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TECHNICAL REPORT NO. 133

A COMPARISON OF KETAMINE AND KETAMINE-XYLAZINE ANESTHESIA IN THE BABOON

Gary L. White and John F. Cummings

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OFFICE OF NAVAL RESEARCH Contract/N00014-76-C-0229 Project No. NR 207-040 TECHNICAL REPORT, NO. 133 6 A COMPARISON OF KETAMINE AND KETAMINE-XYLAZINE ANESTHESIA IN THE BABOON . Gary L. White and John F. Cummings Prepared for Publication in Vet. Med./Small An. Clin. University of Oklahoma Health Sciences Center Department of Pathology Oklahoma City, Oklahoma ACCESSION for the Rection NTIS 12 February 2079 8 + Section D DOM UNANNOUNC D ASIT ICA . Reproduction in whole or in part is permitted for any purpose of the United States Government BY DISTRIBUTION A TAR AD' ITY CODES SPLCIA Dis 411 106 200 vb 79 03 16 028

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Ketamine HCl has gained wide acceptance in several species of animals, including non-human primates, as an anesthetic agent. It produces the dissociate state of anesthesia. Advantages of ketamine include intramuscular administration, rapid induction and safety.^{1,2} Muscular hypertonicity and inadequate analgesia has been reported as undesirable characteristics of ketamine when used alone.^{3,4} The combination of ketamine and xylazine has been found to increase analgesia and produces good muscle relaxation in several species.^{2,5,6} The combination of ketamine and acepromazine in rhesus monkeys has been reported to eliminate muscular movement and produces satisfactory analgesia for short surgical procedures; however, the laryngeal reflexes were maintained thus preventing endotracheal intubation.⁷

The purpose of this study was to compare the induction time (interval between administration and peak effect), sleep time (interval from beginning of peak effect to first observed voluntary muscular movement), heart rate and muscle tone in baboons anesthetized with either ketamine alone or the combination ketaminexylazine.

Materials and Methods

Six female baboons (<u>Papio cynocephalus</u>) weighing 14 to 15 kg were used in this study. Fecal cultures from each baboon were found to be negative for Salmonella and Shigella, and all baboons were negative on intrapalpebral tuberculin testing. All were also found to be negative for ova and parasites on fecal examination.

Group A baboons received 11 mg ketamine hydrochloride (Ketaset, Bristol Laboratories)/kg of body weight administered intramuscularly. Group B baboons received 11 mg ketamine hydrochloride and .5 mg xylazine (Rompum, Haver-Lockhart Laboratories)/kg of body weight administered intramuscularly given in a single injection. The same baboons were used in both groups with a two week interval between each treatment. On the first day 3 baboons received ketamine alone and 3 received the combination of ketamine-xylazine. Then on the fifteenth day each group of 3 baboons was given the alternate treatment. The dosage of ketamine was chosen from a previous report for this species that utilized a mean dose of 11.3 mg/kg of ketamine.² The xylazine dosage was based on approximately half the dosage recommended by the manufacturer for dogs.

The induction time (interval between administration of drugs and peak effect) and sleep time (interval from the beginning of peak effect to first observed voluntary muscular movement) were measured as defined by a previous study in nonhuman primates.⁷ Heart rate was measured with a Model 240 intensive care monitor (The Capston Company). Muscle relaxation and movement were subjective judgements.

The results were analyzed using t tests for paired and unpaired data.

Results

Induction of anesthesia was smooth for both groups of baboons. Induction time for baboons receiving ketamine alone (Group A) ranged from 3 to 7 minutes (mean: 5.0 minutes; standard error of mean: 0.6 minutes; n=6) compared with a range of 2 to 5 minutes (mean: 4.0 minutes; standard error of mean: 0.5 minutes; n=6) for baboons receiving the ketamine-xylazine combination. Unpaired comparisons revealed no significant difference in induction time between the two groups. Sleep time for baboons administered ketamine alone ranged from 64 to 88 minutes (mean: 72.5 minutes; standard error of mean: 3.8 minutes; n=6) contrasted with a range of 90 to 125 minutes (mean: 106 minutes; standard error of mean: 4.7 minutes; n=6) for baboons injected with the ketamine-xylazine combination. The sleep time was prolonged significantly (p<0.001) in the ketamine-xylazine group when compared with the group administered ketamine alone.

Comparisons of heart rate between the two groups are presented in Table I. There were no significant changes in heart rate within the ketamine group from

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10 minutes through 30 minutes; however, at +20 and +30 minutes the baboons administered the ketamine-xylazine had a significant decrease in heart rate when compared with the +10 minute rate. The ketamine-xylazine group of baboons had a lower (p<0.02) heart rate from +10 through +30 minutes when compared with the group receiving ketamine alone.

Several pertinent observations were made during this study. Group A baboons exhibited muscular hypertonicity contrasted with good muscle relaxation in the Group B baboons. Voluntary muscular movement was not observed in the baboons receiving the combination of ketamine-xylazine compared with some voluntary muscle movement of all 6 baboons anesthetized with ketamine alone. Muscle relaxation was sufficient in the Group B baboons to permit excellent ease of abdominal palpation and endotracheal tubes could be passed easily.

Blood gas measurements were not performed; however, no respiratory impairment was evident. All baboons were observed for 2 months with no untoward side effects being noted.

