

RESEARCH PAPER

Effect of anaesthetic maintenance with isoflurane or propofol on ease of endoscopic duodenal intubation in dogs

Mary Emily Tonge^a, Oscar Bautista Diaz-Delgado^b, Jodie Hughes^c, Thomas Maddox^a & Briony Alderson^a

^aDepartment of Small Animal Clinical Science, University of Liverpool, UK

^bDepartment of Anaesthesia and Analgesia, North West Veterinary Specialists, Sutton Weaver, UK

^cDepartment of Anaesthesia and Analgesia, North Downs Specialist Referrals, Bletchingley, UK

Corresponding author. Small Animal Teaching Hospital, University of Liverpool Leahurst Campus, Chester High Road, Neston, Cheshire, UK, CH64 7TE. E-mail: hlmtonge@liverpool.ac.uk

Abstract

Objective To compare the ease of endoscopic duodenal intubation (EDI) in dogs during maintenance of general anaesthesia with isoflurane or propofol infusion.

Study design Prospective, randomized, partially blinded clinical trial.

Animals A total of 22 dogs undergoing upper gastrointestinal tract endoscopy to include EDI were recruited.

Methods Dogs were randomly assigned isoflurane (ISO; $n = 10$) or propofol (PROP; $n = 11$) for maintenance of general anaesthesia. Following anaesthetic premedication with intramuscular medetomidine (0.005 mg kg^{-1}) and butorphanol (0.2 mg kg^{-1}), general anaesthesia was induced with propofol, to effect, maintained with 1.5% (vaporizer setting) isoflurane in 100% oxygen or $0.2 \text{ mg kg}^{-1} \text{ minute}^{-1}$ propofol. The dose of both agents was adjusted to maintain general anaesthesia adequate for the procedure. Degree of sedation 20 minutes post-anaesthetic premedication, propofol induction dose, anaesthetist and endoscopist training grade, animal's response to endoscopy, presence of gastro-oesophageal and duodenal-gastric reflux, spontaneous opening of the lower oesophageal and pyloric sphincters, antral movement and time to achieve EDI were recorded. EDI was scored 1 (immediate entry with minimal manoeuvring) to 4 (no entry after 120 seconds) by the endoscopist, blinded to the agent in use. Data were tested for normality (Shapiro-Wilk test) and differences between groups analysed using independent t test, Mann-Whitney U test and Fisher's exact test as appropriate.

Results There were no significant differences between groups for EDI score [median (interquartile range): 2 (3) ISO, 2 (3) PROP] or time to achieve EDI [mean \pm standard

deviation: 52.50 ± 107.00 seconds (ISO), 70.00 ± 196.00 seconds (PROP)]. Significantly more dogs responded to passage of the endoscope into the oesophagus in group PROP compared with group ISO ($p = 0.01$).

Conclusions and clinical relevance Maintenance of general anaesthesia with either isoflurane or propofol did not affect EDI score or time to achieve EDI.

Keywords endoscopic duodenal intubation, isoflurane, propofol infusion.

Introduction

Many duodenal or gastric conditions primarily affect the mucosal surface of the gastrointestinal tract (GIT) and are best evaluated by endoscopy (Zoran 2001). Endoscopic evaluation of the upper GIT enables visualization and biopsy of the mucosa without painful surgery in animals who may represent a greater surgical risk (Zoran 2001; Simpson & Hall 2005). Gastroendoscopy, requiring intubation of the duodenum, is indicated in veterinary patients presenting with diarrhoea and chronic vomiting (Simpson & Hall 2005).

Endoscopic evaluation of the duodenum, pylorus and cystic antrum may be unachievable even for experienced endoscopists (Happe & Ivd 1983; Hall 1994; Hall 2013). Positioning the animal in left lateral recumbency, avoiding overdistention of the stomach and minimizing time elapsed between commencing the procedure and attempting endoscopic duodenal intubation (EDI) are practical measures reported to aid EDI (Simpson & Hall 2005; Asorey et al. 2020). Active peristalsis and alterations in pyloric and antral tone may impede EDI (Donaldson et al. 1993). Many drugs affect the pyloric sphincter tone and upper GIT motility, and so pharmacological manipulation may also be employed to improve the ease of EDI (Hall 2013; McFadzean et al. 2017).

General anaesthesia is necessary to facilitate endoscopic evaluation of the upper GIT in the dog to ensure endoscopist and animal comfort and to protect expensive equipment (Zoran 2001). Previous studies have evaluated the effects of anaesthetic premedication on EDI (Zoran 2001; Hall 2013; McFadzean et al. 2017; Salla et al. 2020). EDI was more difficult when animals were premedicated with atropine or metoclopramide (Leib et al. 1990) and with morphine and atropine compared to atropine with or without acepromazine (Donaldson et al. 1993). Premedication with butorphanol resulted in easier EDI than that with methadone (McFadzean et al. 2017), but when combined with acepromazine, butorphanol and methadone led to equivalent ease of EDI (Salla et al. 2020). As such, the effect of anaesthetic premedication on EDI should be taken into account when selecting an anaesthetic protocol for upper GIT endoscopy (Zoran 2001; Hall 2013).

