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Clinical and hematological evaluation of glyceryl guaiacolate as an adjuvant to anesthesia in the horse (Equus caballus).

Larry Lavern Jackson
Iowa State University

Clinical and hematological evaluation of glyceryl guaiacolate as an adjuvant to anesthesia in the horse (Equus caballus)

by

Larry LaVern Jackson

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INTRODUCTION

The production of an anesthetic state in the equine species poses problems for the veterinary anesthesiologist not encountered in the handling of smaller species. Horses are not only large and thus difficult to restrain but tend also to be nervous and intractable when subjected to the restraint necessary for the induction of general anesthesia.

Administration of a combination of glyceryl guaiacolate and thiamylal sodium intravenously has been suggested as an adequate chemical restraining agent, used alone for short anesthetic procedures and for the induction of inhalation anesthesia in the horse. Any agent to be used in this manner should produce a state of basal narcosis or surgical anesthesia without contributing to the already nervous and excited state of the subject. The agent should depress both laryngeal and pharyngeal reflexes making the passage of an endotracheal tube possible and should be relatively short acting with a smooth recovery period. It should be compatible with other anesthetic agents used in the horse and ideally should produce no adverse physiological effects on either the respiratory or cardiovascular systems.

The purpose of this study was to evaluate a combination of glyceryl guaiacolate and thiamylal sodium as to its ability to meet the above requirements. More specifically the combination was evaluated as to its ability to produce a state of recumbency and analgesia without depression of respiratory function or alteration of certain hematological factors.

REVIEW OF THE LITERATURE

General Considerations

The utilization of monitoring techniques and clinical pathological tests to determine physiological actions of various anesthetics has produced an abundance of data which the veterinary anesthesiologist can utilize.

A study to determine the effect of inhalant anesthesia on arterial oxygen tension has shown a definite depressant effect[37]. No correlation with age or sex of the subject could be shown in this study. It was concluded that ventilation perfusion abnormalities were the cause of the lowered arterial oxygen tension and that high concentrations of inspired oxygen in the anesthetic circuit could minimize the effect. To prevent the possible production of a hypoxic state when using inhalant anesthesia in the horse, the induction agents utilized should not cause apnea[18]. In the adult horse oxygen flow rates of four liters per minute have been recommended as being sufficient to prevent hypoxia.

Studies to determine the most accurate sampling technique for the determination of blood gas tension have been done[32, 33]. Arterial blood samples, capillary blood samples and tracheal end tidal samples were collected.

Oxygen and carbon dioxide partial pressures and blood pH values were determined. It was concluded that the accuracy of the capillary samples was acceptable only in the case of blood pH determination[33]. The partial pressures of oxygen and carbon dioxide determined from arterial and tracheal end tidal samples compared favorably and either method is acceptable for use in clinical investigation of pulmonary function in horses. The mean value for partial pressure of oxygen in arterial samples was 95.64 $\pm$ 5.4 mm. Hg. The mean value for partial pressure of carbon dioxide in arterial samples was 44.9 $\pm$ 2.47 mm. Hg.[32].

In the dog, narcotics, neuroleptoanalgesics, and other analgesics have been shown to produce depression of ventilation which can be documented by depression of arterial blood gas and pH[44].

In the horse, general anesthesia, in the laterally recumbent position, has been shown to produce a cardiopulmonary dysfunction which is characterized by hypoventilation and depression of alveolar and arterial oxygen tension[23]. This phenomenon was thought to be the result of maldistribution of blood perfusion due to gravitational forces on the dependent lung, development of atelectasis, hypoventilation of the dependent lung, and decrease in cardiac output. These

physiological changes occur with the use of several of the commonly used general anesthetics in the horse.

Horses to which toxic doses of chloral hydrate and chloroform were administered in combination exhibited marked respiratory depression and respiratory acidosis[49]. Arterial oxygen tension after thirty minutes was 52 mm. Hg. Arterial carbon dioxide tension was 38 mm. Hg. and blood pH was 7.35 at the same time interval. The horse died ultimately in cardiac arrest, exhibiting a metabolic acidosis.

Arterial oxygen tension is significantly lowered by anesthesia induced with barbiturates and maintained with halothane-oxygen mixtures in the horse[27]. It has been recommended that the inspired anesthetic mixture be at least 90% oxygen when halothane is utilized as an anesthetic in the horse. Halothane anesthesia also produces a highly significant decrease in cardiac output and left ventricular work[14]. Peripheral vascular resistance is increased however, thus a hypotension does not occur unless arterial oxygen tension decreases and arterial carbon dioxide tension increases sufficiently to produce respiratory acidosis.

Pharmacological Considerations

Glyceryl guaiacolate (3-(0-methoxy phenoxy)-1, 2 propanediol) is a guiaiacol derivative closely related to mephenesin. Its original use in the veterinary drug armamentarium was as an expectorant in various cough medications.

The propanediol derivatives of guiaiacol, of which mephenesin and glyceryl guaiacolate are the two most widely used examples, selectively depress transmission of nerve impulses at the internuncial neurons of the spinal cord, brain stem, and subcortical areas of the brain[24, 25]. Glyceryl guaiacolate is a white crystalline powder which, like mephenesin, is soluble in alcohol, glycerin and propylene glycol. Unlike mephenesin, glyceryl guiaiacolate is also readily soluble in water and therefore requires no special solvent for the preparation of a solution suitable for intravenous injection[25].

Solutions of both mephenesin and glyceryl guaiacolate produce hemolysis when administered intravenously. The degree of hemolysis depends primarily on the concentration of the solution injected. Glyceryl guaiacolate has only slightly less relaxant properties than does mephenesin but has sixty five to seventy five percent less hemolytic activity[24, 36, 48].

Therefore, glyceryl guaiacolate has been recommended as the best of the propanediol derivatives of guaiacol for clinical use[5]. In vitro and in vivo studies have been done to ascertain the best concentration and solvent for use with glyceryl guaiacolate[5, 36]. A 3.66% aqueous solution of glyceryl guaiacolate has been shown to possess no hemolytic activity while a 12.5% aqueous solution has been shown to produce intravenous hemolysis at each administration. The incorporation of isotonic sodium chloride or five percent glucose in combination with glyceryl guaiacolate solution markedly reduces the degree of intravenous hemolysis produced[25]. Evidence has been presented that solutions of glyceryl guaiacolate in concentration of 5-10%, either with or without the incorporation of sodium chloride or glucose, may be administered with little danger of hemolysis[2]. Serum bilirubin and hemochromogen determinations have supported this finding[48].

All of the propanediol derivatives of guaiacol have been shown to possess some hypotensive activity[24]. Studies have been conducted in humans and in many animal species to determine the degree of cardiac depression produced by glyceryl guaiacolate administration[17, 43, 54]. When therapeutic doses of glyceryl guaiacolate are administered intravenously

a slight transitory fall in blood pressure can be demonstrated in all species. In larger doses this hypotensive activity is markedly increased. The average reduction of systolic and diastolic pressure is 20 mm. Hg. and the pressure reduction may be as great as 50 mm. Hg.[13, 35]. This fall in blood pressure is transitory and electrocardiographic studies have reported no pathological changes, with the exception of a short period of tachycardia during the recovery period[30, 46]. As long as only therapeutic doses of glyceryl guaiacolate are administered, its action on the cardiovascular system has been shown to be transitory and insignificant[10, 54].

Although glyceryl guaiacolate has the ability to relax the peripheral musculature to the point of paralysis, it has little effect on the musculature of the diaphragm[13, 29]. A slight decrease in respiratory volume and arterial oxygen tension has been demonstrated during glyceryl guaiacolate administration[17, 46]. Therapeutic doses have been shown to produce neither apnea nor depression of the respiratory center[1, 10, 29]. With doses sufficient to cause the subject to assume a recumbent position, the laryngeal and pharyngeal reflexes are sufficiently depressed to allow endotracheal intubation[1, 54]. Endotracheal intubation is not essential, unless desired, as apnea does not occur and respiration need

not be supported.

The effect of glyceryl guaiacolate on the central nervous system is the reason for its inclusion in the armamentarium of the veterinary anesthesiologist. Its primary effect is to block transmission of nerve impulses through the spinal cord, brain stem and subcortical areas of the brain, resulting in a profound muscular relaxation.

Its effects on the nervous system have been shown to be central, rather than peripheral as in the case of the myo-neural junction blocking agents such as curare or succinylcholine chloride[13, 24]. In addition glyceryl guaiacolate produces a hypnotic and psychic effect mediated through a direct depression of the cortical areas of the brain[20, 26, 29]. In humans this psychic effect is manifested as a feeling of tranquility which progresses to euphoria and, as the dose of solution is increased, an analgesic state[9, 26, 29, 43] is reached. Animal trials have also shown an analgesic effect when solutions of glyceryl guaiacolate are administered at appropriate dosage rates[29, 31, 54].

Glyceryl guaiacolate has been administered to pregnant subjects, both human and animal, with no damage to the fetus being observed. Gynecologists have attributed this phenomenon to the inability of glyceryl guaiacolate to pass the

placental barrier[20, 54].

