

## Clinical Comparison of Recovery from Total Intravenous Anesthesia with Propofol and Inhalation Anesthesia with Isoflurane in Dogs

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**ABSTRACT.** The characteristics of recovery from total intravenous anesthesia (TIVA) with propofol and inhalation anesthesia with isoflurane was clinically compared in 149 client-owned dogs that anesthetized for surgical or diagnostic procedures. In all dogs, anesthesia was induced with an intravenous injection of propofol following premedication with acepromazine or diazepam. As a result, 58 dogs anesthetized with propofol-TIVA showed slower but smoother recovery than 91 dogs anesthetized with isoflurane anesthesia. The dogs stood at  $34.5 \pm 19.3$  and  $27.7 \pm 17.2$  min after propofol-TIVA and isoflurane anesthesia, respectively. Adverse effects, including hypersalivation, neurologic excitement (paddling, muscle tremor/twitching, opisthotonos) and vomiting/retching, were observed in similar infrequent incidences during the recovery from both anesthetic protocols. Propofol-TIVA is suggested to be an alternative anesthetic protocol for canine practice.

**KEY WORDS:** isoflurane, propofol, total intravenous anesthesia.

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Propofol is a newer generation injectable anesthetic agent introduced into veterinary practice in the 1990's. In dogs, it is characterized by rapid onset, short duration, easy titration, rapid clearance, lack of accumulation, rapid and smooth recovery, and some degree of respiratory depression [8, 16].

Total intravenous anesthesia (TIVA) is an alternative to inhalant anesthesia. It provides potential advantages and avoids some drawbacks of inhalant anesthesia, including operating room pollution and the cumbersome anesthetic equipment. TIVA with propofol has become widely adopted in human outpatient anesthesia. In human studies, recoveries from propofol infusion are as rapid as, or even faster than isoflurane or sevoflurane anesthesia and have a low incidence of postoperative nausea and vomiting (PONV) [3, 10, 11].

In this report, a systemic comparative study of the recovery between propofol TIVA and conventional propofol-isoflurane anesthesia in clinical canine cases was carried out. The anesthetic recovery included three observable profiles: (1) the smoothness of recovery, (2) the speed of recovery, and (3) the adverse effects during recovery. The results obtained using the two different anesthetic protocols were compared and analyzed statistically.

One hundred and forty-nine client-owned dogs admitted to the National Taiwan University Veterinary Hospital and the Asia-Pacific Animal Surgical Center requiring general anesthesia for a variety surgical or diagnostic procedures were included in this study. Patients undergoing gastrointestinal procedures were precluded from the study

because of the potential impact on symptoms of vomiting and retching during recovery. Dogs were randomly assigned to 1 of 2 groups of different anesthetic maintenance regimens: (1) isoflurane (Forane, Abbott Labs, Queenborough, England) inhalational anesthesia in oxygen after propofol (Fresofol, Fresenius Kabi, Austria, Germany) induction (Isoflurane group), and (2) propofol TIVA with oxygen supplement (TIVA group).

According to the patients' physical status, laboratory test results and co-existing disorders, dogs were categorized using the American Society of Anesthesiologists (ASA) classification system as ASA 1, 2 or 3. The baseline data including the breed, age, sex, body weight, rectal temperature, heart rate and the nature of the procedure was recorded pre-operatively. A cephalic or lateral saphenous vein was cannulated for the administration of propofol and suitable crystalloid solutions (10 ml/kg/hr) during anesthesia. Dogs were premedicated with either 0.05 mg/kg (with the maximal dose of 3 mg) of acepromazine (Acepromazine Maleate, Boehringer Ingelheim, St Joseph, U.S.A.) or 0.3 mg/kg of diazepam (Diazepam, Oriental, Taipei, Taiwan) intravenously as sedative agents according to their behavior, hemodynamic conditions, and co-existing disorders. Ketoprofen (Ketoprofen, Astar, HsinChu, Taiwan) at the dose of 1 mg/kg was administered intramuscularly in orthopedic patients preoperatively or intraoperatively. Opioids were given only as a rescue remedy for pain as needed postoperatively.

Dogs were induced with propofol at an initial intravenous bolus dosage of 1.5–2 mg/kg. Incremental doses were administered intermittently until intubation of the trachea became possible. Ventilation was manually assisted and maintained at 3–6 ventilations/min with an appropriate airway pressure if dogs did not breathe within 30 sec after intubation. Ventilation was manually assisted until spontaneous

