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ETORPHINE HYDROCHLORIDE ANTAGONISTS USED IN THE CAPTURE OF THE WHITE RHINOCEROS CERATOTHERIUM SIMUM SIMUM

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Summary

Nalorphine hydrobromide, Cyprenorphine hydrochloride, or Diprenorphine hydrochloride were employed to antagonise the narcotic Etorphine hydrochloride used in drug combinations for the immobilization of 320 white rhinos between April 1967 and April 1970. The method of capture and the dosages of each drug used are given, and the relative efficiency of each antagonist in enabling the animal to rise after administration is discussed.

Introduction

Some one thousand white rhinos have been immobilized by the staff of the Natal Parks Board, mainly for the purpose of translocation. (Wallach, 1966 [1]; Player, 1967 [2]). Etorphine hydrochloride was employed in the drug combinations in the vast majority of these captures, and Nalorphine hydrobromide as the antagonist.

Recently Etorphine has been supplied in powder form together with the antagonist Cyprenorphine, in separate bottles in the same pack. An inclusive charge is made for the whole pack, and the two drugs cannot be purchased separately, with the result that in reality the Cyprenorphine is supplied free of charge. Nalorphine is, however, very expensive, and a large dose is required for white rhinos. Trials were therefore undertaken to examine the efficiency of Cyprenorphine and Diprenorphine on a limited number of immobilized white rhinos.

Materials and Methods

The darts containing the immobilizing drugs were projected either by means of the Can Chur gas-gun*, the Palmer Powder-charge gun,* or the Van Rooyen cross-bow**, on foot, or from a moving Land Rover. Projectiles of 2 or 3 c.c. capacity were used with 1½ inch barbed needles.

After darting, the rhino was followed on horse-back, or on foot until immobilized. The distance travelled by the animal following injection of the drug varied from a few yards to three miles, and the time taken eight to twenty minutes.

A lorry was brought to the recumbent animal and the crate on it unloaded and placed in front of the rhino with the door open.

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The narcotic antagonist was then injected into a convenient ear vein. The rhino usually rose from sternal recumbency to its feet within three minutes, often with some artificial stimulus, and was guided forwards into the crate by means of a rope previously positioned under its chin and behind the posterior horn, but in front of the ears.

The following drugs were used:

Etorphine hydrochloride – M99 (Reckitt).

This highly potent drug has been fully described by Harthoorn[3], and other authors recently. It is now used extensively, either alone, or in combination with other drugs, for the immobilization of a large variety of animals. The white powder was dissolved in Acetylpromazine producing a solution containing 5 mgm. Etorphine hydrochloride per c.c.

Acetylpromazine (Boots Pure Drug Company)

This tranquilliser was used primarily as a vehicle for dissolving Etorphine, and was employed in very small doses. The solution proved very stable, having a pH of about 4, and was coloured yellow. It is a phenothiazine derivative and a rapidly absorbed central nervous depressant. It is supplied in a concentration of 10 mgm. Acepromazine per c.c.

Hyoscine hydrobromide.

This alkaloid has an atropine-like action and depresses the central nervous system. When used in drug mixtures it reduced the latent period between darting and capture, and caused temporary, partial blindness, due to pupillary dilation. This prevented the rhino from refusing to enter the crate following the admission of the antidote.

Nalorphine hydrobromide - 'Lethidrone' (Burroughs Wellcome & Co.)

This morphine antagonist was used to reverse the narcotic effect of Etorphine. It acts very rapidly when injected intravenously, but can also be administered parenterally when a slower, more prolonged action is required. The water soluble powder was prepared as a solution containing 25 mgm/c.c. The dosage rate of Nalorphine varied with the weight of the animal and not so much with the dose of narcotic used.

Cyprenorphine hydrochloride – M285 (Reckitt).

This substance is a highly potent specific morphine antagonist, but in contrast to Nalorphine its action is very much less weight dependent. Thus the dose given depends more upon the amount of Etorphine used for immobilization. The prepared solutions contained 10 mgm/c.c.

Diprenorphine hydrochloride – M50 - 50 (Reckitt).