The metabolism and detoxification of glyceryl guaiacolate have been studied in man, the dog and the horse. It has been shown that the intact molecule is the active principle in the dog[34]. Glyceryl guaiacolate exhibits no hepatotoxic properties and is apparently metabolized in the liver[7]. In the horse, plasma levels in excess of 238 ug./ml. were necessary to produce complete muscle relaxation, with the exception of the diaphragmatic musculature[12]. The time required for plasma levels to be halved ranged from 55-85 minutes. At plasma levels of approximately 154 ug./ml. the horses were able to stand and plasma levels of 150 ug./ml. produced no visible effects in the horse. The metabolites of glyceryl guaiacolate are excreted by the kidney in the form of catechol and polar metabolites of catechol[12]. These urinary metabolites could be the active factors in the production of toxic overdose to glyceryl guaiacolate[12, 17]. Catechol toxicity is characterized by tetany, convulsions, hypotension, deep coma, apnea and death due to respiratory failure. These signs are also characteristic of those observed with toxic overdose of glyceryl guaiacolate.

The incidental pharmacological properties of glyceryl guaiacolate neither aid nor hinder anesthesia. It has been

shown to have slight bacteriostatic, antipyretic and anti-phlogistic properties[9].

Clinical Considerations

Glyceryl guaiacolate is not commercially available in the United States in preparations suitable for intravenous administration. Investigators must therefore make up their own formulations[22, 28, 33, 39, 47]. The usual concentration administered is 5% glyceryl guaiacolate either in water, saline or 5% glucose solution. One investigator[47] has utilized combinations of glyceryl guaiacolate and pentothal sodium while others[22, 38] have used glyceryl guaiacolate in combination with thiamyl sodium or thiopental sodium. The barbiturate concentrations reported were approximately 0.2%.

In Europe commercial preparations of glyceryl guaiacolate are available. One preparation which has been utilized extensively in both human and animal subjects[1, 11, 20, 53, 54] is a 5% solution of glyceryl guaiacolate in 5% levulose (My 301[1]) marketed in 20 ml. ampoules. Other preparations available are, 20% glyceryl guaiacolate in 5% levulose (My 301

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[1]Brunnengraber, Lubeck, W. Germany.

forte[1]) supplied in 10 ml. ampoules 20% solution in 5% dextrose (G.G.G.[2]) in 500 ml. bottles, and 5% glyceryl guaiacolate in isostonic saline (Myocain A[3]) in 20 ml. ampoules[(54)]. Preparations in oral form are available but are not used as frequently as the intravenous preparations.

The early investigations on the use of glyceryl guaiacolate as a muscle relaxant were carried out using laboratory animals[(24, 25)]. Studies utilizing white mice indicated the ability of glyceryl guaiacolate to antagonize the toxic effects of strychnine. In rabbits doses of 100 mg./kg. were sufficient to produce a complete paralysis of 15-20 minutes duration. With doses of 200 mg./kg. respiration was not appreciable impaired in the rabbit.

The use of glyceryl guaiacolate in the small species of animal such as the dog and cat has been rather limited. The usual practice in cats is to premedicate the subject with atropine (.2-.4 ml./kg.) and induce the anesthetic state using

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[1]Brunnengraber, Lubeck, W. Germany.

[2]Grunau, Berlin, Germany.

[3]Holzinger, Vienna, Austria.

a barbiturate anesthetic. One author[6] then administered a 20% glyceryl guaiacolate solution intravenously, empirically using the degree of muscle relaxation and relief from pain as the indicators for the dosage necessary. Good clinical results were claimed for this method. Another author[45] administered 50% solutions of glyceryl guaiacolate by either intravenous, intraperitoneal or interosseus routes. The dose again was metered by the relaxation and analgesic state desired but in this case never exceeded 10 ml. of the 50% solution.

The effective dose for use in the dog has been stated to be 200 mg./kg.[17]. The lethal dose in the dog is approximately 700 mg./kg.

A 20% solution of glyceryl guaiacolate is suitable for use in pigs[21]. The administration of 5 ml./10 kg. bodyweight intravenously caused the animal to assume a recumbent position. A total dose of 8-9 ml./10 kg. was necessary to produce a completely relaxed state. The influence of glyceryl guaiacolate on heart rate, respiration and body temperature was found to be minimal in the pig and no adverse physiological alterations could be observed after administration.

The administration of glyceryl guaiacolate solution to

the small ruminant species has been carried out with few adverse effects[20]. A 5% solution of glyceryl guaiacolate in 5% levulose was utilized as the preparation of choice. The administration intravenously of 120-220 ml. of this solution was necessary to cause the animal to assume recumbency. The muscle relaxant effect was found to last 12-15 minutes. The author was able to extend this time by the administration of additional quantities of solution by a slow drip infusion technique. The solution was administered at the rate of 100 drops/minute. By this method the subjects were retained in the recumbent position for periods of one hour without adverse physiological changes, either during or after the administration period. No disturbances in rumen motility were observed. The only undesirable side effect observed was increased salivation during the relaxant period. The author recommended the use of the central acting analeptics to counteract the relaxant effect of glyceryl guaiacolate in the small ruminant species.

In the larger ruminant species, glyceryl guaiacolate has been used alone in the standard concentrations[52], in combination with tranquilizers and thiopental sodium[19] and in combination with pentothal sodium[47]. The same observations have been made in large ruminants as in the small-

er ruminant species. The standard ocular reflexes were of little use in determining the depth of anesthesia in the cow during glyceryl guaiacolate administration[47]. Instead, as the relaxation becomes more profound the eye moves in a counterclockwise rotation, first dorsally, then ventrally and finally returns to center position when the subject is under the full influence of the solution. During recovery the sequence of eye movements was reversed. The dosage rate necessary for recumbency to be assumed is stated to be 1 ml./lb. of body weight of a 5% solution or 4-5 g./50 kg. of body weight[54]. As in the small ruminants the action of glyceryl guaiacolate can be partially inhibited by the use of the central acting analeptics[54].

Glyceryl guaiacolate has been evaluated clinically as a muscle relaxant for use in human subjects. In Europe the drug has been used extensively in the disciplines of surgery and traumatology[1, 3, 7, 10, 11, 16, 29, 35, 50]. The preparation most often used was a 5% glyceryl guaiacolate solution in 5% levulose. The method of administration used by one author[10, 11] was to premedicate the patient with the usual dosages of morphine and atropine. In one series of trials[10], basal narcosis was initiated using barbiturates.

Muscle relaxation and deeper narcosis were achieved by the infusion of 20 ml. of the 5% solution of glyceryl guaiacolate. Good muscle relaxant effects were observed for 4-6 minutes using this method of administration.

In another series of administrations by the same author[11] basal narcosis was maintained using low levels of ether inhalation. An excellent degree of muscle relaxation was observed using this technique.

A study[35], in which inhalant anesthesia was used in conjunction with muscle relaxation by glyceryl guaiacolate infusion, revealed that a dosage rate of 80-120 ml. of the 5% solution to an adult human, markedly potentiated and lowered the dose of inhalant necessary.

Another author[7] commented on the apparent compatibility with, and potentiation of, ether - nitrous oxide narcosis by glyceryl guaiacolate.

When pentothal — nitrous oxide anesthesia was used to provide basal narcosis[1] the dose of 5% glyceryl guaiacolate necessary to produce good muscle relaxation ranged from 20-82 ml. In this study repeated doses were administered with no evidence of cumulative effect.

In one series of clinical trials[50] the commercially

available 20% solution of glyceryl guaiacolate in 5% levulose was evaluated. The muscle relaxant effect was found to be more rapid and longer acting than with the 5% solutions. No hemolysis or intravasal damage was observed. Four to six ml. of the 20% solution were required to produce muscle relaxation in the adult human. A total dose of 30 ml. was administered in this study, achieving 72 minutes of muscle relaxation with no adverse effects being observed clinically.

Infusion of glyceryl guaiacolate solutions to relieve the muscle spasms associated with tetanus[51] and other spastic conditions have been successful in human patients. In the case of tetanus therapy, total doses as high as 73.2 grams over an eight day period have been administered. A dose of 100 mg./lb./day has been administered with few side effects and definite relaxant properties being observed[8].

In a study to determine the ability of the muscle relaxant properties of glyceryl guaiacolate to eliminate post operative urinary retention, 10 ml. doses of a 5% solution were administered intravenously to 40 surgical patients[15]. The drug was effective in fifty-five percent of the patients.

In cases of novocaine shock, 10-20 ml. doses of a 20%

glyceryl guaiacolate solution given intravenously, were found to relieve or eliminate the muscle cramps associated with this condition[29].

The administration of glyceryl guaiacolate solutions has not been incriminated as causing habituation, addiction or allergic responses in human subjects[29].

In the horse glyceryl guaiacolate has been used in combination with many other preanesthetic and anesthetic agents. In Germany most investigators have premedicated the subject with a combination of an ataractic and an analgesic drug before the administration of the glyceryl guaiacolate solution[4, 42, 53]. This ataractic-analgesic combination has been termed a "lytic cocktail"[42]. The dose of 5% solutions of glyceryl guaiacolate required to cause complete relaxation is stated to be .5-1 ml./lb. administered rapidly intravenously[4, 53]. This dose results in a period of profound relaxation of 5-15 minutes duration. As dosage rates of this magnitude abolish pain reflexes previously present an analgesic effect has been concluded for glyceryl guaiacolate in the horse[43].

