Chemical Restraint of African Lions (*Panthera leo*) with Medetomidine-Ketamine

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ABSTRACT. Effects of a combination of medetomidine-ketamine as a chemical restraint and antagonistic effects of atipamezole on this combination were investigated in 5 lions. The medetomidine (47.6–58.4 μg/kg) and ketamine (1.9–5.7 mg/kg) combination provided complete immobilization with good analgesia and muscle relaxation in 4 lions, while one lioness was poorly sedated by medetomidine, and additional injections of medetomidine and ketamine were required. The duration of anesthesia seemed to be much longer than one hour in 4 of the lions. Atipamezole, at four times the preceding dose of medetomidine, provided a smooth recovery and animals were able to stand up 17–61 min after its injection. Side effects were limited to vomiting after walking in 3 of 5 lions. — KEY WORDS: ketamine, lion, medetomidine.

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The handling of carnivores has been facilitated by recent advances in methods of chemical restraint. The chemical restraint of African lions (*Panthera leo*) with anesthetic drugs [1, 6, 9] and drug combinations [2–4] has been previously described in several reports, however, it seems that there are presently no ideal injectable anesthetic agents for lions.

Medetomidine is a novel sedative and an analgesic α_2-adrenoceptor agonist which is mainly intended for use in dogs and cats [10]. Medetomidine potentiates the effects of anesthetic drugs such as ketamine, and the disadvantages of each compound are mutually counterbalanced [12, 13]. Atipamezole is a potent, selective and specific α_2-adrenoceptor antagonist which produces an efficacious and quick reversal of medetomidine-induced sedation [11]. Atipamezole also reverses the effects of the medetomidine-ketamine combination anesthesia efficaciously in cats [14, 15]. The medetomidine-ketamine combination is expected to be an effective anesthesia for lions which belong to the same family as cats, and the purpose of the present study was to determine whether the medetomidine-ketamine combination could be effective for the immobilization of lions and be safely antagonized by atipamezole.

Five healthy African lions (1 male and 4 females) in the Morioka Zoological Park were immobilized for blood sampling to examine FIV titers. The sex, age and body weight of the individual lions, and the doses of drugs given to the animals are shown in Table 1. The lions were starved for 24 hr before immobilization, and were restrained in squeeze cages immediately before the first injection. At first, atropine and medetomidine were injected in the same syringe directly into the quadriceps muscles. After administration of the drugs, the lions were kept quiet in the squeeze cages. Then, ketamine was administrated intramuscularly after sufficient immobilization or sedation was apparent. During immobilization, blood samples were collected from each lion and body weight was measured by an electric weight meter. Atipamezole was injected intramuscularly about an hour after the ketamine injection. The doses of these drugs were determined based on estimated body weight of each lion before administration, and the actual dose of each drug was calculated after measuring body weight (Table 1). The atipamezole dose was four times the preceding medetomidine dose.

The following information was recorded: The time from initial injection to the moment when the first signs of sedation were manifest; the time from the initial injection to the moment when the animal lapsed into deep sedation and immobilization; the time from the atipamezole injection to the moment when the first signs of arousal were manifest; and the time from the atipamezole injection to the moment when the animal stood up and walked about. Rectal temperature, heart rate and respiratory rate of the lions were measured and their ECG was recorded at 5-min intervals after lying down. Any side effects in the course of study were also recorded.

The record of the observations are shown in Table 2. After the initial injection of atropine and medetomidine, four lions reached the sedative state within 1–3 min. They were deeply sedated in a mean time of 5.7 min after the

Table 1. Sex, age and body weight of individual lions, and the dose of drugs given to the animals

Lion No.	Sex	Age (years)	Body weight (kg)	Atropine (μg/kg)	Medetomidine (μg/kg)	Ketamine (mg/kg)	Atipamezole (μg/kg)
1	Male	5	157.5	29	47.6	1.9	190.5
2	Female	5	117.5	26	51.1	2.1	204.3
3	Female	1	87	29	57.5	5.7	229.9
4	Female	1	77	35	58.4	2.3	233.8
5	Female	1	80.5	34	83.9	6.7	335.4

Table 2. The sedation, anesthetic and recovery times of each drug in four lions[a)]

Lion No.	Time (min) after initial injection				Time (min) after atipamezole injection				Remarks
	First signs of sedation	Deep sedation	Ketamine injection	Immobilization	Duration of immobilization[b)] (min)	First signs of vigilance	Standing up	Walking about	
1	3	6	13	20	52	8	17	54	Vomiting
2	3	8	14	17	57	10	34	41	Vomiting
3	1.2	2.5	2.5	4.3	61	1	61	82	
4	1.8	6.3	11.8	14.3	58	8	17	35	Vomiting

a) The recordings in No. 5 lioness are excluded.
b) The moment from onset of immobilization to atipamezole injection.

initial injection. Ketamine was injected on average 10.3 min after the initial injection, and the average duration of immobilization (the moment from onset of immobilization to atipamezole injection) was 57 min. When atipamezole was administered, each lion was completely immobilized. The first signs of arousal were manifest within 1–10 min after the atipamezole injection. The mean times taken for the four lions to stand up, and walk about, after the atipamezole administration were 32 and 53 min, respectively. The recovery was smooth without any excitatory phase. This reversal was lasting and no relapse into a deeper stage of sedation was observed.

