Comparison of quality of induction of anaesthesia between intramuscularly administered ketamine, intravenously administered ketamine and intravenously administered propofol in xylazine premedicated cats

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ABSTRACT

The quality of induction of general anesthesia produced by ketamine and propofol, 2 of the most commonly used anaesthetic agents in cats, was assessed. Eighteen cats admitted for elective procedures were randomly assigned to 3 groups and then premedicated with xylazine 0.75 mg/kg intramuscularly before anaesthesia was induced with ketamine 15 mg/kg intramuscularly (KetIM group), ketamine 10 mg/kg intravenously (KetIV group) or propofol 4 mg/kg intravenously (PropIV group). Quality of induction of general anaesthesia was determined by scoring ease of intubation, degree of struggling, and vocalisation during the induction period. The quality of induction of anaesthesia of intramuscularly administered ketamine was inferior to that of intravenously administered ketamine, while intravenously administered propofol showed little difference in quality of induction from ketamine administered by both the intramuscular and intravenous routes. There were no significant differences between groups in the ease of intubation scores, while vocalisation and struggling were more common in cats that received ketamine intramuscularly than in those that received intravenously administered ketamine or propofol for induction of anaesthesia. Laryngospasms occurred in 2 cats that received propofol. The heart rates and respiratory rates decreased after xylazine premedication and either remained the same or decreased further after induction for all 3 groups, but remained within normal acceptable limits. This study indicates that the 3 regimens are associated with acceptable induction characteristics, but administration of ketamine intravenously is superior to its administration intramuscularly and laryngeal desensitisation is recommended to avoid laryngospasms.

Key words: cat, ketamine, propofol anaesthesia.

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INTRODUCTION

Cats are among the companion animals most commonly anaesthetised by practising veterinarians. The use of injectable anaesthetic agents remains the choice for veterinarians. Fortunately, there is a wide range of injectable anaesthetic agents that can be used in cats[6]. Ketamine and propofol are among the most popular injectable agents used for induction of general anaesthesia in cats[5].

Ketamine (di-2-[(o-chlorophenyl)-2-(methylamino)]-cyclohexanone hydrochloride) is one of the mainstream feline general anaesthesia drugs for many private veterinary practitioners primarily because of its versatility[6,11]. The fact that ketamine can be administered *via* the intramuscular route makes it particularly attractive for use in feral cats. It is one of the very few general anaesthetic agents that can be administered by more than one route (*i.e.* intravenously and the intramuscularly). In addition, it is probably the only general anaesthetic agent with substantial analgesic effects[5]. An interest in the N-methyl-D-aspartate receptor at which ketamine has antagonistic action has recently encouraged re-evaluation of ketamine in human medicine[11]. It is classified as a dissociative anaesthetic agent because its mechanism of action is thought to interrupt the cerebral association pathways, with relative sparing of the reticular and limbic systems and depression of the thalamocortical system[7]. Common effects of ketamine include anaesthesia, analgesia and catalepsy (waxy rigidity of muscles)[5]. To ameliorate the skeletal muscle-related side-effects (twitching rigidity, convulsions), ketamine should be administered concurrently with muscle-relaxing drugs like alpha-2-adrenergic agonists or benzodiazepines[3]. In cats, ketamine is typically administered in combination with medetomidine or xylazine intramuscularly or intravenously[2,12]. Cardiovascular effects of ketamine, which include increases in arterial blood pressure as well as heart rate, can be explained by its central sympathomimetic activity[1]. It is important to note that ketamine has direct myocardial depressant effects independent of heart rate and should therefore be avoided in animals whose cardiovascular function is significantly compromised[6]. The dosage for ketamine in cats ranges from 2–10 mg/kg and 5–20 mg/kg for the intravenous and intramuscular routes, respectively. After administration by the intramuscular route, recumbency is usually attained in 3–5 minutes[5]. Rapid induction and faster recovery with a short duration of anaesthesia (10–15 minutes) occur when ketamine is administered intravenously in cats. Retention of the laryngeal and pharyngeal reflex as well as increased salivation that occur with ketamine anaesthesia makes endotracheal intubation difficult in cats[7].

Propofol (2,6 di-isopropoylphenol) is a rapid-acting (since it is highly lipophilic) short-acting (since it is both lipophilic and rapidly metabolised) intravenous anaesthetic agent. It is widely used in the field of medicine and has been accepted as a useful agent in all domestic animals since its launch in 1986[9,10,11]. It is associated with smooth inductions and recoveries as well as minimal side-effects at low dosages[8]. Propofol can only be administered intravenously and in high dosages produces cardiovascular depression characterised by decreased arterial blood pressure as a result of decreased cardiac output and reduced systemic vascular resistance[9]. Pain has been reported as a side-effect on injection of propofol into small veins in

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humans and dogs[5]. Sneezing and apnoea have been cited as other negative effects that can be caused by propofol in cats during the period of induction of general anaesthesia[8,10]. The dose of induction of propofol is between 6 and 8 mg/kg.

