Evaluation of the intravenous administration of Xylazine hydrochloride on cardiopulmonary function in the bovine species (Bos taurus)

by

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INTRODUCTION

Xylazine hydrochloride was first synthesized in Germany in 1962[9] and has been used in several animal species as a sedative, analgesic and muscle relaxant in many parts of the world.

In the United States of America its usage has been approved by the Food and Drug Administration for the equine, canine and feline species. It has also been administered to some wild animal species.

In spite of the fact that xylazine hydrochloride has been widely used in the bovine species in Europe, Australia and South America, more research is required concerning the intravenous administration of the drug.

Its action on cardiopulmonary function has been studied when administered intramuscularly in the bovine species. As the clinical signs vary with the route of administration, it is possible to project that the effects on the different systems also vary.

Xylazine hydrochloride has been shown to be a useful adjunct for the practitioner and its results have been satisfactory. Therefore, a more detailed study of the action of this drug when injected intravenously in bovine subjects was deemed important.

The purpose of this investigation was to study the effects of the intravenous administration of xylazine hydrochloride on

cardiopulmonary function in the bovine species with the subjects in lateral recumbency.

LITERATURE REVIEW

General Considerations

The action of xylazine hydrochloride, administered intramuscularly and intravenously, on the cardiopulmonary function has been studied in detail in the horse.[8,21,22,26,27,38,39] In the bovine species several authors[7,9,11,12,13] have studied the action of the drug when given intramuscularly and it has been reported that although no harmful effects have been observed following the intravenous injection of xylazine hydrochloride in cattle, the effects of intravenous administration have not been studied in detail.[9]

Blood gas determinations in resting, unanesthetized calves have shown means of 93.6± 7.68 mm of Hg for partial pressure of oxygen in arterial blood (PaO_2), 42.8± 3.28 mm of Hg for partial pressure of carbon dioxide in arterial blood ($PaCO_2$), 7.37±.02 for arterial blood pH, 23.9±1.42 mEq/liter for standard bicarbonate and .0±1.78 mEq/liter for base excess.[16] Gas evaluations using venous blood have shown means of 7.418 for pH, 33.1 mm of Hg for partial pressure of oxygen (PvO_2) and 48.7 mm of Hg for partial pressure of carbon dioxide ($PvCO_2$).[58] Blood gas and pH determinations in cattle anesthetized with halothane have confirmed the development of acidosis in cattle during halothane anesthesia.[23] A study related to the effect of anesthesia and posture on the exchange of respiratory gases and on the heart

in horses showed that oxygenation was impaired by general anesthesia, the effect being more severe in animals maintained in dorsal than in lateral recumbency.[40] According to the same authors, the pulse rate was found to be little influenced by differences of the available oxygen in the inspired air but significantly raised by positioning in dorsal compared to lateral recumbency. Similar studies have confirmed the influence of the body position on arterial oxygenation.[14]

Investigations have shown that there is no statistically significant difference in blood gas data obtained with polypropylene versus glass syringes.[19] The storage of blood samples for gas analysis for up to 3 hours in ice water has shown no effect on the results.[46]

Chronic catheterization of blood vessels in experimental animals is a common procedure and the most commonly used technique is to place a catheter into the blood vessel and suture it in place, having the end of the catheter emerge through the skin.[31] The saphenous artery has shown to be suitable for catheterization in the bovine species.[16]

Electrocardiographic study with normal cows has been done using the standard limb leads.[53] Using the leads I, II and III, in bovine subjects, it has been found that the range of the Q-T interval is .32 to .52 second with an average duration of .409 second and the T-wave magnitude is between .2 and .3 mv.[37] The same author found a great difference in

QRS magnitude. A dipole lead system for electrocardiogram (ECG) has been used in horses.(59) In this lead system the positive electrode is placed on the neck about 12 inches caudal to the wing of the atlas and the negative electrode lies over the apex of the heart. The ground lead is usually placed over the withers or on the shoulder.

Pharmacological Considerations

Xylazine hydrochloride, (2-(2,6-dimethylphenilamino)5-6-dihydro-4H-1,3 thiazine) is a non-narcotic compound with sedative, analgesic and muscle relaxant activities. Its sedative and analgesic properties are elicited through central nervous system depression and its muscle relaxant action is based on inhibition of the intraneural transmission of impulses in the central nervous system.(49) The drug acts at the level of the intraneural transmissions reducing the release of noradrenaline from postganglionic sympathetic fibers. It is an alpha sympathomimetic drug with inhibitory effects on vasomotor centers of the brain stem.(52) Xylazine hydrochloride has a paradoxical temporal positive and negative sympathetic effect with a short-lasting alpha adrenergic receptor-stimulant effect and a longer-lasting, centrally acting, inhibitory effect of the sympathetic outflow.(32) Depending upon the dose the drug does not act uniformly on all sympathetic structures but shows a selective effect: the sympathetic activity is reduced in order of decreasing effect

in the cardiac nerves, in the splanhnic nerves and in the cervical sympathetic trunk.[52] Three main effects on the adrenergic system have been demonstrated in anesthetized cats: a sympathomimetic action, an increased sensibility of the blood pressure and the nictating membrane to adrenaline and noradrenaline and less pronounced to tyramine, and an inhibition of the adrenergic neurofunction.[33]

The compound has shown different levels of sedative effects in different animal species, depending on the dosage rate and the route of administration, but the bovine species has been found to be much more sensitive to the action of the drug than other species investigated.[9,27] Electroencephalographic recordings in cats, in which sedation or hypnosis has been produced by xylazine hydrochloride, resembled those recorded during normal sleep.[27] In the same species it has been reported that the sedative action of xylazine hydrochloride in the central nervous system does not produce hallucination nor excitation.[45]

In comparing the analgesic action of the drug to that of morphine, investigators noted a hypnotic rather than a true anesthetic effect in horses and ponies without the side effects of morphine.[8] The analgesic properties of xylazine hydrochloride have been compared to those of morphine in the cat.[45]

The intravenous administration of xylazine hydrochloride in the horse caused an initial rise in blood pressure

accompanied by a fall in the heart rate and second-degree atrioventricular block. This effect was maximal for one to three minutes after administration, following which the blood pressure declined slowly over the next 15 minutes.[9] Second-degree atrioventricular block has been reported in normal subjects and is frequently found in resting horses.[29] It can be prevented by the use of atropine sulphate.[28] Alteration in T-wave configuration has also been described in the horse.[62] Intramuscular injections of xylazine hydrochloride, in the same species resulted in a slight fall in blood pressure with the heart rate remaining within normal limits.[9] One author reported that the heart rate in the horse remained slower than normal for at least 60 minutes after xylazine hydrochloride was injected.[29] Other investigators have found a significant decrease in heart rate after intravenous and intramuscular administration of the drug, in horses, but have not found significant changes in the mean carotid blood pressure. In the same study the calculated peripheral vascular resistance increased significantly and the calculated vigor of the left ventricular contraction decreased significantly.[39] Studies have suggested that there may be an initial fall in cardiac output following the injection of xylazine hydrochloride in horses, but it rapidly returns to within normal limits.[9] Bradycardia has been reported in the bovine species following intramuscular or intravenous administration of the drug.[7,20,24,25,50] The decrease in the

heart rate in the bovine species was found to be on the order of 30 to 40 percent of normal values.[20] The systolic and diastolic blood pressures have been reported to be lowered by about 15 to 20 percent in the bovine after intramuscular injection of xylazine hydrochloride.[51] Studies of changes in the ECG in bovine subjects under the action of the drug administered intramuscularly have not shown significant alterations.[24] In the canine species a marked bradycardia has been reported within 2 to 10 minutes after xylazine hydrochloride administration.[32,34,60] An investigation of the cardiopulmonary effects of xylazine hydrochloride in dogs indicated three possibilities that could cause the decrease in the cardiac rate: increase in vagal tone, decrease in activity of the sympathetic cardiac nerves or direct depression of the heart.[32] According to the same author, the second possibility would most likely be the primary source of the bradycardia. In some wild animal species under the influence of xylazine hydrochloride the heart rate is reduced.[1,17]

A marked decrease in the respiratory rate has been reported in the equine, bovine, canine, feline and some wild animal species, after xylazine hydrochloride administration.[7, 8,9,20,26,39,50,55] Increase in $PaCO_2$ has been reported in horses after intravenous administration of xylazine hydrochloride. The increases have never exceeded 45 mm of Hg even during periods of deep sedation.[9] A study of blood pH,

packed cell volume (PCV), $PaCO_2$ and PaO_2 in ponies did not show statistically significant changes in these variables under the effect of xylazine hydrochloride.[21] Arterial and venous pH, and PaO_2, PvO_2, $PaCO_2$ and $PvCO_2$, in the equine species, were not affected significantly after intravenous injection of xylazine hydrochloride.[39] In the bovine species the intramuscular administration of xylazine hydrochloride with the animals in the supine and lateral positons caused a significant reduction in the PaO_2 and this reduction was not entirely due to the position in which the animal had been restrained.[13] The same authors established that the pH, standard bicarbonate (HCO_3), base excess and $PaCO_2$ tended to increase but not significantly. The study of the effects of intravenous administration of xylazine hydrochloride in dogs did not show significant changes in blood pH, PaO_2 and $PaCO_2$.[32]

Decrease in ruminal motility has been reported in the bovine species after xylazine hydrochloride administration.[7, 9,24,50] Xylazine hydrochloride often produces emesis in the dog and almost always in the cat.[3,5,6,35,41] Emesis may be prevented by premedication with atropine sulphate.[35]

It has been reported that xylazine hydrochloride produces an increase in the uterine tone in the feline species.[45] One investigator using xylazine hydrochloride in one hundred Caesarian sections in the bovine species did not observe an increase in the uterine tone and attributed that to the uterine musculature being close to atonicity at the stage the surgery was done.[20]

Hematological studies developed with bovine subjects under the effect of xylazine hydrochloride given intramuscularly have shown some deviations which are more evident around the third hour following the administration of the drug. The main deviations were a considerable reduction in the hemoglobin values and an increase in the white blood cell number in association with a slight increase in the percentage of neutrophils and a drop in leukocyte numbers.(24) A decrease in the leukocyte count has been reported when xylazine hydrochloride was administered daily for ten days in cattle.(7)

Elimination of xylazine hydrochloride has been demonstrated as 70 percent via the kidneys and 30 percent by the liver in the feline species.(45) Excretion was almost complete 10 to 15 hours after administration of the drug, in a study involving rats.(18)

Clinical Considerations

Xylazine hydrochloride is supplied as a clear, colorless two percent and ten percent solution for intravenous and intramuscular injection. The solutions are miscible with both water and saline.(9) The dose and route of administration depend on the animal species and the desired level of sedation, analgesia and muscle relaxation. Investigators have used dosage rates between .5 mg to 2.2 mg per kilogram of body weight for intravenous administration and

dosage rates between 1 mg to 3.0 mg per kilogram of body weight for intramuscular administration in the horse.[8,9,22,26,28,29,39,55,57]

