International Journal of Clinical Pharmacy (2020) 42:652–661
https://doi.org/10.1007/s11096-020-00992-8

RESEARCH ARTICLE

Significance of a clinical pharmacist-led comprehensive medication management program for hospitalized oncology patients

Rashida Muhammad Umar[1] · **Sule Apikoglu-Rabus**[2] · **Perran Fulden Yumuk**[3]

Received: 30 August 2018 / Accepted: 10 February 2020 / Published online: 20 February 2020

Abstract

Background The use of highly toxic drugs in cancer treatment and supportive care medications exposes patients to an increased number of drug-related problems (DRPs). Clinical pharmacists contribute to the optimal use of medications by intervening in identified drug-related problems. *Objective* To evaluate the relevance of a comprehensive medication management service in oncology patients. *Setting* Marmara University Teaching and Research Hospital Medical Oncology Ward, Istanbul, Turkey. *Methods* This prospective study was carried out between December 2015 and April 2016 with adult patients with confirmed malignancy. Comprehensive medication management was performed by the clinical pharmacist throughout the patient's hospital stay. The medication-related data as well as data regarding demographic and general health status of the patients were reviewed for the presence of drug-related problems. The identified problems, interventions and acceptance rate by physicians were recorded with the help of the Pharmaceutical Care Network Europe V6.0 (PCNE) classification. *Main outcome measures* Number and causes of drug-related problems, nature and acceptance rate of clinical pharmacist interventions and rate of problems solved. *Results* The study included 137 patients. The mean (SD) age of the patients was 58 (14.6) years. A total of 481 drug-related problems were recorded. The most frequent drug-related problems were 'adverse drug events [including drug interactions]' (n = 376), 'untreated indications' (n = 59) and 'unnecessary drug treatment' (n = 25). Inappropriate combination of drugs was the cause of 73.2% of the total problems. Interventions were made to stop administration of a suitable drug if the combination with another drug was contraindicated while prescribers were mostly informed about major drug interactions. The prescribers approved 93% of the total intervention proposals. The majority (90.9%) of the identified problems were totally solved. *Conclusion* Integration of clinical pharmacy services through a comprehensive medication management program in oncology will help to reduce the number of drug-related problems.

Keywords Clinical pharmacist · Drug-related problems · Medication management · Oncology · Turkey

Impact on practice

- Cancer patients, especially those with comorbidities, renal impairment, polypharmacy or poor health status, need special care and appropriate pharmaceutical care from clinical pharmacists
- A comprehensive medication management program in oncology will help to reduce drug-related problems
- One of the most frequent drug-related problems encountered in oncology practice is 'drug interactions', which can be prevented by the input of the clinical pharmacist.

Rashida Muhammad Umar and Sule Apikoglu-Rabus are contributed equally to this work.

✉ Rashida Muhammad Umar
rmumar@medipol.edu.tr

Sule Apikoglu-Rabus
sulerabus@yahoo.com

[1] Clinical Pharmacy Department, Istanbul Medipol University Faculty of Pharmacy, Istanbul, Turkey

[2] Clinical Pharmacy Department, Marmara University Faculty of Pharmacy, Istanbul, Turkey

[3] Division of Medical Oncology, Marmara University School of Medicine, Istanbul, Turkey

Introduction

Cancer is the second leading cause of death globally and a major life-threatening condition, which requires aggressive use of drugs with multiple side effects. Therefore, cancer patients are at high risk for drug-related problems (DRPs) due to the use of many drugs for the management of cancer, side effects of chemotherapy drugs, malignancy-related complications and comorbidities. A study covering 11,804 patients over 65 years revealed that major drug-related problems included inadequate therapy (56.9%), non-adherence (14.9%), adverse drug reactions (14.7%), doses higher than needed (6.8%) and unnecessary therapy (6.7%) [1]. To reduce these drug-related problems and optimize therapeutic outcomes, pharmacist-led comprehensive medication management is needed [2, 3].

Comprehensive medication management is defined by the American College of Clinical Pharmacy as "the standard of care that ensures each patient's medication (including nonprescription drugs, traditional and alternative therapies and supplements) are individually assessed to determine that each medication is appropriate for the patient, effective for the medical condition, safe given to comorbidities and other medications taken, and able to be taken by the patient as intended" [1].

Clinical pharmacists work in alliance with other healthcare providers to deliver comprehensive medication management that optimizes patient outcomes [4]. On oncology wards, the main aim of the clinical pharmacist as a member of the multidisciplinary healthcare team is to ensure the provision of the safest chemotherapy regimens, effective supportive care and treatment of comorbidities through comprehensive medication management.

Many studies have shown the positive impact of clinical pharmacy services on patient outcomes under different conditions [5–8]. Similarly, clinical pharmacists made positive contributions to the care of oncology patients through identification of medication errors and drug-specific interventions in both inpatient and outpatient settings [9–12], and the outcomes of these interventions included improved medication appropriateness, fewer adverse drug events, higher patient satisfaction and favorable economics [3, 13]. However, studies in the literature evaluating the impact of a clinical pharmacist-led comprehensive medication management program on the management of oncology patients are very scarce [14, 15].