The ease of EDI during general anaesthesia induced and maintained with halothane, isoflurane and enflurane has been evaluated and compared, with no significant differences between volatile anaesthetic agents identified (Leib et al. 1990). Intravenous (IV) propofol and isoflurane delivered at 1.0–1.5% \times minimal alveolar concentration (MAC) have both been recommended to facilitate EDI and upper GIT examination (Leib et al. 1990; Donaldson et al. 1993; Sap & Hellebrekers 1993; Zoran 2001; McFadzean et al. 2017). The duration of upper GIT endoscopy including EDI was shortened when general anaesthesia was maintained with propofol boluses rather than with inhaled halothane and nitrous oxide (Sap & Hellebrekers 1993), as has been our clinical experience. Optimizing conditions for EDI may decrease time to achieve EDI, reduce mechanically induced GI trauma, increase clinic throughput, increase clinician satisfaction and facilitate the development of less experienced endoscopists.

To the best of our knowledge, no study has directly compared the effect of maintenance of general anaesthesia using inhaled isoflurane with an IV infusion of propofol, on the ease of EDI.

The purpose of this study was to compare the effect of maintenance of general anaesthesia with inhaled isoflurane or propofol infusion on the ease of EDI in dogs undergoing upper GIT endoscopy. We hypothesized that the maintenance of general anaesthesia with propofol infusion would enable easier EDI during upper GIT endoscopy than maintenance of general anaesthesia with isoflurane.

Materials and methods

Ethical approval was obtained from the University of Liverpool Research Ethics Committee (VREC969). Dogs were recruited to the study following informed owner consent. Using previously published work (Donaldson et al. 1993; McFadzean et al. 2017), the EDI scoring system (Matz et al. 1991) and

adjusting for use of the Mann-Whitney *U* test for comparison (Thrushfield 2018), a minimum of 10 dogs in each group were required to detect a difference of one point in EDI scoring system with 80% power and 95% confidence level.

Animals

A group of 22 dogs, all of whom were scheduled to undergo upper GIT endoscopy which included EDI, were prospectively recruited for the study by the attending medical clinician. Exclusion criteria included animals who were deemed unsuitable for the study anaesthesia protocol, dogs with body mass < 5 kg or dogs with a gastric foreign body who were undergoing gastric endoscopy only. Recruitment was ended when the data of 10 animals per group were available for analysis.

Study protocol

The study was designed as a prospective, randomized, partially blinded clinical trial in accordance with the consolidated standards of reporting trials (Table S1). The attending anaesthetist performed a clinical examination of the dog on the day of the scheduled procedure and confirmed their suitability for the study anaesthetic protocol. Animal age, sex, body mass, body condition score (BCS) and American Society of Anesthesiologists (ASA) physical status score (I–V) were recorded by the attending anaesthetist. Using an envelope system, dogs were assigned randomly to one of two groups: group ISO, general anaesthesia would be maintained with inhaled isoflurane (IsoFlo; Zoetis, UK) in 100% oxygen; and group PROP, anaesthesia would be maintained with a propofol (Propofol-Lipuro; Virbac, UK) infusion. Food, but not water, was withheld for 8–16 hours prior to induction of general anaesthesia. If required (in dogs undergoing colonoscopy examination following completion of upper GIT endoscopy), oral doses of a laxative agent (KleanPrep; Norgine, UK) and warm water enema were administered as directed by the attending medical clinician.

Senior lecturers and lecturers were deemed to be experienced at performing endoscopy. Residents and interns were deemed inexperienced. The same system was used to grade the experience of the attending anaesthetist.

Anaesthetic premedication included medetomidine (Sedator; Dechra, UK) 0.005 mg kg⁻¹ and butorphanol (Dolorex; MSD Animal Health, UK) 0.2 mg kg⁻¹ administered by intramuscular injection of the cervical muscles. The dog was returned to its assigned kennel, left undisturbed and monitored at a distance. After 20 minutes, a sedation score was assigned to the dog by the attending anaesthetist using a subjective sedation scale ranging 0–15 (no sedation to well sedated) by Gurney et al. (2009). A peripheral vein was cannulated using a cannula (Jelco; Smiths Medical, UK) of a gauge (23–18 gauge) appropriate for animal's size. Dogs were moved to the