Xylazine was the 1st α_2 adrenergic agonist to be used as a sedative and analgesic agent by veterinarians in dogs and cats before the advent of medetomidine, a more specific and potent α_2 adrenergic agonist[5]. Despite the obvious positive effects of xylazine such as dose-dependent sedation of 1 to 2 hours' duration, analgesia of 15 to 30 minutes' duration and muscle relaxation, its use should be limited to normal, healthy animals due to concerns about negative cardiovascular effects such as hypotension and bradycardia[1,2,13]. Premedication with xylazine can reduce the required dose of an induction agent by as much as 30–80 %[5] and significantly slows delivery of intravenously induction drugs related to the low cardiac output.

Both ketamine and propofol are induction agents commonly used in cats. No data are available in the literature that compares induction characteristics of these 2 drugs in cats. The aim of this investigation was to compare the quality of induction of anaesthesia produced by propofol and ketamine in clinically relevant settings.

The hypothesis was that ketamine administered intramuscularly or intravenously produces the same quality of induction of general anaesthesia as propofol administered intravenously in normal, healthy cats premedicated with xylazine.

MATERIALS AND METHODS

A total of 18 client-owned healthy cats admitted for elective procedures to the University of Zimbabwe Veterinary Teaching Hospital were used in this investigation. This study was approved by the Faculty of Veterinary Science's Final Year Scientific Projects Coordinating Committee. Owner consent to use the cats was obtained.

The cats were assigned randomly to 3 groups of 6 each related to induction anaesthesia: the KetIM Group received ketamine intramuscularly for induction of anaesthesia, the KetIV Group that received ketamine intravenously for induction of anaesthesia and the PropIV Group that received propofol intravenously for induction of anaesthesia.

All cats were starved for 12 hours and deprived water for at least 2 hours before commencement of the clinical trial. A physical examination and analysis of blood samples for haematocrit and total serum protein were done prior to administration of the preanaesthetic agent.

All cats were sedated with xylazine 2 % (Chanazine®, Centaur Laboratories, Isando, South Africa) at a dose of 0.75 mg/kg intramuscularly. The degree of sedation was assessed 20 minutes after administration of xylazine on a 0–3 scale where:

0: poor – active interest in surroundings and no evidence of 3rd eyelid prolapse;

1: mild – active interest in surroundings and evidence of 3rd eyelid prolapse;

2: moderate – quiet or asleep, but arousable and 3rd eyelid prolapsed;

3: deep – unarousable.

Thirty minutes after administration of xylazine, general anaesthesia was induced using ketamine 10 % (Anaket–V®, Centaur Labs, Isando, South Africa) at a dose of 15 mg/kg administered intramuscularly into the dorsal lumbar muscles (KetIM Group), ketamine 10 % at a dose of 10 mg/kg administered intravenously through an over-the-needle indwelling catheter placed in the cephalic vein (KetIV Group) or propofol (Propofol 1 %®, Fresenius, Bodene, trading as Intramed, Port Elizabeth, South Africa) at a dose of 4 mg/kg administered intravenously through an over-the-needle indwelling catheter placed in the cephalic vein (PropIV Group). Intravenous administration of ketamine and propofol at fixed dosages indicated above was done slowly over a period of 2 minutes. For intramuscularly administered ketamine, induction of anaesthesia was considered complete by the time that pinching a lateral digit and toe-web for 5 seconds elicited no vocalisation or movement. Toe-pinching began when the patient had relaxed and was applied every 30 seconds until induction was deemed complete.

Endotracheal intubation, which was done by 1 person on all cats, was then attempted. If this was not possible, halothane 3 %® (Halothane, M & B, Safeline Pharmaceuticals, Florida South Africa) was administered with a face mask to facilitate intubation. Ease of intubation was then assessed on a 0 – 3 scale where:

0: very easy – successful on 1 attempt with no evidence of laryngospasms;

1: easy – successful on 1 attempt with evidence of physical movement of cat;

2: difficult – successful after more than 1 attempt with or without evidence of physical movement of cat;

3: very difficult – unsuccessful due to, for example excessive jaw tone, laryngospasms or physical movement of cat.

Besides ease of intubation to determine quality of induction, degree of vocalisation and struggling during intubation were also assessed separately on a 0–3 scale where:

0: no vocalisation or movement;

1: mild vocalisation or movement;

2: moderate vocalisation or movement;

3: severe vocalisation or movement.

The overall quality of induction score was obtained by adding together the ease of intubation score, vocalisation score and the struggling score.

