Comparison of the efficacy of three premedicants administered to cats

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Abstract

Healthy cats (n = 90), anesthetized for minor procedures, were included in a study designed to evaluate the efficacy of three premedicant mixtures. The drug combination was assigned randomly and the evaluations were made by individuals unaware of the treatment used. The mixtures and their final concentrations were as follows: acepromazine (1.0 mg/mL) and atropine (0.25 mg/mL) with either meperidine (20.0 mg/mL), ketamine (25.0 mg/mL), or oxymorphone (0.2 mg/mL). The dose used was 0.2 mL/kg$^{0.75}$. There was no significant difference ($p < 0.05$) among drug combinations in the degree of sedation achieved, difficulty of handling for IV catheter placement, induction dose of thiopental, or heart or respiratory rate following induction. All combinations were considered satisfactory for premedication of healthy cats. The ketamine combination had a tendency for more consistent sedation ($0.05 < p < 0.01$).

Résumé

Comparaison de l'efficacité de trois prémédications chez le chat

L'efficacité de trois préparations de médicaments administrées comme prémédication a été évaluée chez 90 chats en santé, anesthésiés pour des procédures mineures. Chacune d'entre elles a été donnée au hasard et les observations ont été faites par des individus qui ignoraient la nature du traitement administré. Les préparations et leur concentration étaient comme suit : acépromazine (1 mg/ml), atropine (0,25 mg/ml) combinée avec soit de la mépéridine (20 mg/ml), soit de la kétamine (25 mg/ml) ou soit de l'oxymorphone (0,2 mg/ml). La dose utilisée était de 0,2 ml/kg$^{0.75}$. Les résultats indiquent qu'il n'y a pas de différence significative ($p < 0,05$) entre les préparations de médicaments en ce qui concerne le degré de sédation, la facilité de contention pour la mise en place d'un cathéter intraveineux, la dose d'induction du thiopental, ou aux rythmes cardiaque et respiratoire suite à l'induction. Toutes les préparations se sont avérées satisfaisantes comme prémédication chez le chat en bonne santé. Le mélange comprenant de la kétamine avait cependant tendance à fournir une sédation plus constante ($0,05 < p < 0,1$).

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Introduction

Premedication is indicated in all animals undergoing general anesthesia, unless their physiological status is such that central nervous system depression is present. Premedication in cats reduces the stress of handling and may reduce the requirement for induction and maintenance anesthesia by as much as 50% (1). Cats are often difficult to restrain for IV administration of anesthetic drugs, a fact which emphasizes the benefits of adequate sedation (2). Salivation is often profuse when cats are in unfamiliar environments or when they are exposed to inhalant anesthetics either via a mask or in an induction chamber. Atropine and glycopyrrolate are effective antisialogogues in cats (3), improving visualization of the larynx and reducing the chance of aspiration of saliva during the induction of anesthesia. Premedicants such as acepromazine, ketamine, or meperidine may be used alone or in association with atropine; however, their efficacy as sedatives in healthy cats varies considerably (1).

Combined neuroleptanalgesics (droperidol/fentanyl or acepromazine/oxymorphone) produce profound sedation in dogs, superior to either agent when used alone (4). Combining a tranquilizer with an analgesic or a dissociative anesthetic may result in improved restraint of cats. At the Ontario Veterinary College, a combination of acepromazine, meperidine, and atropine is used for sedation of healthy cats. The cardiovascular effects of this combination in cats have been evaluated (5).

The purpose of our study was to compare the efficacy of three drug combinations, namely acepromazine/meperidine/atropine, acepromazine/oxymorphone/atropine, and acepromazine/ketamine/atropine, as sedatives in healthy cats.

Materials and methods

Healthy cats (n = 90), admitted to the Veterinary Teaching Hospital for minor surgical procedures, were assigned randomly to one of three premedicant treatments: M = meperidine (20 mg/mL) (Pethidine, Glaxo, Mississauga, Ontario), acepromazine (1.0 mg/mL) (Atravet, Ayerst, Montreal, Quebec), atropine (0.25 mg/mL) (Atropine, Glaxo); K = ketamine (25 mg/mL) (Ketaset, Pfizer, London, Ontario), acepromazine (1.0 mg/mL), atropine (0.25 mg/mL); or O = oxymorphone (0.2 mg/mL) (Numorphan, Dupont, Mississauga, Ontario), acepromazine (1.0 mg/mL), atropine (0.25 mg/mL). The mixtures were prepared in advance at the final concentrations listed by dilution with saline as required to allow equal volume dosing (0.2 mL/kg$^{0.75}$). The dose chosen was based on effective metabolic size (6) and historical experience with the mixture M. Following a preoperative examination which included a subjective assessment of behavior (friendly, timid, aggressive, other), the cats were given the premedicant by IM injection. The cats were left undisturbed, and level of sedation was judged at 20–30 min. The evaluation of each cat was made by one of three individuals