The most satisfactory dosage rate for the horse is considered to be 1.1 mg per kilogram of body weight for intramuscular administration.[26,39] Repeated intramuscular injections of xylazine hydrochloride in equine subjects over a 10-day period have produced muscle necrosis and abscesses at injection sites.[8] According to the same author subcutaneous injections of the drug in horses caused swellings under the skin persisting for several months. In the bovine species investigators have worked with dosage rates between .04 mg per kilogram of body weight to 1.6 mg per kilogram of body weight with both intravenous and intramuscular injections, with the intramuscular route attaining the most favor.[7,9,11,12,13,20,27,47,49,50] Dosage rates on the order of .05 to .1 mg per kilogram of body weight have been reported as within safe limits for intramuscular administration in cattle.[9]

No correlation between breeds of cattle and dosage rates have been found.[50] The dosage rate of .3 mg per kilogram of body weight has been considered optimal for the sheep.[36] In dogs and cats dosage rates between 1 to 5 mg per kilogram of body weight for intravenous administration and between .5 to 10 mg per kilogram of body weight for intramuscular administration have been used.[4,5,6,35,41,45] Dosage rates

between 2 mg and 10 mg per kilogram of body weight via intramuscular administration have been reported for some wild animal species.[1,15]

It has been reported that intravenous injection of .5 mg per kilogram of body weight of xylazine hydrochloride produces almost immediate effects in horses. The head lowers and eyelids and lower lip droop. This state lasts for 15 to 20 minutes and during this period response to stimuli such as loud noises is usually absent. The recovery period is 10 to 15 minutes. Normal behavior is usually resumed within 30 minutes of the time of administration. Intramuscular injections of 2 to 3 mg per kilogram of body weight of xylazine hydrochloride result in similar but apparently less profound sedation. Larger doses given by intravenous injection do not produce more profound sedation, but the duration of both the sedated and recovery period is increased. The animals are reluctant to walk during the period of deep sedation and are particularly sensitive to noise during the recovery period.[9]

Other investigators using xylazine hydrochloride intravenously in 254 horses reported the sedation as excellent in 177 horses, good in 49, fair in 22 and poor in 6.[26] In the same study penile paralysis did not occur in any of the males. Among the 254 horses, analgesia was evaluated in 158 horses as follows: 75 excellent, 54 good, 17 fair and 12 poor.

Very high doses of xylazine hydrochloride seldom cause a horse to become recumbent, but such horses may become so ataxic that working on them becomes difficult.(39) A pregnant mare foaled normally 41 days after intramuscular xylazine hydrochloride injection.(38)

Bovine subjects have been found to be much more sensitive to the compound.(9) Intramuscular administration of xylazine hydrochloride has caused deep sedation in cattle from 15 to 50 minutes after administration and the type of sedation has been compared to that produced by chloral hydrate.(9) In an investigation involving 125 cattle it was described that the effect of the drug depends on the dosage rate, the route of administration and the homeostatic balance of the animal at the time of the administration. The same author identified three distinct levels of response to the action of the drug: sedation, analgesia and muscle relaxation. These three stages corresponded to three dosage rates of xylazine hydrochloride given by intramuscular injection: .09 mg, .18 mg and .35 mg per kilogram of body weight, respectively.(27) The "milk fever" position has been described as characteristic after xylazine hydrochloride administration in the bovine species.(47, 50) When xylazine hydrochloride was administered intravenously the effect was immediate.(25) Increase in salivation and in rectal temperature have been reported in the bovine species.(7, 20,27) Decrease of corneal and palpebral reflexes were

evident in cattle under the action of xylazine hydrochloride.[7] Among 67 bulls sedated with xylazine hydrochloride, 3 showed penile prolapse.[50] Ten cows at the 8 to 9 months of pregnancy presented uterine movements at 8 to 12 minutes after intramuscular injection of .3 mg per kilogram of body weight of xylazine hydrochloride. Seven of these cows had calves within 25 to 62 hours following the drug administration. Eight cows among the 10 had retained placentas. The drug was also used in 37 other cows at different stages of pregnancy including 5 in the third trimester with no alterations.[50] The same authors advised not to use the drug during the last month of pregnancy.

Results of toxicity trials in the bovine species have shown that the minimum lethal dosage rate of xylazine hydrochloride in adult cattle is 3 times the highest recommended intramuscular dosage rate of .3 mg per kilogram of body weight.[27] Three cases of respiratory paralysis have been reported with the death of one subject which had erroneously received 10 times the highest recommended intramuscular dose.[7] One or two reinjections of the initial dose have proved to be efficient when the surgical procedure requires the patient sedated for an extended period.[50]

Xylazine hydrochloride has been reported to produce remarkable analgesic effects in the cutaneous portions of the body, particularly the head region and excellent relaxation

of the musculature in the abdomen as well as the back, neck and limbs in the canine species.[34] In a study involving 570 dogs the anesthetic effect was considered good in 454 subjects and lasted 2 to 3 hours.[6] The maximum effect was reached in 5 to 15 minutes following intravenous administration and in 10 to 20 minutes after the subcutaneous administration of the drug in dogs.[5] Studies in cats revealed that with 214 subjects the effect was good in 173 cases, sufficient in 19, poor in 15 and insufficient in 7.[6] In the same species the effect has lasted at accepted levels for a period of 45 to 60 minutes.[5] The drug produced vomition in 27 out of 30 experimental cats.[35] The death of 3 cats with respiratory infection following intramuscular administration of 4.4 mg per kilogram of body weight of xylazine hydrochloride was reported.[3]

Xylazine hydrochloride has been used by intramuscular injections in different wild animal species.[1,15,42,48] The use of 2 mg per kilogram of body weight in Camelus dromedarius showed that the animal became recumbent within 15 to 20 minutes after intramuscular injection.[15]

Xylazine hydrochloride has been used in association with local anesthetics in horses for procedures such as repair of lacerations, cauterizations, castrations, myotomies, tenotomies and obstetrical procedures.[57] Marked relief from acute abdominal pain has been reported in 3 horses

given xylazine hydrochloride intravenously at the dosage rate of 1.1 mg per kilogram of body weight.[26] The same authors reported the use of xylazine hydrochloride as especially valuable in laryngoscopic examinations, passing a stomach tube and loading intractable horses for transportation. Xylazine hydrochloride has been used in horses in combination with several general anesthetics. Marked sedation and smooth induction resulted when it was given intravenously with thiamylal sodium, pentobarbital sodium-thiopental sodium, pentobarbital sodium-thiopental sodium-glyceryl guaiacolate and thiamylal sodium-halothane.[26] It has also been used in association with methadone and chloral hydrate in horses.[57] A preliminary report has recently been published about the combination of xylazine hydrochloride and morphine to provide standing restraint, sedation and analgesia in horses.[30] Other investigators working with the same animal species showed that the amount of general anesthetic could be reduced satisfactorily from one-third to one-half the usual dosage when combined with xylazine hydrochloride, but the full amount could be given if longer action was desired.[8]

The use of xylazine hydrochloride alone or in association with local anesthesia has been reported for most of the common surgical procedures in the bovine species.[7,50] Investigators have said that the use of xylazine hydrochloride in procedures such as rumenotomy and intestinal resection

presents a disadvantage because the patient may become recumbent during the surgery.[7] A study of 100 Caesarian sections in the bovine species reported 51 were performed in the standing position and 49 in lateral recumbency, all under the action of xylazine hydrochloride. On the patients in the standing position local anesthetic was infiltrated along the incision line. Of the cows in lateral recumbency 33 received local anesthetic and xylazine hydrochloride and 16 were operated on under the action of xylazine hydrochloride only.[25] A preliminary report of xylazine hydrochloride as a sedative agent in bulls for electroejaculation and semen collection has been published.[49] In this report is is emphasized that the depression of the pulse and respiratory rates persisted in spite of the agitation of the electro-stimulation. Rectal gynecological examination became easier after the administration of xylazine hydrochloride due to the relaxation of the rectum.[2]

The drug has been used alone or with supplementary doses of barbiturates in dogs.[6] The analgesic effect of xylazine hydrochloride studied in 884 dogs proved to be sufficient in 75 percent of the cases.[7] It was reported that the depth of anesthesia induced by xylazine hydrochloride alone is not enough to permit endotracheal intubation before administration of an inhalation anesthetic in dogs and cats, but anesthesia could be easily induced via a face mask followed by endo-tracheal intubation. Following intravenous injection of

xylazine hydrochloride in dogs and cats the barbiturate dosage rate could be reduced by 75 percent or more and after intramuscular injections the reduction ranged from 30 to 50 percent.(41) Another report indicated an average reduction of 42 percent of the total calculated dose of pentobarbital sodium and gave an average recovery period of 155 minutes in dogs.(36)

A variety of central nervous system depressants and a skeletal muscle paralyzing agent were evaluated for restraining dogs and cats during air cystometry. Xylazine hydrochloride was the only drug which provided adequate restraint without blocking the micturition reflex.(44)

Xylazine hydrochloride has been used as a preanesthetic medication before ketamine hydrochloride administration in cats.(4,48) When used prior to the administration of ketamine hydrochloride the required dose of the latter was approximately one third to one half of the maximum label recommendations for surgical anesthesia.(43) After premedication with xylazine hydrochloride the muscle hypertonicity associated with ketamine hydrochloride anesthesia in cats was absent.(4) The emetic property of xylazine hydrochloride in cats has been emphasized and the maximal effectiveness of the compound as an emetic has been reported as occurring at 1.1 mg per kilogram of body weight given intramuscularly.(3) The subcutaneous injection has been advised as the most effective for producing emesis.(61)

Comparative studies in horses have shown that the sedative and analgesic effects of xylazine hydrochloride given intravenously (1.1 mg per kilogram of body weight) are greater than that of the acetylpromazine maleate given intravenously (.066 mg per kilogram of body weight) which in turn is greater than that of xylazine hydrochloride given intramuscularly (2.2 mg per kilogram of body weight).[28] The same investigators have reported that a comparison of xylazine hydrochloride with acetylpromazine maleate as a preanesthetic agent indicated that less respiratory depression and greater cardiovascular stability were present in general anesthesia after using xylazine hydrochloride. Investigators studying the comparative effects of xylazine hydrochloride, promazine and halothane on serum electrolytes in the horse concluded that little change was seen following the administration of xylazine hydrochloride.[55]

When penile prolapse is required it has been shown that xylazine hydrochloride is not as useful as propionylpromazine.[47]

MATERIALS AND METHODS

Laboratory Animals

Twelve cows of various breeds and ages were used in the investigation. The cows were owned by the Department of Veterinary Clinical Sciences, College of Veterinary Medicine, Iowa State University. The cows were weighed prior to the administration of the drug and the weight, breed and age were recorded. The cows were clinically healthy.

Xylazine Hydrochloride

The drug evaluated was xylazine hydrochloride, (2-(2,6-dimethylphenilamino)5-6-dihydro-4H-1,3 thiazine)[1] in a 10 percent solution.