Discussion

The combination of ketamine-xylazine has been shown to have advantages over ketamine alone in cats, rabbits and rats.^{2,5,6} This study was conducted to compare the induction time, sleep time, heart rate and muscle tone in baboons anesthetized with either ketamine alone or the combination ketamine-xylazine. Ketamine, a "dissociative anesthetic", suppresses the corticothalmic system and concurrently activates areas of the limbic system;^{8,9} however, ketamine alone has been shown to give inadequate analgesia and muscle relaxation.^{5,10} Xylazine is a sedative and analgesic with good muscle relaxant properties. The sedative and analgesic properties result from its central nervous system properties, while the muscle relaxation is due to inhibition of intraneual impulse transmission

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in the central nervous system.¹¹ The combination of ketamine and xylazine has been reported to produce good analgesia, anesthesia and muscle relaxation in rabbits and rats.^{5,6}

The ketamine-xylazine combination did not decrease the induction time; however, it did prolong the sleep time when compared with ketamine alone. In contrast, an earlier study revealed that the combination of ketamine and acepromazine caused no significant different in either induction time or sleep time.⁷

Heart rate was decreased in baboons anesthetized with ketamine-xylazine compared with ketamine alone. Ketamine given alone has been previously reported to depress heart rate when compared to measurements with physical restraint in rhesus monkeys.⁸ Another recent study found that excitement with physical restraint increased the pulse rate of non-human primates and this could account for the relative decrease when comparing physically restrained and anesthetized non-human primates.¹² An earlier study in man revealed that ketamine alone increased the blood pressure and heart rate.¹³

Muscle hypertonicity, characteristic of anesthesia with ketamine alone, was eliminated with the combination of ketamine-xylazine. This finding is in agreement with earlier findings in cats and rabbits.^{2,5} Good muscle relaxation found with ketamine-xylazine is a definite asset permitting good abdominal palpation and ease of surgical manipulations. Another advantage of the ketamine-xylazine combination is the fact that this combination permits passage of an endotracheal tube in contrast with persistence of the laryngeal reflex found with either ketamine alone or the combination of ketamine-acepromazine.⁷

This study revealed that the combination ketamine-xylazine in the baboon produced increased sleep time, decreased heart rate, provided good muscle relaxation, prevented voluntary muscle movement and permitted passage of an endotracheal

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tube. Further studies should investigate more physiological measurements, blood gas analyses and hematological effects associated with this anesthetic combination.

REFERENCES

- Beck, C. C. and Dresner, A. J.: Vetalar (ketamine HCl) a cataleptoid anesthetic agent for primate species. <u>Vet Med Small Anim Clin</u> 67:1082-1084, , 1972.
- Amend, J. F., Klavano, P. A. and Stone E. C.: Premedication with xylazine to eliminate muscular hypertonicity in cats during ketamine anesthesia. <u>Vet Med Small Anim Clin</u> 67:1305-1307, 1972.
- Reid, J. S. and Frank, R. J.: Prevention of undesirable side effects of ketamine anesthesia. J Am Anim Hosp Assoc 8:115, 1972.
- Prince, M. D., White, G. L. and Holmes, D. D.: Ketamine vs. ketaminexylazine anesthesia in guinea pigs and rabbits. AALAS Publication 77-9:98, 1977.
- White, G. L. and Holmes, D. D.: A comparison of ketamine and ketaminexylazine for effective surgical anesthesia in the rabbit. <u>Lab Anim Sci</u> 26: 804-806, 1976.
- 6. Van Pelt, L. F.: Ketamine and xylazine for surgical anesthesia in rats. JAVMA 171:842-844, 1977.
- Connolly, R. and Quimby, F. W.: Acepromazine-ketamine anesthesia in the rhesus monkey (Macaca mulatta). Lab Anim Sci 28:72-74, 1978.
- Ochsner, A. J.: Cardiovascular and respiratory responses to ketamine hydrochloride in the rhesus monkey (Macaca mulatta). Lab Anim Sci 27:69-71, 1977.
- Corssen, G., Miyasaka, M. and Domino, E. F.: Changing concepts in pain control during surgery. Dissociative anesthesia with CI-581. A Progress Report. Anesth & Analg 47:746-748, 1968.
- Green, C. J.: Neuroleptanalgesia drug combination in the anesthetic management of small laboratory animals. Lab Anim 9:161-178, 1975.

 Shmidl, J. A.: Experimental use of rompum in the exotic species. J Zool Anim Med 5(4):8-11, 1974.

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- 12. Bush, M., Caster, R., Smeller, J. and Bush, L. M.: Physiologic measures of non-human primates during physical restraint and chemical immobilization. JAVMA 171:866-869, 1977.
- Vayden, S., Hunt, J., Willis, K. W. and Stephen, C. R.: Cardiovascular and respiratory function with CI-581. Anesth & Analg 47:760-768, 1968.

TABLE I. HEART RATE (Mean +SE)

TIME	NIM 01+	+20 MIN	+30 MIN
Group A*	135 (+6)	131 (+4)	131 (+3)
Ketamine			
۵.		SN	NS
Group B**	106 (+8)	(9 -) 96	(6+) 26
Ketamine-xylazine			
С,		.025	.02
P ₄	.02	.005	.005

Group A (N=6) were administered 11 mg/kg ketamine hydrochloride

** Group B (N=6) were administered 11 mg/kg ketamine and .5 mg/kg
xylazine

Paired comparisons for +20 and +30 minutes compared to+10 minutes = d

 P_{\neq} = Unpaired comparisons between Groups A and B

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