Aim of study

In this study, we aimed to evaluate the relevance of a comprehensive medication management service provided by a clinical pharmacist to hospitalized oncology patients as well as to explore the association between patient factors and the identified DRPs.

Ethics approval

Ethics approval was obtained prior to the commencement of the research from the ethics committee of Marmara University Faculty of Medicine (Protocol No: 09.2015/36770737436-050.06.04).

Methods

This prospective study was carried out between December 2015 and April 2016 at the oncology ward of a university-affiliated state hospital. All adult patients with confirmed malignancy admitted to the ward were informed about the study, and those who agreed to be involved were enrolled in the study within 48 h of their admission and were followed throughout their stay on the ward. All participating patients or their caregivers signed consent forms before they were enrolled in the study; relevant consent and information regarding the unconscious patients were taken from these patients' legal guardians who were the accompanying family members who signed all of the therapy-related consent forms. Two patients who were discharged within 48 h of admission were excluded from the study.

A comprehensive medication management service was carried out by the clinical pharmacist from admission to discharge or demise. The pharmacist-led 'Comprehensive Medication Management" service involved four steps: assessment of the patient; evaluation of medication therapy; development and initiation of a plan; and follow-up and medication monitoring. In this study, one clinical pharmacist (RMU; MSc) actively worked on the ward, and one clinical pharmacist (SAR; PhD) provided consultation.

Assessment of the patients

This step involved collection and documentation of the complete medication history, collection and interpretation of patient data and review of the medical records to determine the clinical status of the patient within 24 h of admission. A comprehensive list of patients' medications, including prescription drugs, nonprescription drugs, and herbal and nutritional supplements, was performed. The purpose and duration of use, dosage and source of each drug in the list were also noted. All clinical and medication data were collected from the hospital database, pharmacy database, hospital files, patients and their caregivers. The patients' laboratory test results and hospital medication orders were

collected daily after the ward rounds throughout their stay in the hospital.

Evaluation of medication therapy

This step involved assessing the appropriateness of current medications, evaluating the effectiveness, safety and affordability of the therapies, and assessing medication use and adherence. All these items were conducted through medication reconciliation and identification of drug-related problems.

Medication reconciliation was performed for all patients within 48 h of admission. Medication discrepancies identified at admission were also recorded as drug-related problems.

Medications were reviewed daily considering the patient's health condition, new indications and resolved problems. The appropriateness of each drug given to a patient was checked in terms of patients' demographics, renal and hepatic functions, comorbidities and other drugs used. The Micromedex online drug reference was used as a source of drug information. Drug interactions were checked using the 'Micromedex Drug Interaction Checker' (Access dates: December 2015–April 2016). Interactions were classified as contraindicated, major, moderate and minor. Interactions were first checked after medication reconciliation and completion of a comprehensive medication list. Interactions were subsequently checked when changes in the patients' medication orders occurred. The number of these medication orders reflecting the frequency of changes in the individual patient drug list was also recorded.

Identification and classification of potential or manifest drug-related problems that may delay or influence therapeutic goals were performed using Pharmaceutical Care Network Europe's (PCNE) Classification Scheme for Drug-Related Problems V6.2. Problems that might present during treatment were coded as 'potential problems', while problems that had already been present in the respective patients were coded as 'manifest problems'.

Assessment of the association between patient factors and the DRPs

The association between the presence and number of DRPs and the following patient features were also investigated: sex, age, educational status, BMI, smoking status, renal function, primary cancer type, length of disease, presence of metastasis, cancer stage, purpose of admission, presence of comorbidities, number of comorbidities, number of orders, presence of polypharmacy, length of hospital stay, and average number of drugs used.

Development and initiation of plan

This step involved clinical pharmacists' decision making regarding drug-related problems, making suggestions regarding the resolution of DRPs based on their causes and developing a collaborative plan after communication with the physician responsible for the patient. Intended interventions/clinical decisions were communicated with the physician; all interventions intended for other healthcare providers or patients/caregivers were communicated after the physicians' approval. The rate of acceptance of all intended interventions was recorded. All accepted interventions were performed, and relevant education was provided to the patients/caregivers. The outcome of each intervention was recorded as 'totally solved', 'partially solved' or 'not solved'. A problem was classified as 'totally solved' if the pharmacist's intervention resulted in the total resolution of a manifest problem or the prevention of a potential problem.

Follow-up and medication monitoring

This step involved coordinating with other healthcare providers to ensure that the patient follow-up was in line with the patient's medication-related and medical needs; revisiting medical records to acquire updates on the clinical status and medication-related needs; conducting ongoing evaluations and refining the care plan to optimize drug therapy; and monitoring and managing the care plan.