Sampling Technique

One and one half millimeters inside diameter and 2.31 mm outside diameter, 30 cm teflon catheters[2] were implanted in the saphenous artery and great saphenous vein, to obtain anaerobic arterial and venous blood samples for blood gas determinations, venous blood samples for hematological and serum electrolyte evaluations and to record the arterial blood pressure. The catheters were implanted within a variable period of time between 2 hours and 24 hours before the

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[1]Rompun, Chemagro, Kansas City, Missouri.

[2]Becton-Dikinson, Rutherford, New Jersey.

administration of xylazine hydrochloride. The cows were restrained in left lateral recumbency on a surgery table.

The saphenous artery is a branch of the femoral and emerges between the sartorius and gracilis muscles on the medial surface of the thigh. It continues distally over the stifle joint and in the region of the tarsus it divides into the medial and lateral plantar arteries. The saphenous artery lies cranial to the great saphenous vein and saphenous nerve and can be palpated subcutaneously.

The surgical site was located approximately 20 cm above the tuber calcanei, over the saphenous artery and great saphenous vein on the medial aspect of the hind limb. The skin and subcutaneous tissue were infiltrated with lidocaine hydrochloride containing epinephrine 1:100,000[1] at the elected surgical site. A 5 cm incision was made through the skin and the vessels were separated from the adjacent connective tissue by means of blunt dissection. Two ligatures were made around the artery using a number 5-0 cardiovascular silk[2] and the artery wall was incised between the ligatures. The catheter was filled with a .5 percent heparinized saline solution and occluded with a stopper. It was then inserted into the artery for a distance of 15 cm in a cranial

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[1]2% Xylocaine HCl - Jensen-Salsbury Laboratories, Kansas City, Missouri.

[2]Deknatel cardiovascular silk - Deknatel, Queens Village New York.

direction and the ligatures around the vessel were tied. The same procedure was followed to implant a catheter into the greater saphenous vein. Both catheters were exteriorized through another smaller skin incision and fixed to it with polyglycolic acid suture material.[1] Continuous suture pattern with the same suture material was used to close the subcutaneous tissue and the original skin incision.

The catheters were flushed with heparinized saline solution every 12 hours during the period of time between implantation and final sampling. The blood samples for gas determinations were collected in sterile 3 ml disposable syringes[2] through a needle[3] adapted to each catheter. The needles were closed by means of a three way valve.[4] The syringes were previously treated with heparin sodium[5] and all air was evacuated leaving a drop of heparin sodium in the tip of the syringes to maintain anaerobic conditions. Each syringe was closed with a 23 gauge needle[6] inserted into

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[1]O Dexon - American Cyanamid Company, Pearl River, New York.

[2]Monoject - Sherwood Medical Industries, Inc., Deland, Florida.

[3]B-D19 - Becton-Dikinson, Rutherford, New Jersey.

[4]B-D MS02 - Becton-Dikinson, Rutherford, New Jersey.

[5]Sodium heparin injection - Wolins Pharmacological Corp., Melville, New York.

[6]Monoject 200 - Sherwood Medical Industries, Inc., Deland, Florida.

a rubber stopper. The samples were stored in an ice bath until the recovery samples were taken and then transported to the laboratory where blood gas and blood pH determinations were done. The venous blood samples for the other hematological parameters in this study were collected with a sterile disposable syringe[1] and deposited in commercially available ethylene diamine tetracetic acid (EDTA) vacuum tubes.[2]

Electrocardiogram and Arterial Blood Pressure Recording Techniques

The ECG and the arterial blood pressure were recorded using a physiograph.[3] The ECG was recorded using the dipole lead system. The positive electrode was placed at the level of the fourth thoracic vertebra and the negative electrode over the apex of the heart. The ground lead was placed over the acromion.

The arterial blood pressure was taken by means of a transducer[4] connected to the three way valve in the catheter implanted into the saphenous artery.

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[1]Monoject - Sherwood Medical Industries, Inc., Deland, Florida.

[2]Vacutainer - Becton-Dikinson, Rutherford, New Jersey.

[3]Physiograph Four - E and M Instrument Co., Inc., Houston, Texas.

[4]Physiologic Pressure Transducer - Statham Laboratories Inc., Hato Rey, Puerto Rico.

Administration, Sampling and Recording Procedures

Pre-catheterization blood samples were collected from the external jugular vein before catheter implantation. These samples were taken in EDTA vacuum tubes for hematological evaluations other than blood gas determinations. Immediately prior to the administration of xylazine hydrochloride control arterial and venous blood samples were collected for blood gas determinations as well as control venous blood samples for other hematological evaluations. At the same time control ECG and arterial blood pressure records were recorded. Xylazine hydrochloride was then administered at the dosage rate of .22 mg per kilogram of body weight through the catheter implanted into the great saphenous vein.

With the cow in lateral recumbency a further set of blood samples and physiographic recordings were taken. This procedure was repeated every 10 minutes during a period of 40 minutes. Recovery samples and recordings were taken when the subject was in a standing position. The recovery control, arterial and venous blood samples for all hematological evaluations were collected after approximately 18 hours. The catheters were then removed from the blood vessels.

Clinical Pathological Determinations

The eight arterial blood samples and the eight venous blood samples collected from each animal for blood gas studies were subjected to PaO_2, $PaCO_2$, PvO_2, $PvCO_2$ and blood

pH determinations in the laboratory of the Department of Veterinary Anatomy, Pharmacology and Physiology, College of Veterinary Medicine, Iowa State University. The instrument used was a pH and blood gas analyzer[1] using three electrode systems to measure quantitatively blood pH, partial pressure of oxygen in the blood and partial pressure of carbon dioxide in the blood. Serum bicarbonate concentration (HCO_3), whole blood base excess and total serum carbon dioxide (CO_{2ct}) were calculated by the instrument based on the measured values. The instrument was adjusted for the local barometric pressure factor. The partial pressures of the gases in the blood were measured in mm of Hg. The base excess and HCO_3 were measured in mEq per liter and the CO_{2ct} in mmol per liter.

Venous blood samples for the remaining hematological variables were evaluated by medical technologists in the clinical pathology laboratory, Department of Veterinary Pathology, College of Veterinary Medicine, Iowa State University. The hemoglobin (Hb) values were determined by the cyanmethemoglobin method and the results obtained were recorded in grams percent. The packed cell volume (PCV) of each sample was determined by the microhematocrit method.[2]

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[1]IL513 Digital pH Blood Gas Analyzer/Acid Base Calculator-Instrumental Laboratory Inc., Lexington, Massachusetts.

[2]International micro-capillary Centrifuge and Reader - International Equipment Company, Boston, Massachusetts.

The results were recorded in volumes percent. White blood cell (WBC) count was made by means of an electronic particle counter[1] and the data was recorded in cells per mm^3. Blood smears were made and stained with Wright's stain for differential leukocyte counts done by manual reading and recorded in units percent. Plasma protein and fibrinogen were determined by means of a TS meter[2] and a T/C refractomer.[3] The data was recorded in grams percent for plasma protein and milligrams percent for fibrinogen. Serum sodium (Na) and potassium (K) were determined using a flame photometer.[4] The values obtained were measured in mEq per liter. Serum calcium (Ca) and magnesium (Mg) were determined by means of colorimetric analysis.[5,6] The data was recorded in milligrams percent. Serum phosphorus (P) values were evaluated by the phosphomolybdic acid method[7] and recorded in milligrams percent.

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[1]Coulter Counter Model F - Coulter Electronics, Inc., Hialeah, Florida.

[2]10400 - American Optical Company, Buffalo, New York.

[3]American Optical Company, Buffalo, New York.

[4]IL Model 343 flame photometer - Instrumental Laboratory, Inc., Lexington, Massachusetts.

[5]Calcium Rapid Stat Kit - Pierce, Rockford, Illinois.

[6]Magnesium Rapid Stat Kit - Pierce, Rockford, Illinois.

[7]Hycel Phorphorus Test - Hycel, Inc., Houston, Texas.

Electrocardiogram and Arterial Blood Pressure Evaluations

The ECG recordings were evaluated for heart rate, QRS magnitude, T-wave magnitude, Q-T interval and S-T segment depression or elevation. The heart rate was measured in beats per minute, the Q-T interval in seconds, and the remaining variables in millivolts.

The arterial blood pressure recordings were evaluated for systolic and diastolic arterial pressure and the data obtained was recorded in mm of Hg.

Statistical Analysis

The data was collected, grouped and coded for computer analysis. One way analysis of variance was used to detect the presence of statistical differences between the mean values of the various samples or records in the same variable. The differences, when present, were given at 2 levels of significance: $P < .05$ and $P < .01$. By means of the multiple range test the differences between groups were identified. The Student-Newman-Keuls test was the procedure basically used and gave the results at .05 level of significance. The more conservative Scheffe's test was used when a more accurate result was desired. That test gave the results at 2 levels of significance, .05 and .01. The statistical procedures were done by the Iowa State University Computation Center.

RESULTS

Clinical Evaluation

The intravenous administration of xylazine hydrochloride at a dosage rate of .22 mg per kilogram of body weight resulted in an almost immediate effect. With no exceptions the 12 experimental animals adopted the lateral recumbent position within 1 to 2 minutes following administration of the drug. Nine cows remained in that position for an average period of 50 minutes. Two of the other 3 cows adopted sternal recumbency within 25 to 40 minutes following administration of the drug. The last cow stood up 35 minutes after the injection. All the cows manifested salivation and moderate tympany. Deep sedation was present for at least 20 minutes. Some cows showed a mild degree of dyspnea. A mucous vaginal discharge was characteristic in all the subjects. The period of deep sedation was followed by a phase of mild sedation lasting several hours.

Evaluation of Cardiovascular Function

The mean values of ECG variables are listed in Table 1. The one way analysis of variance revealed differences among the values recorded at different times for heart rate, Q-T interval and S-T segment elevation significant at the .01 level. The mean values for those variables are plotted in Graphs 1, 2 and 3 respectively. The mean value for heart

rate of the control record was 72 beats per minute decreasing to 41 beats per minute in the immediate post-injection record. This decrease proved to be significant at the .05 level by the multiple range test. The differences between the mean value for heart rate of the control record and the mean values of the remaining records were also significant at the .05 level. The Q-T interval presented a continuous increase. The multiple range test evidenced differences between the mean values of the 30 minute, 40 minute and recovery records significant at the .05 level. The decrease presented in the S-T segment elevation between the mean value of the control record and the mean values of the 40 minute and recovery records was significant at the .05 level. Xylazine hydrochloride administration had no significant effect on the T wave and QRS magnitudes.

The mean values for systolic and diastolic arterial pressure are presented in Table 2 and plotted in Graph 4. The effect of xylazine hydrochloride on systolic and diastolic arterial pressure was significant at the .01 level. The decrease in the systolic arterial pressure between the mean value of the control record and the mean values of the 20, 30 and 40 minute records was significant at the .05 level. The differences in the mean values of the control, immediate post-injection, 10 minute and recovery records were not statistically significant. The differences between the mean

value for diastolic arterial pressure of the control record and the remaining records were significant at the .05 level with the exception of the mean value of the immediate post-injection record.

