THE EFFECT OF PREMEDICATION ON THE INDUCTION DOSE OF PROPOFOL IN DOGS AND CATS

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ABSTRACT

The effect of premedication on the induction dose of propofol was determined in 15 cats and 25 dogs undergoing elective surgical procedures. The induction dose of propofol in dogs younger than 8 years old was 6,9 ± 0,9 mg kg^{-1} (n = 4) without premedication and 4,3 ± 1,4 mg kg^{-1} (n = 12) with premedication with acetylpromazine maleate. The induction dose in cats younger than 3 years old was 7,8 ± 1,1 mg kg^{-1} (n = 8) with atropine alone and 7,1 ± 0,9 mg kg^{-1} (n = 7) with the inclusion of acetylpromazine maleate. The reduction in the induction dose of propofol was statistically significant in dogs, but not in cats. When atropine was used together with a fentanyl-droperidol combination or pethidine and acetylpromazine maleate in dogs, the mean induction dose of propofol was reduced to 2,1 ± 0,1 mg kg^{-1} (n = 4) and 2,4 ± 0,3 mg kg^{-1} (n = 5), respectively. Propofol was also evaluated as an induction agent in patients undergoing non-elective surgical procedures.

Key words: Propofol, dogs, cats, premedication, dose, induction, anaesthesia

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INTRODUCTION

Propofol [Diprivan Injection 10 mg ml^{-1}, Stuart Pharmaceuticals, (South Africa) (Pty) Limited] is an alkyl phenol (2,6 diisopropylphenol), which is marketed as a white sterile oil-in-water emulsion. It has anaesthetic properties following intravenous administration and is currently registered for use in man. The original solvent, Cremophor-EL (polyoxyethylated castor oil), caused a release of histamine in dogs which prevented its use as an anaesthetic agent in this species[19]. It was also believed to be associated with a significant incidence of anaphylactoid reactions in man[2 3 10 15]. The current formulation is a soya-bean emulsion and exhibits some loss of potency in man when compared to the Cremophor-EL formulation[16 19]. Although the frequent occurrence of a cutaneous flush was noted with the use of the emulsion formulation for the induction of anaesthesia in man, no tendency to develop anaphylactoid reactions was observed, as determined by measurement of immunoglobulin levels, complement C3 levels and plasma histamine concentrations[3]. No allergic-type reactions have been recorded in dogs or cats with the emulsion formulation[1 6 15].

In man, propofol causes a rapid induction of anaesthesia and is extensively distributed from the blood into the tissues following intravenous administration[16]. Metabolism is rapid and occurs via hepatic and extrahepatic mechanisms with inactive metabolites excreted by the kidney[15 16]. It lacks cumulative properties[15]. Recovery from anaesthesia is smooth and rapid and is associated with minimal postoperative confusion[15]. Thus, propofol is used in man as an alternative to methohexitone for the maintenance of general anaesthesia during brief outpatient procedures[4].

The potential of propofol for use as an anaesthetic in veterinary science was recognised from clinical trials performed on experimental animals during the development of propofol for use in man[6]. Its use in animals was associated with a rapid smooth induction which was of short duration and a smooth recovery[6 15 19].

Induction doses of propofol for dogs and cats with and without premedication, using acetylpromazine maleate, have been reported[1 12 19]. The effect of tranquillising premedication on the induction dose for cats, produced conflicting results[1 12]. One study examined the effect of tranquillising premedication on the induction dose in dogs and cats, but did not appear to differentiate between the different types of tranquillising premedication when the induction doses were statistically analysed[12]. The induction dose of propofol for dogs and cats, when an opioid was used in the premedication, had not been reported. This has been shown to decrease the induction dose of propofol in man[4].

The purpose of this investigation was to establish if the induction dose of propofol for dogs and cats was affected by the different types of routine premedication drugs used in the small animal section of the Department of Surgery, Faculty of Veterinary Science, University of Pretoria. Propofol was also assessed as an induction agent in patients considered to be anaesthetic risks.

MATERIALS AND METHODS

Propofol was used as an intravenous induction agent in cats (n = 15) and dogs (n = 25) undergoing elective surgical procedures and assigned an American Society of Anaesthesiologists (ASA) status of one[5]. The decision of whether to give premedication and the type of premedication was determined on a random basis. If premedication was given prior to induction, it was administered as outlined in Tables 1 & 2.