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breathing resumed. Anesthesia was maintained either with isoflurane in oxygen (Isoflurane group) or with intravenous propofol infusion using a syringe pump ( Infusion Pump, Model AS40A, Baxter, U.S.A.) (TIVA group). The vaporizer setting or the propofol infusion rate was adjusted to achieve an appropriate anesthetic plane determined by the patients eyeball position, muscle tone, palpebral reflex, pupil aperture and cornea moisture. All dogs were connected to a semiclosed circle rebreathing anesthetic machine to provide pure oxygen with (Isoflurane group) or without (TIVA group) isoflurane. The propofol or isoflurane was discontinued toward the end of the procedure. Dogs were extubated upon the return of the swallowing reflex. Adverse effects during recovery (e.g., salivation, retching/vomiting and any neurological signs, including paddling, muscle tremor/twitching and opisthotonos) were recorded. The smoothness of recovery was scored with the value of 1 to 4, with 4 representing excellent recovery and the values of 3, 2 and 1 representing good, fair and poor recovery, respectively. An "excellent" recovery was designated as without struggling, vocalization, or excitement and requiring little or no physical restraint to prevent self-injury to the patient. If any one of the former conditions was observed, recovery was judged as "good". Recovery with two or more above conditions was considered as "fair" and "poor", respectively. The time of head lifting, regaining sternal recumbency, standing, and unaided walking after extubation were also recorded for the analysis of the speed of recovery.

Descriptive (categorical) variables and the observed adverse effects were analyzed using a chi-square test. Age,

duration of procedure, the smoothness and speed of recovery (time to first head lifting, regaining sternal recumbency, standing and unaided walking after extubation) were compared by using two-sample *t*-test. A *p* value <0.05 was considered significant for all tests. Stepwise multiple logistic regressions were performed for multivariate analysis.

No significant statistical differences were observed between the two groups regarding gender, age, categorized surgical procedures, duration of procedure, ASA status, or the sedative agents given (Table 1).

The vaporizer settings were adjusted to 1.5~3 % and the propofol infusion rates were adjusted to 0.1–0.6 mg/kg/min for maintenance. No any dog received opioids in this study.

The score of smoothness of anesthetic recovery in this study is shown in Table 2. The TIVA group was significantly better than the Isoflurane group (*p*<0.05).

The parameters for speed of recovery (time to first head lifting, regain of sternal recumbency, standing and unaided walking after extubation) are shown in Table 3. Dogs in the Isoflurane group generally recovered faster than those in the TIVA group.

During recovery, adverse effects were observed in 31 of 91 dogs (34%) in the Isoflurane group and in 18 of 58 dogs (31%) in the TIVA group. There was no significant difference between the two groups. The recorded adverse effects during recovery in this study are shown in Table 4.

Hypersalivation was observed in both groups and generally lasted for approximately one half to one hour; all resolving spontaneously without medical intervention. The hypersalivation was observed as a continuous flooding of

Table 1. The signalment, categorized surgical procedures, physical status and type of sedative agents between groups

	Isoflurane group (n=91)	TIVA group (n=58)
<i>Signalment</i>		
Mean age (years)	8.04	8.44
Gender	Male: 45; Female: 46	Male: 26; Female: 32
Mean body weight (kg)	11.73	8.38*
<i>Type of sedative agents</i>		
	Acepromazine: 33 Diazepam: 58	Acepromazine: 18 Diazepam: 40
Mean induction dosage of propofol (mg/kg)	4.89	5.54
Mean duration of procedures (min)	78.15	76.75
<i>Categorized surgical procedures</i>		
Soft tissue surgery	63	43
Oral surgery	12	11
Orthopedic surgery	7	2
Others	9	2
<i>Physical status</i>		
ASA 1	25	14
ASA2	54	35
ASA3	12	9
Total	91	58

\* Significant difference between compared with isoflurane group (*p*<0.05).

Table 2. Smoothness of anesthetic recovery between the two groups

	Isoflurane group (n=91)	TIVA group (n=58)
Excellent (score= 4 points)	n=67 (73.6%)	n=52 (89.7%)
Good (score= 3 points)	n=16 (17.6%)	n=4 (6.9%)
Fair (score= 2 points)	n= 6 (6.6%)	n=2 (3.5%)
Poor (score= 1 point)	n= 2 (2.2%)	n=0 (0%)
Average scores	3.63	3.86*

\*Significantly better smoothness of recovery compared with isoflurane group ( $p<0.05$ ).

Table 3. Speed of recovery after extubation

	Isoflurane group (n=91)	TIVA group (n=58)
Time to first head lifting	1.87 $\pm$ 2.53	6.14 $\pm$ 5.98*
Time to first regain of sternal recumbency	5.17 $\pm$ 5.65	12.76 $\pm$ 15.38*
Time to first standing	27.7 $\pm$ 17.2	34.5 $\pm$ 19.34*
Time to first unaided walking	35.55 $\pm$ 17.16	41.879 $\pm$ 17.99*

\*Significant difference compared with isoflurane group ( $p<0.05$ ).  
Results expressed as mean  $\pm$  SD, time in minutes.

Table 4. Observed adverse effects during recovery

	Isoflurane group (n= 91)	TIVA group (n=58)
None	60 (65.9%)	40 (69.0%)
Hypersalivation	19 (20.9%)	12 <sup>#</sup> (20.7%)
Neurologic signs	8 (8.8%)	6 <sup>#</sup> (10.3%)
Vomiting / retching	4 (4.4%)	1 (1.7%)

<sup>#</sup> One dog developed hypersalivation and neurological signs concurrently.