Evaluation of Pulmonary Function

The mean values of arterial blood gas determinations are listed in Table 3 and those of venous blood gas determinations are listed in Table 4. The mean values for PaO_2 and $PaCO_2$ are plotted in Graphs 5 and 6, respectively. The effect of xylazine hydrochloride on PaO_2, $PaCO_2$, arterial blood HCO_3, arterial blood base excess and arterial blood CO_{2ct} was significant at the .01 level. Xylazine hydrochloride had no significant effect on arterial blood pH. The mean value for PaO_2 of the control sample, taken immediately prior to the xylazine hydrochloride administration was 102.76 mm of Hg which was within the normal values for the bovine species. The difference between that value and the mean values of the remaining samples were significant at the .05 level with the exception of the mean value of the recovery control sample collected approximately 18 hours after the administration of the drug. The differences among the mean values for PaO_2 of the immediate post-injection, 10, 20 and 30 minute samples were not significant. However, the same values were found to be significantly different at the .05 level when compared with the 40 minute and recovery samples. The recovery sample,

collected immediately after the subject adopted the standing position, showed an increase significant at the .05 level when compared with the mean value of the 40 minute sample. The $PaCO_2$ revealed an increase which was significant at the .05 level between the mean value of the control sample and the mean values of the remaining samples except those of the immediate post-injection and recovery control samples. The latter presented differences significant at the .05 level when compared with the mean values of the 10, 20, 30 and 40 minute samples and the recovery sample. The arterial blood HCO_3 showed an increase between the mean value of the control sample and the mean values of the 30 and 40 minute samples and the recovery sample which was significant at the .05 level. The mean value of the recovery control sample decreased at a level which was not significantly different from the mean value of the control sample. The increase in the base excess in arterial blood mean values was significant at the .05 level between those of the control sample and of the recovery sample. The mean values of the 40 minute and recovery samples differed significantly from those of the recovery control sample at the .05 level. The mean values for arterial CO_{2ct} of the control and recovery control samples did not reveal significant differences but both were significantly lower at the .05 level than those of the 30 and 40 minute and recovery samples.

The venous blood pH was not significantly affected by xylazine hydrochloride. The mean values for PvO_2 of the control and recovery control samples did not differ significantly. The control sample mean value was significantly higher than those of the remaining samples at the .05 level. The mean values for $PvCO_2$ did not differ significantly between those of the control and recovery control samples at the .05 level. The mean value for base excess in venous blood of the recovery control sample was significantly lower at the .05 level than those of the 40 minute and recovery samples. The increase in venous HCO_3 between the mean values of the control and recovery control samples and the mean values of the 40 minute and recovery samples was significant at the .05 level. The same pattern was followed by the increase in the mean values of CO_{2ct} in venous blood.

Hematological and Serum Electrolyte Evaluations

The mean values for hematological evaluation including Hb, WBC count, differential WBC count, PCV, plasma protein, and fibrinogen, are listed in Table 5. The one way analysis of variance indicated differences significant at the .01 level among the mean values of the samples collected at different times for segmented neutrophils, lymphocytes, Hb, PCV and plasma protein. The differences between the mean values for segmented neutrophils and lymphocytes of the pre-catheterization sample and those of the other samples were significant at the

.05 level. The mean values for Hb of the pre-catheterization sample and of the control, immediate post-injection and recovery control samples were not different at the .05 level of significance. The mean values for PCV of the pre-catheterization sample, control sample and recovery control sample were not different at the .05 level of significance. The mean value for this variable of the pre-catheterization sample was significantly higher than those of the 10, 20, 30 and 40 minute and recovery samples at the .05 level. The mean value of the control sample was significantly higher than those of the 10, 20, 30 and 40 minute and recovery samples at the .05 level. The mean values for plasma protein presented no significant differences at the .05 level between the pre-catheterization, control, immediate post-injection and recovery control samples.

The mean values for serum electrolyte evaluation including Na, K, Ca, Mg and P are listed in Table 6. The mean values for Ca and Mg were significantly different at the .05 level among the samples collected at different times. By means of the Student-Newman-Keuls procedure the difference between the mean values for Ca of the pre-catheterization and the 10 minute sample was significant at the .05 level. The differences detected among the mean values for Mg by the one way analysis of variance could not be identified by the multiple range test. No significant differences were found

among the mean values of the samples collected at different times for the remaining variables studied in the serum electrolyte evaluation.

DISCUSSION

Clinical Evaluation

The dosage rate of .22 mg per kilogram of body weight of xylazine hydrochloride seemed to be more than adequate for intravenous injection in cattle. The effect was almost immediate and little help was needed to make the cows adopt lateral recumbency. Once in lateral recumbency the experimental animals presented a state of deep sedation and a level of analgesia which would make some minor surgical procedures possible without the supplementation of a local anesthetic. Treated animals showed no response to the manipulation of catheters and jugular puncture. For the first 15 minutes of sedation, at least, the cows did not present the characteristic "milk fever" position described as following the intramuscular administration of the drug. However, that position was adopted at the end of the state of deep sedation and near the time the subjects assumed sternal recumbency or stood up. All the subjects maintained palpebral and corneal reflexes. The abundant salivation did not offer any problems because the pharyngeal reflex was present. Some difficulty in respiration was noticed which was probably due to the compression caused by moderate tympany and muscle relaxation following the administration of xylazine hydrochloride. A vaginal mucous discharge was present in all animals. An

increase in uterine tone has been reported in the feline species under the action of xylazine hydrochloride.(45)

Evaluation of Cardiovascular Function

The decrease in heart rate was significant at the .01 level. The multiple range test was used to identify that difference by means of two different procedures. The Student-Newman-Keuls procedure gave the interpretation at the .05 level. The more conservative Scheffe's test interpreted the significance at .05 and .01 levels. In the present case using the Student-Newman-Keuls procedure there were statistically significant differences between the mean value of the control record and those of the other records. Checking the same variable by means of the Scheffe's test the results proved to be significant at the .01 level. If examined from a numerical point of view those results were sufficiently meaningful to reach the conclusion that xylazine hydrochloride was responsible for a dramatic decrease in the heart rate. Although a decrease in heart rate was expected based on previous investigations the control mean value looked higher than normal. That increase in heart rate preceding the administration of the drug was explained by the excitation the cows exhibited during the restraining procedures. The exact action of xylazine hydrochloride in lowering the heart rate has not been completely elucidated. Among the three possible causes of the decrease in the cardiac rate viz. increase in

vagal tone, decrease in activity of the sympathetic cardiac nerves and direct depression of the heart, the second possibility is the most probable.[32] The increase of the Q-T interval could be expected as that variable was related to the heart rate. However, that increase was statistically significant only between the mean value of the control record and those of the final three records.

The S-T segment depression or elevation would be a sign of cardiac hypoxia. In the present study the S-T segment was elevated but showed a decrease towards the base line. An increase in the S-T segment depression or elevation could have been expected due to the marked drop in PaO_2 and increase in $PaCO_2$ which were present. An increase in the S-T segment depression or elevation could also make evident a very low potassium level. The other findings which would constitute signs of cardiac hypoxia were an enlarged T-wave and atrial or ventricular arrhythmias.[59] The increase in the T-wave magnitude was not significant and arrhythmias were absent. The values of the curves in PaO_2 decrease and $PaCO_2$ increase supported the ECG findings related to cardiac oxygenation. The increase in PaO_2 following the accentuated decrease showed during the first 10 minutes after administration of xylazine hydrochloride, although moderate, prevented the cardiac muscle from chronic hypoxia.

The curves showing the decrease in systolic and diastolic arterial pressures followed the same pattern, keeping an

almost perfect proportion. An inhibitory effect of xylazine hydrochloride on vasomotor centers of the brain stem has been reported to be responsible for that decrease.(52) According to other studies the arterial pressure should have presented an increase during the first few minutes following the administration of the drug with a later decrease in the mean values. Due to the fact that the experimental animals were not connected to the pressure transducer during the period lasting from the control record to the immediate post-injection record, that supposed increase in the blood pressure was not recorded in the present study. The reported biphasic blood pressure response is probably due to the paradoxical temporal positive and negative sympathetic effects of the drug.(32)

Evaluation of Pulmonary Function

The curve of the mean values for PaO_2 evidenced a very acute decrease between the values of the control and immediate post-injection samples. The period of time between those samples was not the same for all subjects because it depended on the time required for the cows to assume lateral recumbency, however, it did not exceed 3 minutes in any of the animals. Investigators found that the decrease in PaO_2 was not only due to the position in which the animal was restrained when xylazine hydrochloride was used intramuscularly.(13) The lowest mean value was that of the 10 minute sample following which the mean values increased slowly but consistently

reaching values which were significantly higher in the 40 minute sample. The mean value of the recovery sample also showed a significant difference when compared with that of the 40 minute sample by means of the Student-Newman-Keuls procedure. The mean values of the control sample and the recovery control sample did not show significant differences. The Scheffe's test showed no differences among the mean values for PaO_2 of the control, recovery and recovery control samples at the .01 level. Even considering the conservative characteristics of that test, those results gave a meaningful support to the clinical signs evidenced during the experimental procedures. The central depression produced by xylazine hydrochloride, its muscle relaxant action and the lateral recumbency might be considered among the possible causes of the decrease in PaO_2. The central depression and muscle relaxant action are characteristic of xylazine hydrochloride. The lateral recumbency probably influenced in the oxygenation but two facts have to be considered which would keep this influence within certain limits. The decrease in PaO_2 was sharper between the first two samples which was a period when the cows had not been in lateral recumbency for more than a few seconds. The other point to be emphasized was the increase in the mean values for PaO_2 evidenced after the 10 minute sample, when the cows continued in lateral recumbency.

The probable hypothesis would be a combination of these factors resulting in the decrease in PaO_2.

The increase in $PaCO_2$ was continuous and consistent until it reached the highest mean value at the 40 minute sample. There was a small drop in the mean values of the 30 minute sample but there were no significant differences among the values of the immediate post-injection, 10 minute, 20 minute, 30 minute, 40 minute and recovery samples. The Student-Newman-Keuls procedure did not indicate significant differences between the mean values of the control and recovery control samples. This fact was clinically meaningful and showed a return to the normal values in a relatively short period of time. The clinical significance of the increase in $PaCO_2$ has been reported as more important than the decrease in PaO_2. The $PaCO_2$ is considered to be the direct and immediate reflection of the adequacy of alveolar ventilation in relation to the metabolic rate.(54) Both PaO_2 decrease and $PaCO_2$ increase proved to be acute and did not continue into a chronic hypoxia. It has been reported that intramuscular reinjections of the initial dose proved to be efficient when the surgical procedure required the patient sedated for an extended period.(50) Intravenous administration of xylazine hydrochloride was used as a second dose and the author did not report clinical consequences.(10) Blood gas determinations in these cases were not reported. Other investigators reported a significant reduction in PaO_2 following intramuscular administration of

.3 mg per kilogram of body weight of xylazine hydrochloride.[13] It seems logical to expect another drop in the PaO_2 values and increase in the $PaCO_2$ values following an intravenous or even intramuscular second dose of xylazine hydrochloride. If true, a condition of poor oxygenation would be repeated at a stage during which the animal was not completely recovered from the action of the first injection of the drug. It would be possible to expect at that time the ECG findings related to the cardiac muscle hypoxia which were absent in the present study. The fall in the PaO_2 has been interpreted as generally tolerated by healthy animals but has not been considered without danger and might be a fatal course in animals with acute or chronic anemia, or with disorders having an unfavorable effect on tissue oxygenation.[13]

The increase in the HCO_3, base excess and CO_{2ct} in the arterial blood were expected due to the fact that these variables were calculated based on the PaO_2 and $PaCO_2$ values. The action of xylazine hydrochloride was not significant on the arterial blood pH. This fact evidenced a response of the buffer system to the $PaCO_2$ increase.