This substance was in its early experimental stage, and only a very limited trial was undertaken. It is closely related to Cyprenorphine, and its mode of action probably very similar. It is one and one half times the potency of Cyprenorphine, and is said to have far less of a respiratory depressant action. The white powder was prepared as a solution containing 3 mgm./c.c. using acid sterile water.

Results

The amounts of drugs used in immobilizing combinations, and antidotes injected, for different weight groups of white rhinos, are shown in Tables 1, 2, and 3.

TABLE 1:
Dosages of all drugs in mgm.

Group Numbers	Estimate weight in pounds	Etorphine	Acetylpromazine	hyoscine	Nalorphine 1/v	Numbers of animals.
1	600 to 1000	¼	½	25	50	2
2	600 to 1000	½	1	25	100	3
3	800 to 1250	½	1	50	90 to 175	7
4	1250 to 1800	1	2	50	75 to 112	3
5	1250 to 1800	1	2	50	200 to 250	6
6	1250 to 2500	¾	1½	50	150 to 250	6
7	1250 to 2500	¾	1½	25	125 to 200	6
8	1250 to 2500	¾	1½	None	175 to 250	5
9	1250 to 2500	¾	None	None	250	2
10	1250 to 2500	1	2	25	175 to 200	33
11	1250 to 2500	1	2	None	175 to 250	7
12	1250 to 2500	1	None	None	200	1
13	1250 to 2500	1¼	2½	25	200 to 250	7
14	1250 to 2500	1¼	2½	None	175 to 250	6
15	1250 to 2500	2	4	100	150 to 225	2
16	2500 to 5000	1½	3	100	250 to 300	48
17	2500 to 5000	1½	3	100	375	9
18	2500 to 5000	1½	3	50	375	22
19	2500 to 5000	1½	3	None	250 to 350	9
20	2500 to 5000	2	4	100	225	16
21	2500 to 5000	2	4	100	255 to 330	34
22	2500 to 5000	2	4	25	375	15
23	2500 to 5000	2	4	50	375	28
24	2500 to 5000	2	4	None	300 to 375	8
25	2500 to 5000	2¼	4½	50	375	7
26	2500 to 5000	2¼	4½	None	325 to 375	5

TABLE 2:
Dosages of all drugs in mgm. Animals unable to stand within 10 minutes of antidote being given, were lifted & pushed into the crates. All stood ½ to 3 hours after crating.

Estimated weight in pounds	Etorphine	Acetylpromazine	hyoscine	Cyprenorphine 1/v	Reaction following administration of antidote.
1000	½	1	50	20	Very light anaesthesia when antidote administered. Could not rise after antidote administered.
1300	¾	1½	50	20	Respiratory rate increased and ears moved. No effort made to rise onto its feet.
1500	¾	1½	40	2	Attempted to rise, but unable to stand.
2000	1	2	25	3	Stood up within two minutes.
2000	1¼	2½	25	5	Respiratory rate increased, but unable to stand.
2500	1	2	25	10	Respiratory rate increased, but unable to stand.
4000	2	4	100	50	Attempted to rise, but unable to stand.
5000	1½	3	100	3	Attempted to rise, but unable to stand.
3000	1½	3	50	5	Attempted to rise, but unable to stand.
2000	1	2	None	4	Attempted to rise, but unable to stand.
2250	1½	3	None	5	Attempted to rise, but unable to stand.
2250	1½	3	None	10	Respiratory rate increased but made no effort to stand. Stood up 2 hours later.
1500	1	None	None	4	Rose onto its feet after several efforts 6 minutes after antidote administered.
2000	1	None	None	5	Stood up within three minutes
2500	1	None	None	3	Unable to stand in ten minutes

TABLE 3:
Dosage of all drugs in mgm.

Estimated weight in pounds	Etorphine	Acetylpromazine	hyoscine	Diprenorphine	Reaction following the administration of the antidote.
3000	1½	3	50	2	No visible effect. Inject 375 mgm. Nalorphine ⅓v. Stood up 1½ minutes later, and walked away.
3500	1½	3	50	4	Stood up in 3 minutes.
4000	1½	3	50	4	Respiratory rate increased. Slight effort made, but unable to rise even with stimulus.
4500	1½	3	50	6	Struggled from lateral to sternal recumbency in 2 minutes. Stood up in 14 minutes.
1500	1	2	25	2	Stood up in 8 minutes with stimulus.
1750	½	1	None	2	Stood up from lateral recumbency, and was very lively within 3 minutes.
2000	1¾	3½	None	3	Stood up and walked away
2000	1¾	3½	None	3	Stood up and walked away
4500	2	4	None	5	Stood up from lateral recumberency without stimulus within three minutes.