All parameters showed no statistical differences.

saliva without tongue licking. The only drawback noted from excessive salivation was in long-haired toy breed dogs, where the hair on the ventral neck might become wet and need constant wiping and drying. Most dogs that developed hypersalivation showed excellent recovery and displayed no sign of major discomfort.

Statistically, the incidence of hypersalivation was similar in both groups (20.9% in the Isoflurane group and 20.7% in the TIVA group). Multiple logistic regression analysis disclosed that maintenance agent, anesthetic risk, the nature of the procedure and the sedative agent given was not related with post-operative hypersalivation. The present study indicates a 20.8% (31 out of 149 dogs) overall incidence of hypersalivation after propofol administration regardless of the maintenance protocol used.

The incidence of neurological signs (including paddling, muscle tremor/twitching and opisthotonos) during recovery was similar in both groups (8.8% in the Isoflurane group and 10.3% in the TIVA group). All animals with neurological signs recovered uneventfully without medical intervention.

Isoflurane is a widely adopted anesthetic agent in both

veterinary and human practice. Recovery from isoflurane is generally rapid and smooth with occasional short periods of excitement and/or disorientation. Propofol is also reported to provide excitement-free anesthetic recoveries in dogs given single or repeated bolus injections [8, 16]. In the present study, the smoothness of recovery after propofol TIVA was significantly superior to the propofol induced, isoflurane maintained anesthesia. Recovery after propofol TIVA was characterized by a minimal amount of struggling, vocalization, and excitement and required little or no physical restraint. This study concludes that anesthesia maintenance by propofol is recommended over isoflurane if a smooth and quiet anesthetic recovery is a main concern for a canine patient.

Propofol has been reported as the intravenous anesthetic agent least likely to cause postoperative nausea and vomiting in the human [7]. More recently, chemotherapy-related nausea and vomiting in humans was also reported to respond well to propofol infusion at subhypnotic doses [1, 12]. In a previous report, propofol infusion was associated with a 16% incidence of vomiting in the recovery period in the dog [4]. However, with gastrointestinal procedures precluded, the incidence of postoperative vomiting was low in the present study regardless of the maintenance agents given (4.4% in the Isoflurane group and 1.7% in the TIVA group).

The present study indicates a total of 20.8 % incidence of postoperative hypersalivation after propofol administration. There was no significant difference between the two groups tested and there was no evidence linking this sign to post-operative pain. In one study, excessive salivation had been noticed in only one out of 68 unpremedicated dogs during propofol anesthesia [16]. In humans, only one study regarded hypersalivation as the most important side-effect associated with propofol administration, with the exact cause unidentified [2]. In most veterinary studies, atropine has been routinely given with propofol administration. Atropine is also frequently administered in human patients to prevent opioid induced bradycardia during surgery. This might explain the reason that postoperative hypersalivation was infrequently reported in prior human and canine studies.

Documentation and study of postoperative nausea in veterinary patients has been relatively limited. Animals with nausea usually show signs of depression, salivation, licking of lips, and increased swallowing motions [15]. In a previous report, post-operative salivation with concurrent retching and/or vomiting developed in 8 out of 40 dogs after propofol administration with various preanesthetic regimens. The authors speculated the salivation was a result of nausea, developed without the antiemetic effects of acepromazine [14]. In the present study, the majority of hypersalivation was not associated with signs of nausea, and it was not related to which sedative agent was given. A positive link between hypersalivation and nausea can not be established from our data.

Salivation may also be a result of post-operative pain. Although the general recovery quality was excellent, a pain

score system was not used to evaluate the influence of postoperative pain. However, since the hypersalivation was independent of the procedures preformed, and no significant postoperative pain/discomfort was documented by anesthesiologists, pain was temporarily excluded as the sole etiology of hypersalivation. The exact causes of postoperative hypersalivation in the present study require further investigation.

Transient signs of neurologic excitement (paddling of limbs, muscle twitching, opisthotonos) during or after propofol administration have been reported in dogs and humans [13]. The incidence of neurologic signs has been variably reported in the literature. In this study, neurologic signs developed in 8% of the isoflurane group and 10.3% of the TIVA group, which is statistically similar. The results suggest that the continued dosing of propofol for anesthetic maintenance will not further predispose the patients to more neurological signs, and any that develop will spontaneously disappear without treatment. Although care should still be taken, neurological problems may be regarded as rare and mostly harmless in dogs with propofol administration.

In humans studies, recovery after propofol TIVA was as rapid as isoflurane anesthesia [9, 11]. However, in one study, dogs recovered slower with propofol TIVA than with propofol/isoflurane anesthesia [6]. The present study showed similar results. The prolongation of recovery using propofol TIVA is not compatible with the hypothesis that propofol provides lighter anesthetic planes [5, 6]. The slower but smoother recovery in dogs with propofol TIVA may be a physio-pharmacologic feature of the agent and requires further investigation.

In conclusion, propofol TIVA provides a slower but smoother recovery compared with propofol induced, isoflurane maintained anesthesia in dogs. Adverse effects were similar in both protocols. The continued propofol dosing

with total intravenous maintenance did not further predispose canine patients to more neurological signs.

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