Propofol was also used as an intravenous induction agent in cats (n = 7) and dogs (n = 18) that were to undergo non-elective surgical procedures and that had been assigned an ASA status greater than one. These cases either received no premedication or premedication was given as determined by the condition of the animal and the surgical procedure to be performed (Tables 3 & 4).

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An over-the-needle Teflon catheter (Jelco, Critikon) was inserted, using an aseptic technique, in the cephalic vein of the animal prior to the induction of anaesthesia. The amount of propofol drawn up in the syringe was based on an approximate dose of 7,0 mg kg^{-1} for dogs and 8,0 mg kg^{-1} for cats which had previously been established for unpremedicated patients[12]. The initial amount of propofol in the syringe was recorded. A bolus intravenous injection was given intravenously at 2,0 mg kg^{-1} with incremental doses titrated within 15 to 20 sec to the stage where there was sufficient relaxation of the jaw and suppression of protective laryngeal reflexes to allow endotracheal intubation. The amount of propofol not used was noted and the total dose of propofol used was recorded.

Lignocaine [Xylocaine, Astra (Keatings)] was sprayed onto the larynx of cats as a routine procedure prior to intubation. Anaesthesia was maintained with halothane (Fluothane, ICI) in all cases except dental procedures and thoracotomies. In these cases, enflurane (Ethrane, Abbott) and isoflurane (Forane, Abbott) were used, respectively.

Post intubation, the patient was connected to an inhalation anaesthetic system, and the vaporiser setting was increased in increments of 0,5% with every

Table 1: **Induction dose of propofol in dogs younger than 8 years undergoing elective surgical procedures (ASA status I)**

Premedication (*)	Species	Surgical procedure	Age	Sex	Body mass (kg)	Dose (mg kg^{-1})	Mean induction dose (mg kg^{-1})
No premedication	Maltese	ovariohysterectomy	7 months	F	3,75	8,0	6,9 ± 0,9
	Pug	nictitating membrane flap (corneal ulcer)	2 years	M	7,10	6,3	
	GSD	ovariohysterectomy	young adult	F	22,00	5,9	
	GSD	ovariohysterectomy	young adult	F	27,50	7,2	
Acetylpromazine maleate (1) 0,10 mg kg^{-1} SC	ST	ovariohysterectomy	2,3 years	F	11,00	3,6	4,3 ± 1,3
	GSD	ovariohysterectomy	young adult	F	20,00	3,3	
	GSD	ovariohysterectomy	young adult	F	17,50	2,6	
	Mongrel	ovariohysterectomy	1,5 years	F	5,50	3,6	
	Mongrel	ovariohysterectomy	6 months	F	5,00	5,2	
	Mongrel	ovariohysterectomy	1,5 years	F	6,40	2,0	
	Rottweiler	caudectomy	3 months	F	10,50	4,8	
	Bullterrier	ovariohysterectomy	6 months	F	18,00	5,1	
	Dachshund	ovariohysterectomy	8 months	F	6,80	6,8	
	BT	ovariohysterectomy	11 months	F	8,70	4,6	
	Fox terrier	orchidectomy	1,3 years	M	12,00	5,8	
	Poodle	ovariohysterectomy	1 year	F	4,75	4,1	
Acetylpromazine maleate (0,05 mg kg^{-1} SC); Atropine (2) 0,05 mg kg^{-1} SC and Pethidine (3) 2,00 mg kg^{-1} IM	Maltese	front leg amputation (radial paralysis)	3 years	M	10,50	2,9	2,4 ± 0,3
	Bulldog	congenital elbow luxation repair	2 months	M	6,50	2,2	
	Chihauhua	orchidectomy	1 year	M	1,60	2,4	
	GSD	vasectomy	young adult	M	31,50	2,3	
	Labrador	stifle arthrotomy	7 years	?	36,00	2,1	
Fentanyl 0,4 mg ml^{-1} droperidol 20 mg ml^{-1} (4) IV (**) 1 ml 60 kg^{-1} and atropine 0,05 mg kg^{-1} SC	GSD	vasectomy	young adult	M	32,50	2,0	2,1 ± 0,1
	GSD	ovariohysterectomy	young adult	F	28,06	2,1	
	GSD	vasectomy	young adult	M	35,00	2,0	
	GSD	ovariohysterectomy	young adult	F	28,50	2,3	

(*) Given one hour before induction unless otherwise indicated
(**) Given 15 min prior to induction

GSD = German Shepherd dog ST = Staffordshire terrier BT = Boston terrier
? = Unknown M = male F = female
IM = intramuscular SC = subcutaneous IV = intravenous

(1) ACP 2 mg ml^{-1}, Centaur
(2) Atropine 0,5 mg ml^{-1}, Centaur
(3) Pethidine 50 mg ml^{-1}, Centaur
(4) Innovar vet, Jansen Pharmaceutica

3 or 4 breaths of the animal. The patient was initially maintained on a halothane concentration of 3,0% on a closed circuit system or 2,5% on a semi-open system. Once the animal was stabilised, a vaporiser setting of 2,0% for a closed circuit system and 1,5% for a semi-open system on halothane was used.