The use of glyceryl guaiacolate in horses was introduced in the United States in 1965[41]. It was described as being

preceded by the "lytic cocktail" combination in common use in Germany. The preparation described was a 5% solution of glyceryl guaiacolate and a .2% solution of barbiturate in 5% dextrose. American investigators[22, 38, 39, 40] have since completed extensive clinical trials. The "lytic cocktail" in use by some investigators[38, 39] consisted of atropine sulfate, promazine, and meperidine. Ten minutes after the administration of the lytic cocktail a 5% glyceryl guaiacolate and .2% thiopental-sodium solution was administered rapidly intravenously. The subject was described as falling gently after approximately .5 ml./lb. of this combination had been administered. A "blitz" or crash type induction was not observed. A total dose of 1 ml./lb. of body weight resulted in excellent relaxation. In a study[38] to determine what, if any, irritation would result from accidental perivascular injection of the glyceryl guaiacolate-thiopental mixture, 25-50 cc. doses were given subcutaneously. Only a mild inflammation of surrounding tissue resulted.

In a study in which a 5% glyceryl guaiacolate and .2% thiamylal sodium combination was evaluated[22] as an induction agent, this combination was found to be compatible with both

methoxyflurane (Metofane[1]) and halothane (Fluothane[2]). The lethal dose of this combination was found to be three times the therapeutic dose.

In studies comparing the effectiveness of glyceryl guaiacolate to that of succinylcholine chloride as induction agents for inhalation anesthesia[28, 46], glyceryl guaiacolate was shown to have far less depressant action on cardio-pulmonary function than did succinylcholine chloride. Succinylcholine chloride was extremely hypertensive while glyceryl guaiacolate exhibited a minimal physiological response[28]. Dosage rates of 160 mg./kg. of 5% solution of glyceryl guaiacolate caused recumbency while causing only minor depression of mean arterial blood pressure and arterial oxygen tension[46]. Eighty mg./kg. of glyceryl guaiacolate in combination with 3.5 mg./kg. of thiopental sodium was as effective in relaxant properties but caused more profound, though minor, changes in arterial blood pressure and oxygen tension.

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[1]Pitman-Moore Inc., Fort Washington, Pa.

[2]Ayerst Laboratories Inc., New York, New York.

Solutions of glyceryl guaiacolate have been shown to be effective in the treatment of tetanus in the horse[17]. One hundred mg./kg. doses of glyceryl guaiacolate administered as needed through the course of treatment relieved the muscle spasms associated with tetanus. Glyceryl guaiacolate was shown to have a cumulative effect when used in this manner.

MATERIALS AND METHODS

Laboratory Animals

Thirty horses of various breeds were used in the investigation. The horses were selected randomly from those presented to the Veterinary Clinic at Iowa State University for surgical procedures requiring general anesthesia. The horses were characterized as to breed, sex, age, and weight, and this information was recorded. The weight of each horse was obtained by estimation. The medical histories of the horses were variable and were not recorded.

Glyceryl Guaiacolate Solution

The solution evaluated in the study was a glyceryl guaiacolate-thiamylal sodium combination prepared by dissolving fifty grams of sterile glyceryl guaiacolate powder (Gecolate[1]) and two grams of thiamylal sodium (Surital[2]) in one liter of sterile water. It was necessary to warm the preparation to facilitate the formation of the

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[1]Summit Hill Labs, Summit, New Jersey.

[2]Parke Davis and Co., Detroit, Michigan.

solution. A warm water bath was utilized for this purpose. The glyceryl guaiacolate-thiamylal sodium mixture was prepared immediately prior to each administration, so that fresh solutions were administered in every instance.

Sampling Technique

A technique was devised to obtain anaerobically drawn arterial blood samples for the blood gas determinations. The carotid artery was chosen as the most accessible site when the subject was either standing or recumbent. The jugular vein was raised and its dorsal border was marked as the dorsal landmark at which the needle puncture would be made. At this landmark, in the ventral one-third of the jugular furrow, (Figure 1), a sterile twenty gauge, one and one-half inch needle was inserted through the skin. The needle was directed medially and ventrally, medial to the jugular vein, until the pulsations of the carotid artery could be felt with the tip of the needle. The needle was then inserted into the lumen of the carotid artery (Figure 2).

The sample was collected in a two and one-half milliliter disposable syringe. The syringe was wetted with heparin

sodium (Heparin[1]) prior to its use and all air was evacuated leaving a drop of heparin sodium in the tip of the syringe to maintain anaerobic conditions. Immediately after the syringe was filled and withdrawn from the subject, the tip of the needle was closed by insertion into a rubber stopper and the sample was placed in an ice bath (Figure 3). The sample was then transported to the clinical pathology laboratory as soon as possible and blood gas and blood pH determination were done immediately.

Formation of a hematoma in the carotid sheath or surrounding structures was prevented by either the application of a compression bandage or finger pressure over the area of the carotid puncture (Figure 4).

The venous blood samples required for the remainder of the hematological parameters investigated were collected by jugular puncture into commercially available, ethylene diamine tetracetic acid vacum tubes (Vacutainer[2]).

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[1] 1000 units/ml. -- Upjohn Co., Kalamazoo, Michigan.

[2] Becton-Dickinson, Columbus, Nebraska.

Administration and Sampling Procedure

An arterial blood sample and a venous blood sample were collected at four time intervals on each subject. The first set of samples was taken while the horse was standing quietly in a box stall and prior to the administration of any pre-anesthetic or anesthetic preparation. This sample was the "normal" control for purposes of statistical analysis.

The subject was then administered .5 mg./kg. of promazine (Sparine[1]) to induce a state of ataraxia. A period of time ranging from ten to thirty minutes was allowed to pass so that the full effect of the promazine developed. A second set of samples was then collected with the horse still in a quiet stall. These were the post-tranquilization samples.

The horse was then led to a padded area suitable for casting and the intravenous infusion of the glyceryl guaiacolate-thiamylal sodium solution was begun. The solution was administered as rapidly as possible through a twelve gauge needle (Figure 5). The dosage necessary to cause the horse to assume a recumbent position was noted and recorded.

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[1]Wyeth Laboratories Inc., Philadelphia, Pennsylvania.

The post-infusion blood samples were collected as soon as possible after the horse was recumbent.

In one group of 4 horses the infusion was stopped at this time and a mouth speculum was applied. An endotracheal tube of appropriate size was inserted and connected to a closed circuit circle system anesthetic machine (I Fraser Sweatman VML[1]). The presence or absence of laryngeal and pharyngeal reflexes and the ease with which the endotracheal tube could be passed were noted and recorded. The horse was then subjected to a period of general anesthesia with halothane during which the surgical procedure required was performed.

In another group of 26 horses the infusion of the glyceryl guaiacolate-thiamylal sodium solution was continued until a state of surgical anesthesia was attained. The dosage of the solution necessary to achieve a state of surgical anesthesia was noted and recorded. Numerous surgical and diagnostic procedures were performed on this group of horses. Surgical anesthesia was maintained for

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[1]Fraser Sweatman Inc., Lancaster, New York.

varying periods of time in this group of horses by a slow infusion technique in which monitored doses of the glyceryl guaiacolate-thiamylal sodium mixture were administered as needed to maintain an absence of pain responses. The amount of time surgical anesthesia was maintained and the total dose of solution necessary to do so were noted and recorded.

The horses in both groups were allowed to recover from the effects of either the glyceryl guaiacolate-thiamylal sodium mixture or the halothane, and the time required for the animal to regain its feet was noted and recorded.

The fourth set of blood samples collected were the recovery samples. The thirty horses investigated were divided into two groups for the purpose of the collection of the recovery samples. In the first group of 23 horses the recovery blood samples were drawn immediately after the subject had regained its feet and before it was returned to its stall. In the second group of 7 horses the subject was returned to its stall upon regaining its feet and the recovery samples were collected twenty four hours later.

Clinical Pathological Determinations

The four arterial blood samples collected from each subject were subjected to oxygen partial pressure, carbon

dioxide partial pressure and blood pH determination in the clinical pathology laboratory at Iowa State University Veterinary Clinic. The instrument used was a micro-sample blood gas analyzer and glass pH electrode apparatus (Model 113 - S2[1]) (Figure 6). The blood gas partial pressures were corrected for the local barometric pressure factor and recorded using m.m. Hg. as the unit of measure. The blood pH values were read directly from the apparatus and recorded.

The venous samples were divided into appropriate quantities and various hematological parameters were determined. Blood glucose determination was carried out utilizing a modified glucose oxidase reaction and colorimetric methods (Unimeter 250[2]). The data was recorded in milligrams percent.

Hemoglobin determination was done utilizing the cyanmethemoglobin method and spectrophotometric apparatus (Coleman Jr. Model 620 Spectrophotometer[3]). Values thus

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[1]Instrumentation Laboratories Inc., Lexington, Massachusetts.

[2]Biodynamics Inc., Indianapolis, Indiana.

[3]Coleman Instrument Corp., Maywood, Illinois.

obtained were recorded in grams percent.

The packed cell volume of each sample was determined by the microhematocrit method (International micro-capillary Centrituge and Reader[1]) and was recorded in units of percent.

Erythrocyte counts were done using isotonic saline as the diluent in a 1:50,000 dilution. The counts were made using an electronic particle counter (Coulter Counter[2]). The data obtained was recorded in cells/m.m.[3].