Data analysis

The mean outcome measures of the study were as follows:

- Number and causes of the DRPs: For each patient, the existence of any DRP was checked, and identified DRPs were noted together with their causes.
- Nature and acceptance of the pharmacist's intervention: The level (prescribers/patients/drug level) and the acceptance rate of the proposed interventions by the relevant healthcare provider were recorded.
- Rate of problems solved: The outcome of the interventions and the rate of problems solved were recorded.

Data from this study were analyzed using SPSS (Statistical Package for Social Sciences) Version 16.0. Continuous variables are expressed as mean ± standard deviation; ordinal and nominal data are expressed as n (%). The Pearson correlation was used to study the relationships between patient variables and the number and type of DRPs. A p value < 0.05 within a confidence interval of 95% was considered significant.

Results

A total of 137 patients, 56.9% of whom were male, participated in the study. Ten (7.3%) patients died during the study, while 127 of the patients were monitored until discharge. Data analysis was conducted using the data from 137 patients. The mean (SD) age of the patients was 58 (14.6) years (range 19–82 years); 50 patients were aged ≥ 65 years. Approximately half of the patients were ex-smokers. Comorbidities were present in 85 patients. Polypharmacy (use of ≥ 5 drugs) was present in 81.8% (n = 112) of the patients. The mean (SD) length of hospital stay was 8.55 ± 6.3 days (range 2–40 days). Details on patient demographics and other clinical characteristics are given in Table 1.

The cancer-related features of the patients are presented in Table 2. Cancer-related complications were the reason for admission for 40% of the patients, while 18% were admitted for receiving palliative treatment. The most common primary malignancy was lung cancer (22.6%); the majority (79.6%) of the patients had metastasis and were at Stage 4. Older patients (≥ 65 years) presented with higher numbers of comorbid diseases ($p < 0.001$) and poor renal function ($p = 0.003$), as presented in Table 3. The most common comorbid diseases present in patients were hypertension, diabetes and chronic obstructive respiratory disease affecting 30% (n = 41), 19% (n = 26) and 7% (n = 10) of the patients, respectively. The presence of comorbidities was associated with the use of a higher number of medications (r = 0.22; $p < 0.05$), the presence of polypharmacy (r = 0.18; $p < 0.05$) and increasing age (r = 0.33; $p < 0.01$). The patients with polypharmacy had more frequent medication order changes (r = 0.34; $p < 0.01$), probably due to their extended hospital stay (r = 0.25; $p < 0.05$). A longer hospital stay was associated with more medication order changes (r = 0.61; $p < 0.01$) and higher mortality (r = 0.17; $p < 0.01$).

The most frequently used drug classes included antiemetics, analgesics, antibiotics, corticosteroids, antidepressants and other medications for comorbidities, mostly antihypertensives, inhaler bronchodilators and antidiabetic agents. All patients were on stress ulcer prophylaxis with a proton pump inhibitor or histamine-2 receptor antagonist and anticoagulants. Only a few patients (n = 24; 17.5%) received cancer therapy during the study. The chemotherapy regimens included bevacizumab (n = 2, 7.7%), capecitabine (n = 1, 3.8%), carboplatin (n = 1, 3.8%), cetuximab (n = 1, 3.8%), cisplatin (n = 1, 3.8%), cyclophosphamide (n = 1, 3.8%), doxorubicin (n = 2, 7.7%), etoposide (n = 1, 3.8%), exemestane (n = 2, 7.7%), fluorouracil (n = 1, 3.8%), gemcitabine (n = 1, 3.8%), ifosfamide (n = 3, 11.5%), irinotecan (n = 2, 7.7%), lapatinib (n = 1, 3.8%), paclitaxel (n = 2, 7.7%), oxaliplatin (n = 1, 3.8%), pemetrexed (n = 1, 3.8%), rituximab (n = 1, 3.8%) and vincristine (n = 1, 3.8%).

Table 1 Demographic and general clinical characteristics of the patients (n = 137)

Demographic and general clinical characteristics	n (%)
Age (years); mean ± SD	58 ± 14.60 (range 19–82)
Gender	
Male/Female	78 (56.9)/59 (43.1)
Educational status	
No formal education	30 (21.9)
Primary school graduate	68 (49.6)
Secondary school graduate	14 (10.2)
High-school graduate	16 (11.7)
University graduate	7 (5.1)
Post-graduate	2 (1.5)
Ex-smokers	71 (51.8)
Alcohol use	37 (27)
Weight status	
Obese	17 (12.4)
Over-weight	39 (28.5)
Normal	70 (51.1)
Under-weight	11 (8.0)
Renal function stage [GFR (mL/min)]	
G1 [≥ 90]	78 (56.9)
G2 [60–89]	37 (27)
G3a [45–59]	8 (5.9)
G3b [30–44]	11 (8)
G4 [15–29]	2 (1.5)
G5 [< 15]	1 (0.7)
Number of comorbid diseases	
No comorbidity	52 (37.9)
One comorbidity	42 (30.7)
Two comorbidities	20 (14.6)
Three comorbidities	12 (8.8)
Four comorbidities	7 (5.1)
Five comorbidities	4 (2.9)
Length of hospital stay (days); mean ± SD	8.55 ± 6.3 (range 2–40)
Number of drugs used	
< 5	25 (18.2)
≥ 5	112 (81.8)