endoscopy suite and pre-oxygenated via mask and a small animal circle (for dogs > 10 kg) or Mapleson-D (for dogs < 10 kg) breathing system. In both groups, general anaesthesia was induced by the attending anaesthetist with propofol (Propofol Plus; Zoetis) via slow IV injection to enable endotracheal intubation. For group ISO, maintenance of general anaesthesia was with isoflurane vaporized in 100% oxygen delivered at 1.5% of fresh gas flow and adjusted by increments of 0.2% to maintain an adequate plane of anaesthesia. For group PROP, propofol was infused commencing at a rate of 0.2 mg kg⁻¹ minute⁻¹ and the infusion rate adjusted in increments of 0.05 mg kg⁻¹ minute⁻¹ to maintain an adequate plane of anaesthesia. For both groups, for the duration of the study period, a propofol bolus of 0.5 mg kg⁻¹ IV was administered if the animal moved, swallowed or showed a sympathetic response to the procedure.

Following endotracheal intubation and after commencing administration of the ascribed anaesthetic maintenance agent, dogs were positioned in left lateral recumbency and instrumented to record heart rate, oscillometric arterial blood pressure, saturation of arterial haemoglobin with oxygen, respiratory rate, temperature and end-tidal carbon dioxide concentration via multiparameter monitor (Datex-Ohmeda; GE, UK) every 5 minutes during the study protocol period.

To blind the endoscopist to the maintenance agent used, screens covered all anaesthetic and infusion equipment. The endoscopist did not enter the endoscopy suite until the maintenance phase of general anaesthesia had commenced. Upper GIT endoscopy was performed prior to colonoscopy examination in those dogs scheduled for both procedures. The endoscope [5.7 mm diameter (dog < 8 kg) or 7.9 mm diameter (dog > 8 kg)] (TL-100; Karl Storz, UK) was introduced into the stomach via the oesophagus. Swallowing or movement in response to the passage of the endoscope through the oesophagus into the stomach, the presence of gastroesophageal reflux fluid within the oesophagus, spontaneous opening of the lower oesophageal sphincter and the presence of gastric antral movement were recorded (yes or no). The endoscope was manipulated to enable visualization of the pyloric sphincter and the presence of duodenal reflux and spontaneous opening of the pyloric sphincter were recorded by the anaesthetist as reported by the endoscopist (yes or no). The ease of EDI was then scored (EDI score) by the endoscopist using a previously reported four-point scale (Matz et al. 1991): 1) immediate entry with minimal manoeuvring required; 2) rapid entry with moderate manoeuvring; 3) difficult entry with multiple attempts required; and 4) no entry after 2 minutes. The duration of time (seconds) needed to achieve EDI was measured using a mobile phone stopwatch by the attending anaesthetist. This time began when the endoscopist reported the start of this manoeuvre and stopped when the endoscopist positively confirmed the duodenum had been intubated. At the

point of confirmed EDI, the study period was deemed to be complete and for the remainder of the endoscopic examination and recovery period anaesthesia management was determined by the attending anaesthetist.

On completion of the procedure, dogs were disconnected from the anaesthetic machine and breathing circuit and moved to a quiet recovery room. Recovery from general anaesthesia was observed and a recovery score assigned ranging from 1 (poor; marked excitement or struggling and needed sedation) to 4 (excellent, smooth recovery) using a previously described subjective scale (Ambros et al. 2008) by the attending anaesthetist.

Statistical analysis

Missing animal data (age, sex, body mass, BCS and ASA classification) were retrieved from anaesthetic and clinical records made during the same hospitalization period for the same condition. If time to achieve EDI was greater than 120 seconds, an EDI score of 4 was automatically applied at the time of data analysis.

Statistical analysis was performed using computer software (IMB SPSS Statistics for Windows, version 27; IBM Corp, NY, USA). Continuous variable data were tested for normality using the Shapiro-Wilk test. Descriptive statistics for normally distributed continuous variables are reported as mean \pm standard deviation (SD). Descriptive statistics for categorical data are reported as frequencies, and non-normally distributed or ordinal data are reported as median (interquartile range). Statistical significance was set at $p < 0.05$. Differences between groups for normally distributed variables were determined using the *t* test, for non-normally distributed continuous variables using the Mann-Whitney *U* test and for categorical

Table 1 Age, sex, body mass, body condition score (1–9) and American Society of Anesthesiologists physical status score (ASA I–V) of 21 dogs undergoing upper gastrointestinal tract endoscopy during general anaesthesia. Anaesthetic premedication consisted of medetomidine (0.005 mg kg⁻¹) and butorphanol (0.2 mg kg⁻¹) administered intramuscularly. General anaesthesia was induced with propofol, given to effect, and maintained with 1.5% (vaporizer setting) isoflurane in 100% oxygen (group ISO) or 0.2 mg kg⁻¹ minute⁻¹ propofol (group PROP). Data are shown as mean \pm standard deviation or median (interquartile range).