Leukocyte counts were done using isotonic saline in a 1:500 dilution. The erythrocytes were lysed using a commercially available lysing agent (Zap-Isoton[3]). Cell counts were done by means of the electronic particle counter and recorded in cells/m.m.[3].

Blood smears were made, stained using Wright's stain, and differential leukocyte counts were done. Differential counts were recorded in units of percent.

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[1]International Equipment Co., Boston, Massachusetts.

[2]Coulter Electronics Inc., Hialeah, Florida.

[3]Coulter Electronics Inc., Hialeah, Florida.

Statistical Analysis

The data was collected, grouped and coded for computer analysis. Descriptive analysis and correlation analysis using the correlated T test were done by the Iowa State University Computation Center.

RESULTS

Clinical Evaluation

The physical properties of the glyceryl guaiacolate-thiamylal sodium formulation prepared for this study were found to be adequate. The solution was easily prepared and remained stable for a period of approximately forty eight hours without flocculation occurring. Although solutions used in this investigation were prepared fresh before each administration, solutions up to forty eight hours old have been utilized without special preparation or adverse consequences.

Rapid administration of the glyceryl guaiacolate-thiamylal sodium solution proved to be a necessary prerequisite for a smooth and uneventful induction phase. It was found the faster the infusion could be carried out the more rapid was the onset of the muscle relaxation and the less apprehension was observed in the subject. In those few administrations in which difficulty was encountered in the infusion process, due to improper jugular puncture or intractability of the patient, the subject seemed to be more aware of the onset of the muscular relaxation and was more inclined to resist the restraint applied. The induction

phase, even when difficulties were encountered, was routinely smooth and uneventful. The action of the solution was so rapid and insidious that even the most intractable horses exhibited a minimum of apprehension.

The mean dosage rate necessary to produce a degree of muscular relaxation resulting in sternal recumbency was 65 mg./kg. of glyceryl guaiacolate and 2.6 mg./kg. of thiamylal sodium (1.3 ml./kg. of a 5% glyceryl guaiacolate-.2% thiamylal sodium solution). At this dosage rate the pharmacological effects were profound enough to permit manipulation of the extremities and repositioning of the animal. None of the thirty horses in this study exhibited signs of respiratory distress or apnea during the induction phase. The horses did not object to the carotid puncture which was necessary to collect the arterial samples although pain reflexes were still present at this dosage rate. In those horses which were to be subjected to general anesthesia with a closed circuit circle system halothane unit this dose resulted in sufficient depression of the pharyngeal and laryngeal reflexes to allow endotracheal intubation. The duration of the anesthetic state was sufficient to allow a smooth transition to the halothane unit and resulted in a short and uneventful halothane induction. Respiration

continued when the subject was connected to the halothane circuit so that voluntary apnea was not a problem.

In those 23 horses in which the glyceryl guaiacolate-thiamylal sodium solution was used as the only anesthetic a mean dosage rate of 115 mg./kg. glyceryl guaiacolate and 4.6 mg./kg. of thiamylal sodium (2.3 ml./kg. of the 5% glyceryl guaiacolate-.2% thiamylal sodium solution) produced a state of surgical anesthesia of 25 minutes duration. The anesthetic state produced was characterized by profound muscular relaxation, immobility, and absence of previously present pain reflexes. The ocular reflexes historically utilized as indicators of anesthetic depth were of limited value. Nystagmus was usually not observed during the induction or anesthetic periods. Palpebral and corneal reflexes were routinely present at anesthetic dosage rates but were of limited value in evaluating anesthetic plane. Cardiac function was uneffected. Cardiac rates while under the influence of glyceryl guaiacolate-thiamylal sodium anesthesia were in the range of 40-60 beats/min. No pathological abnormalities were observed in those horses which were monitored electrocardiographically. Respiratory function was altered in that during the period of surgical

anesthesia, respiration was almost entirely diaphragmatic. Respiratory rates ranged from 4-12 breaths/min. No attempt was made to monitor respiratory volume. None of the horses in which the glyceryl guaiacolate-thiamylal sodium solution was used as the only anesthetic agent exhibited apnea.

The longest period of time that a horse was maintained in a state of anesthesia using glyceryl guaiacolate-thiamylal sodium solution as the only anesthetic agent was ninety minutes. The total dose required for this horse was 222 mg./kg. of glyceryl guaiacolate and 9 mg./kg. of thiamylal sodium (4.4 ml./kg. of a 5% glyceryl guaiacolate-.2% thiamylal sodium solution) administered by a slow infusion monitored dose technique. Cardiac and respiratory function remained uneffected during the anesthetic procedure.

The period required for recovery in those horses in which general anesthesia was maintained with halothane averaged 39 minutes. Recovery was smooth and characteristic of a typical recovery from inhalation anesthesia. These horses did not appear to have any residual pharmacological effect from the glyceryl guaiacolate-thiamylal sodium infusion.

In those horses in which glyceryl guaiacolate-thiamylal sodium solution was used as the only anesthetic agent recovery was routinely smooth. The mean time required for recovery in

this group of horses was 25 minutes. The horses remained quiet during the recovery period with only minor evidence of apprehension observed. The pharmacological effects of the infusion appeared to disappear from the higher central nervous centers first. Muscular function returned first to the head and forequarters. The laryngeal and pharyngeal reflexes became functional early in the recovery period. The hindquarters were the last area to regain muscular tone. If left alone in a quiet recovery area the horses assumed sternal recumbency and voluntarily remained in that position for a few minutes. They then stood with very little difficulty. Some muscular weakness and ataxia were exhibited just after standing.

Hematological Evaluation

The mean values for the blood cell determinations are listed in Table 1. The values obtained by analysis of the control sample were all within the published normal range for blood cell determination of the horse. Administration of the ataractic had no appreciable effect on these values. Infusion of the glyceryl guaiacolate-thiamylal sodium solution had no significant effect on the mean blood cell counts of the thirty horses investigated. The recovery sample did indicate

an increase in the mean number of leukocytes and a corresponding neutrophilia and lymphopenia as shown by the differential leukocyte count. This leukocytosis was more apparent in those horses in which 24 hours were allowed to elapse before the recovery sample was collected (Table 4).

The mean value for blood glucose level of the control samples was 101.1 mg.% (Table 2). Administration of the ataractic had no appreciable effect on blood glucose level. Infusion of the glyceryl guaiacolate-thiamylal sodium solution had no predictable effect on the blood glucose level of the horses in this study. The mean value for blood glucose of the post infusion sample was 103.3 mg.%. The mean value for blood glucose of the recovery sample was 108.5 mg.%. Although this was slightly higher than the other three samples it is not a significant increase in circulating blood glucose.

The mean values of the blood gas determinations of all subjects are listed in Table 3. The blood pH did not change significantly with either the administration of the ataractic or the glyceryl guaiacolate-thiamylal sodium solution. The mean value for partial pressure of oxygen of the control sample was 94.3 mm. Hg. (Table 3). Administration of the ataractic resulted in a slight decrease in mean partial

pressure of oxygen. Infusion of glyceryl guaiacolate-thiamylal sodium solution resulted in a further decrease so that the mean value of oxygen partial pressure was 84.3 mm. Hg. for the post infusion sample. The partial pressure of oxygen increased during the recovery phase so that the mean value for the recovery sample was 88.5 mm. Hg. Neither the administration of the ataractic or the glyceryl guaiacolate-thiamylal sodium solution had an effect on the carbon dioxide partial pressure. The mean value of carbon dioxide partial pressure was approximately 40 mm. Hg. in the post tranquilization, and post infusion sample as well as in the control and recovery sample.

The effect of glyceryl guaiacolate-thiamylal sodium infusion on blood gas partial pressure is even more apparent if a comparison is made between those horses which received no extrinsic oxygen source and those which received oxygen via a closed circuit circle system anesthetic machine. The mean value for oxygen partial pressure of the post infusion sample in those horses receiving no extrinsic oxygen was 72.4 mm. Hg. (Table 6). The mean value for partial pressure of oxygen of the post infusion sample in those horses which were connected to the anesthetic apparatus immediately on assuming sternal

recumbency was 162.8 mm. Hg. In both of these groups of horses the recovery sample indicated a return to the normal control value of oxygen partial pressure when the subject had recovered from the effects of the anesthetic agent.

In those horses which received extrinsic oxygen via the anesthetic apparatus there was a significant increase in partial pressure of carbon dioxide in the post infusion sample. The mean value for carbon dioxide partial pressure in this group of horses was 45.9 mm. Hg. There was a corresponding decrease in blood pH in this group of horses (Table 6). The collection of the recovery sample twenty four hours after clinical recovery had no predictable effect on the mean values of partial pressures of blood gas or blood pH (Table 5).

DISCUSSION

Clinical Evaluation

The intravenous infusion of 5% glyceryl guaiacolate-.2% thiamylal sodium solution proved to be an effective and safe method for the induction and maintenance of anesthesia in the horse.

The solution as formulated for this study had adequate physical properties. The glyceryl guaiacolate and thiamylal sodium were readily soluble at the concentrations utilized. The use of a warm water bath was necessary to attain the critical temperature for the preparation to go into solution but this was not a major problem. A shelf life of approximately 48 hours was observed after which time flocculation occurred. Although it was possible, by warming, to redissolve the formulation it was thought that some decrease in efficacy resulted and thus it is recommended that only fresh solutions be used.