GRF glomerular filtration rate, *SD* standard deviation

Evaluation of medication therapy through identification of drug-related problems

Problems

A total of 481 DRPs were identified in 114 patients. At least one DRP was recorded in the majority (83.2%) of the patients. The problems were recorded into the primary domains of 'treatment effectiveness', 'adverse reactions', 'treatment cost' and 'others' as presented in Table 4. An

Table 2 Cancer-related features of the patients (n = 137)

Cancer-related features	n (%)
Purpose of admissions	
Cancer-related complications	54 (39.4)
Cancer treatment	24 (17.5)
Diagnosis of primary malignancy	6 (4.4)
Treatment of other conditions not related to malignancy	21 (15.3)
Management of chemotherapy side-effects	7 (5.1)
Palliative treatment	25 (18.3)
Primary malignancy	
Lung cancer	31 (22.6)
Colon cancer	16 (11.7)
Gastric cancer	13 (9.5)
Breast cancer	12 (8.8)
Other/unknown primary malignancy	65 (47.4)
Disease stage	
Stage 4	109 (79.6)
Stage 3	7 (5.1)
Disease stage unknown[a]	21 (15.3)

[a]This information could not be found in the patient records

Table 3 Status of comorbidities and renal function according to age groups (n = 137)

	Age		*p**
	< 65; n = 87 n (%)	≥ 65; n = 50 n (%)	
Number of comorbidities			
0	41 (47.1)	11 (22)	< 0.001
1–2	38 (43.7)	23 (46)	
3–5	8 (9.2)	16 (32)	
Renal function			
GFR ≥ 90 mL/min	58 (66.7)	20 (40)	0.003
GFR 60–89 mL/min	21 (24.1)	16 (32)	
GFR 45–59 mL/min	3 (3.5)	5 (10)	
GFR 30–44 mL/min	3 (3.5)	8 (16)	
GFR 15–29 mL/min	1 (1.1)	1 (2)	
GFR < 15 mL/min	1 (1.1)	0 (0)	

*Significance between age groups; GRF: glomerular filtration rate

average of 3.5 problems/patient was recorded. Seventy-five percent (n = 362) of the identified problems were potential problems, while 24.7% (n = 119) were manifest problems.

The number of DRPs increased with increasing malignancy stage (r = 0.182; $p < 0.05$), length of hospital stay (r = 0.405; $p < 0.01$), number of drugs (r = 0.612; $p < 0.01$), frequency of order change (r = 0.573; $p < 0.01$) and presence of polypharmacy (r = 0.360; $p < 0.01$).

Causes of problems

A single cause was recorded for each problem. Drug selection issues made up 89.2% (n = 429) of the causes of problems. The most common cause was inappropriate drug combinations (n = 352, 73.2%), which included drug interactions and unsuitable drug selection based on patients' clinical features. Drug interactions made up most of the causes of the problems.

Unnoticed indications requiring drug treatment made up six percent (n = 29) of the problems that involved medication discrepancies after reconciliation (n = 15), lack of routine stress ulcer and emboli prophylaxis (n = 8) and specific prophylaxis (n = 6). The 10 (2.1%) causes regarding prescribing errors were reordering of a previously stopped drug (n = 7), unintended elimination of routinely administered drugs in patient orders (n = 2), and inappropriate dilution of vancomycin (n = 1). The problems involving unnecessary drug use were caused by a lack of indication for drug use (n = 7, 1.5%) or inappropriate duplication of therapeutic group or active ingredient (n = 9, 1.9%). Details of the causes of the DRPs are given in Table 4.

Interventions

The majority (69%, n = 332) of interventions were made at the prescriber level, while 29.3% (n = 141) interventions were made at the drug level, most of which included beginning a new medication (11.4%, n = 55) or stopping a medication (9.6%, n = 46).

Table 5 shows an elaborate explanation of interventions based on the causes of the DRPs. No interventions were made in 7 cases with manifest problems because there was no need or possibility to solve the problem. For 13 (2.7%) DRPs, dose modifications were proposed for the resolution of the related problem.

Interventions involving medication withdrawal were proposed for 30 manifest problems and 16 potential problems that involved inappropriate drug combinations. The prescribers were only informed of approximately 317 potential major drug interactions. They were alerted to the possibility of problems and informed about the resolution options.