The patient was placed in a recovery room after the surgical procedure and monitored during recovery. Recovery times were not recorded.

The reduction in the induction dose with the use of premedication in dogs and cats undergoing elective surgical procedures was analysed, using the Student's *t* test with $p < 0,05$ taken as the minimal level of statistical significance. The doses of propofol given in animals undergoing non-elective surgical procedures were not analysed statistically.

RESULTS

The induction doses which would allow endotracheal intubation for animals undergoing elective procedures, using no premedication and different types of premedication, are shown in Tables 1 & 2. There was a significant reduction ($p < 0,05$) in the mean induction dose of propofol with the use of premedication in dogs. When acetylpromazine maleate (ACP 2 mg ml^{-1}, Centaur) was used, there was a 38% reduction in the mean induction dose of propofol of dogs. When an opioid was included in the premedication in dogs, there was more than a 60% reduction in the mean induction dose of propofol. Use of acetylpromazine maleate in cats however, did not cause a significant reduction ($p > 0,05$) in the mean induction dose of propofol.

Induction doses of propofol used in dogs and cats undergoing non-elective surgical procedures are shown in Tables 3 & 4. The induction dose was administered too slowly in 2 dogs undergoing non-elective surgical procedures (Table 3). This resulted in further incremental doses of propofol being given before endotracheal intubation could be achieved.

Transient apnoea accompanied by a slightly blue discolouration of the tongue was occasionally seen at the time of endotracheal intubation in cats undergoing elective surgical procedures. Respiration returned spontaneously in each case.

The induction of anaesthesia in the English Bulldog (Table 1) with propofol was smooth and intubation was easily achieved. The geriatric patient undergoing a short dental procedure (Table 3) recovered from the anaesthetic with a return to an alert habitus within a short period of time.

DISCUSSION

This study found that the mean induction dose of propofol in dogs was significantly reduced ($p < 0,05$) when premedication was used. The affect of acetylpromazine maleate on the induction dose of propofol in dogs was found to be similar to that of other work which reported a mean induction dose of $5,95 \pm 1,86$ mg kg^{-1} in unpremedicated dogs and $3,81 \pm 2,07$ mg kg^{-1} in dogs given acetylpromazine maleate[19]. Inclusion of an opioid in the premedication in dogs undergoing elective surgery, reduced the mean induction dose by over 60%.

The inclusion of acetylpromazine maleate in the premedication of cats, was not shown to significantly affect ($p > 0,05$) the induction dose of propofol. This supported the results of another study which established that the mean induction dose of 6,8 mg kg^{-1} in cats was not significantly affected by prior administration of acetylpromazine maleate[1].

The effect of atropine alone on the in-

Table 2: **Induction dose of propofol for cats younger than 3 years undergoing elective surgical procedures (ASA status I)**

Premedication (*)	Surgical procedure	Age (months)	Sex	Body weight (kg)	Dose (mg kg^{-1})	Mean induction dose (mg kg^{-1})
	orchidectomy	8	M	3,2	6,3	
	ovariohysterectomy	6	F	3,3	8,8	
	ovariohysterectomy	young adult	F	3,1	7,7	
Atropine (1)	ovariohysterectomy	36	F	2,5	6,8	$7,8 \pm 1,1$
0,05 mg kg^{-1}	dental procedure	24	?	3,2	9,4	
	orchidectomy	12	M	3,8	7,9	
	ovariohysterectomy	8	F	2,5	7,0	
	orchidectomy	18	M	4,1	8,8	
Acetylpromazine	orchidectomy	9	M	4,0	7,5	
maleate (2)	ovariohysterectomy	9	F	3,0	6,2	
0,10 mg kg^{-1}	ovariohysterectomy	18	F	2,8	6,1	
and	orchidectomy	24	M	4,8	6,9	
atropine	ovariohysterectomy	young adult	F	3,2	8,8	$7,1 \pm 0,9$
0,05 mg kg^{-1}	orchidectomy	9	M	3,5	6,7	
	ovariohysterectomy	12	F	3,3	7,3	