TABLE 4

Estimated weight in lbs.	Immobilizing Mixture in mgm. Etorphine	Acetyl-promazine	Hyoscine	Antidote. Nalorphine mgm.
800 to 1250	½	1	25	90 to 175
1250 to 2500	1	2	25	175 to 250
2500 to 5000	1½ to 2	3 to 4	50	375

All three animals in group 4 were rather slow rising to their feet, that is, they took more than four minutes. All six animals in group 5, however, were standing within two minutes. The amount of antidote given to these latter animals was probably 50 mgm. more than was absolutely necessary. All the rhinos in groups 1, 2 and 3 behaved normally.

Three animals in group 6 were slow to rise in spite of receiving a small ¾ mgm. dose of Etorphine. This was probably due to their receiving 50 mgm. of Hyoscine, instead of 25 mgm. All six in group 7 stood up quickly after receiving 25 mgm. of Hyoscine.

All animals in groups 8, 9, 11, 12 and 14 rose very quickly, and were immediately aware of their surroundings, and proved difficult to crate.

Two of the smaller animals, out of thirty-three, in group 10, were slow getting up. All the rest were up within four minutes.

Both rhinos in group 15 received large doses of both Etorphine and Hyoscine, and small doses of antagonist. Both were nearly 2500 pounds body weight, and both stood up satisfactorily, but the number in the group was insufficient to come to any conclusions.

All seven rhinos in group 13 behaved normally.

One animal in group 21 could not regain its feet and was lifted into the crate. Two in group 20 behaved in a similar fashion, and, in fact, never did rise, and died some hours later in the crates. They were both females heavy in calf.

Some of the rhinos in group 16 were slow to rise, then became recumbent again in the crates and relapsed into deep narcosis, with sweating and distressed breathing. This was particularly noticeable in very hot weather. The amount of antidote was then increased to 375 mgm. in group 17 with better results as far as rising onto their feet was concerned. But again recumbency and distress followed in the crates in hot weather. The dose of hyoscine included in the immobilizing mixture was then reduced to 50 mgm., from 100 mgm., in groups 18, 23 and 25, with the result that all fifty-seven animals rose quickly and did not show distress following crating.

In group 22 the dose of Hyoscine was reduced even farther, to 25 mgm., and that of Nalorphine retained at 375 mgm. All fifteen animals stood up quickly, but were too lively, and difficulty was experienced in getting some of them to enter the crates.

All the rhinos in groups 19, 24 and 26 rose quickly, and in most cases a smaller dose of Nalorphine was employed. None received any hyoscine, and none was crated, all being released where they fell following immobilization. Great difficulty would have been experienced had attempts been made to crate them due to their weight and ability to see.

Discussion

Following the intravenous administration of either Nalorphine or Cyprenorphine, zebra and cloven hoofed wild animals, immobilized with drug combinations similar to those employed on white rhinos, rise to their feet very quickly, usually in 40 to 60 seconds. Pienaar (1967) [4] describes how immobilized elephants stand up in about two minutes following the intravenous injection of Cyprenorphine; and Kind (1969)[5] has found it a satisfactory antidote to Etorphine on immobilized black rhinos. Members of this latter species rise very quickly and are often immediately very aggressive following the intravenous administration of Nalorphine. The white rhino shows greater difficulty in rising, and having done so, remains much more phlegmatic. In fact, it is possible to sit upon a white rhino's back for several hours after the administration of this antidote.

The dosage of Lethidrone received by the two hundred and ninety-six animals included in Table I varied from one mgm. per seven to one mgm. per thirteen pounds, with a maximum total dose of 375 mgm. even for the largest fullgrown male of about 5000 pounds body weight. All body weights were estimated in the field from experience gathered following the accurate weighing and measuring of some dead individuals, and also some crated individuals on a heavy-duty weigh bridge. This dosage compares with one mgm. per 5 to 6 pounds body weight employed for blue wildebeest and zebra, a mgm. per 7 pounds for eland, and one mgm. per 8 pounds for buffalo. The dose therefore diminishes per pound body weight the heavier the total weight of the animal.