The decrease in PvO_2 presented a curve which followed a pattern similar to that of the decrease in PaO_2. The increase in $PvCO_2$ was in relationship to the mean values for $PaCO_2$. The relation between the values for blood gas determinations in the arterial and venous blood were expected.

As a consequence the mean values for HCO_3, base excess and CO_{2ct} in the venous blood showed an increase. The mean values for venous blood pH similarly to those for arterial blood pH were not affected at a significant level.

Hematological and Serum Electrolyte Evaluations

The increase in segmented neutrophils and decrease in lymphocytes were significant between the mean values of the pre-catheterization sample and those of the remaining samples. That fact showed the influence of the surgical procedure rather than the action of xylazine hydrochloride on those variables. The decrease in Hb proved to be significant at the 10, 20, 30 and 40 minute samples and at the recovery sample. The mean values of the recovery control sample and of the control sample were not significantly different. The decrease in the PCV confirmed previous investigation.[13]

The differences found among the mean values for Ca and Mg of the various samples were at levels which were not clinically meaningful.

SUMMARY AND CONCLUSIONS

Twelve cows were administered xylazine hydrochloride intravenously at a dosage rate of .22 mg per kilogram of body weight. Teflon catheters had been previously implanted into the saphenous artery and great saphenous vein. Venous blood samples were collected prior to catheter implantation for hematological evaluation including Hb, WBC count, differential WBC count, PCV, plasma protein and fibrinogen and for serum electrolytes including Na, K, Ca, Mg and P. Arterial and venous blood samples for blood gas determinations and hematological and serum electrolyte evaluations were collected immediately before and after the administration of xylazine hydrochloride. Blood sampling was repeated every 10 minutes during the 40 minutes following the administration of the drug and at the time the cows stood up. Recovery control arterial and venous blood samples were collected approximately 18 hours later. Arterial blood pressure and ECG were recorded at the same time intervals the blood samples were collected with the exception of the final one.

The dosage rate selected proved to be more than sufficient for the bovine subjects to adopt lateral recumbency and the state of sedation, analgesia and muscle relaxation seemed to be adequate for minor surgical procedures.

The increase in Q-T interval and decrease in the cardiac rate and systolic and diastolic blood pressures were significant

at the .01 level. The PaO_2 and PvO_2 were sharply decreased and the $PaCO_2$ and $PvCO_2$ increased. Arterial and venous blood pH were not significantly affected by xylazine hydrochloride. The results approached normal values at the recovery period. The mean values of the control and recovery control samples were not statistically different. The hematological and serum electrolyte evaluations showed the primary influence of the surgical procedure of implanting the catheter. The decrease in PaO_2 and increase in $PaCO_2$ were acute and the subjects did not present clinical signs of hypoxia. The findings suggested that repeated doses of the drug could lead to repeated phases of low PaO_2 and high $PaCO_2$ levels. The absence of apparent clinical alterations in the experimental animals in this study seemed to give support to the affirmation that healthy animals generally tolerate the changes caused by the administration of xylazine hydrochloride. According to previous investigation the drug should be avoided in patients with disorders having an unfavorable effect on tissue oxygenation. This was confirmed by the results of this study as well. More studies are necessary but it could be suggested that the dilution of xylazine hydrochloride in saline solution for intravenous administration would moderate the acute and marked alterations in the cardiopulmonary function which were found in this investigation.

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Finally, I want to express my special thanks to my family and friends, in Brazil, who have given me the encouragement to pursue higher education.

APPENDIX

Table 1 - MEAN VALUES OF ECG VARIABLES OF ALL SUBJECTS

Record / Variable	Control	Immediate Post-Injection	10 Minute	20 Minute	30 Minute	40 Minute	Recovery
HEART RATE Beats/Minute	72	47	50	51	49	49	49
QRS MAGNITUDE mv	.94	1.06	1.04	1.02	.98	.98	.82
QT INTERVAL seconds	.28	.31	.31	.31	.32	.33	.34
ST SEGMENT ELEVATION mv	.085	.063	.066	.066	.062	.037	.040
T WAVE MAGNITUDE mv	.41	.41	.45	.46	.45	.43	.37

Table 2 - MEAN VALUES OF ARTERIAL BLOOD PRESSURE OF ALL SUBJECTS

Record / Variable	Control	Immediate Post-Injection	10 Minute	20 Minute	30 Minute	40 Minute	Recovery
SYSTOLIC BLOOD PRESSURE mm of Hg	131.45	122.17	114.06	103.88	98.77	99.77	108.24
DIASTOLIC BLOOD PRESSURE mm of Hg	109.72	96.72	87.12	82.31	76.78	78.95	86.54

Table 3 - MEAN VALUES OF ARTERIAL BLOOD GAS DETERMINATIONS OF ALL SUBJECTS

Variable \ Sample	Control	Immediate Post-Injection	10 Minute	20 Minute	30 Minute	40 Minute	Recovery	Recovery Control
pH	7.45	7.43	7.42	7.43	7.45	7.46	7.48	7.44
PaO_2 mm of Hg	102.76	58.05	53.91	54.42	60.92	69.17	85.56	97.51
$PaCO_2$ mm of Hg	37.08	41.26	45.28	45.56	45.37	46.58	44.89	38.51
HCO_3 mEq/l	25.44	27.03	28.90	29.75	31.40	32.34	32.53	25.61
BASE EXCESS mEq/l	2.67	3.77	5.18	5.74	7.31	8.24	8.83	2.28
CO_{2ct} mmol/l	26.58	28.20	30.15	31.22	32.68	33.65	33.75	26.68

Table 4 - MEAN VALUES OF VENOUS BLOOD GAS DETERMINATIONS OF ALL SUBJECTS

Sample / Variable	Control	Immediate Post-Injection	10 Minute	20 Minute	30 Minute	40 Minute	Recovery	Recovery Control
pH	7.41	7.40	7.40	7.40	7.42	7.42	7.42	7.41
PvO_2 mm of Hg	47.76	27.06	31.62	33.05	33.66	33.85	33.37	41.93
$PvCO_2$ mm of Hg	43.10	48.09	49.27	49.77	49.88	51.47	53.32	43.07
HCO_3 mEq/l	27.08	28.91	29.55	30.32	31.34	33.10	33.74	26.51
BASE EXCESS mEq/l	3.57	5.09	5.38	6.10	7.14	8.79	9.23	2.78
CO_{2ct} mmol/l	28.42	30.38	31.08	31.85	32.91	34.70	35.38	27.85

Table 5 - MEAN VALUES OF THE HEMATOLOGICAL VARIABLES OF ALL SUBJECTS

Variable \ Sample	Pre-Catheterization	Control	Immediate Post-Injection	10 Minute	20 Minute	30 Minute	40 Minute	Recovery	Recovery Control
Hb gm%	10.7	10.0	9.60	8.80	8.50	8.50	8.40	8.11	9.83
PCV %	32	30	28	26	25	25	24	24	30
WBC count/ mm^3	8,700	9,300	7,791	7,225	7,500	7,441	7,058	8,025	9,033
Differential WBC count/ mm^3									
Segmented Neutrophils	28	45	49	54	49	50	46	51	48
Non-Segmented Neutrophils	1	2	2	3	4	4	3	2	1
Lymphocytes	64	48	44	38	43	44	47	41	46
Eosinophils	8	8	8	8	6	7	8	4	7
Monocytes	1	1	1	2	2	2	1	1	1
Plasma Protein gm%	7.78	7.17	7.17	7.02	6.88	6.93	6.88	6.82	7.35
Fibrinogen	433	500	467	400	392	408	383	350	483

Table 6 - MEAN VALUES OF SERUM ELECTROLYTES OF ALL SUBJECTS

Sample / Variable	Pre-Catheterization	Control	Immediate Post-Injection	10 Minute	20 Minute	30 Minute	40 Minute	Recovery	Recovery Control
Na mEq/l	137	137	137	137	137	138	137	138	138
K mEq/l	3.83	3.54	3.58	3.52	3.47	3.46	3.42	3.47	3.85
Ca mg%	8.27	7.72	7.63	7.48	7.58	7.58	7.58	7.58	7.81
Mg mg%	1.50	1.58	1.57	1.56	1.54	1.56	1.53	1.53	1.65
P mg%	5.02	4.88	4.87	4.58	4.39	4.32	4.18	4.58	4.58

Codes for the following graphs:

1 - Control

2 - Immediate post-injection

3 - 10 minute

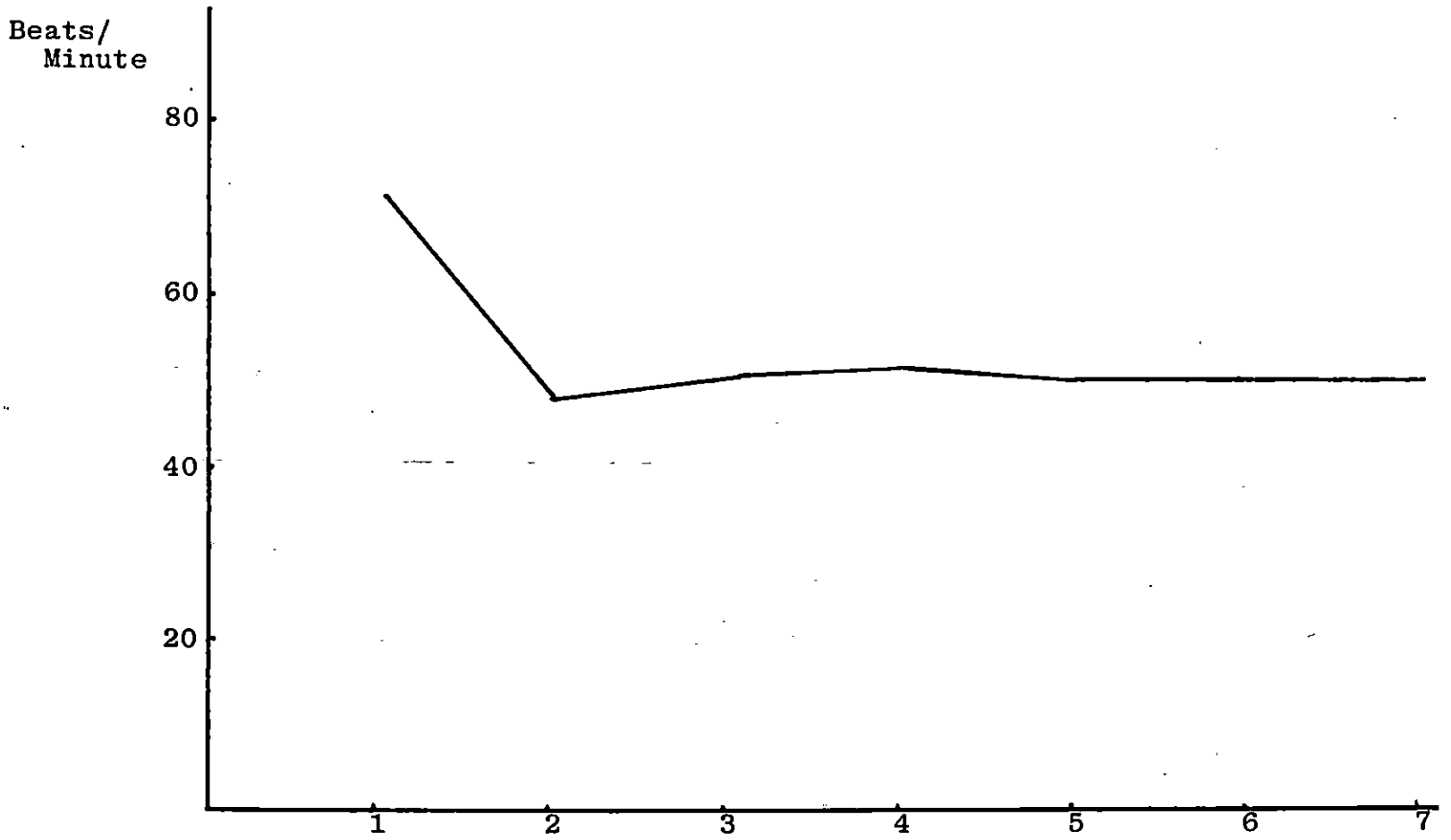
4 - 20 minute

5 - 30 minute

6 - 40 minute

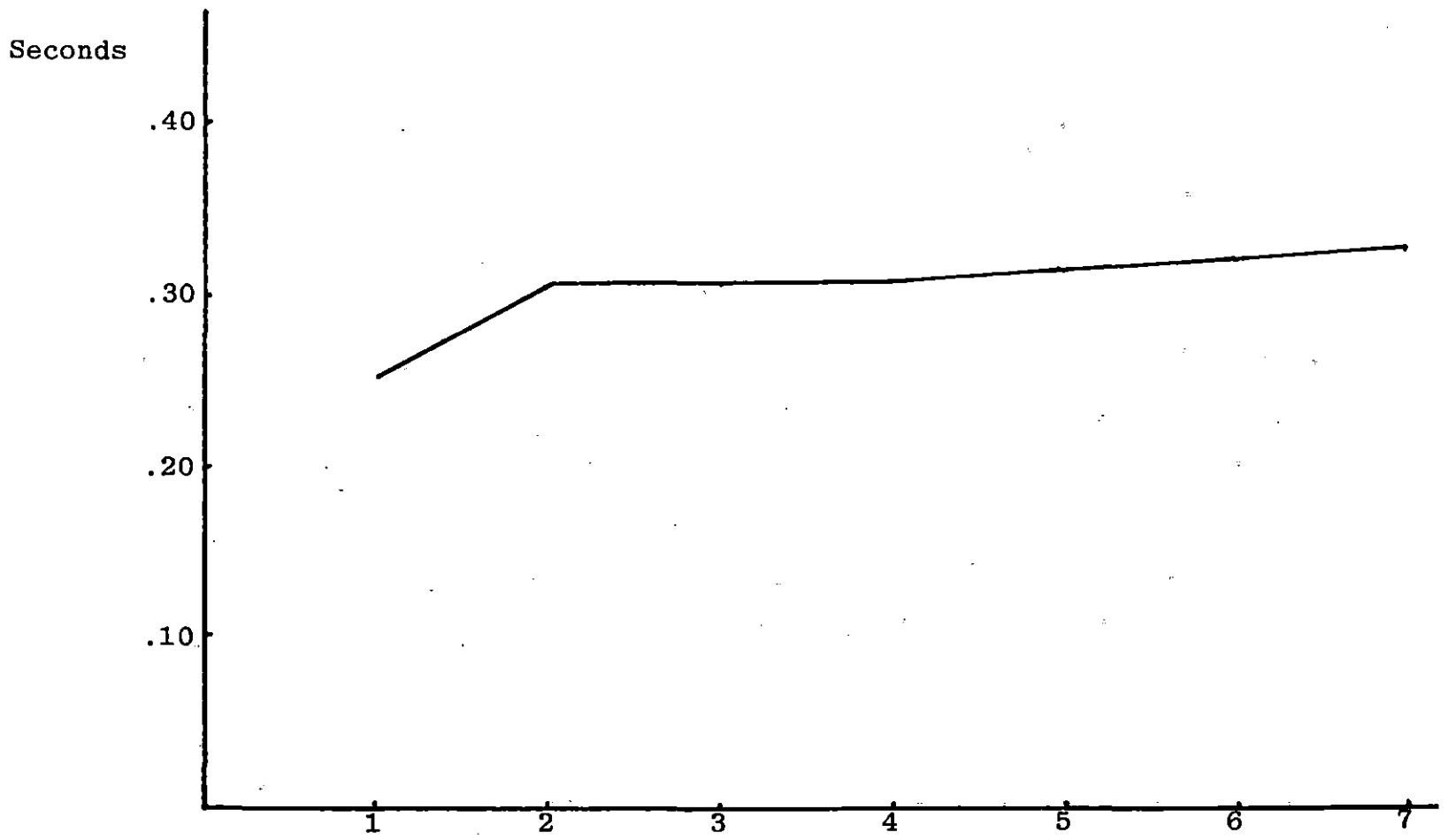
7 - Recovery

8 - Recovery control



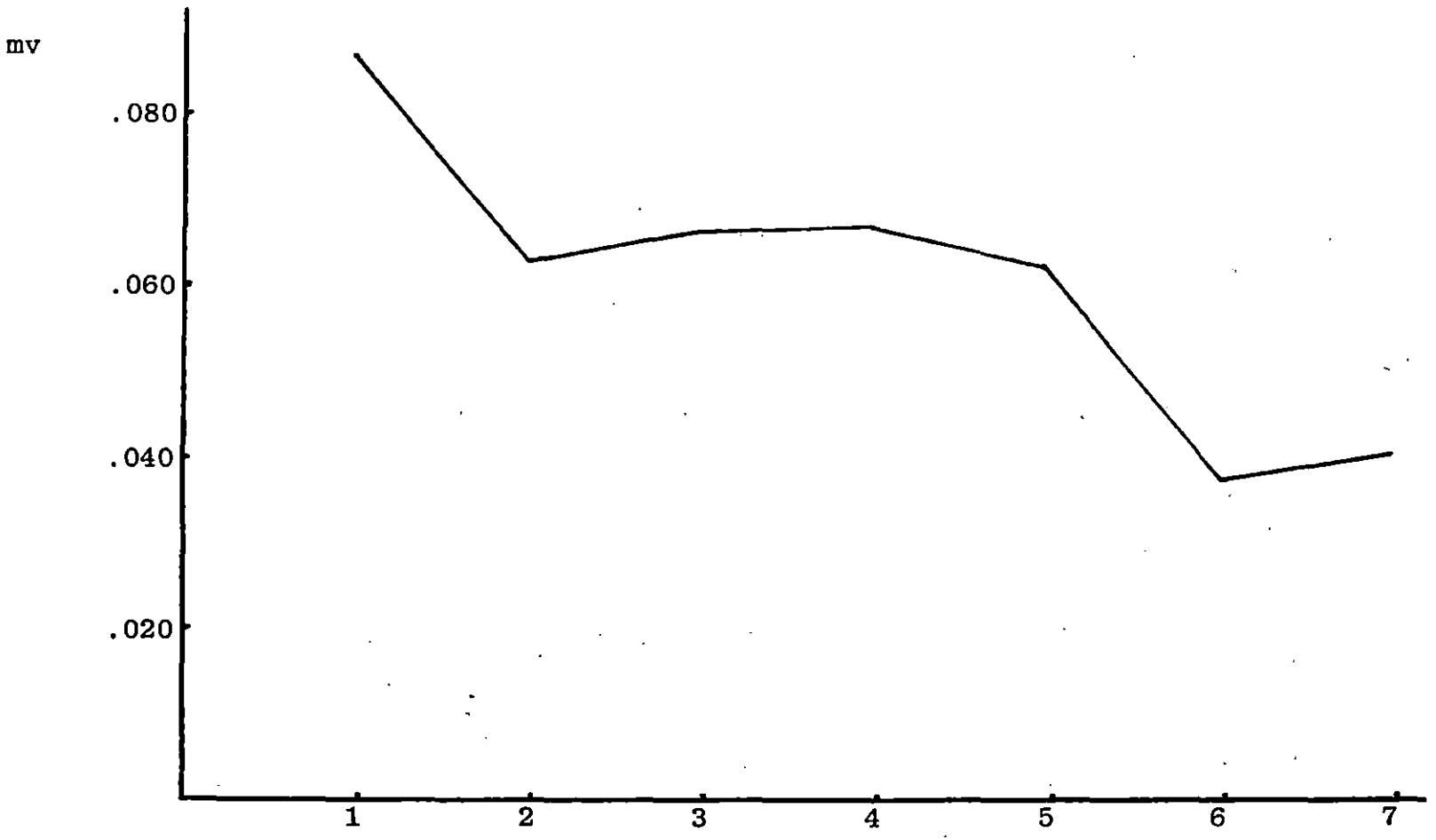
Graph 1 - MEAN VALUES OF HEART RATE OF ALL SUBJECTS

(See Page 60 for Codes for Abscissa)