The information provided to the prescribers was not limited to but included the following: necessity for laboratory tests (such as vancomycin and phenytoin blood level monitoring, measurement of TSH, T4, INR, iron, cholesterol and triglyceride levels, and repeating the laboratory tests); drug adverse effects (such as those experienced during the use of quetiapine, morphine, cefepime and chemotherapeutics [i.e., for tumor lysis syndrome]); drug interactions (recommendations included changing drug administration times, monitoring for possible/increased adverse effects such as seizures, monitoring for signs and

Table 4 Classification and causes of the drug-related problems (n = 481)

	n (%)
Classification of the drug-related problems	
Treatment effectiveness	
No effect of drug treatment/therapy failure	8 (1.7)
Effect of drug treatment not optimal	11 (2.3)
Untreated indication	59 (12.3)
Adverse reactions	
Adverse drug event (non-allergic)	376 (78.2)
Treatment cost	
Unnecessary drug-treatment	25 (5.2)
Others	
Patient dissatisfied with therapy despite optimal clinical and economic treatment outcomes	2 (0.4)
Causes of the drug-related problems	
Drug selection	
Inappropriate drug (including contraindicated)	4 (0.8)
No indication for drug use	7 (1.5)
Inappropriate combination of drugs, or drugs and food	352 (73.2)
Inappropriate duplication of therapeutic group or active ingredient	9 (1.9)
Indication for drug-treatment not noticed	29 (6.0)
Too many drugs prescribed for indication	1 (0.2)
New indication for drug treatment presented	27 (5.6)
Drug form	
Inappropriate drug form	5 (1.0)
Dose selection	
Drug dose too low	1 (0.2)
Drug dose too high	5 (1.0)
No therapeutic drug monitoring	8 (1.7)
Pharmacokinetic problem requiring dose adjustment	9 (1.9)
Deterioration/improvement of disease state requiring dose adjustment	2 (0.4)
Drug use process	
Inappropriate timing of administration and/or dosing intervals	5 (1.0)
Drug not taken/administered at all	1 (0.2)
Logistics	
Prescribed drug not available	2 (0.4)
Prescribing error (necessary information missing)	10 (2.1)
Others	
No obvious cause	4 (0.8)
Total	481 (100)

symptoms of serotonin syndrome, stopping/changing the most relevant one of the interacting drugs, monitoring the effect of clopidogrel, monitoring the effect of clarithromycin, monitoring bleeding risk, monitoring for respiratory distress, monitoring for hypotension and bradycardia, monitoring for fentanyl toxicity, monitoring for signs and symptoms of QT prolongation, monitoring for myopathy, monitoring mental status, monitoring TSH levels, etc.)

The prescribers accepted 93.5% (n = 450; 96 manifest and 354 potential problems) of the proposed interventions, while they did not accept 23 (5%) interventions (15 manifest and 9 potential problems). Table 5 shows the proposed interventions and their rates of acceptance.

Outcomes

The vast majority (n = 437; 90.9%) of the problems were totally solved, while 4 (0.8%) problems were partially solved. There was no possibility or need to solve 10 (2.1%) problems. These were problems that did not require immediate solution or those that had already affected the patient and could not have been undone or changed. Twenty-two

Table 5 Proposed interventions and their acceptance rates for the resolution of drug-related problems (n = 481)

Proposed intervention	Total n (%)	Acceptance rate n (%)	
		Approved by prescriber	Not approved by prescriber
No intervention	7 (1.5)	0	0
Prescriber informed only	330 (68.6)	325 (67.6)	5 (1)
Prescriber asked for information	2 (0.4)	1 (0.2)	1 (0.2)
Patient (medication) counselling	1 (0.2)	1 (0.2)	0
Drug changed to ….	7 (1.5)	5 (1)	2 (0.4)
Dosage changed to ….	13 (2.7)	11 (2.3)	2 (0.4)
Formulation changed to ….	3 (0.6)	3 (0.6)	0
Instructions for use changed to ….	16 (3.3)	16 (3.3)	0
Drug stopped	46 (9.6)	44 (9.2)	2 (0.4)
New drug started	55 (11.4)	43 (8.9)	12 (2.5)
Other intervention	1 (0.2)	1 (0.2)	0
Total	481 (100)	450 (93.6)	23 (4.8)

(4.6%) problems were not solved due to lack of cooperation from the prescribers, and one patient did not cooperate in solving a problem. The outcome of six (1.2%) interventions was unknown.

Associations between patient factors and the DRPs

The presence and number of drug-related problems was associated with extended hospital stays, more frequent medication order changes, higher number of drugs used and presence of polypharmacy ($p \leq 0.001$, for all) (Table 6). In addition, the number of DRPs not involving drug interactions was higher in patients with poor renal function (r = 0.172; $p < 0.05$) and was associated with the presence (r = 0.224; $p < 0.01$) and higher number (r = 0.258; $p < 0.01$) of comorbidities (Table 6).

On the other hand, sex, age, educational status, BMI, smoking status, length of disease, purpose of admission, primary cancer type and presence of metastasis were not found to be associated with the presence and/or number of drug-related problems (whether involving drug interactions or not) ($p > 0.05$, for all).