Variable	Group ISO (n = 10)	Group PROP (n = 11)	<i>p</i>
Age (months)	87 \pm 49.6	67 \pm 43.5	0.35
Sex, <i>n</i>	M, 7/F, 3	M, 9/F, 2	0.64
Body mass (kg)	12.2 (31.2)	12.8 (7.1)	0.86
Body condition score	4.5 (3)	4 (2)	0.83
ASA physical status score	II (0)	II (0)	0.48

F, female; M, male.

variables using Fisher's exact test. The effect of anaesthetist and endoscopist experience on the main outcomes were controlled for using ordinal (EDI score) and linear (time to achieve EDI) regression analysis.

Results

A total of 22 dogs were recruited to the study (group ISO: $n = 11$, group PROP: $n = 11$). For one dog, general anaesthetic maintenance agent was changed from isoflurane to propofol infusion without explanation following induction of general anaesthesia, and this case was excluded from the subsequent analysis.

There were no significant differences between the groups for demographic variables including age ($p = 0.35$), sex ($p = 0.64$), body mass ($p = 0.86$), BCS ($p = 0.83$) or ASA classification ($p = 0.48$) (Table 1).

There were no significant differences for pre-, intra- and post-procedure anaesthetic variables: sedation score ($p = 0.08$), propofol induction volume ($p = 0.08$), propofol bolus volume ($p = 0.61$) and recovery score ($p = 0.07$) or for anaesthetist ($p = 0.15$) or endoscopist experience between the groups ($p = 0.99$) (Table 2).

There were no significant differences between the two groups for the presence of gastroesophageal reflux fluid within the oesophagus ($p = 0.39$), spontaneous opening of the lower oesophageal sphincter ($p = 0.67$), gastric antral movement ($p = 0.06$), the presence of gastroduodenal reflux ($p = 0.20$) or spontaneous opening of the pyloric sphincter ($p = 0.39$), assessed during endoscopy. Of the 11 dogs in group PROP, six responded to passage of the endoscope into the oesophagus compared with none in group ISO ($p = 0.01$; Table 3).

Neither EDI score (Table 4) nor the time to achieve EDI were significantly different between the groups ($p = 0.39$ and $p = 0.75$, respectively; Table 5).

Table 2 Sedation score [range 0 (no sedation) to 15 (well sedated)], propofol induction volume, propofol bolus volume and recovery score [range 1 (poor) to 4 (excellent)], anaesthetist and endoscopist experience in 21 dogs undergoing upper gastrointestinal tract endoscopy in dogs under general anaesthesia as per the protocol described in the legend of Table 1. Data are shown as mean \pm standard deviation or median (interquartile range). $p < 0.05$ significant.

Variable	Group ISO ($n = 10$)	Group PROP ($n = 11$)	p
Sedation score	9 (9)	12 (5)	0.08
Propofol induction volume (mL)	4.5 \pm 2.8	2.7 \pm 1.6	0.08
Propofol bolus volume (mL kg ⁻¹)	0.1 (0.1)	0.1 (0.1)	0.61
Recovery score	2 (3)	4 (1)	0.07
Anaesthetist's experience, n	E, 1/I, 9	E, 5/I, 6	0.15
Endoscopist's experience, n	E, 6/I, 4	E, 7/I, 4	0.99

E, experienced; I, inexperienced.

Of the six procedures with an EDI score of 4 (no entry after 2 minutes), two were in group ISO; time to achieve EDI (inexperienced endoscopist) was 315 seconds and (experienced endoscopist) 214 seconds; whereas four were in group PROP; time to achieve EDI (inexperienced endoscopist) 323 seconds and (experienced endoscopist) 200, 227 and 341 seconds (Table 6). When anaesthetist and endoscopist experience were controlled for using regression analysis, there was no significant association with either EDI score (anaesthetist experience $p = 0.45$, endoscopist experience $p = 0.84$) or time to achieve EDI (anaesthetist experience $p = 0.63$, endoscopist experience $p = 0.62$).

Discussion

In dogs undergoing upper GIT endoscopy, maintenance of general anaesthesia with inhaled isoflurane compared with propofol infusion did not affect the ease of EDI, as measured by EDI score or time to achieve EDI. All dogs were premedicated with medetomidine and butorphanol, and general anaesthesia was induced with propofol. However, significantly more dogs anaesthetized with a propofol infusion responded (swallowing, movement) to passage of the endoscope into the oesophagus than those in which anaesthesia was maintained with isoflurane ($p = 0.01$).