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unaware of the contents of the premedicant used. Cats were assessed relative to adverse response to injection (no objection, minor, moderate, severe, other), degree of sedation following premedication (none, mild, moderate, deep, other) and difficulty of IV catheter placement (impossible, difficult to place, cat concerned, cat unconcerned, other). Comments were requested to clarify the selection of "other", which was chosen whenever distinction was not obvious. Results were compiled and graded further, according to comments, as 0-3 by a single "blinded" individual to reduce bias. The choice and dose of inducing agent and maintenance drug were also recorded. Anesthesia was induced with halothane (Fluothane, Ayerst, Montreal, Quebec) in an induction chamber, in all cats that could not be catheterized (difficulty = impossible (0)). All cats were intubated following induction and laryngeal desensitization with lidocaine (Xylocaine Endotracheal Aerosol, Astra Chemical, Mississauga, Ontario). A small number of cats in each group were maintained with methoxyflurane (Metofane, MTC, Cambridge, Ontario) (3%), isoflurane (Aerrane, Anaquest, Mississauga, Ontario) (3%), or further thiopental (Intraval Sodium, MTC) (7%), while the remainder received halothane. Heart and respiratory rates were recorded at 5, 15 and 30 min after induction, if the duration of the procedure permitted.

The three groups were compared for similarity in age, sex, and initial behavior. Consideration was made for size and age by analysis of separated data. The effects of the drug combinations were compared using a one-way analysis of variance (general linear models procedure). A p value <0.05 was considered significant.

Results

The random distribution of cats within the three groups resulted in similar weight and age groupings. The majority of the cats were ≤ 2 yr and this group was analyzed separately. Behavior prior to premedication indicated variation among groups. There were more timid cats (n = 14) in group O than in groups M (n = 6) or K (n = 7). Groups K and O had one aggressive cat in each. More cats were classified as friendly in group M (n = 14) than groups K (n = 9) or O (n = 6). Adverse response to the IM injection was greater in group K than in groups M and O; moderate or severe objection was demonstrated by 15 cats in group K, seven in group M, and 10 in group O.

The degree of sedation produced tended to be greater or more consistent in group K ($0.05 < p < 0.1$) (Table 1). One cat in group K showed no visible sign of sedation compared to four in group M and six in group O. Cats in group M appeared to be less sedated: 27% were moderately sedated versus 47% in group K, and 53% in group O. There was no significant difference among groups in the response to the placement of an intravenous catheter (Table 2) and no difference in the quantity of thiopental used for induction (10.7, 11.3, 11.3 mg/kg) for groups M, K and O, respectively), despite variation in the degree of sedation. There was no apparent difference among groups in the ability to transfer patients to the inhalant chosen.

Table 1. Degree of sedation following: M = meperidine, acepromazine, atropine; K = ketamine, acepromazine, atropine; or O = oxymorphone, acepromazine, atropine

Sample	Drug combination	Degree of sedation[a] 0	1	2	3	n
All animals	M	6	14	8	1	29
	K	1	12	16	1	30
	O	4	12	14	0	30
Animals ≤ 2 yr	M	3	10	6	1	20
	K	0	6	13	0	19
	O	3	8	9	0	20
Animals ≤ 3 kg	M	2	3	6	0	11
	K	0	6	6	0	12
	O	3	3	8	0	14
Animals > 3 kg	M	4	11	2	1	18
	K	1	6	10	1	18
	O	1	9	6	0	16

[a]Sedation level: 0 (no visible effect), 1 (mild), 2 (moderate), 3 (deep)

Table 2. Difficulty of IV catheter placement following: M = meperidine, acepromazine, atropine; K = ketamine, acepromazine, atropine; or O = oxymorphone, acepromazine, atropine

Drug combination	Difficulty of cathether placement[a] 0	1	2	3	n
M	5	4	6	11	26
K	2	5	5	15	27
O	5	4	10	9	28

[a]Difficulty level: 0 (impossible), 1 (difficult to place), 2 (cat concerned), 3 (cat unconcerned)

There were no significant differences in heart or respiratory rates among groups at 5 or 15 min (Table 3). At 30 min one cat in each group was bradycardic as defined by HR ≤ 100 (n = 15, 13, 17 for M, K and O, respectively).