Discussion

The results of this study demonstrate that a clinical pharmacist-led comprehensive medication management program was feasible and effective at identifying drug-related problems and improving safe medication use among adult cancer patients. A total of 481 DRPs were identified in 114 patients. At least one DRP was recorded in the majority (83.2%) of our patients, reflecting the high prevalence of DRPs in our patients, the majority of whom had terminal illness and comorbid conditions. The willingness of the physicians regarding the clinical pharmacist's integration into the clinic setting was reflected in the high (93.5%) acceptance rate of the pharmacist's intervention proposals. The acceptance rate of interventions was similar to those reported in other studies [9, 16], while it was higher than that (46%) reported by Nightingale et al. [15].

Most of the identified problems involved supportive care needs associated with advanced disease, complication(s) of previous cancer treatment(s) and other care needs, while a few problems were directly related to cancer therapy, as only 18% of the patients were admitted for cancer-specific treatment. This is in concordance with the findings of a large prospective study in a hematology and oncology department, which revealed that only 3.9% of 552 DRPs identified were associated with anti-cancer agents [9].

The identified DRPs involved adverse drug reactions, including drug interactions, untreated indications,

Table 6 Factors that affect the presence and number of drug-related problems

	Presence of drug-related problems		Number of drug-related problems		Presence of drug-related problems involving drug interactions		Presence of drug-related problems NOT involving drug interactions	
	Pearson's r	*p*	Pearson's r	*p*	Pearson's r	*p*	Pearson's r	*p*
Malignancy stage	0.134	0.119	0.182*	0.033	0.182*	0.033	0.082	0.340
Length of hospital stay	0.282**	0.001	0.405**	0.000	0.313**	0.000	0.364**	0.000
Average number of drugs used	0.441**	0.000	0.612**	0.000	0.605**	0.000	0.286**	0.001
Presence of polypharmacy	0.336**	0.000	0.360**	0.000	0.321**	0.000	0.238**	0.005
Frequency of order change	0.274**	0.001	0.573**	0.000	0.465**	0.000	0.472**	0.000

*Correlation is significant at the 0.05 level (2-tailed); **Correlation is significant at the 0.01 level (2-tailed)

unnecessary drug use, nonoptimal treatment effect of the drug, no effect of drug treatment or therapy failure, and patient dissatisfaction. Slightly different frequencies of DRPs were recorded in two different studies involving oncology patients. The most frequent problems recorded in other studies were inappropriate medication selection (20.6%) [9] and inappropriate dose (25.0%) [16]. Delpeuch et al. reported a rate of untreated indications (14.8%) similar to our results. The fact that the majority of DRPs identified in our study involved drug interactions might be due to unawareness of the physicians of the possible negative outcomes of drug interactions.

In a study regarding comprehensive medication management in elderly oncology patients, Nightingale et al. reported a total of 123 medication-related problems at baseline. As a result of pharmacist involvement, medication-related problems were reduced to 78 at 30-day and 67 at 60-day follow-ups. They concluded that despite a few problems in communicating their recommendations, pharmacist intervention was feasible and effective in reducing medication-related problems [15]. A 10-year review of medication therapy management revealed that the program improved clinical and economic outcomes with high patient satisfaction [17]. Although Shaya et al. [18] reported that they could not find any advantages of a pharmacist-led medication therapy management program, they recommended conducting additional studies to investigate whether pharmacist involvement in the transition of care could reduce rehospitalization and healthcare expenditures post discharge. The ACCP pursues the continuous provision of comprehensive medication management in collaborative practice settings by competent clinical pharmacists to enhance recognition of their positive impact on medication-related outcomes [19].

The presence of major health problems such as cancer is associated with undertreatment [20], a decline in the control of comorbid chronic diseases [21] and nonadherence to treatment of other chronic conditions [22]. Medication reconciliation in our study revealed the omission of 15 chronic disease medications in some patients. Interventions in this respect were readily accepted by prescribers, and some prescribers showed appreciation for this particular service provided by the pharmacist. Unintended medication discrepancies are the most common and significant type of medical errors that occur at transitions between sites of health care [23, 24]. It has been reported that 94% (77/82) of self-reported medication lists had at least one discrepancy with clinic medication lists, with a median of 4 discrepancies per patient list [25]. According to the report of Hanigan et al., medical records generally failed to report 24% of prescription medications, 84% of nonprescription medications and 83% of other remedies [26]. The implementation of a pharmacist-initiated pharmaceutical handover of patients from an oncology and hematology unit to a critical care unit improved the medication use process in cancer patients [27]. Clinical pharmacists have an important role in managing medication discrepancies that occur at transitions between sites of health care [28, 29].