Previous studies have shown the control of pyloric motility to be highly complex (Donaldson et al. 1993) with several hormones, neurotransmitters and receptors involved in its regulation (Donaldson et al. 1993; Salla et al. 2020). Gastroduodenal peristaltic activity results in changes in the size of the pyloric aperture, which can affect ease with which an endoscope passes into the duodenum (Donaldson et al. 1993). Excessive peristaltic activity of the gastric antrum may lead to retroflexion of the endoscope and ultimately failure to achieve EDI (Happe & Ivd 1983). Increased intestinal and duodenal tone may decrease the diameter of the pyloric lumen and thereby increase the difficulty of EDI (Donaldson et al. 1993). Gastric and small bowel motility may be influenced by general anaesthetic maintenance agent (Schurizek et al. 1989a; Schurizek et al. 1989b; Torjman et al. 2005; Boscan et al. 2014; Desmet et al. 2016) and so the choice of general anaesthetic maintenance agent may influence the ease of EDI.

Volatile anaesthetic agents and propofol cause smooth muscle relaxation and affect gastric and intestinal motility when used to maintain general anaesthesia in humans and other animals (Schurizek et al. 1989a; Schurizek et al. 1989b; Torjman et al. 2005; Dryn et al. 2018; Li et al. 2021).

Data relating to the effect of propofol on the GIT are mostly associated with human intensive care unit sedation, where short-term propofol administration prolonged oro-caecal transit time (Hammam et al. 1998). In mice, propofol inhibited gastric emptying and prolonged intestinal transit time

Table 3 Endoscopically derived observations in 21 dogs undergoing upper gastrointestinal tract endoscopy under general anaesthesia maintained with either isoflurane in oxygen (group ISO) or propofol infusion (group PROP). For study details, see Table 1 legend.

	Group	Dogs, <i>n</i>		<i>p</i>
		Yes	No	
Response to passing the endoscope	ISO	0	10	0.01*
	PROP	6	5	
Gastro-oesophageal reflux present	ISO	5	5	0.39
	PROP	3	8	
Spontaneous opening of the lower oesophageal sphincter	ISO	3	6	0.67
	PROP	5	6	
Antral movement present	ISO	1	9	0.06
	PROP	6	5	
Gastro-duodenal reflux present	ISO	7	3	0.20
	PROP	4	7	
Spontaneous opening of the pyloric sphincter	ISO	3	7	0.39
	PROP	6	5	

*Significant difference between the groups ($p < 0.05$); *n*: number.

(Inada et al. 2004). *In vitro* propofol decreased spontaneous peristaltic activity of the human GIT, possibly owing to calcium channel blockade and reduction in muscarinic receptor-induced contraction (Lee et al. 1999).

Maintenance of general anaesthesia with propofol boluses rather than a volatile anaesthetic agent has been shown to reduce the procedure time for upper GIT endoscopy, including EDI by 20–30 minutes (Sap & Hellebrekers 1993), as was our subjective, clinical impression. The results of the present study do not support this hypothesis; furthermore, our study showed no significant differences between the groups ISO and PROP for endoscopically derived observations associated with alteration in gastroduodenal and sphincter motility. Though not a statistically significant difference ($p = 0.06$), antral movement was abolished in nine of 10 cases in group ISO compared with five of 11 cases in group PROP. This finding reflects that of studies during human general anaesthesia (Schurizek et al. 1989a; Schurizek et al. 1989b). Failure to achieve EDI has been attributed to an excessively flaccid gastric antrum (Happe & Ivd 1983). Different volatile anaesthetic agents may be considered to have similarly reductive effects on gastrointestinal motility (Boscan et al. 2014). Human gastric antral motility was almost abolished during enflurane and halothane anaesthesia (Schurizek et al. 1989a; Schurizek et al. 1989b), gastric emptying and intestinal motility in rats were reduced following a short period of isoflurane anaesthesia (Torjman et al. 2005) and in dogs sevoflurane anaesthesia reduced gastric and small intestinal propulsive motility (Boscan et al. 2014). The molecular mechanisms by which isoflurane administration causes alterations in GIT motility are yet to be fully elucidated but involve inhibition and disruption of muscarinic receptor G-protein coupling at several levels as well as alterations in plasma membrane transient receptor potential channels (Desmet et al. 2016; Dryn et al. 2018).

We believe the effect of anaesthetic maintenance agent on antral motility warrant further investigation and may have contributed to our impression of increased difficulty of EDI during isoflurane general anaesthesia.