One lioness (No. 5) was poorly sedated by the initial injection. Therefore, a single additional injections of medetomidine and two more of ketamine were required. Total doses of medetomidine and ketamine were 83.9 μg/kg and 6.7 mg/kg, respectively. After the last administration, the lioness was completely immobilized for more than 59 min. Thereafter, atipamezole at four times the total dose of medetomidine was injected.

Figure 1 shows the changes which occurred in the rectal temperature after the administration of ketamine in the four lions. The initial rectal temperature in each animal ranged from 37.8–40.8°C and thereafter decreased gradually. Before the atipamezole injection (50–60 min after initial values were obtained), the rectal temperature was 0.9–2.2°C lower than the initial temperature, and recovered incompletely after injection of atipamezole. The changes in heart rate after the ketamine injection are shown in Fig. 2. The heart rate remained stable at approximately 60–80/min during immobilization. There was a rapid increase in the heart rate of each animal 5–10 min after the injection of atipamezole. ECG revealed no significant changes throughout the experimental period in all animals. The changes in respiratory rate are shown in Fig. 3. The respiratory rate was varied in individual animals, however it did decrease in most of the lions. No cyanosis was noted during immobilization in any of the animals. Vomiting after walking was observed as a side effect in three of the lions.

The recommended dose of medetomidine for cats is 80–110 μg/kg intramuscularly [10]. The dose of medetomidine used in the four lions (47.6–58.4 μg/kg) was about half of the recommended dose for cats. Jalanka [8] applied

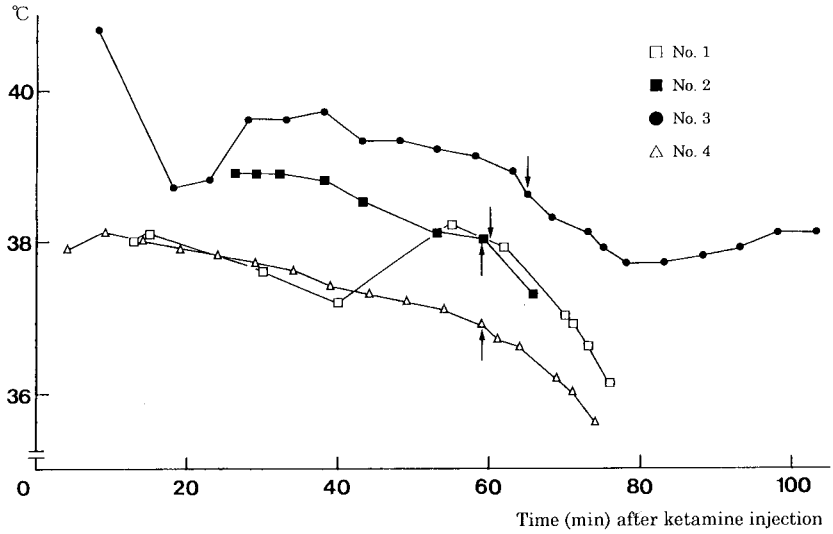

Fig. 1. Changes in rectal temperature after ketamine injection in four lions (No. 1–4) sedated with atropine and medetomidine. Arrows represents intramuscular injection of atipamezole.

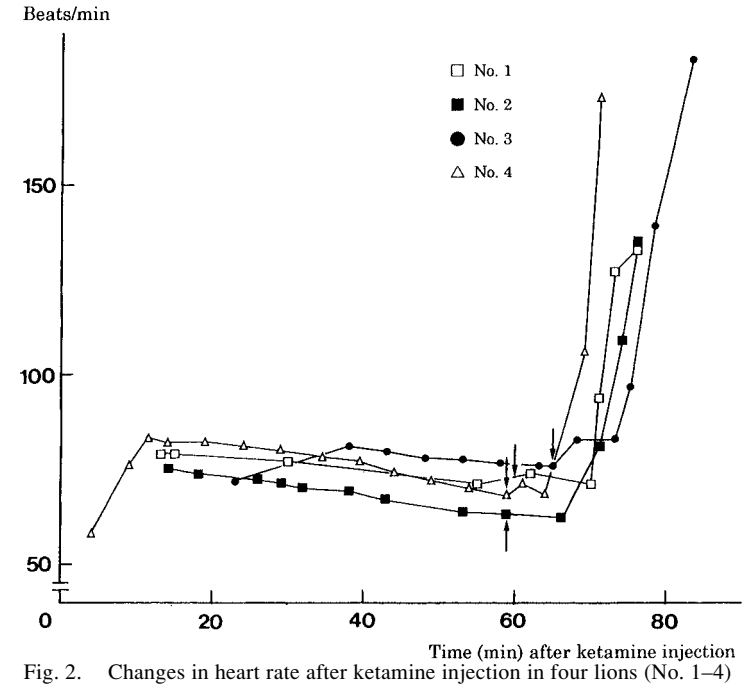

Fig. 2. Changes in heart rate after ketamine injection in four lions (No. 1–4) sedated with atropine and medetomidine. Arrows represent intramuscular injection of atipamezole.