Drug interactions were the cause of 352 (73.2) problems, of which only 9 interactions involved anticancer agents. Most reported interactions were associated with supportive care medications, which is in accordance with other studies [29–32]. In their study, Delpeuch et al. [9] reported 79 drug interactions among 552 medication-related problems, where they monitored patients and only intervened in major issues. On the other hand, we recorded all interactions that required monitoring because physicians were not familiar with most of the interactions. Drug interactions are major problems in cancer patients because they concurrently receive multiple drugs [32, 33], and the number of drugs used by a patient is an independent factor that increases the risk of drug interactions [30, 32]. Most (81.8%) of our study population were taking 5 or more drugs, which may have increased the number of recorded drug interactions. Detection of drug interactions in patients with cancer is fundamental in the management of pharmacotherapy in these patients, and a routine systematic review of all patients' medications is necessary to avoid interactions [29, 34].

Lustig et al. [2] reported that in their study, the highest medication error rate was recorded in the oncology-hematology unit. Study results have consistently provided evidence of the positive impact of clinical pharmacists on preventing medication errors, optimizing drug usage and maintaining patient safety [33, 35]. The multidisciplinary approach to patient care is becoming more acceptable, and the awareness of the importance of pharmacists has increased [7]. This was reflected in our study because the majority (93%) of our interventions were readily accepted and implemented by physicians and other healthcare providers.

The results of the study show the positive impact of a comprehensive medication management service provided by a clinical pharmacist, particularly in settings where the usual care does not involve ward-based clinical pharmacy practice.

Comprehensive medication management services are conducted based on the regulations of individual countries. It may be difficult to cover all patients in this service, but high-risk patients may be given the privilege to benefit. Introduction of pharmaceutical care programs that enable integration of clinical pharmacists in the multidisciplinary team of patient care will improve therapeutic outcomes and reduce health-related expenditures.

Limitations

This study had a number of limitations, some of which include the following: the clinical applicability of comprehensive medication management could have been best

measured with a multicenter randomized controlled study instead of a single cohort, single-institution study; and the effects of interventions on long-term health outcomes were not measured as there was no follow-up after the patients were discharged. There is a need for a future randomized controlled study involving mid- and long-term follow-up of patients.

Conclusions

Integration of clinical pharmacy services through a comprehensive medication management program in oncology will help reduce DRPs.

Acknowledgements The authors are grateful to the staff of Marmara University teaching and research hospital for their support.

Funding The authors have no funding to declare.

Conflicts of interest The authors have no conflicts of interest to declare.