The duration of the induction period was recorded as time between beginning of administration of the induction agent and loss of response to toe-pinching. The occurrence of breath-holding and any other adverse effects during induction were also noted.

The heart rates and respiratory rates at baseline (before sedation), at 20 minutes after sedation and at the time immediately after onset of induction were measured and recorded.

Statistical analysis

Statistical significance was set at a value of $P < 0.05$. The data were analysed using the R Statistical software (R®, The R Foundation for Statistical Computing, Vienna, Austria). The means of patient descriptive data (age, body weight) and analytical data (haematocrit and total serum protein) were compared between groups using 1-way analysis of variance (ANOVA). Where differences were noted, pair-wise comparisons were done using *t*-test with a Bonferroni adjustment for multiple testing. The same tests (1-way ANOVA and pair-wise *t*-test) were used to compare mean heart rate and respiratory rate reading between groups and within groups. Values for the mean duration of the induction period were compared using the same tests. Median scores between groups (KetIM Group, KetIV Group and PropIV Group) were compared using the Kruskal-Wallis rank sum test.

Where statistical differences were noted, pair-wise comparisons were performed using the Wilcoxon rank sum test with a Bonferroni adjustment for multiple testing.

RESULTS

There were no significant differences between the 3 groups in patient descriptive data (age, body weight) and analytical data (haematocrit and total serum protein).

The sedation scores expressed as median (ranges) were 2 (0–3), 2 (0–3) and 3 (1–3) for the KetIM, KetIV and PropIV groups, respectively; and were not significantly different between groups.

There were no significant differences between groups in the intubation scores. Vocalisation scores, struggling scores and total induction quality scores were significantly different between groups. More specifically, vocalisation and struggling

were more common in cats that received ketamine intramuscularly than in those that received intravenously administered ketamine or propofol for induction of general anaesthesia. One cat from the KetIM group required halothane administered by a mask to complete the induction because intubation was unsuccessful due to excessive movement. Two cats from the PropIV group required halothane administered by a mask to complete the induction because intubation was unsuccessful due to development of laryngospasms. Overall quality of induction produced by intramuscularly administered ketamine was inferior to that produced by intravenously administered ketamine, while intravenously administered propofol showed no difference in quality of induction from ketamine administered by either the intramuscular or intravenous routes (Table 1).

Table 1: **Quality of induction scores presented as median (range) for the KetIM Group** (ketamine 15 mg/kg intramuscularly)**, KetIV Group** (ketamine 10 mg/kg intravenously) **and PropIV Group** (propofol 4 mg/kg intravenously) **in xylazine premedicated cats.**

Parameter	Group	Score	*P*-value (between groups)
Ease of intubation	KetIM	1.5 (0-3)	NS
	KetIV	1.0 (0–1)	
	PropIV	2.0 (0–3)	
Vocalisation	KetIM	2.0 (1–3)	0.023
	KetIV	0.5 (0–1) #	
	PropIV	0.5 (0–2) #	
Struggling	KetIM	2.0 (2–3)	0.002
	KetIV	0.0 (0–1) #	
	PropIV	0.0 (0–2) #	
Total induction quality	KetIM	5.5 (3–8)	0.006
	KetIV	1.5 (0–6) #	
	PropIV	2.5 (1–7)	

NS: no significant differences ($P < 0.05$) between the 3 groups.
#Significantly different ($P < 0.05$) from KetIM.

The duration of the induction period was 4.4 ± 0.5, 1.5 ± 0.4 and 1.4 ± 0.5 minutes for the KetIM, KetIV and PropIV groups, respectively, and was significantly longer in cats that received ketamine intramuscularly than in cats that received intravenously administered ketamine or propofol.

There were no significant difference in pre-sedation, pre-induction and post-induction heart rates and respiratory rates between the 3 groups, but there were some differences within groups across the 3 time points (Table 2).

DISCUSSION

Uniformity in distribution of the cats among the 3 groups is supported by the lack of differences in the mean age, body weight, haematocrit and total serum protein of the groups. The study was also designed to minimise differences at induction by using the same premedication agent at the same dosage since the type of drug used for premedication and the dosage used influences the amount of the induction agent required to achieve complete induction of general anaesthesia[5]. It should be emphasised that the premedication agent used (xylazine) as expected, caused moderate to deep sedation in all 3 groups and this would imply a marked reduction in the induction dose needed. We chose to use a uniform dose of the induction agents, and not to induce to effect, as a way of standardising the dose received by cats within the same group, but this could be viewed from another angle as a limitation to the study because induction drugs are usually administered to effect. By the time the induction agents were administered, the predominant cardiovascular effects from xylazine would be cardiac output depression and bradycardia, and bradycardia would imply that the onset of central nervous system effects of the induction agents would be delayed, especially for intramuscularly administered drugs.