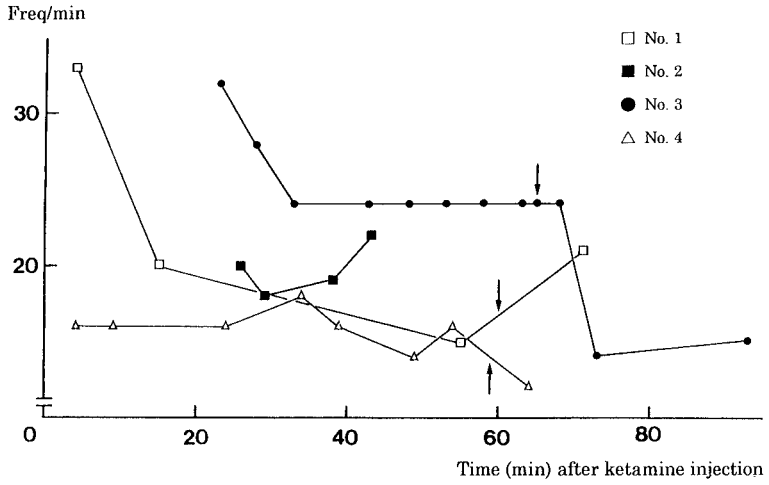

Fig. 3. Changes in respiratory rate after ketamine injection in four lions (No. 1–4) sedated with atropine and medetomidine. Arrows represent intramuscular injection of atipamezole.

medetomidine-ketamine anesthesia to snow leopards. The mean ± SD (range) medetomidine and ketamine dose, were 67.0 ± 16.1 (38–107) μg/kg and 2.7 ± 0.8 (1.3–5.7) mg/kg, respectively. With the mean doses, the animals became completely immobilized in 4–9 min, and the effect lasted for about 45 min. The doses of medetomidine and ketamine in this study were quite similar to those reported by Jalanka. The average duration of immobilization (the moment from onset of immobilization to the atipamezole injection) was 57 min in the present study. However, when atipamezole was administered, each lion was completely immobilized. Therefore, the actual duration of immobilization might have lasted much longer than an hour. Even if the number of lions was limited, the sedative and anesthetic effects of the medetomidine-ketamine combination were considerably potent in this study.

Medetomidine highly potentiates the anesthetic effects of ketamine and the disadvantages of each compound are mutually counterbalanced [12, 13]. The ketamine doses were minimal compared with the doses used in other studies [4, 6], but were adequate for satisfactory immobilization, analgesia and muscle relaxation in the present study. The

degree of anesthesia and immobility might increase with the dose of ketamine. According to the ketamine dose, therefore, medetomidine-ketamine combination could be used appropriately for examination, treatment or operation in lions.

Furuya and others [4] reported that the heart rate in the lions ranged from 60-78/min during xylazine and ketamine anesthesia. Their results agree with those obtained in this study. With regard to cardiovascular function, ketamine has a stimulating effect in cats. Medetomidine has the typical cardiovascular effects of α_2 agonistic compounds. It mainly induces centrally mediated bradycardia and peripheral vasoconstriction [13]. Because the centrally stimulating effects of ketamine appear to balance the depressive effects of medetomidine when taken together, the heart rates in almost all of the animals were stable during immobilization in the present study.

Atipamezole was able to reverse medetomidine-ketamine induced anesthesia smoothly and rapidly. Jalanka [7] found that atipamezole produced a reversal after medetomidine-ketamine induced immobilization in snow leopards. The results of Verstegen and others in cats [14], together with the present results, indicate that a reduction in the ketamine dose may enhance the effectiveness of atipamezole and result in a more complete recovery. It has been demonstrated that atipamezole minimized the danger of hypothermia and cardiovascular depression during the recovery period [14, 15]. Atipamezole immediately increased the heart rate which was depressed by the medetomidine-ketamine combination in the present study, however, the hypothermic effect of medetomidine-ketamine anesthesia was not rapidly recovered by the atipamezole injection. These results were different from those of Verstegen and others [14] which showed that the hypothermic effect of medetomidine-ketamine anesthesia disappeared rapidly following an atipamezole injection in cats. This may have been due to the dose of ketamine or room temperature.

The most prominent side effect of medetomidine was vomiting in cats. Vähä-Vahe [10] reported that vomiting was seen in 50–65% of the cats after medetomidine administration. Verstegen and others [12] described that vomiting occurred in 9.5–10% of cats with medetomidine-ketamine anesthesia, and suggested that ketamine reduced the incidence of vomiting induced by medetomidine [13]. On the other hand, Hikasa and others [5] reported that vomiting induced by α_2-adrenoceptor agonists was effectively antagonized by α_2-adrenoceptor antagonists. Vomiting was, however, observed after the atipamezole injection in this study. It is unknown why vomiting occurred in the course of the recovery in the lions.

In conclusion, the use of medetomidine-ketamine and atipamezole has several benefits compared to previously used methods for immobilization and reversal in lions.

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