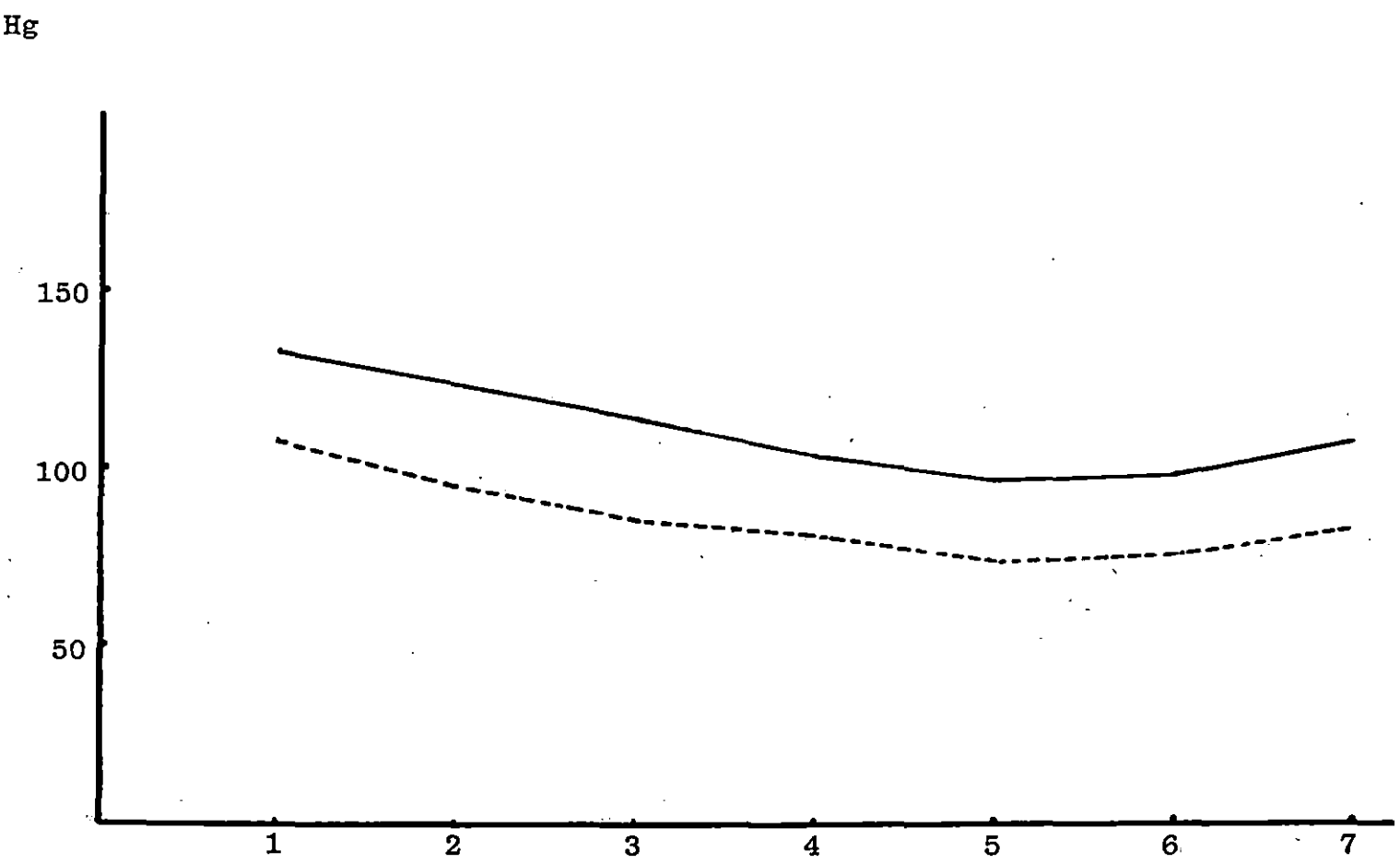
Graph 2 - MEAN VALUES OF Q-T INTERVAL OF ALL SUBJECTS

(See Page 60 for Codes for Abscissa)



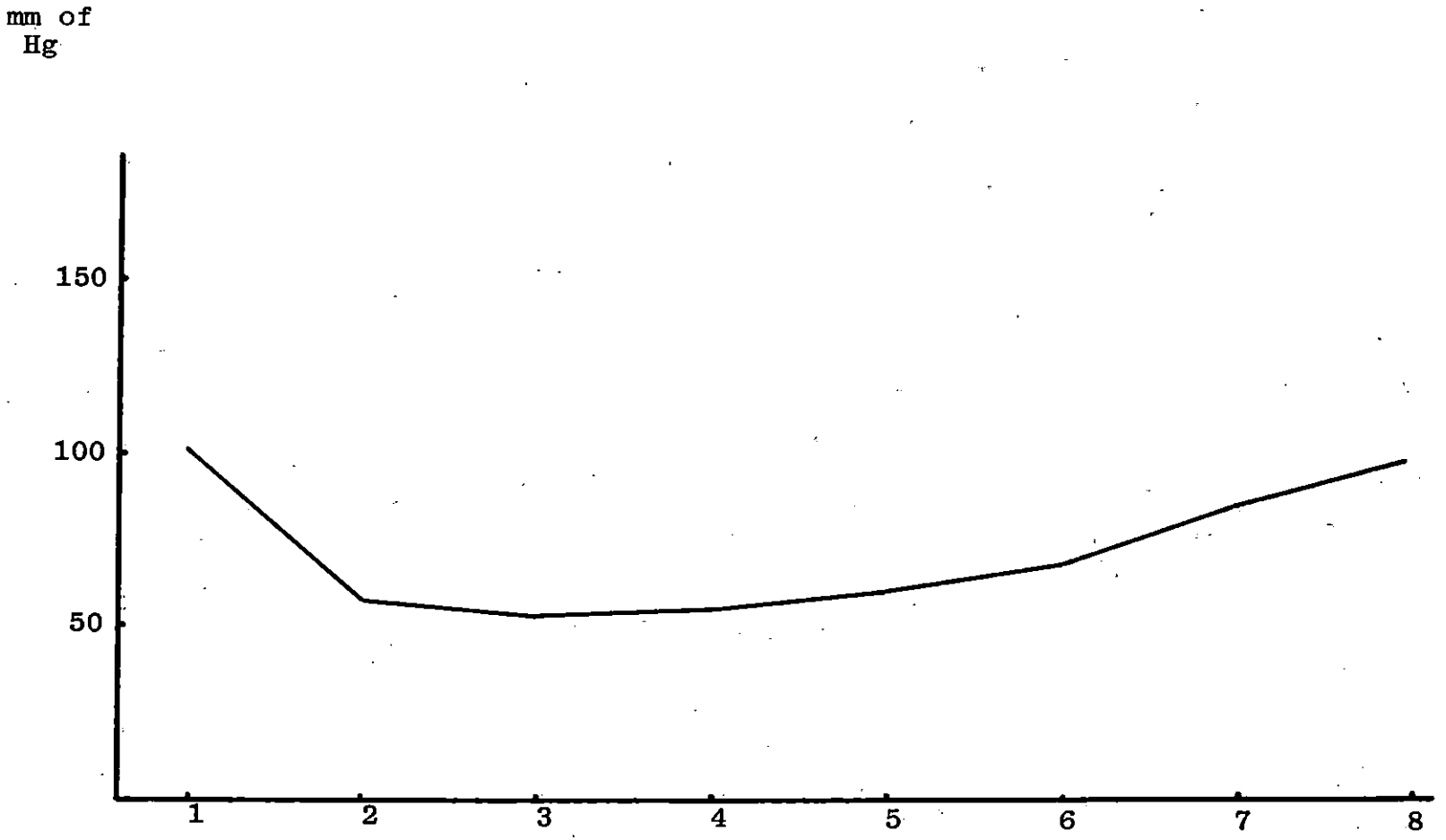
Graph 3 - MEAN VALUES OF S-T SEGMENT DEPRESSION OF ALL SUBJECTS

(See Page 60 for Codes for Abscissa)



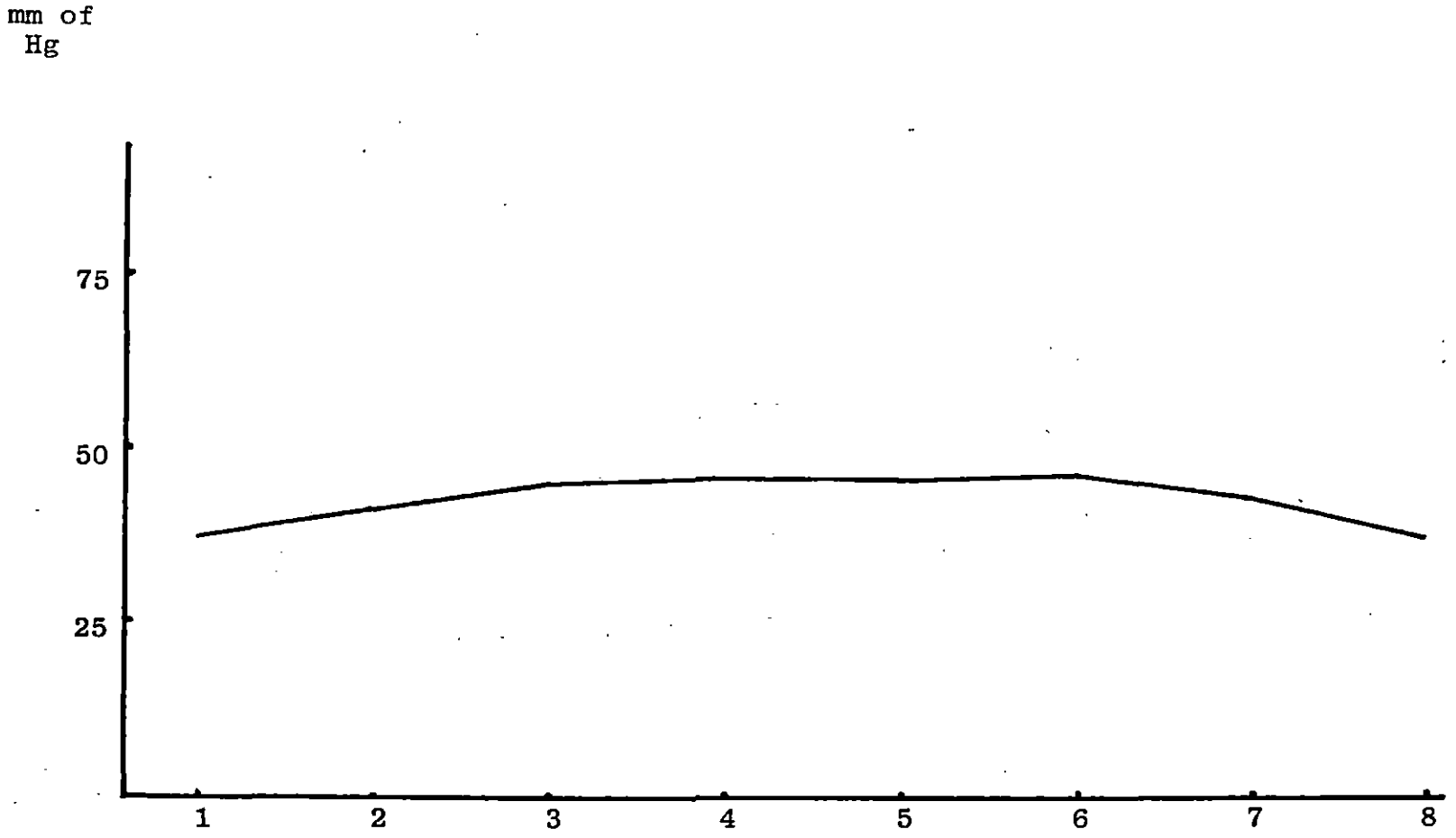
Graph 4 - MEAN VALUES OF SYSTOLIC AND DIASTOLIC BLOOD PRESSURE OF ALL SUBJECTS

(See Page 60 for Codes for Abscissa)



Graph 5 - MEAN VALUES OF PaO_2 OF ALL SUBJECTS

(See Page 60 for Codes for Abscissa)



Graph 6 - MEAN VALUES OF $PaCO_2$ OF ALL SUBJECTS
(See Page 60 for Codes for Abscissa)

Figure 1 - The saphenous artery and great saphenous vein are located on the medial aspect of the hind limb, above the tarsus, lying between the sartorius and gracilis muscles.