(*) Given one hour prior to anaesthesia by subcutaneous injection
M = male F = female ? = unknown

(1)Atropine 0,5 mg ml^{-1}, Centaur (2)ACP 2 mg ml^{-1}, Centaur

Table 3: **Induction doses of propofol for dogs undergoing non-elective surgical procedures**

Premedication (*)	Species	ASA status	Surgical procedure	Age	Sex	Body mass (kg)	Dose (mg kg^{-1})
	Rottweiler	III	diaphragmatic hernia repair	3 months	F	7,5	5,2
No premedication	Boxer	III	laparotomy	5 months	M	14,0	2,9
	Mongrel	III	diaphragmatic hernia repair	Adult	?	4,5	3,6
	Poodle	III	dental scaling and tooth extraction	19 years	M	6,6	4,6
	Maltese	II	laparotomy	2 years	M	4,0	(+)10,0
Acetylpromazine maleate (1)	Mongrel	II	fracture femur/open reduction	4 months	M	2,5	4,8
0,10 mg kg^{-1} SC	Chow	II	rectopexy	8 weeks	F	3,2	3,8
	Scottish terrier	II	laparotomy	5 years	M	14,0	2,0
Acetylpromazine maleate	Staffordshire terrier	II	thoracotomy	3 years	F	10,0	3,0
0,05 mg kg^{-1} SC;	Maltese	II	laminectomy	4 years	F	4,5	2,0
	Pug	III	femur luxation/open reduction	4 years	M	8,9	4,3
Atropine (2) 0,05 mg kg^{-1} SC and	Mongrel	II	slot decompression	12 years	M	10,0	(+)6,0
	Maltese	II	laminectomy	3 years	F	3,9	4,1
pethidine (3) 2,00 mg kg^{-1} IM	Staffordshire terrier	II	ulna fracture/open reduction	Adult	?	21,5	1,4
Fentanyl 0,4 mg ml^{-1} droperidol 20 mg kg^{-1} (4) 1 ml 60 kg^{-1} IV (**) and atropine 0,05 mg kg^{-1} SC	Maltese	IV	perineal herniorrhaphy	10 years	M	4,7	4,3
	Pomeranian	IV	inguinal herniorrhaphy	14 years	M	3,4	1,2
	Bull Mastiff	II	humeral fracture/open reduction	Adult	M	31,4	3,2
	Red Setter	III	patent ductus arteriosus ligation	12 weeks	F	11,5	2,5

(*) Given one hour prior to induction of anaesthesia unless otherwise indicated
(**) Given 15 min prior to induction of anaesthesia
(+) Drug administered too slowly

SC = subcutaneous IM = intramuscular IV = intravenous
M = male F = female ? = unknown

(1) ACP 2 mg ml^{-1}, Centaur (2) Atropine 0,5 mg ml^{-1}, Centaur
(3) Pethidine 50 mg ml^{-1}, Centaur (4) Innovar vet, Jansen Pharmaceutica

duction dose of propofol was not evaluated in this study. Atropine has not been found to significantly affect the induction dose in dogs[19]. However, it may cause a prolonged recovery in cats[12]. Other factors, not evaluated in this study, that could affect the induction dose of propofol, include the effect of sex and age on induction dose. Male dogs have been found to require slightly larger induction doses than females[12 19]. In man, elderly patients have been shown to require a lower induction dose of propofol than young patients[4 11 13 15].

The incidence of apnoea after induction, was not monitored in this study. However, propofol is a profound respiratory depressant and a high incidence of apnoea post administration of propofol is reported in man[14 15]. It has been found to cause a significant decrease in minute volume immediately after administration and in patients receiving an opioid premedication[15]. Thiopentone and propofol were not shown to differ significantly in the percentage of patients experiencing apnoea post induction[15]. A similar clinical impression was obtained on the incidence of apnoea in dogs induced with propofol when compared with the induction of anaesthesia using thiopentone and methohexitone[19]. However, the low blood oxygen tensions, found in animals anaesthetised with propofol and breathing air, indicate the necessity of the routine use of endotracheal intubation and the possible need to support respiration with intermittent positive pressure ventilation[19].

