you use tramadol to help you in increasing your physical efforts in parties .					
40	Did you take tramadol during pregnancy.					
41	Are you smoking .					
42	Are you a heavy smoker .					
43	Did the use of tramadol affect in increasing the number of cigarettes and change the euphoria of smoking.					
44	Do you take alcoholic drinks					
45	Did you misuse another drug with tramadol.					
Attitudes of tramadol abusers.						
46	Do you Support the measures of concerned people to stop the spread of this phenomenon.					
47	Do you support programs of mass media to stop the spared of this phenomena.					
48	Did you try to stop the using tramadol due to some circumstances.					

N.o	Sentence	Strongly agree	Agree	Hesitant	Disagree	Strongly disagree
49	Did you try stop using tramadol due to the hardness of getting it.					
50	Did you feel of the stigma because of taking tramadol .					
51	Was there any one who expected that you were taking tramadol .					
52	Did any one around you suffer from your taking tramadol .					
53	Did you neglect your family because of using tramadol .					
54	Were you exposed to confrontation or embarrassments due to taking tramadol .					
55	Did you Try to stop on your own.					
56	Were you engaged in a treatment program.					
57	Were you Committed to the instructions of the treatment program.					
58	Were you able to get rid of the using tramadol for more than a month.					
59	Were you able to stop taking tramadol.					
60	Are the reasons behind stopping the use of tramadol, religious.					
61	Are the reasons behind stopping the use of tramadol social .					
62	Are the reasons behind stopping the use of tramadol economic .					
63	Are the reasons behind stopping the use of tramadol healthy .					

The psychological state of the abusers of tramadol.

N.o	Sentence	Strongly agree	Agree	Hesitant	Disagree	Strongly disagree
64	Did you take this drug while you were suffering from psychological stress.					
65	Were you suffering from anxiety.					
66	Were you suffering from a sleep disorder.					
67	Did you deal with tramadol to escape from reality .					
68	Did you use tramadol to avoid social problems .					

The presence of side effects related to tramadol abuse.

69	Did you suffered from gastrointestinal disorders that caused by misuse of tramadol .					
70	Did you suffer from convulsions or coma that caused by the misuse of tramadol .					
71	Did you Suffer from itching feeling in the feet or electrical waves during the misusing tramadol.					
72	Did you Suffer from a rise in body temperature during the misuse of tramadol .					
73	Did you Suffer from tremor when you did not use tramadol .					
74	Did you feel dizzy while you were taking tramadol .					
75	Did you have physical symptoms when you stop using tramadol.					

76	Did you have high blood pressure when you stop using tramadol					
77	Did you have excessive sweating when you stop using tramadol.					

78- What is the daily dose that you rely on?

.....

.....

.....

79 - Have you experienced any symptoms during the use of tramadol, or when you stop taking it?

.....

.....

.....

Annex 4

بسم الله الرحمن الرحيم

استبيان

"معرفة وسلوك وممارسات الاشخاص الذين اساؤوا استخدام عقار الترامال"

الإخوة و الأخوات المشاركين في الدراسة.

هذه الدراسة يقوم بها الباحث كمتطلب للحصول على درجة الماجستير في الصحة النفسية المجتمعية –الجامعة الاسلامية .

يشكر الباحث لكم حسن المشاركة في هذه الدراسة من خلال الإجابة على أسئلة الاستبيان والتي لا تستغرق اكثر من ٢٠ دقيقة من وقتكم الثمين وان مشاركتكم تسهم في إنجاح الدراسة التي تهدف للتعرف على معرفة وسلوك وممارسات الاشخاص الذين اساؤوا استخدام وتعاطى عقار الترامال .

يود الباحث التأكيد على أن المعلومات ستبقى سرية و لهدف البحث العلمي لذلك لا داعي لذكر الأسماء.
علما بأنه من حق المشارك الامتناع عن إجابة أي سؤال أو رفض المشاركة.