The concentration of glyceryl guaiacolate-thiamylal sodium solution evaluated in this study proved to be an excellent formulation for clinical use. The inclusion of an ultra-short acting barbiturate in the formulation is recommended. There appears to be a synergistic effect

between the glyceryl guaiacolate and the barbiturate which reduces the dosage of each required to attain a desired depth of anesthesia. Concentrations and combinations other than the one investigated have been recommended by other authors[38, 40, 41] for use in the horse. The 5% glyceryl guaiacolate-.2% thiamylal sodium aqueous solution was excellent in that it was highly efficacious, did not cause intravenous hemolysis or other toxic side effects, and did not require the infusion of awkwardly large amounts of solution.

Rapid infusion of the solution was found to be necessary for a smooth induction. If the infusion rate was sufficiently slow the subject became very ataxic and apprehensive before the muscular relaxation became sufficiently profound to cause sternal recumbency. An adequate rate of infusion could be attained through the use of a 12 gauge intravenous needle. The rapid metabolism and short plasma half-life of glyceryl guaiacolate are probably responsible for this phenomenon. Rapid infusion of the solution is necessary to achieve plasma levels of a sufficient magnitude to cause the desired pharmacological effect before metabolic detoxification can reduce plasma concentration to an ineffective level.

Induction of anesthesia was routinely smooth, even when difficulties with the infusion were encountered. The rapid onset of action and insidious nature of the solution were such that even the most intractable subjects could be cast with a minimum of danger to the horse or the operator. Before the animal was aware of the loss of function, the muscular relaxation was so profound that only ineffectual resistance could be manifested. The blitz or crash type induction observed with the use of the peripheral neuro-muscular agents or barbiturate anesthetics alone was not observed. The subject appeared to succumb to a profound muscular relaxation and sank gently into sternal recumbency. A minimum of physical restraint was necessary so that three operators, one administering the infusion, one supporting the head and one supporting the hind quarters, could cast most subjects. If extremely gentle handling was necessary, as in the case of casting an animal with a fracture of a limb or a pregnant female, then physical support was applied and the animal was lowered to the floor of the casting area after the maximum pharmacologic effects had been achieved.

The 5% glyceryl guaiacolate-.2% thiamylal sodium solution was administered to several pregnant females in various stages of pregnancy with no adverse effects being

observed. The observation lends support to those investigations in which it has been stated that glyceryl guaiacolate does not pass the placental barrier[20, 54].

This could be an indication for the use of glyceryl guaiacolate solutions for the induction and maintenance of anesthesia for cesarean section.

Endotracheal intubation is recognized as an essential technique for the maintenance of a patent airway when inhalation anesthetics are administered to the horse. In this respect glyceryl guaiacolate-thiamylal sodium infusion is an excellent induction method for use with inhalant anesthetics, as dosages which cause sternal recumbency to be assumed also depress pharyngeal and laryngeal reflexes sufficiently to allow endotracheal intubation.

Glyceryl guaiacolate-thiamylal sodium solution was clinically compatible with halothane. The duration of action of the glyceryl guaiacolate-thiamylal sodium solution was sufficient to allow a smooth transition to the closed circuit circle system halothane unit. None of the horses in which anesthesia was induced using glyceryl guaiacolate-thiamylal sodium infusion exhibited apnea so that the transition to the halothane unit was very smooth. The rapid metabolic detoxification of the glyceryl guaiacolate-thiamylal sodium

solution is an excellent feature in that most procedures requiring general anesthesia with halothane are of sufficient length so that the plasma concentration of glyceryl guaiacolate has decreased to ineffective levels during the time the subject is under the influence of halothane. The horse is therefore able to recover from the inhalant anesthesia without residual action by the glyceryl guaiacolate-thiamylal sodium solution.

The use of glyceryl guaiacolate-thiamylal sodium infusion as the exclusive anesthetic agent in procedures requiring a short period of surgical anesthesia is recommended. The anesthetic state produced by the infusion of glyceryl guaiacolate-thiamylal sodium solution is characterized by a profound muscular relaxation and analgesia. The state of immobility and muscular relaxation allows repositioning and manipulation of the horses legs for diagnostic procedures such as radiographic examination. The muscular relaxation necessary to allow closed reduction and cast application to leg fractures in the horse is easily achieved by the infusion of a glyceryl guaiacolate-thiamylal sodium solution. As very little apprehension is exhibited by the subject during the recovery phase there is little danger of damage

to the plaster cast or disruption of the fractured bone ends due to panic or struggling.

The degree of analgesia produced by glyceryl guaiacolate-thiamylal sodium infusion is not as profound as can be produced by other anesthetic agents. It is profound enough, however, to allow surgical procedures which do not require an extreme depth of anesthesia but do require a marked muscular relaxation. The analgesic properties coupled with the profound muscular relaxation make glyceryl guaiacolate-thiamylal sodium infusion an excellent agent for use in such procedures as castration, cryptorchid castration, and umbilical herniorraphy.

During the course of the investigation glyceryl guaiacolate-thiamylal sodium infusion was used as the only anesthetic agent in many other short procedures such as posterior digital neurectomy, ventriculotomy, excision of benign tumors and repair of lacerations. In those procedures which required a longer period of anesthesia glyceryl guaiacolate-thiamylal sodium solution was administered by a slow infusion monitored dose technique over an extended period of time. Metered quantities were administered as needed to maintain a state of surgical anesthesia characterized by profound muscular relaxation, absence of peripheral pain

response, and intact ocular reflexes.

The classical ocular signs of anesthetic depth were of limited value as pain responses were sometimes present when nystagmus was absent and the palpebral reflex was depressed. It was more reliable to gauge the dosage rate necessary based on the degree of muscular relaxation, absence of pain response and character and rate of respiration. Respiration was altered in that it was almost entirely diaphragmatic during the period of surgical anesthesia. This can be explained by the predilection of glyceryl guaiacolate to abolish nerve transmission in internuncial neurons supplying peripheral musculature at a much lower dosage rate than is necessary to obtund function of neurons supplying the diaphragmatic musculature.

Respiratory rate and volume were not altered sufficiently to cause adverse clinical manifestations.

The infusion of glyceryl guaiacolate-thiamylal sodium solution by the monitored dose technique prolongs the period of surgical anesthesia much longer than the dosage required would be assumed to do.

This phenomenon can be explained by the cumulative effect of both glyceryl guaiacolate and thiamylal sodium. The deposition of thiamylal sodium in body lipids and its

subsequent slow release is a well known phenomenon. The mechanism of action of the cumulative effect of glyceryl guaiacolate is not known but is stated to occur[17].

In those horses which were administered glyceryl guaiacolate-thiamylal sodium solution by the monitored dose technique, doubling the total dose more than quadrupled the total anesthetic time. The longer the period of anesthesia maintained, the longer was the time required for recovery. This may be a function of the thiamylal sodium component of the solution rather than the glyceryl guaiacolate but could also support the claims in the literature of a cumulative effect for glyceryl guaiacolate.

In the course of one administration of the glyceryl guaiacolate-thiamylal sodium solution a small quantity was inadvertently injected perivascularly. This resulted in a local soft tissue reaction characterized by heat, swelling, and edema. Treatment with intravenous phenylbutazone (Butazolidine[1]) and hydrotherapy was successful in alleviating the local tissue reaction. In one investigation[38]

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[1]Jensen-Salsbery Laboratories, Kansas City, Missouri.

in which 25-50 ml. doses of glyceryl guaiacolate-thiopental sodium solution were injected subcutaneously only a mild inflammation of surrounding tissue resulted.

The local reaction resulting from accidental perivascular injection may be due to the barbiturate component of the solution. It should not be assumed, however, that perivascular injection of glyceryl guaiacolate-thiamylal sodium solutions are of little consequence. Glyceryl guaiacolate in the proper concentration may by itself be capable of producing a local tissue reaction resulting in edema and the formation of a sterile abscess. Care should be taken that glyceryl guaiacolate-thiamylal sodium solutions not be accidentally administered perivascularly.

Hematological Evaluation

The infusion of a 5% glyceryl-guaiacolate-.2% thiamylal sodium solution intravenously was shown to have no acute adverse effect on the blood cell components of the horses investigated. There was no significant alteration in hemoglobin, erythrocyte count or packed cell volume, nor was there a consistent degree of hemolysis observed grossly in the post infusion samples. The use of a 5% concentration of glyceryl guaiacolate would appear to alleviate the

intravenous hemolysis which occurs with the intravenous administration of more concentrated glyceryl guaiacolate solutions.

The leukocytosis that was observed in the recovery sample was not statistically significant although it was a constant observation. The neutrophilia and lymphopenia observed were significant ($P < .05$). When the recovery sample was collected 24 hours after clinical recovery the leukocytosis was more pronounced than if the recovery sample was collected as soon as the subject assumed a standing position. This phenomenon was probably the result of the subject's normal response to the stress of the anesthetic and surgical procedure performed.

Infusion of the glyceryl guaiacolate-thiamylal sodium solution had no significant effect on circulating blood glucose. The inclusion of glucose in the solution to be administered would therefore not be necessary as a means of maintaining blood glucose levels on the anesthetic subjects. The inclusion of 5% glucose in the formulation has been advocated as a method of decreasing the incidence of intravenous hemolysis resulting from the intravenous administration of glyceryl guaiacolate solutions. The

results of this study indicate that the inclusion of glucose in the formulation is not necessary as long as solutions of 5% glyceryl guaiacolate or less are administered. If concentrations greater than 5% glyceryl guaiacolate are administered the inclusion of 5% glucose in the formulation is recommended.