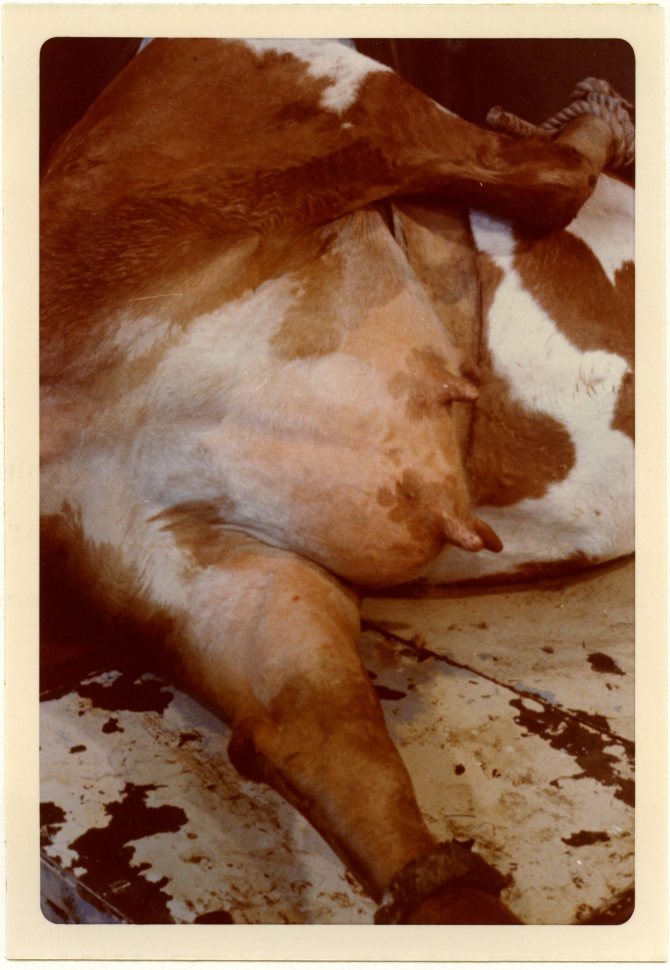


Figure 2 - The Teflon catheters implanted into the saphenous artery and great saphenous vein.

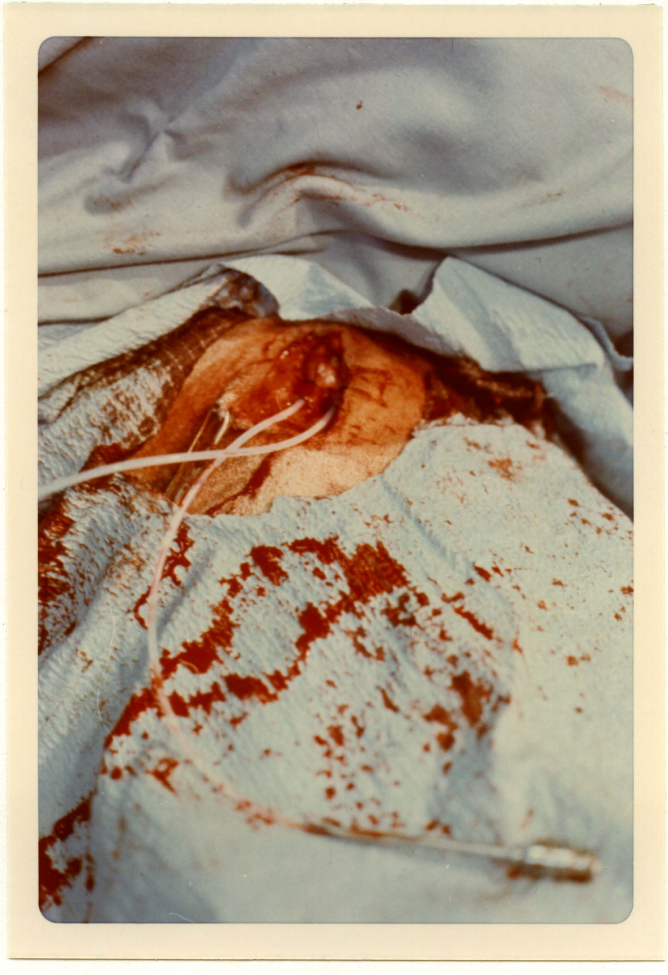


Figure 3 - The catheters fixed on the skin.

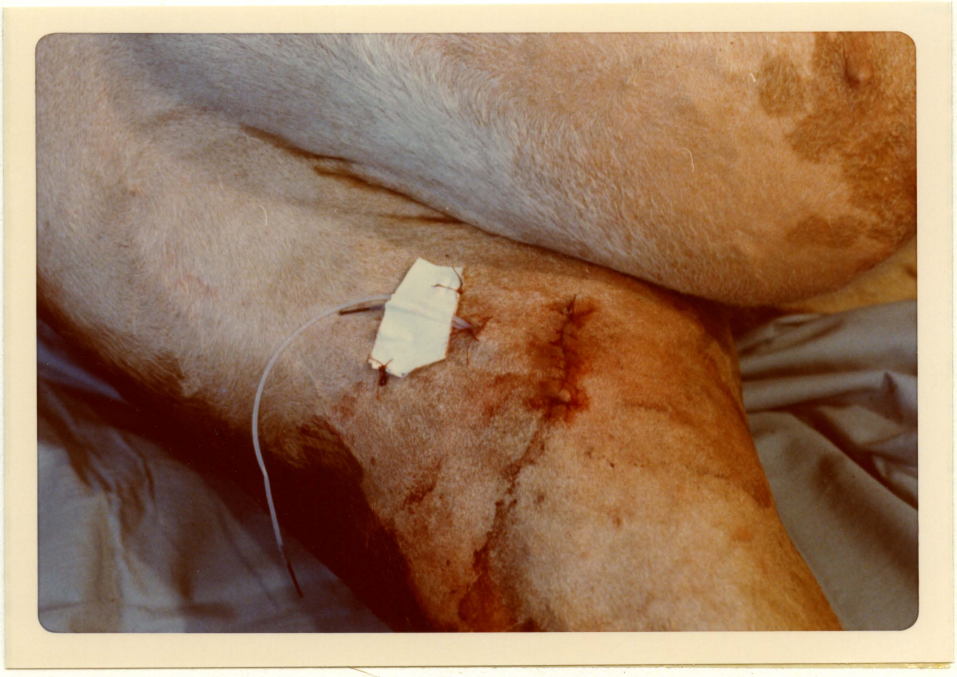


Figure 4 - The subjects adopted lateral recumbency immediately after the administration of xylazine hydrochloride and remained in that position for a period of time not shorter than 20 minutes.

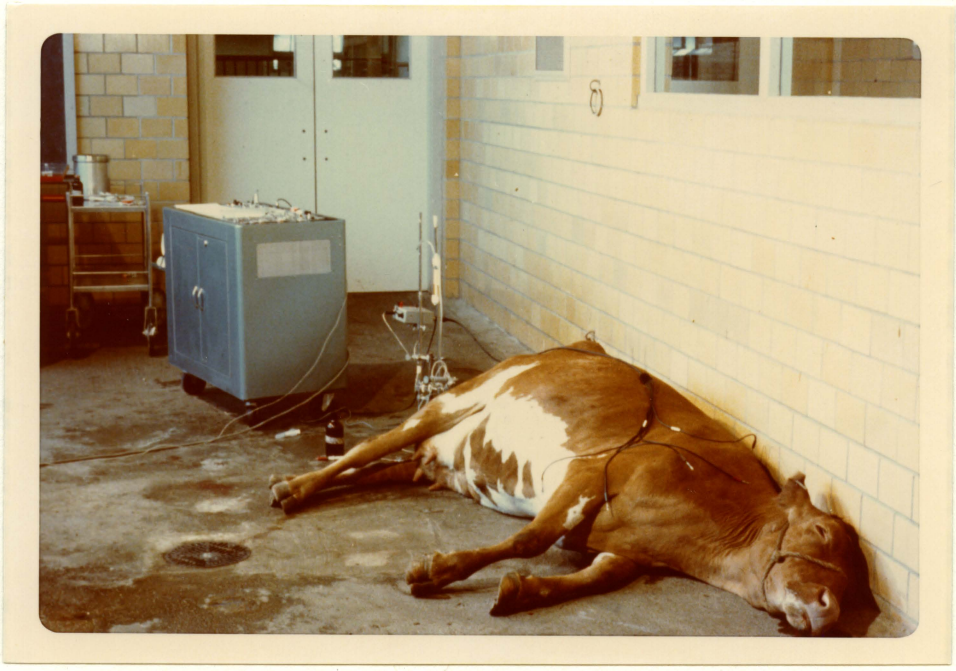
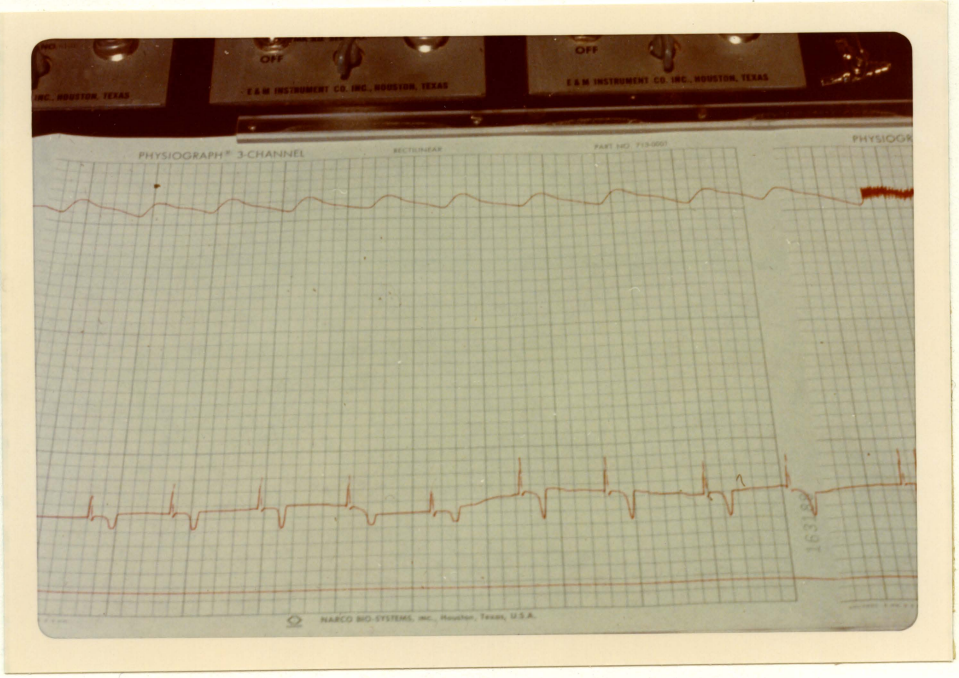


Figure 5 - Recording of systolic and diastolic blood pressures and ECG.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