شكرا لكم على المشاركة

الباحث
محمد رفيق حسن طافش
0598-910907

بسم الله الرحمن الرحيم

رقم الاستبيان ☐.....خاص بالباحث

البيانات الشخصية

من فضلك ضع/ى إشارة × في المربع المناسب لك/ى

١-العمر ----------سنة

٢-الجنس: ☐ ذكر ☐ أنثى

٣-العنوان

☐ محافظة الشمال ☐ محافظة غزة ☐ محافظة الوسطى

☐ محافظة خان يونس ☐ محافظة رفح

٤-الحالة الاجتماعية:

☐ أعزب/ آنسة ☐ متزوج/ ة

☐ أرمل/ ة ☐ مطلق/ ة

٥-عدد أفراد الأسرة الذين يقيمون معك في نفس السكن:----------.

٦-الدخل الشهري بالشيكل:

☐أقل من ١٠٠٠ شيكل ☐ ١٠٠٠-٢٠٠٠شيكل ☐ ٢١٠٠-٣٠٠٠

☐ ٣١٠٠ فأكثر

٧- المستوى العلمي:

☐ أقل من ثانوية عامة ☐ ثانوية عامة

☐ دبلوم سنتين بعد الثانوية العامة ☐ بكالوريوس ☐ دراسات عليا .

٨-المهنة:

☐ موظف ☐عامل ☐طالب ☐عاطل ، اخرى "حدد".....

معرفة مسيئ استخدام عقار الترامال.

الرقم	العبارة	موافق بشدة	موافق	متردد	غير موافق	غير موافق بشدة
٩	تعرف/ى عقار الترامال.					
١٠	تعتقد/ى أن تعاطي الترامال مشكلة في قطاع غزة.					
١١	تعتقد/ى أن هناك فئة معينة تتعاطى الترامال.					
١٢	تعتقد/ى أن تناول عقار الترامال يؤثر في مسار الشخص اليوم اليومي.					
١٣	تعرف/ى أن عقار الترامال هو عبارة عن مسكن للآلام.					
١٤	تعتقد/ى أن للحصار اثر في انتشار تعاطى هذا العقار.					
١٥	تعتقد/ى أن تناول الترامال يؤثر في الحياة الجنسية.					
١٦	كنت/ى على علم بجرعات هذا العقار عند تناولك له .					
١٧	تعتقد /ى أن تعاطي هذا العقار يسبب الإدمان.					
١٨	تأثر عملك/ى بسبب استخدامك الترامال بصورة سلبية .					
١٩	تأثر عملك/ى بسبب استخدامك للترامال بصورة ايجابية .					
٢٠	تعتقد/ى أن تعاطي الترامال حرام شرعا .					
٢١	تعتقد/ى ان التدخين حرام شرعا .					

ممارسات مسيئ استخدام الترامال .

الرقم	العبارة	موافق بشدة	موافق	متردد	غير موافق	غير موافق بشدة
٢٢	يتم الحصول على العقار من خلال الصيدليات .					
٢٣	الحصول على العقار من تجار المخدرات .					
٢٤	الحصول على العقار من الأصدقاء .					
٢٥	الحصول على العقار ممن يعمل في الأنفاق .					
٢٦	هل تناولت العقار من اجل علاج القذف المبكر .					

الرقم	العبارة	موافق بشدة	موافق	متردد	غير موافق	غير موافق بشدة
٢٧	هل ساعدك العقار في تأخير القذف .					
٢٨	هل ساعدك العقار في الحصول على المدة المطلوبة في تأخير القذف					
٢٩	تناولت العقار وأنت لا تعانى من القذف المبكر .					
٣٠	تناولت/ى هذا العقار من اجل السهر لمدة طويلة .					
٣١	بدأت/ى بتناول حبات من عيار ١٠٠ملجم .					
٣٢	قمت/ى بزيادة عدد الحبات بين الفترة والاخرى .					
٣٣	تناولت هذا العقار للحصول على حالة من النشوة والصهللة .					
٣٤	تناولت/ى هذا العقار من اجل مساعدتك في عملك .					
٣٥	كنت/ى تتناول العقار في نفس وقت آخر جرعة .					
٣٦	قمت/ى بأعمال غير قانونية للحصول على الترامال .					
٣٧	زيادة تأثير العقار كانت تتأثر بحجم الجرعة وعدد الحبات .					
٣٨	تناولت/ى الترامال من اجل مساعدتك في الدراسة .					
٣٩	تناولت/ى الترامال من اجل مساعدتك في الجهد البدني للحفلات .					
٤٠	تناولتى العقار أثناء فترة الحمل .					
٤١	هل انت/ى مدخن للسجائر .					
٤٢	تعتبر/ى مدخن بشكل كبير للسجائر .					
٤٣	اثر استخدامك/ى للعقار في زيادة عدد السجائر وتغير نشوة التدخين .					
٤٤	هل تتناول/ى المشروبات الكحولية .					
٤٥	أسأت/ى استخدام عقار مصاحب لعقار الترامال.					