The decrease in oxygen partial pressure observed immediately after administration of the glyceryl guaiacolate-thiamylal sodium solution was a consistent and significant ($P < .10$) observation. This phenomenon was the result of the decreased respiratory capability of the subject. The glyceryl guaiacolate thiamylal sodium solution effectively blocked transmission in internuncial neurons responsible for innervation of the intercostal and abdominal musculature. Paralysis of these muscles effectively decreased the respiratory capability of the subject. The fact that the animals were in a laterally recumbent position when the post infusion samples were collected may have contributed to this decrease in respiratory function. This is doubtful, however, as the post infusion samples were collected within a very few minutes of the time lateral recumbency was assumed, limiting the effect of the venous congestion, gravitational

forces, and the venous to arterial shunt that occurs in the dependent lung when anesthetized horses are maintained in lateral recumbency for long periods of time.

Though the decrease in arterial partial pressure of oxygen was consistent and significant it was not sufficiently high to cause manifestation of clinical signs of hypoxia. Respiratory rate and volume remained constant throughout the anesthetic procedure though respiration was entirely diaphragmatic. The administration of oxygen via a closed circuit circle system anesthetic apparatus effectively increased the arterial oxygen partial pressure in horses anesthetized with glyceryl guaiacolate-thiamylal sodium solution. The use of glyceryl guaiacolate-thiamylal sodium infusion as an induction agent for general anesthesia with volatile anesthetics is highly recommended.

Infusion of glyceryl guaiacolate-thiamylal sodium solution had no significant effect on arterial partial pressure of carbon dioxide. The increase in carbon dioxide tension observed in the post infusion samples of those horses in which anesthesia was maintained using a closed circuit circle system anesthetic apparatus was the result of the inability of the carbon dioxide absorption apparatus to effectively remove the carbon dioxide from the expired air.

It is probable that no closed circuit anesthetic apparatus can be designed which is totally effective in the removal of carbon dioxide from the expired air. In accordance with other authors it is recommended that the carbon dioxide absorption apparatus not be depended upon and that whenever possible a semiclosed system be utilized.

SUMMARY AND CONCLUSIONS

Thirty horses were administered a 5% glyceryl guaiacolate -.2% thiamylal sodium solution intravenously. Arterial and venous blood samples were collected prior to administration, immediately after administration, and upon full recovery from the anesthesia resulting from this infusion. Hemoglobin, packed cell volume, erythrocyte count, leukocyte count, differential leukocyte count and blood glucose determinations were performed on the venous blood samples. The arterial samples were subjected to blood gas partial pressure and pH determination. The values obtained were analyzed and the effect of the infusion was determined.

The infusion of the glyceryl guaiacolate-thiamylal sodium solution had no significant effect on hemoglobin, packed cell volume, erythrocyte count, leukocyte count, differential leukocyte count or blood glucose value in the horses investigated.

The glyceryl guaiacolate-thiamylal sodium infusion depressed the arterial partial pressure of oxygen due to its ability to block transmission in internuncial neurons supplying the intercostal and abdominal musculature. This depression was statistically significant but resulted in no

clinical manifestation of hypoxia in the horses studied. The glyceryl guaiacolate-thiamylal sodium solution exerted no influence on arterial partial pressure of carbon dioxide or blood pH. The depression of arterial partial pressure of oxygen was effectively counteracted by the administration of oxygen via a closed circuit circle system anesthetic apparatus.

Infusion of the glyceryl guaiacolate-thiamylal sodium solution was evaluated clinically as a method of general anesthesia in the horse. Infusion of a 5% glyceryl guaiacolate-.2% thiamylal sodium solution intravenously at a dosage rate of 2.3 ml./kg. was found to produce 15-25 minutes of surgical anesthesia characterized by a smooth induction, a good degree of analgesia, profound muscular relaxation and a smooth and uneventful recovery. Infusion of additional amounts of the glyceryl guaiacolate-thiamylal sodium solution by a monitored dose technique was found to effectively prolong the period of surgical anesthesia. Using glyceryl guaiacolate-thiamylal sodium solution as the only anesthetic agent such surgical procedures as umbilical herniorraphy, cryptorchid castration and repair of lacerations were performed.

The use of a 5% glyceryl guaiacolate-.2% thiamylal

sodium solution as an agent for induction of anesthesia maintained with inhalant anesthetics was evaluated. Infusion of the glyceryl guaiacolate-thiamylal solution produced a smooth induction, abolished the laryngeal and pharyneal reflexes allowing endotracheal intubation, and was compatible with halothane.

Glyceryl guaiacolate was shown to be a valuable addition to the armamentarium of drugs used in anesthesia of the horse.

LITERATURE CITED

1. Atanasov, A. Application of the muscle relaxant guaiacol glycerol ether in abdominal surgery. Translated title. Kirurgiia. 2: 328-333. 1958. (English Summary).

2. Badura, R., Kwiatkowski, T., Modrakowski, A., Osinski, B. and Zaleska, H. Haematuria in cows after use of guaiacol glyceryl ether (Translated title). Med. Vet. 20: 489-490. 1964. (English Summary).

3. Beghe, R., Luccardi, V., and Alonzo, F. Guaiacol glycerin ether in orthopedic surgery and traumatology, (Translated title). Policlinico Sez. Prat. 64: 1157-1159. 1957.

4. Berge, Ewald and Westhues, Melchior. Veterinary Operative Surgery 1st ed. Baltimore Md., Williams and Wilkins Co.

5. Berger, F. M., Hubbard, C. V. and Ludwig, B. J. Hemolytic action of water soluble compounds related to mephenesin. Proc. Soc. Exp. Biol. Med. 82: 532-535. 1953.

6. Bolz, W. and Loeffler, K. About cat narcosis with guaiacol glycerol ether. (Translated title). Kleintier-Prax. 11: 99-105. 1966. (English Summary).

7. Caramia, M. Use in surgery of glyceryl guaiacolic ether as a muscle relaxant, (Translated title). Minerva Anest. 24: 221-223. 1958.

8. Carter, C. H. Muscle relaxant properties of glyceryl guaiacolate. Western Med. 7: 206-211. Aug. 1966.

9. Chemnitius, K. H., Boltze, K. H. and Hofmann, H. Effect of guaiacol glycerin ether in combination with pyrazoline in animal experiments (Translated title). Pharmazie 12: 391-396. 1957.

10. Crone-Munzebrock, A. Glyceryl guaiacolate as an adjunct to anesthesia in surgery (Translated title). Zentralbl. F. Chir. 79: 171-172. 1954.

11. Crone-Munzebrock, A. and Wyeth, K. Glyceryl guaiacolate, a valuable adjunct to anesthesia in surgery (Translated title). Chirurg. 24: 263-266. 1953.

12. Davis, Lloyd E. and Wolff, William A. Pharmacokinetics and metabolism of glyceryl guaiacolate in ponies. Am. J. Vet. Res. 31: 469-473. 1970.

13. Deiwick, J. and Graudenz, E. Clinical experiences with the new muscle relaxant guaiacol glycerol ether (Translated title). Deut. Gesundwes. 12: 980-984. 1957.

14. Eberly, V. E., Gillespie, J. R., Tyler, W. S. and Fowler, M. E. Cardivascular values in the horse during halothane anesthesia. Am. J. Vet. Res. 29: 305-313. 1968.

15. Fioccardi, R. Postoperative urinary retention. Clinical research on the action of muscle relaxants (Translated title). Archivio per le Scienze Mediche 120: 58-59. July 1965.

16. Forgacs, I. Clinical experiences with the muscle relaxant guaiacol glycerol ether (Translated title). Orv. Hetil. 99: 59-60. 1958.

17. Fritsch, R. Suitability of guaiacol glyceryl ether for casting horses and cattle and for prolonged relaxation in tetanus therapy (Translated title). Zentralbl. Vet. Med. 12A: 278-314, 315-354 and 415-446. 1965.

18. Gabel, A. A., Heath, R. B., Ross, J. N., Smith, C. R. Hypoxia - Its prevention in inhalation anesthesia in horses. Proc. A.A.E.P. 12: 179-196. 1966.

19. Gakhniyan, P. and Drummer, A. Action of guaiacol glyceryl ether in combination with other drugs: tranquilizer, muscle relaxant and narcotics. Translated title. Nauch. Trud. Vissh. Vet. Med. Inst. Sofia. 12: 180-190. 1964.

20. Gehring, W. Experiments with glyceryl guaiacolate on small ruminants (Translated Title). Berl. Munch. Tierarztl. Wchschr. 70: 384-386. 1957.

21. Gehring, W. and Lukang, A. Guaiacol glyceryl ether as a muscle relaxant for pigs (Translated title). Deut. Tierarztl. Wchschr. 69: 280-282. 1962.

22. Gertsen, K. E. and Tillotson, P. J. Clinical use of glyceryl guaiacolate in the horse. Vet. Med. and Small Anim. Clinic. 63: 1062. 1968.

23. Gillespie, J. R., Tyler, W. S., and Hall, L. S. Cardiopulmonary dysfunction in anesthetized, laterally recumbent horses. Am. J. Vet. Res. 30: 61-72. 1969.