References

1. Comprehensive medication management in team-based care. American College of Clinical Pharmacy. www.accp.com/docs/positions/misc/CMMBrief.pdf. Accessed 1 Aug 2018.
2. Lustig A. Medication error prevention by pharmacists—an Israeli solution. Pharm World Sci. 2000;22(1):21–5.
3. Leveque D, Delpeuch A, Gourieux B. New anticancer agents: role of clinical pharmacy services. Anticancer Res. 2014;34:1573–8.
4. American College of Clinical Pharmacy. Standards of practice for clinical pharmacists. Pharmacotherapy. 2014;34(8):794–7.
5. Abunahlah N, Elawaisi A, Velibeyoglu FM, Sancar M. Drug-related problems identified by clinical pharmacist at the internal medicine ward in Turkey. Int J Clin Pharm. 2018;40:360–7.
6. Mousavi M, Hayatshahi A, Sarayani A, Hadjibabaie M, Javadi M, Torkamandi H, et al. Impact of clinical pharmacist-based parenteral nutrition service for bone marrow transplantation patients: a randomized clinical trial. Support Care Cancer. 2013;21(12):3441–8.
7. Chieng R, Coutsouvelis J, Poole S, Dooley MJ, Booth D, Wei A. Improving the transition of highly complex patients into the community: impact of a pharmacist in an allogeneic stem cell transplant (SCT) outpatient clinic. Support Care Cancer. 2013;21(12):3491–5.
8. Han JM, Ah YM, Suh SY, Jung SH, Hahn HJ, Im SA, et al. Clinical and economic impact of pharmacists' intervention in a large volume chemotherapy preparation unit. Int J Clin Pharm. 2016;38(5):1124–32.
9. Delpeuch A, Leveque D, Gourieux B, Herbrecht R. Impact of clinical pharmacy services in a hematology/oncology inpatient setting. Anticancer Res. 2015;35(1):457–60.
10. Ranchon F, Salles G, Späth HM, Schwiertz V, Vantard N, Parat S, et al. Chemotherapeutic errors in hospitalised cancer patients: attributable damage and extra costs. BMC Cancer. 2011;11(1):478.
11. Tezcan S, Izzettin FV, Sancar M, Turhal NS, Yumuk PF. Role of clinical oncology pharmacist in determination of pharmaceutical care needs in patients with colorectal cancer. Eur J Hosp Pharm. 2018;25:e17–20.
12. Abunahlah N, Sancar M, Dane F, Özyavuz MK. Impact of adherence to antiemetic guidelines on the incidence of chemotherapy-induced nausea and vomiting and quality of life. Int J Clin Pharm. 2016;38(6):1464–76.
13. Schwinghammer T. The patient care plan. In: Schwinghammer T, Koehler J, editors. Pharmacotherapy casebook: a patient-focused approach. 9th ed. New York: McGraw Hill Education; 2011. p. 23–30.
14. Marr TD, Pinelli NR, Jarmul JA, Waldron KM, Eckel SF, Cicci JD, et al. Continuous care provided through comprehensive medication management in an acute care practice model. Ann Pharmacother. 2018;52(4):314–24.
15. Nightingale G, Hajjar E, Pizzi LT, Wang M, Pigott E, Doherty S, et al. Implementing a pharmacist-led, individualized medication assessment and planning (iMAP) intervention to reduce medication-related problems among older adults with cancer. J Geriatr Oncol. 2017;8(4):296–302.
16. Langebrake C, Hilgarth H. Clinical pharmacists' interventions in a German University Hospital. Pharm World Sci. 2010;32(2):194–9.
17. Ramalho de Oliveira D, Brummel AR, Miller DB. Medication therapy management: 10 years of experience in a large integrated health care system. J Manag Care Pharm. 2010;16(3):185–95.
18. Shaya FT, Chirikov VV, Rochester C, Zaghab RW, Kucharski KC. Impact of a comprehensive pharmacist medication-therapy management service. J Med Econ. 2015;18(10):828–37.
19. McBane SE, Dopp AL, Abe A, Benavides S, Chester EA, Dixon DL, et al. Collaborative drug therapy management and comprehensive medication management—2015. Pharmacotherapy. 2015;35(4):e39–50.
20. Earle CC, Neville BA, Landrum MB, Ayanian JZ, Block SD, Weeks JC. Trends in the aggressiveness of cancer care near the end of life. J Clin Oncol. 2004;22(2):315–21.
21. Zanders MMJ, Haak HR, van Herk-Sukel MPP, van de Poll-Franse LV, Johnson JA. Impact of cancer on adherence to glucose-lowering drug treatment in individuals with diabetes. Diabetologia. 2015;58(5):951–60.
22. Calip GS, Elmore JG, Boudreau DM. Characteristics associated with nonadherence to medications for hypertension, diabetes, and dyslipidemia among breast cancer survivors. Breast Cancer Res Treat. 2017;161(1):161–72.
23. Sanchez SH, Sethi SS, Santos SL, Boockvar K. Implementing medication reconciliation from the planner's perspective: a qualitative study. BMC Health Serv Res. 2014;14(1):290.
24. Wortman SB. Medication reconciliation in a community, non-teaching hospital. Am J Health Syst Pharm. 2008;65(21):2047–54.
25. Lee KP, Nishimura K, Ngu B, Tieu L, Auerbach AD. Predictors of completeness of patients' self-reported personal medication lists and discrepancies with clinic medication lists. Ann Pharmacother. 2014;48(2):168–77.
26. Hanigan MH, Dela Cruz BL, Shord SS, Medina PJ, Fazili J, Thompson DM. Optimizing chemotherapy: concomitant medication lists. Clin Pharmacol Ther. 2011;89(1):114–9.
27. Coutsouvelis J, Corallo CE, Dooley MJ, Foo J, Whitfield A. Implementation of a pharmacist-initiated pharmaceutical handover for oncology and haematology patients being transferred to critical care units. Support Care Cancer. 2010;18(7):811–6.
28. Farley TM, Shelsky C, Powell S, Farris KB, Carter BL. Effect of clinical pharmacist intervention on medication discrepancies following hospital discharge. Int J Clin Pharm. 2014;36(2):430–7.
29. Lopez-Martin C, Garrido Siles M, Alcaide-Garcia J, Faus Felipe V. Role of clinical pharmacists to prevent drug interactions in cancer outpatients: a single-centre experience. Int J Clin Pharm. 2014;36(6):1251–9.

30. Hadjibabaie M, Badri S, Ataei S, Moslehi AH, Karimzadeh I, Ghavamzadeh A. Potential drug–drug interactions at a referral hematology-oncology ward in Iran: a cross-sectional study. Cancer Chemother Pharmacol. 2013;71(6):1619–27.
31. Kannan G, Anitha R, Rani V, Thennarasu P, Alosh J, Vasantha J, et al. A study of drug–-drug interactions in cancer patients of a south Indian tertiary care teaching hospital. J Postgrad Med. 2011;57(3):206–10.
32. Riechelmann RP, Tannock IF, Wang L, Saad ED, Taback NA, Krzyzanowska MK. Potential drug interactions and duplicate prescriptions among cancer patients. J Natl Cancer Inst. 2007;99(8):592–600.
33. Conde-Estévez D. Targeted cancer therapy: interactions with other medicines. Clin Transl Oncol. 2017;19(1):21–30.
34. van Leeuwen RW, Swart EL, Boom FA, Schuitenmaker MS, Hugtenburg JG. Potential drug interactions and duplicate prescriptions among ambulatory cancer patients: a prevalence study using an advanced screening method. BMC Cancer. 2010;10:679.
35. Walton SM. The pharmacist shortage and medication errors: issues and evidence. J Med Syst. 2004;28(1):63–9.