The recommended dose of Cyprenorphine is three times the Etorphine dose used for immobilizing the animal.[6] The dose employed on the fifteen rhinos listed in table 2 varied from two to twenty-five times the Etorphine dose. The respiratory rate increased in every case, and in most, ear movement also increased. This latter movement is always an excellent indication that the antidote is taking effect. However, in the majority of cases the animal was quite unable to rise to its feet, often for several hours after administration of the antidote, whether hyoscine or Acetylpromazine was included in the mixture or not.

The results obtained using Diprenorphine as the Etorphine antagonist, on a limited number of animals, were more encouraging than those when Cyprenorphine was employed. The rhinos took longer to stand up than when Nalorphine was used, particularly when hyoscine was included in the immobilizing mixture.

The suggested dose of Diprenorphine was two-thirds or a half of the normal Cyprenorphine dose[6]. Brief trials on horses and dogs had shown that satisfactory results had been obtained using an Etorphine/Diprenorphine ratio of 1:1.3 to 1:4.0.

The sex of the rhino had little bearing upon the reaction to the various antidotes, except in the case of two females which received 100 mgm. hyoscine in the immobilizing mixture and only

225 mgm. of Nalorphine (Table I, group 2). They were both about 3500 lbs. body weight and were heavily pregnant. It was also mid winter when the nutritional value of the food-grass was low. In fact, it was noticed that from the middle of the winter to shortly after the first rains, when the overall condition of the rhinos was at its worst, animals frequently took longer to regain their feet after administration of antidote, than during the summer months. Zululand is a summer rainfall area, and subject to frequent prolonged droughts.

The time which elapsed between the darting and the administration of the antidote had a bearing upon the animals readiness to rise. When this time was over one and a half hours they stood up quicker and with less struggling than at a shorter interval. If no antidote was given at all most white rhinos stood up on their own in from two to four hours after darting.

If the rhino did not regain its feet soon after the antidote had been injected, it was found to be quite useless to administer a further quantity either intravenously or intramuscularly within about two hours. After this time an additional dose was found to be beneficial. For example, some individuals of group 16 received an additional 150 mgm. of Nalorphine about three hours after crating.

When catching rhinos for translocation it is absolutely essential that each one rises to its feet, and is capable of walking forward into the crate, within five minutes of the intravenous administration of an antidote. At the same time, hyoscine has to be included in the immobilizing mixture, at least in adult animals, so that, as a result of impaired vision, they will enter the crate without resistance. Young animals due to their lighter weight, can be forced to enter the crate if hyoscine is not used, but this is undesirable.

Conclusions

Provided the rhinos are not for transportation following immobilization, hyoscine, and in some circumstances also the tranquilliser, can be omitted. Any one of the three antidotes under discussion can then be used to antagonise the Etorphine, although the recovery time will probably be prolonged in the case of Cyrenorphine.

However, when translocation is the objective, an Etorphine, Acetylpromazine and hyoscine mixture should be employed for immobilization, and Nalorphine the antidote of choice.

The dosages recommended for this purpose for the various weight categories are given in Table 4.

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REFERENCES

1. Wallach, J. D. (1966) Immobilization and Translocation of White (Square-lipped) Rhinoceros. J. Am. vet. med. Ass. 149 871-874.
2. Player, I. C. (1967) Translocation of White Rhinoceros in South Africa. Oryx 9: 137-154.
3. Harthoorn, A.M. (1965). Application of Pharmacological and Physiological Principles in Restraint of Wild Animals. Wildl. Monogr. No. 14:39.
4. Pienaar, U. de V. (1967) Operation 'Khomandlopfu' Koedoe. No. 10: 158-164.
5. King, J. M. (1969) The Capture and Translocation of the Black Rhinoceros. E. Afr. Wildl. J. 7: 115-130.
6. Dr. G. F. Blane, Reckitt and Sons Ltd., Hull, England. Personal communication.