Previous reports investigating the ease of EDI in dogs has focused on choice of anaesthetic premedication (Donaldson et al. 1993; Zoran 2001; Simpson & Hall 2005; Hall 2013; McFadzean et al. 2017; Salla et al. 2020). Butorphanol 0.2 mg kg⁻¹, the most commonly used dose at our institution, facilitates EDI and has been recommended for anaesthetic premedication prior to upper GIT endoscopy (McFadzean et al. 2017). Medetomidine at a dose of 0.005 mg kg⁻¹, rather than the recommended anaesthetic premedication dose of 0.01 mg kg⁻¹ (Murrell & Hellebrekers 2005), was used to provide reliable preanaesthetic sedation and anxiolysis for a duration of approximately 1 hour. Its use in combination with propofol anaesthesia has also resulted in rapid and successful EDI (Sap & Hellebrekers 1993). Dexmedetomidine, the active enantiomer of medetomidine, significantly reduced gastrointestinal motility in mice (Li et al. 2021). The use of medetomidine for anaesthetic premedication may have contributed to ease of EDI through a reduction in gastrointestinal motility. There was no significant difference between groups in anaesthetic premedication sedation score ($p = 0.08$); therefore, it seems improbable that premedication drugs affected the ease of EDI in the two groups.

Dogs in both groups received propofol for induction of general anaesthesia. As a clinical study, using client-owned animals, the induction of general anaesthesia using inhaled isoflurane was deemed ethically inappropriate and previous work comparing the use of isoflurane and propofol for maintenance of general anaesthesia used a similar protocol (Caines et al. 2014). We found no significant difference between either the induction volume of propofol (mL kg⁻¹; $p = 0.08$) or

Table 4 Ease of duodenal intubation score (1–4) in 21 dogs undergoing upper gastrointestinal tract endoscopy under general anaesthesia maintained with either isoflurane in oxygen (group ISO) or propofol infusion (group PROP). For study, details see Table 1 legend.

Ease of duodenal intubation score	Group ISO, <i>n</i>	Group PROP, <i>n</i>
1	4	3
2	4	4
3	0	0
4	2	4

Ease of duodenal intubation score: 1 = immediate entry with minimal manoeuvring required, 2 = rapid entry with moderate manoeuvring, 3 = difficult entry with multiple attempts required and 4 = no entry after 2 minutes (Matz et al. 1991); *n*: number.

Table 5 Time for endoscopic duodenal intubation and ease of duodenal intubation score (1–4) during upper gastrointestinal tract endoscopy in 21 dogs under general anaesthesia as per the protocol described in the legend of Table 1. Data are shown as mean \pm standard deviation, median (interquartile range).

Variable	Group ISO	Group PROP	<i>P</i>
Time for endoscopic duodenal intubation (seconds)	52.50 \pm 107.00	70.00 \pm 196.00	0.39
Ease of duodenal intubation score	2 (3)	2 (3)	0.75

Ease of duodenal intubation score: 1 = immediate entry with minimal manoeuvring required, 2 = rapid entry with moderate manoeuvring, 3 = difficult entry with multiple attempts required and 4 = no entry after 2 minutes (Matz et al. 1991).

propofol bolus dose (mL kg⁻¹; *p* = 0.61) between the groups. Gastric emptying and therefore motility are affected to a similar degree following induction and maintenance of general anaesthesia with propofol alone or IV propofol followed by maintenance with a volatile anaesthetic agent (Bennett et al. 1994). We believe that the propofol bolus doses used in group ISO are unlikely to have led to a failure to detect a difference in the ease of EDI between groups.

Significantly more dogs responded to passage of the endoscope through the oesophagus into the stomach in group PROP than in group ISO (*p* = 0.01). A light plane of general anaesthesia (Simpson & Hall 2005) or, following anaesthetic premedication, isoflurane at 1 \times MAC (McFadzean et al. 2017) has been reported as adequate to maintain general anaesthesia and to facilitate upper GIT endoscopy. MAC isoflurane in unpremedicated dogs is approximately 1.2–1.3% (Steffey & Howland 1977; Ewing et al. 1993; Barletta et al. 2016). Anaesthetic premedication with medetomidine reduces MAC isoflurane by up to 50% (Ewing et al. 1993). While a propofol infusion rate of 0.2 mg kg⁻¹ minute⁻¹ produced a light plane of general anaesthesia in dogs (Aguiar

et al. 2001) and accordingly was selected as the initial postinduction propofol infusion rate for this work. However, following anaesthetic premedication with medetomidine at 0.005 mg kg⁻¹, a propofol infusion rate of 0.4 mg kg⁻¹ minute⁻¹ reportedly led to difficulty maintaining a stable plane of general anaesthesia (Hammond & England 1994). In unpremedicated dogs, a propofol infusion rate of approximately 0.3 mg kg⁻¹ minute⁻¹ compared with an end-tidal isoflurane concentration of 0.73% was required to maintain general anaesthesia adequate for magnetic resonance imaging (Caines et al. 2014). There was no significant difference in anaesthetic premedication sedation score between groups ISO and PROP (*p* = 0.08), so it seems improbable that different background sedation levels between groups caused the reported difference in animal response to passage of the endoscope. The attending anaesthetist scored the level of sedation following anaesthetic premedication (Gurney et al. 2009); however, this scoring system was adapted from a previously published system (Kuusela et al. 2000) with intra- and inter-rater variability. We believe that our initial isoflurane administration rate was relatively higher than that of propofol infusion and may have led to an increased plane of anaesthesia at the start of the procedure resulting in the differences in response rate.