توجهات مسيئ استخدام الترامال .

الرقم	العبارة	موافق بشدة	موافق	متردد	غير موافق	غير موافق بشدة
٤٦	تؤيد/ى إجراءات الجهات المعنية لوقف انتشار هذه الظاهرة.					

٤٧	تؤيد/ى وجود برامج إعلامية لوقف هذه الظاهرة.					
٤٨	حاولت/ى التوقف عن استخدام الترامال بسبب الظروف المحيطة.					
٤٩	حاولت/ى التوقف عن الترامال بسبب صعوبة الحصول علية .					
٥٠	هل شعرت/ى بالوصمة لتناول الترامال.					
٥١	توقع من حولك/ى تعاطيك للترامال .					
٥٢	عانى من حولك/ى لاستخدامك الترامال .					
٥٣	أهملت/ى عائلتك لاستخدامك للترامال.					
٥٤	تعرضت/ى لوجود مواجهات أو احراجات لاستخدامك للترامال.					
٥٥	حاولت/ى التوقف بمفردك .					
٥٦	انخرطت/ى في برنامج علاجي .					
٥٧	التزمت/ى بتعليمات البرنامج العلاجي .					
٥٨	استطعت/ى التخلص من تعاطي الترامال لمدة أكثر من شهر .					
٥٩	نجحت/ى في التوقف عن تعاطى العقار .					
٦٠	الأسباب التي دفعتك للتوقف عن استخدام الترامال **دينية** .					
٦١	الأسباب التي دفعتك للتوقف عن استخدام الترامال **اجتماعية** .					
٦٢	الأسباب التي دفعتك للتوقف عن استخدام الترامال **اقتصادية** .					
٦٣	الأسباب التي دفعتك للتوقف عن استخدام الترامال **صحية** .					

الحالة النفسية لمسيء استخدام عقار الترامال .

٦٤	عند تناولك/ى لهذا العقار كنت تعانى من ضغوط نفسية .					
٦٥	هل كنت/ى تعانى من القلق .					
٦٦	هل كنت/ى تعانى من اضطراب في النوم .					
٦٧	تناولت/ى عقار الترامال للهروب من واقعك .					
٦٨	تناولت/ى عقار الترامال لتفادى مشاكل اجتماعية .					

وجود أعراض جانبية لإساءة استخدام الترامال .

الرقم	العبارة	موافق بشدة	موافق	متردد	غير موافق	غير موافق بشدة
٦٩	عانيت/ى من اضطرابات معوية لتعاطيك الترامال .					
٧٠	عانيت/ى من تشنجات او اغماءات لتعاطيك الترامال .					
٧١	عانيت/ى من حكة في القدمين او شعور بماس كهربي لتعاطيك الترامال.					
٧٢	عانيت/ى من ارتفاع في درجة حرارة الجسم أثناء تعاطيك للترامال.					
٧٣	عانيت/ى من رجفة لعدم تناولك لعقار الترامال .					
٧٤	عانيت/ى من دوخة أثناء تناولك لعقار الترامال .					
٧٥	عند توقفك عن اخذ الترامال عانيت من أعراض جسمانية .					
٧٦	عند توقفك عن اخذ الترامال عانيت من ارتفاع في ضغط الدم .					
٧٧	عند توقفك عن اخذ الترامال عانيت من التعرق .					

٧٨-ما هي الجرعة اليومية التي كنت/ى تعتمد عليها ؟

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٧٩-هل واجهتك أي اعراض اثناء تعاطيك للترا مال او عند التوقف عن اخذها ؟

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Annex 5

Panel of expert

The questionnaire were examined by a group of experts. Some items were added, modified or excluded as a result of their comments .