The speed of administration of propofol in this study affected the dose requirement and rapidity of onset of anaesthesia in dogs. Propofol was administered slowly, over approximately 60 sec, on 2 occasions (Table 3) which resulted in larger doses being used and a longer time before endotracheal intubation could be achieved. In man, the administration of a 2 mg kg^{-1} induction dose of propofol is reported to produce a satisfactory level of anaesthesia more

rapidly and more reliably if injected over 5 sec than over 60 sec[14 15]. The speed of injection has not been found to affect the incidence or duration of apnoea or the degree to which blood pressure dropped[15]. Transient apnoea with cyanosis was occasionally seen on endotracheal intubation of cats undergoing elective surgical procedures in this study. This was not considered to be associated with too rapid an administration of propofol. Respiration returned spontaneously in each case.

Induction of anaesthesia with propofol in man, causes a decrease in arterial pressure which is more severe in the elderly[4 15 18]. The cardiovascular depression obtained with propofol is greater than that obtained with thiopentone and methohexitone and may be dose-related[4 14 18]. As the diastolic pressure falls to a proportionally greater degree than the systolic pressure, it was suggested that there may be a decrease in peripheral resistance[15]. Recent work has shown that propofol may have a direct venodilatory effect, causing a reduction in preload with a secondary decrease in cardiac output[7]. If preload is maintained, cardiac output and arterial pressures are well preserved at normal anaesthetic blood concentrations[7].

It must still be established whether the reduced induction dose of propofol in dogs given premedication is associated with less cardiovascular and respiratory depressant effects.

Thiopentone is still the most popular, cheap and widely used intravenous anaesthetic for dogs. It is often used as the sole anaesthetic agent for short minor surgical procedures. The solution for injection is alkaline and can produce tissue necrosis if injected perivascularly, and arterial spasm if injected into an artery[8]. It has a short induction time and has anti-convulsant properties following anaesthesia[6 8 15]. It is not rapidly metabolised and has a cumulative effect which can lead to prolonged anaesthesia and unconsciousness[8]. This can be a serious hazard postoperatively[8]. Propofol also has a short induction time but lacks anti-convulsant properties[6 15]. No tissue damage occurs after perivascular or intra-arterial injection[6]. One of the desirable characteristics of propofol is its lack of cumulative properties when compared with thiopentone[12]. This allows it to be used for continuous intravenous infusion for maintenance of anaesthesia[1 4 10 15 17 19]. Emergence from anaesthesia is rapid with a rapid return to an alert habitus[15]. However, one study on dogs premedicated with acetylpromazine maleate and atropine and induced and maintained on propofol, found that although cardiovascular and respiratory effects were similar to those in dogs anaesthetised with halothane and nitrous oxide, maintenance on propofol was associated with a higher incidence of vomiting in the recovery period[9].

An initially higher halothane concentration was used after induction with propofol than was normally used after induction with thiopentone. This was found to be necessary to prevent lightening of anaesthesia between induction and sta-

Table 4: **Induction dose of propofol in cats undergoing non-elective surgical procedures**

Premedication (*)	ASA status	Surgical procedure	Age	Sex	Body mass (kg)	Dose (mg kg^{-1})
	III	Diaphragmatic hernia repair	5 months	M	3,4	5,9
Atropine (1) SC 0,05 mg kg^{-1}	III	Pelvic fracture/open reduction	2 years	F	2,6	6,5
	III	Penile urethrostomy	Adult	M	5,0	3,2
Acetylpromazine maleate (2) 0,10 mg kg^{-1} SC and atropine 0,05 mg kg^{-1} SC	II	Bite wounds	8 months	?	3,5	7,7
	I	Pinnectomy-squamous cell carcinoma	8 years	M	3,5	6,7
Acetylpromazine maleate 0,05 mg kg^{-1} SC;	II	Femur fracture/open reduction	5 months	M	2,7	4,8
Pethidine (3) 1,00 mg kg^{-1} IM and atropine 0,05 mg kg^{-1} SC	II	Maxilla fracture/open reduction	3 years	F	2,0	6,0

(*)Given one hour prior to anaesthesia
(1)Atropine (0,5 mg ml^{-1}, Centaur) (2)ACP (2 mg ml^{-1}, Centaur) (3)Pethidine (50 mg ml^{-1}, Centaur)
SC = subcutaneous IM = intramuscular
M = male F = female ? = unknown

bilisation with halothane.

As it causes a rapid, smooth induction and is rapidly metabolised, propofol may be a useful induction agent in the anaesthetic management of diaphragmatic hernias, where rapid access to the airway is needed, and in the anaesthetic management of the English Bulldog. In the latter case, a rapid access to the airway and a rapid recovery with early return of protective reflexes is desirable as a result of this breed's potential to develop an upper airway obstruction syndrome.

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