24. Ginzel, K. H. Comparative investigation of an anti-convulsive active glycerin ether (Translated title). Arch. Exper. Path. U. Pharmakol. 212: 331-338. 1954.

25. Ginzel, K. H., Leupold-Lowenthal, H. and Weis, C. Experiments on animals with myocain (Translated title). Wien. Med. Wchschr. 99: 229-300. 1949.

26. Hafner, H. and Wageneder, F. M. Signs and symptoms during intravenous administration of the muscle relaxant reorganin without premedication (Translated title). Wien. Med. Wchschr. 114: 523-524. 1964.

27. Hall, L. W. Halothane anesthesia in horses. Proc. Europeon Soc. Vet. Surg. Cong. 8: 87. Abstracted in Journal of A.V.M.A. 156: 465. 1970.

28. Heath, R. B. and Gabel, A. A. Evaluation of thiamylal sodium, succinylcholine and glyceryl guaiacolate prior to inhalation anesthesia in horses. Jour. of A.V.M.A. 157: 1486-1494. 1970.

29. Hodum, H. Investigations with the muscle relaxant reorganin (Translated title). Wien. Wochschr. 110: 669-670. 1960.

30. Kraft, H. ECG and narcosis in the horse (Translated title). Berl. u. Munch. Tierarzt. Wsch. 75: 165-168. 1962.

31. Kuna, S. and Pircio, A. W. Process for analgesia and muscle relaxation by glycerol guaiacolate and salicylamide. U.S. Patent 3,140,228. July 7, 1964.

32. Littlejohn, A. Acid-base and blood gas studies in horses II. Tracheal end-tidal and arterial blood gas tensions in horses. Res. Vet. Sci. 10: 263-266. 1969.

33. Littlejohn, A. and Mitchell, B. Acid-base and blood gas studies in horses. I. A comparison of capillary and arterial blood samples for the extimation of acid-base values in horses. Res. Vet. Sci. 10: 260-262. 1969.

34. Morgan, A. M., Truitt, E. B., Jr., and Little, J. M. Plasma levels of mephenesin, mephene carbamate, guaiacol glyceryl ether and methocarbamol after oral and intravenous administration in the dog. Jour. Amer. Pharm. Assoc. 46: 374-377. 1957.

35. Mostert, J. W. A centrally acting relaxant in anaesthesia (Guaiacol glycerol ether). S. African Med. Jour. 37: 1281-1284. 1963.

36. Mostert, J. W. and Metz, J. Observations on the haemolytic activity of guaiacol glycerol ether. Brit. Jour. Anaesth. 35: 461-464. 1963.

37. Panday, J. Serial changes in arterial oxygen tension during anaesthesia with spontaneous respitation. Brit. Jour. Anaesth. 38: 662. 1966.

38. Roberts. W. D. The role of glyceryl guaiacolate in a balanced equine anesthetic. Veterinary Medicine/Small Animal Clinician 63: 157-160. Feb. 1968.

39. Roberts, W. D. The role of glyceryl guaiacolate in balanced equine anesthesia. Proc. A.A.E.P. 13: 171-178. 1967.

40. Roberts, W. D., Rosborough, J. P., Garner, H. E., Tillotson, P. J. Panel - glyceryl guaiacolate. Proc. A.A.E.P. 14: 297-307. 1968.

41. Schebitz, H. A method of intravenous anesthesia. Proc. A.A.E.P. 11: 325-328. 1965.

42. Schebitz and R. Tronicke. Equine sedation and narcosis (Translated title). Berl. Munch. Tierarztl. Wschr. 77. 5: 93-97. 1964.

43. Schmidt, V. and Johne-Liersch, S. Testing various types of anesthesia by continuous blood pressure measurement with special reference to anesthetic combinations with guaiacol glyceryl ether (Translated title). Mh. Vet. Med. 19: 41-48. 1964. (English summary).

44. Short, Charles E., Greenwald, William, and Bendick, Fred. Oxygen, carbon dioxide, and pH responses in arterial blood of dogs given analgesic, neuroleptanalgesic, and ataractic agents. Jour. of A.V.M.A. 156: 1406-1410. 1970.

45. Simon. Anesthesia in cats with a combination of thialbarbitone, O methoxphenyl glyceryl ether and atropine sulphate (Translated title). Magy. Alator. Zap. 19: 484-486. (English summary).

46. Tavernor, W. D. Influence of guaiacol glycerol ether on cardiovascular and respiratory function in a horse. Research in Veterinary Science 11: 91. 1970.

47. Thurmon, J. C., Romack, F. E., and Garner, H. E. Excursions of the bovine eyeball during gaseous anesthesia. Veterinary Medicine and Small Animal Clinician 63: 967-970. Oct. 1968.

48. Truitt, E. B. and Patterson, R. B. Comparative hemolytic activity of mephenesin, guaiacol glycerol ether and methacarbamol in vivo and in vitro. Proc. Soc. Exp. Biol. Med. 95: 422-424. 1957.

49. Turner, D. M., and Davis, P. E. Cardiac failure in a horse during chloral hydrate-chloroform anaesthesia. Australian Vet. Journal 45: 423. 1969.

50. Von Ondarza, R. Experiences with guaiacol glycerol ether in surgery (Translated title). Zentralbl. f. Chir. 80: 1471-1474. 1955.

51. Von Ondarza, R. and Wichman, G. Treatment of spasms of tetanus with guaiacol glycerin ether (Translated title). Zentralbl. f. Chir. 77: 2514-2520. 1952.

52. Weaver, A. D. Recent developments in anesthesia of large animals. Vet. Rec. 79, Clinical Suppl. No. 3: i-iv. 1966.

53. Westhues, M. Narcosis, an extract (Translated title). Schweiz. Arch. Tierheilk. 96: 503-517. 1954.

54. Westhues, Melchior and Fritsch, Rudolf. Animal anesthesia: general anaesthesia. Philadelphia, Pa., J. B. Lippincott Co. 1965.

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APPENDIX

Table 1. Mean values for hematological determinations of all subjects

Parameter	Control Sample	Post Tranquilization Sample	Post Infusion Sample	Recovery Sample
Hemoglobin gm.%	13.2	11.5	11.5	11.7
Packed Cell Volume %	36.6	32.0	32.2	32.4
Erythrocyte Count/mm.^{3}	8.47 mill.	7.79 mill.	7.85 mill.	7.89 mill.
Leukocyte Count/mm.^{3}	11,863	10,387	10,156	12,230
Differential Leukocyte Count %				
Segmented Neutrophils	50	52	53	58
Nonsegmented Neutrophils	1	1	1	2
Lymphocytes	44	43	42	36
Eosinophils	5	4	4	4
Monocytes	1	1	1	1
Basophils	1	1	1	1

Table 2. Mean values for blood glucose levels of all subjects

Parameter	Control Sample	Post Tranquilization Sample	Post Infusion Sample	Recovery Sample
Glucose mg.%	101.1	104.7	103.3	108.5

Table 3. Mean values of blood gas determination of all subjects

Parameter	Control Sample	Post Tranquilization Sample	Post Infusion Sample	Recovery Sample
pH	7.43	7.43	7.42	7.43
O_2 partial pressure mm. Hg.	94.3	89.3	84.3	88.5
CO_2 partial pressure mm. Hg.	40.0	40.1	40.3	39.4

Table 4. The effect of immediate versus 24 hour post recovery collection of recovery samples on hematological values

Parameter	Recovery Sample collected immediately	Recovery Sample collected 24 hours after recovery
Hemoglobin gm%	11.5	12.4
Packed Cell Volume %	31.8	34.3
Erythrocyte Count/mm.^{3}	7.88 mill.	7.91 mill.
Leukocyte Count/mm.^{3}	11,974	13,071
Differential Leukocyte Count %		
Segmented Neutrophils	57	61
Nonsegmented Neutrophils	2	1
Lymphocytes	38	33
Eosinophils	3	4
Monocytes	1	1
Basophils	1	1

Table 5. The effect of immediate versus 24 hour post recovery collection of samples on blood pH and blood gas determination

Parameter	Recovery Sample collected immediately	Recovery Sample collected 24 hours after recovery
pH	7.42	7.44
O_2 partial pressure mm. Hg.	89.1	86.3
CO_2 partial pressure mm. Hg.	38.9	40.9

Table 6. The effect of oxygen administration by a closed circuit anesthetic apparatus on blood gas values

Parameter	No oxygen source		Oxygen supplied	
	Post infusion sample	Recovery sample	Post infusion sample	Recovery sample
pH	7.43	7.43	7.33	7.43
O_2 partial pressure mm. Hg.	72.4	88.2	162.8	90.0
CO_2 partial pressure mm. Hg.	39.5	39.1	45.9	41.5

Figure 1. The arterial blood samples necessary for blood gas and blood pH analysis were collected from the carotid artery in the ventral one-third of the neck. At this point the carotid artery was located medial to the dorsal border of the jugular vein.