Some data were either missed in the original recording or unable to be assessed by the "blinded" individual interpreting the forms. Each table includes the sample size available for that individual variable although the entire data collection was from 90 different forms.

Discussion

One purpose of premedication is to facilitate the induction of anesthesia. Our study showed that each regime provided adequate sedation for this purpose and that there was little advantage with any one. However, none provided adequate chemical restraint on every occasion.

A second purpose for premedication is to provide analgesia. This is desirable during the induction period for humane reasons and because an animal in such a state is more likely to tolerate the placement of an IV catheter. Analgesics are also beneficial during the

Table 3. Heart and respiratory rates (mean ± standard deviation) at 5 and 15 min following anesthetic induction. M = meperidine, acepromazine, atropine; K = ketamine, acepromazine, atropine; or O = oxymorphone, acepromazine, atropine

Drug combination	Heart rate (/min) 5 min	Heart rate (/min) 15 min	Respiratory rate (/min) 5 min	Respiratory rate (/min) 15 min	n
M	157 ± 23	148 ± 24	29 ± 16	33 ± 15	25
K	162 ± 36	155 ± 24	28 ± 11	28 ± 11	25
O	157 ± 30	148 ± 32	31 ± 19	31 ± 20	24

intraoperative period since they reduce anesthetic demands and the responses to noxious stimuli (1,7). Opioid agonists, when given prior to surgery, may reduce the intensity of postoperative pain, dependent upon their duration of effect. Students with limited experience were allowed to catheterize the cats in this study; this tested the level of sedation and analgesia to a greater degree than the practice situation. Although each combination provided adequate analgesia for many of the catheter placements, some cats resisted this intervention (20%). The ketamine-treated group had fewer animals which could not be catheterized, and this finding is in keeping with the sedative and somatic analgesic properties of the drug (8,9).

Premedication should reduce the amount of induction drug required to produce anesthesia. There were no differences among the three groups, each producing a marked reduction in the thiopental dose as compared to that recommended for unpremedicated animals (10). No significant differences in heart rate or respiratory rate occurred during the first 30 min of anesthesia. This lack of difference in heart rate may have resulted from the achievement of a similar surgical plane of anesthesia and the inclusion of atropine in the combinations of premedicants. Atropine was included in all the combinations because it reduces salivation and upper airway secretion, improving the ability of the anesthetist to visualize the larynx for easier intubation. Atropine is contraindicated in patients that are unable to tolerate an increase in heart rate (11). The cats in our study were all healthy patients with no apparent cardiac abnormalities.

It has been reported that drug dosage is more accurately related to effective metabolic size than body weight (6). We had to decide what the average dose for cats should be to allow us to apply effective metabolic size calculations to the mixtures. Various dose recommendations are found in the literature and therefore our results may have been different if other recommended doses had been chosen. Each 3.5 kg cat (average) in our study received 0.5 mg acepromazine and 0.12 mg atropine, with either 10.0 mg meperidine, 12.5 mg ketamine, or 0.1 mg oxymorphone. The doses of the sedative/analgesics are less than those chosen when the drugs are used individually (60–70% of doses found in the literature) due to the additive effect of combinations. There was more variability in the results of sedation in the larger cats (Table 1) which may be a function of dosage calculation on actual weight rather than lean body weight. No attempt was made in our study to account for differences in body fat.

Our study demonstrated that all of the regimes produced effective premedication in cats, and, although they all facilitated the handling of these animals, they did not produce adequate chemical restraint in all individuals. Cats that are very difficult to handle may be restrained more effectively with higher doses of ketamine. Ketamine/acepromazine has been shown to be safe at anesthetic levels in cats when given IM (12,13).

The premixed drug combinations as used in our study are convenient and safe for premedication when followed by thiopental and volatile anesthetics in healthy cats. We did not evaluate the response in older, depressed, or clinically unstable patients, where individual drugs may be safer when used alone or mixed at levels deemed appropriate for the individual animal.

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