Previous work suggested that differing anaesthetist's experience in the use of propofol infusion and volatile anaesthetic agents may affect their administration rates (Caines et al. 2014) and subsequently the conditions during upper GIT endoscopy and EDI. Endoscopist's experience likewise influences the ease of EDI, with more experienced endoscopists finding the procedure less difficult (Matz et al. 1991). As a busy teaching institution, we were unable to ensure that all procedures were performed by the same endoscopist and anaesthetist, and this represents a limitation of this study. However, we used regression analysis to control for anaesthetist and endoscopist experience and did not identify a significant association between anaesthetist or endoscopist experience and time for EDI.

Another limitation is the clinical, and hence heterogeneous, nature of our study population. The inherently smaller volume of the gastric antrum of smaller dogs may increase the difficulty of EDI (Matz et al. 1991); therefore, dogs < 5 kg in weight were not included in this study. The dose of volatile anaesthetic agent required to maintain general anaesthesia (Yamashita et al. 2009) and its effect on GIT smooth muscle contraction and ease of EDI varies with patient age. We found no significant differences between groups for age, sex, body mass, BCS and ASA physical status score and therefore believe such factors did not affect our findings.

In conclusion, when isoflurane and propofol were compared, the use of both anaesthetic maintenance agents allowed successful EDI in all cases. Neither agent led to significantly easier

Table 6 Breed, presenting signs, diagnosis and ease of duodenal intubation (EDI) score in 21 dogs undergoing upper gastrointestinal tract endoscopy during general anaesthesia maintained with either isoflurane in oxygen (group ISO) or propofol infusion (group PROP). For study details, see [Table 1](#) legend.

Group	Breed	Presenting signs	Diagnosis	EDI score (time to achieve EDI, seconds)
ISO	Pug	Haematemesis	Lymphocytic infiltration with suspicion of lymphoma (not confirmed)	2 ^E (40)
	Small Cross-breed	Vomiting	Lymphoplasmacytic gastritis with gastric lymphoid hyperplasia and <i>Helicobacter spp.</i>	1 ^E (10)
	Curly Coat Retriever	Vomiting, diarrhoea	Neutrophilic gastritis with <i>Helicobacter spp.</i> , neutrophilic and eosinophilic enteritis	4 (315)
	Weimaraner	Borborygmi, vomiting, intermittent diarrhoea	Follicular gastritis with multifocal fibrosis	2 (65)
	Alaskan Malamute	Hyporexia, weight loss	Oesophagitis, lymphoplasmacytic and eosinophilic duodenitis	2 (90)
	Small Cross-breed	Vomiting	Sliding hiatal hernia, suspected chronic enteropathy	2 ^E (88)
	Cross-breed	Hypoalbuminaemia	Gastritis, severe duodenitis, protein-losing enteropathy, suspected pancreatitis	4 ^E (214)
	Norfolk Terrier	Diarrhoea	Lymphoplasmacytic gastroenteritis	1 (16)
	Small Cross-breed	Vomiting, diarrhoea	Neutrophilic and eosinophilic enteritis	1 ^E (5)
	Newfoundland	Panhypoproteinaemia	Protein-losing enteropathy	1 ^E (30)
PROP	Japanese Akita	Intermittent regurgitation, chronic diarrhoea	Gastritis, small intestinal inflammation	4 ^E (200)
	Staffordshire Bull Terrier	Diarrhoea	Lymphoplasmacytic enteritis	1 ^E (31)
	French Bulldog	Diarrhoea, ulcerative colitis	Erosive histiocytic and lymphoplasmacytic enteritis with neutrophilic infiltrate and fibrosis	4 ^E (227)
	Cross-breed	Diarrhoea	<i>Helicobacter spp.</i>	2 (120)
	Pug	Panhypoproteinaemia, hypothyroidism	Duodenal epitheliotropic T-cell lymphoma	2 (60)
	Labrador	Weight loss	Lymphoplasmacytic enteritis, lacteal distention	2 ^E (70)
	Border Collie	Diarrhoea, hypoalbuminaemia	Protein-losing enteropathy, inflammation, lymphangiectasis	1 ^E (39)
	Jack Russell Terrier	Regurgitation, hypoadrenocorticism	Lymphoplasmacytic gastroenteritis, <i>Helicobacter spp.</i>	1 (13)
	French Bulldog	Vomiting, diarrhoea	Lymphoplasmacytic enteritis	4 ^E (341)
	Cross-breed	Chronic gastric ulceration	Oesophagitis, gastric ulceration, neutrophilic and lymphoplasmacytic gastroenteritis	2 ^E (13)
	Miniature Schnauzer	Vomiting, diarrhoea	Lymphoplasmacytic gastroenteritis	4 (323)

Ease of duodenal intubation (EDI) score: 1 = immediate entry with minimal manoeuvring required, 2 = rapid entry with moderate manoeuvring, 3 = difficult entry with multiple attempts required and 4 = no entry after 2 minutes ([Matz et al. 1991](#)). ^EAn experienced endoscopist (Lecturer/Senior Lecturer) performed the procedure.

