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ANTAGONISTIC EFFECT OF DOXAPRAM* AFTER ROMPUN** TREATMENT WITH SPECIAL REFERENCE TO ACID-BASE BALANCE IN GOATS

(With 3 Table)

By

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التأثير المضاد لعقار الدوكسبرام بعد حقن الرمبون مع الإشاره الخاصه للتغيرات فى الإتزان الحامضى القاعدى فى الماعز

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لقد استخدمت عشرة من الماعز لهذه الدراسة حيث قسمت الى مجموعتين متساويتين. حقنت المجموعه الاولى عقار الرمبون بجرعه ٥ر٠ مجم لكل من وزن الحيوان فى العضل. وفى المجموعه الثانيه حقن عقار الدوكسبرام فى الوريد بعد خمسون دقيقه من حقن الرمبون. هذا وقد أعطى عقار الدوكسبرام تأثير منبه جيد للماعز المهدئه بعقار الرمبون لذلك يمكن الاشاره باستخدام عقار الدوكسبرام بأمان لعلاج التغيرات الغير مرغوب فيها فى الاتزان الحامضى – القاعدى وغازات الدم وكذلك لتجنب الرقاد الطويل بعد استخدام الرمبون فى الماعز.

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* : Dopram–V, registered trademark of A.H. Robins, Richmond, Va., USA (distribu–tion in germany: A.Albrecht GmbH u.Co., Aulendorf).

**: Registered trademark of Bayer AG, Leverkusen.

SUMMARY

Ten goats of both sexes were used in this investigation. The animals were divided into two equal groups. The first group received rompun (xylazine) only in a dose rate of 0.5 mg/Kg.B.Wt. intramuscularly. Doxapram was given intravenously to the animals of group II, 50 minutes after xylazine injetion. Clinical examination including body temperature, pulse and respiratory rates before and after treatment were recorded. Blood gases and acid-base balance were also demonestrated. Doxapram gave a good stimulant effect for goats sedated with xylazine. Doxapram can be used safely in a dose rate of 5 mg/Kg.B.Wt. to avoid the undesirable alteration in acid-base balance and blood gases as well as prolonged recumbency induced by xylazine injection in goats.

INTRODUCTION

Rompun in a non narcotic sedative analgesic with muscle relaxant properties. It is widely used in different animal species. Ruminants especially goats are more sensitive to xylazine *(HALL, 1971)*. When higher dose rates are used, marked CNS depression may be induced. In these cases antagonist must be used to overcome xylazine-induced CNS depression *(DENDI & PARADA, 1981; HSU et al.,1987 and MOHAMMAD, 1987)*.

Some studies had shown that a combination of 4-amino-pyridine plus yohimbine would antagonise xylazine sedation in dogs and cats *(HATCH et al., 1982 & 1983)*. cattle *(KITZMAN et al., 1984)*. *HSU et al. (1987)* compared the ability of tolazoline and yohimbine to antagonize xylazine-induced CNS depression in sheep.

The purpose of the present investigation is to study the antagonistic effect of doxapram in goats and its possible safe rate and sustained reversal of xylazine sedation. Special attention was made toward the changes in blood gases and acid-base balance as well as the clinical signs.

MATERIAL and METHODS

The study was carried out on ten clinically healthy native breed goats (2 males and 8 females) with body weight ranging from 17 to 40 Kg. The animals were divided randomly into two

equal groups each of five animals. The first group was injected with rompun in a dose rate of 0.5 mg/Kg.B.Wt. intramuscularly and served as a control. The second group rcveived the same dose of rompun as in group (I) and doxapram in a dose of 5 mg/Kg B.Wt. was injected intravensouly 50 minutes after rompun injection.

Pulse, rectal temperature and respiratory rates were recorded before rompun administration and at thirty-minute intervals until the end of experiment (240 minutes). Other clinical observations were also noticed and recorded. Blood samples for blood gas analysis were collected anaerobically from jugular vein into 1 ml disposable syringes whose dead space had previously been filled with 1:1000 sodium heparin at the same time intervals. These samples were immediately placed on ice-bath and measured within 30 minutes of collection. Blood pH, oxygen tension (P02: mmHg), standard bicarbonate concentration (HC03 :mmol/L.), total carbon dioxide (TC02:mmol/L.) and base-excess (B.E.:mmol/L) were determined in each sample using Corning pH-blood gas analyser (Model 168. Halstead, Essex, Great Britian).

RESULTS

Clinicl observations and reflexes:

Group I (0.5 mg/Kg.B.Wt. Rompun I/M): The symptoms of sedation were noticed after about three minutes post-injection and were recognized by lowering of the head and neck, partial drooping of the upper eyelid, protrusion of the nictitating membrane and tongue, muscular incoordination and staggering gait. All animals layed down after 5-7 minutes. At this stage, pronounced watery salivation and frequent urination of a considerable amount of urine were observed. Skin sensibility to pin pricks and interdigital reflex were abscent. Tympany was noticed in all animals during recumbency but disappeared after returning of the animals to standing position. The animals began to stand after about two hours from rompun injection.

Group II (5 mg/Kg.B.Wt. Doxapram I/V after 0.5 mg/Kg.B.Wt. Rompun I/M): The clinical observations and reflexes were similar to those of the animals in group (I). After one minute from intravenous injection of doxapram all animals in this group returned to sternal recumbency and then to standing position. Salivation was stopped. One goat returned to lateral recumbency again after ten minutes but stood quickly when external stimuli were applied. Another goat cried just after doxapram injection and there was a momentery increase in respiratory rate.

The mean values of respiratory rate, pulse rate and body temperature before and after drugs administration are shown in table (1).