Ketamine administration by the intramuscular route was associated with significant struggling and vocalisation and also produced an inferior quality of induction of general anaesthesia when compared with administration by the intravenous route. The bioavailability of drugs is generally less predictable following intramuscular administration when compared with intravenous administration where a drug directly enters the circulation, thereby avoiding potential absorption barriers[5]. In clinical practice, anaesthesia from intramuscularly administered ketamine may be supplemented by intravenously administered propofol to achieve a level of anaesthesia deep enough to allow successful intubation[3]. Intramuscular administration of ketamine has a big role in clinical practice especially in restraint of feral and aggressive client-owned cats that practitioners encounter[5]. Presence of laryngeal and pharyngeal reflexes in ketamine anesthetised cats, did not seem to prevent successful tracheal intubation in most cats, but made the procedure more difficult, especially following intramuscular administration of ketamine.

The quality of induction produced by propofol was generally good, although laryngospasms were observed in some cats. Literature indicates that the quality of induction of anaesthesia produced by propofol is better than that produced by ketamine[4]. This study was not able to show any differences in quality of induction between propofol and intravenously administered ketamine. This could be a result of the low dosages of propofol used in this study whereas high dosages of

Table 2: **Heart rate and respiratory rate readings** (mean ± standard deviation) **obtained before sedation** (baseline)**, 20 minutes after sedation** (pre-induction) **and immediately after induction** (post-induction) **for the KetIM Group** (ketamine 15 mg/kg intramuscularly), **KetIV Group** (ketamine 10 mg/kg intravenously) **and the PropIV Group** (propofol 4 mg/kg intravenously) **in xylazine premedicated cats.**

Group	Heart rate			Respiratory rate		
	Baseline	Pre-induction	Post-induction	Baseline	Pre-induction	Post-induction
KetIM	177.3 ± 13.6	110.7 ± 51.8*	110.0 ± 41.2*	63.3 ± 31.0	48.0 ± 16.8	34.3 ± 14.8
KetIV	157.3 ± 40.4	135.3 ± 44.6	143.0 ± 32.3	59.0 ± 25.8	46.0 ± 9.0	24.0 ± 16.4*
PropIV	164.7 ± 35.0	156.7 ± 42.6	142.7 ± 23.6	56.0 ± 40.1	50.0 ± 10.4	23.3 ± 12.8
	NS	NS	NS	NS	NS	NS

NS: no significant differences ($P < 0.05$) between the 3 groups.
*Significantly different ($P < 0.05$) from baseline (pre-sedation) value.

ketamine were used[5,8]. We used propofol at 4 mg/kg because that is the dosage at which it was used in the clinic at the time. In clinical practice development of laryngospasms during tracheal intubation in cats is usually minimised by applying a local anaesthetic spray on the larynx before attempting endotracheal intubation[3]. We did not use local anesthetic spray in this study because of concerns about possible interference with assessment of ease of intubation as a result of induction agent effects. If the propofol had been given at doses producing desired effect and/or a local anaesthetic spray used, the quality of induction from propofol may have been better. Since higher doses of drugs are usually associated with more adverse effects, use of laryngeal desensitisation would be recommended[13]. Our analysis failed to show significant differences in intubation quality, but laryngospasm is a significant complication and only noted in the propofol cats. Had sequelae been assigned a higher score, which might be more appropriate, significance may have been shown.

The duration of the induction period obtained for intramuscularly administered ketamine (4.4 ± 0.5 minutes) is the same as that from other studies[5]. As was largely expected, the onset of the induction onset was significantly longer in cats where ketamine was administered intravenously than in those that received intravenously administered ketamine or propofol. Drugs administered intramuscularly as opposed to intravascularly generally take longer to attain effective concentrations in the brain[5].

The heart rate and respiratory rates were within the normal range for cats throughout the period of the study and no interesting significant differences were observed between the 3 groups[5]. It is difficult to draw any tangible conclusions on physiological effects on vital body systems of the anaesthetic regimens assessed in this study because inadequate cardiopulmonary variables were assessed.

Another weakness of our study is that we did not devise an objective way of assessing the quality of recovery from anaesthesia. Although the main purpose of the study was to compare induction characteristics of the 3 protocols, the study would have been more valid if the quality of recovery from anaesthesia was also assessed.

We conclude that the quality of induction of anesthesia from intramuscularly administered ketamine is inferior to that of intravenously administered ketamine and that there is little to distinguish propofol induction from ketamine inductions by either the intramuscular or intravenous route in xylazine premedicated normal, healthy cats. However, tracheal intubation could have been improved by laryngeal desensitisation, especially in propofol-induced cats where laryngospasms were observed. We recommend that if ketamine is administered intramuscularly for induction of general anaesthesia in cats, the depth of anaesthesia should be improved, as needed, by intravenously administered propofol or other agents before tracheal intubation is attempted.

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