1-Dr .Youssef ALjeesh .

2- Dr .Abed ALkareem Radwan .

3-Dr .Mohammed Abu Sebah .

4-Dr .Nafez Barakat .

5-Dr .Habeeb ALhawajery.

Annex 6

ملخص

مقدمة :

لا شك ان قضية المخدرات والادمان عليها تعتبر من القضايا التي تؤرق العالم بأسرة ولقد ظهرت في الآونة الاخيرة ظاهرة انتشار اساءة استخدام عقار الترامادول . يعتبر الترامادول هيدروكلوريك عقار مسكن للآلام المتوسطة والشديدة وهو يعمل على الجهاز العصبي المركزي. وتبرز في الآونة الاخيرة مخاوف عالمية بشان ادمان الترامادول .

أهداف الدراسة :

كان الهدف العام لهذه الدراسة هو دراسة تقييمية للمراجعين للعيادات النفسية الخاصة في مدينة غزة، والذين يتعالجون من الادمان على عقار الترامادول ، وقد اهتم الباحث بدراسة مدى معرفة عينة الدراسة بالترامادول ، وكيف كانت ممارستهم في اساءة استخدام هذا العقار ، وتوجهاتهم حول اساءة استخدام هذا العقار ، وايضا تم تسليط الضوء على الحالة النفسية لعينة الدراسة ، وهل عانوا من تأثيرات جانبية لإساءة استخدام هذا العقار، او عند التوقف عن اخذة .

منهجية الدراسة :

كانت الدراسة وصفية ، تحليلية ، مستعرضة وكان معدل الاستجابة لدى المشاركين في هذه الدراسة حوالى٨٣.٣%، تم اخذ 100 مريض عينة لهذه الدراسة حيث تم اخذ اربع مرضى يوميا من عيادتين خاصتين وذلك خلال شهر .

قام الباحث ببناء اداة البحث ، حيث انها كانت تتمثل في ستة محاور (العوامل الديموغرافية ، مستوى المعرفة ،الممارسات ، التوجهات ، الحالة النفسية ، وجود اثار جانبية ، لمسيء استخدام عقار الترامادول). تم جمع المعلومات عن طريق الاستبيان وكان نسبة الصدق والثبات كرو نباخ الفا مرتفعة حيث كانت ٨٦٣٣ .٠.

اهم النتائج :

* اظهرت النتائج ان ٨٦ % من العينة هم من فئة الذكور ،١٤% من فئة الاناث ، وانهم بدأوا بأخذ كبسولات من عيار ١٠٠ملجم حتى وصلوا الى حد ١٨٠٠ملجم يوميا ،يشار الى ان الجرعة الدوائية هي (٤٠٠- ٦٠٠ ملجم يوميا)

*أظهرت النتائج ان ٩٦% من العينة يعتقدون ان اساءة استخدام عقار الترامادول مشكلة في قطاع غزة.

* أظهرت النتائج ان٩٤.٤% يدركون ان الترامادول يسبب الادمان .

* أظهرت النتائج ان ٨٠% من العينة كانوا مدخنين .

* أظهرت النتائج ان ٩٢.٤% استخدموا الترامادول للحصول على حالة من النشوة .

* أظهرت النتائج ان ٧٩.٤ % استخدموا الترامادول لمساعدتهم في تأخير القذف .

* أظهرت النتائج ان ٦٣.٤ % لجأوا الى طرق غير قانونية للحصول على الترامادول .

* أظهرت النتائج ان ٧٦.٢٤% كانوا يعانوا من اضطرابات نفسية .

* أظهرت النتائج ان ٩٠ % عانوا من اعراض انسحابيه عند توقفهم عن استخدام الترامادول .

* اظهرت النتائج ان ٧١.٨ % عانوا من نوبات تشنج بسبب اساءة استخدام الترامادول .

* اظهرت النتائج ان هناك فروق ذات دلالة احصائية عند مستوى دلالة $\alpha \geq$ ٠.٠٥ من حيث المهنة لصالح العمال.