Alteration in acid-balance and blood gases values: Mean values of blood pH, PCO2, PO2, HCO_3^-, TCO2 and B.E. before and after treatment are shown in table 2 (group I) and table 3 (group II).

DISCUSSION

A large number of drugs possess the ability to stimulate the CNS. Stimulant drugs vary markedly in their total pharamacological action. Some can be used for therapeutic stimulation within narrow limits of dosage and others have wide safety margin. Doxapram has a marked stimulant effect in cattle sedated with rompun. In animals treated with CNS depressants, the normalisation of respiration is achieved with dose rates which are 70-75 times lower than those which would be necessary to provoke convulsions in unsedated animals *(DENDI and PARADA, 1981).*

In horses, a clinical evaluation of doxapram (0.25 mg/lb) as a respiratory stimulant was conducted during and after general anaesthesia with intravenous injection of chloral hydrate alone and chloral hydrate in combination with pentobarbital and magnesium sulfate *(SHORT et al., 1970).* The arousal time was reduced, respiratory volume and rate increased immediately following administration of the drug. No toxic or adverse effects were noticed. A similar clinical evalution of doxapram (0.21 mg/lb) in the horse during and after general anaesthesia with halothane and methoxyflurane revealed comparable effects *(SHORT and CLOYD, 1970).*

The results of this study indicated that doxapram at the studied dose had a marked antagonistic effect on the sedative and bradycardic effects of xylazine in goats. The respiratory rate was increased immediately after administration of the antagonist and the arousal time was shortened. The stimulation effect of doxapram is believed to be related to a direct action upon the chemorecptors of the carotid and aortic regions as well as stimulation of the medullary respiratory center *(JONES et al., 1978).*

There were a marked drop in the pH values within 60 minutes post administration, a concamitant drop in the mean values of HCO_3^- and TCO2 then gradual increase in pH value was observed in group (I) after administration of rompun in a large dose until 210 minutes (7.529). This increase in pH values were

also accompanied by increase in the $HCO3^-$ and TCO2 values. These values at 210 minutes were 32.7 and 33.9 mmol/L respectively. Base excess values give a sharp indication for this change. Screening the data of acid-base balance, it was observed that there were no marked change in PCO2 and PO2 values, while the bicarbonate values were slightly elevated during the period of administration. Base excess go in similar manner without marked changes in their mean values. It could be concluded that administration of high dose of rompun alone exert its action and had a marked effect on the values of acid-base balance toward the alkalosis side specially after about 3 hours post-injection.

In group (II) the changes in acid-base balance and blood gases were not similar to that of group (I). Increase in pH was in steady manner and did not reach the maximum alkalosis range if compared with the changes in group (I). It could be concluded that combination of administration of rompun and doxapram, gave no marked alteration in the values of acid-base balance.

It has been observed through the field visit in many veterinary stations that rompun may be used in an over dosage, such usage may subject the animals to risk of rompun over dosage. From our clinical observation in this study it could be concluded that under such cases the usage of doxapram as rompun antagonist, give a great chance to minimize the risk of marked CNS depression accompanying the high dosage of rompun and ensure utmost safety usage of rompun.

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Table (1): Mean values of respiration, pulse and body temperature under the effect of rompun (group I) and rompun and doxapram (group II).

Time (min.)	Respiratory rate GROUP I	GROUP II	Pulse rate GROUP I	GROUP II	Body temperature GROUP I	GROUP II
0	39	37	107	97	39.7	39.2
30	55	47	59	62	39.6	39.6
60	41	37	81	57	39.4	39.5
90	40	50	55	60	39.2	39.5
120	37	27	60	52	38.9	39.9
150	31	29	58	64	38.7	40.1
180	34	45	63	81	38.7	40.2
210	40	42	65	84	38.8	40.5
240	43	45	69	93	39.0	40.5

Table (2): Mean values of blood gases and acid-base balance in goats after I/M injection of 0.5 mg/kg.B.Wt.Rompun (group I).

Time (min.)	pH	PCO2 mm Hg	PO2 mm Hg	HCO3 mmol/L.	TCO2 mmol/L.	B.E. mmol/L.
0	7.399	37.9	41.4	23.2	24.6	0.5
30	7.259	42.3	43.4	18.9	20.2	-7.8
60	7.332	45.1	46.2	24.0	25.3	-0.5
90	7.425	46.6	44.8	30.6	31.7	6.0
120	7.442	44.0	47.3	31.1	32.5	7.0
150	7.527	36.1	66.3	29.2	30.4	7.6
180	7.514	41.2	51.1	34.1	35.3	11.0
210	7.529	39.2	44.8	32.7	33.9	10.4
240	7.436	43.3	43.2	29.7	31.1	5.7

Table (3): Mean values of blood gases and acid-base balance in goats. Doxapram was injected 50 minutes after Rompun injection (group II).

Time (min.)	pH	PCO2 mm Hg	PO2 mm Hg	HCO3 mmol/L	TCO2 mmol/L	B.E. mmol/L
0	7.396	37.6	44.0	23.0	26.1	0.9
30	7.336	41.4	44.5	22.3	23.5	-3.1
60	7.401	40.9	37.5	25.3	26.5	1.0
90	7.444	39.2	35.9	27.3	28.5	3.7
120	7.463	41.3	36.4	29.7	31.0	6.2
150	7.426	42.2	41.4	28.8	30.2	3.2
180	7.460	39.5	35.2	28.1	29.3	4.8
210	7.431	42.2	41.2	28.5	29.9	4.6
240	7.407	39.2	35.5	24.4	25.5	0.8