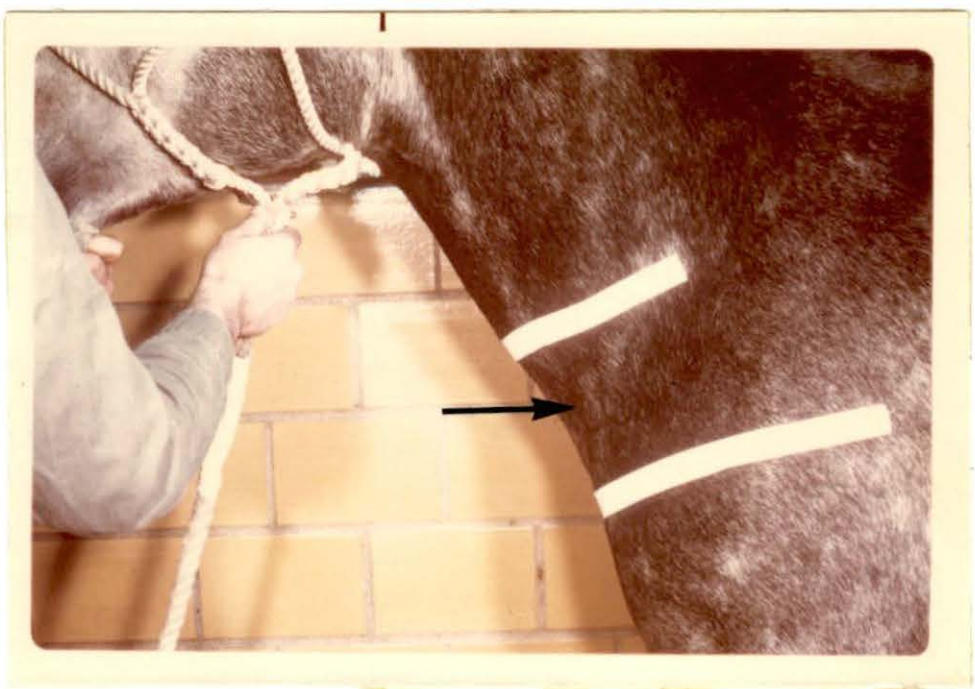

Figure 2. The carotid artery could be palpated medial to the jugular vein. A one inch twenty gauge disposable needle was inserted into the lumen and arterial samples were collected anaerobically.

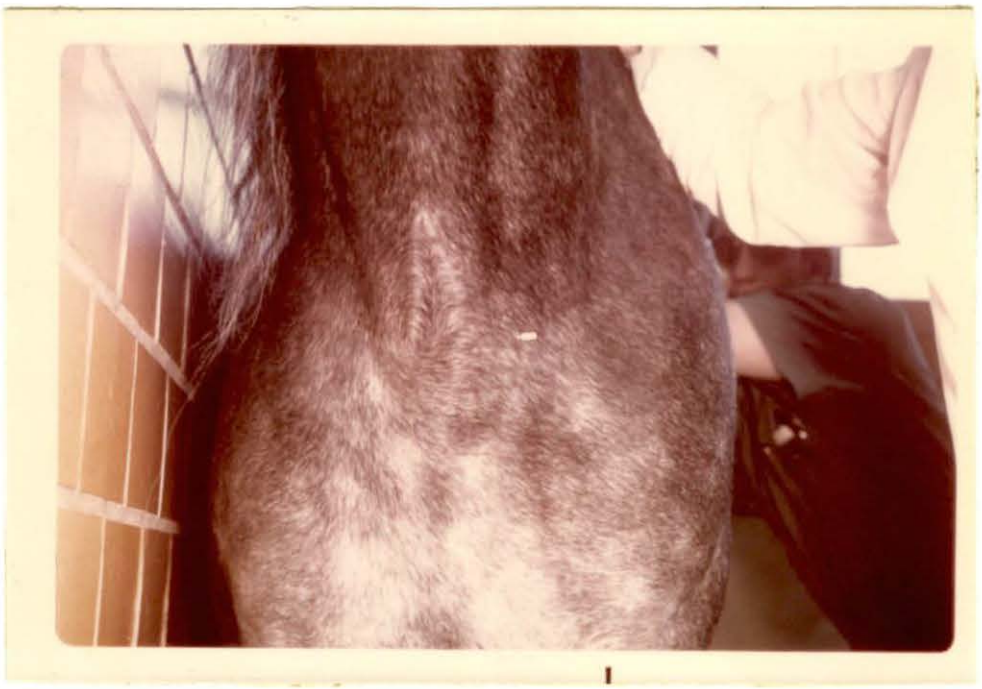

Figure 3. The arterial blood samples were collected in disposable two and one-half milliliter syringes. The syringes were wetted with heparin solution prior to the collection procedure. The syringes were capped by inserting the needle into a rubber stopper to maintain anaerobic conditions.

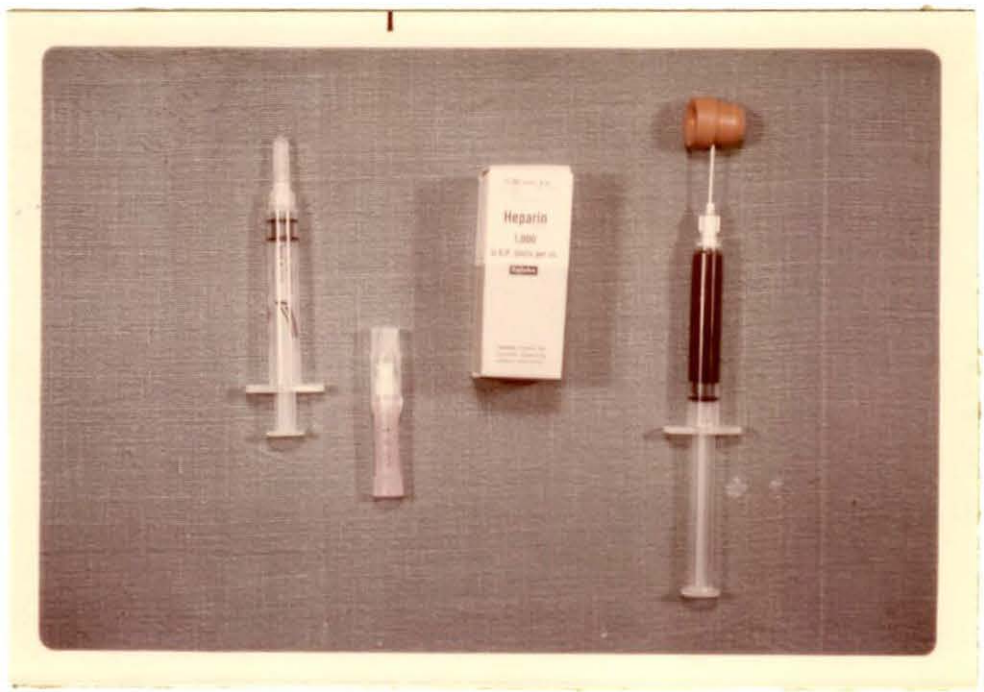
Heparin

Figure 4. A compression tourniquet was applied to forestall the formation of a hematoma in the carotid sheath or surrounding tissue after the carotid puncture.

Figure 5. The glyceryl guaiacolate-thiamylal sodium solution was prepared in one liter quantities using sterile water as the diluent. The infusion of the solution was through an intravenous infusion apparatus and a 12 gauge trocar point intravenous needle.

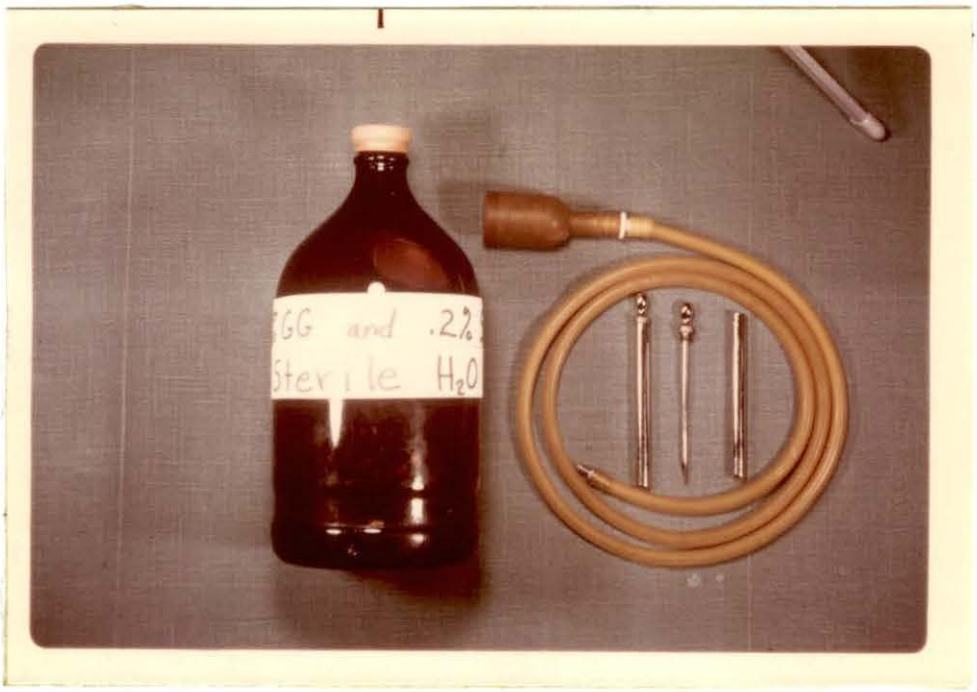
GG and .2%
Sterile H_2O

Figure 6. The equipment utilized for the determination of blood gas tensions and blood pH was the Instrumentation Laboratories Model 127 Blood gas analyzer.