EDI or reduced time to achieve EDI. However, significantly fewer dogs responded to the passage of the endoscope through the oesophagus into the stomach during general anaesthesia maintained with isoflurane compared to propofol. Practitioners may wish to consider this finding when selecting a propofol infusion rate for upper GIT endoscopy and other similarly invasive procedures. The abolition of antral movement, which may increase the difficulty of EDI, was recorded in more cases where general anaesthesia was maintained with isoflurane

compared to propofol, and this finding may warrant future investigation.

Acknowledgements

The authors thank the staff, especially the medicine service and theatre staff of the University of Liverpool Small Animal Teaching Hospital, for their assistance with this work. This research was not supported by any funding.

Authors' contributions

MET: data management, data interpretation, statistical analysis and preparation of manuscript. OBD: study design, data management and preparation of manuscript. JH and BA: study design and preparation of manuscript. TM: data interpretation, statistical analysis and preparation of manuscript.

Conflict of interest statement

The authors declare no conflict of interest.

References

- Aguiar AJ, Luna SP, Oliva VN et al. (2001) Continuous infusion of propofol in dogs premedicated with methotrimeprazine. *Vet Anaesth Analg* 28, 220–224.
- Ambros B, Duke-Novakovski T, Pasloske KS (2008) Comparison of the anesthetic efficacy and cardiopulmonary effects of continuous rate infusions of alfaxalone-2-hydroxypropyl- β -cyclodextrin and propofol in dogs. *Am J Vet Res* 69, 1391–1398.
- Asorey I, Sambugaro B, Bhalla RJ, Drozdzyńska M (2020) Ultrasound-guided serratus plane block as an effective adjunct to systemic analgesia in four dogs undergoing thoracotomy. *Open Vet J* 10, 407–411.
- Barletta M, Quandt J, Hofmeister E (2016) Determination of minimum alveolar concentration of isoflurane in dogs and cats using the up-and-down method. A preliminary study. *Res Vet Sci* 106, 81–83.
- Bennett M, Bembridge J, Shah M (1994) A comparison of the effect on gastric emptying of either enflurane or propofol given during maintenance of anaesthesia for minor surgery. *Anaesthesia* 49, 675–677.
- Boscan P, Cochran S, Monnet E et al. (2014) Effect of prolonged general anesthesia with sevoflurane and laparoscopic surgery on gastric and small bowel propulsive motility and pH in dogs. *Vet Anaesth Analg* 41, 73–81.
- Caines D, Sinclair M, Valverde A et al. (2014) Comparison of isoflurane and propofol for maintenance of anesthesia in dogs with intracranial disease undergoing magnetic resonance imaging. *Vet Anaesth Analg* 41, 468–479.
- Desmet M, Vander Cruyssen P, Pottel H et al. (2016) The influence of propofol and sevoflurane on intestinal motility during laparoscopic surgery. *Acta Anaesthesiol Scand* 60, 335–342.
- Donaldson L, Leib M, Boyd C et al. (1993) Effect of preanesthetic medication on ease of endoscopic intubation of the duodenum in anesthetized dogs. *Am J Vet Res* 54, 1489–1495.
- Dryan D, Luo J, Melnyk M et al. (2018) Inhalation anaesthetic isoflurane inhibits the muscarinic cation current and carbachol-induced gastrointestinal smooth muscle contractions. *Eur J Pharmacol* 820, 39–44.
- Ewing K, Mohammed H, Scarlett J, Short CE (1993) Reduction of isoflurane anesthetic requirement by medetomidine and its restoration by atipamezole in dogs. *Am J Vet Res* 54, 294–299.
- Gurney M, Cripps P, Mosing M (2009) Subcutaneous pre-anaesthetic medication with acepromazine–buprenorphine is effective as and less painful than the intramuscular route. *J Small Anim Pract* 50, 474–477.
- Hall E (1994) Small intestinal disease—is endoscopic biopsy the answer? *J Small Anim Pract* 35, 408–414.
- Hall EJ (2013) Flexible endoscopy: upper gastrointestinal tract. In: *BSAVA manual of canine and feline endoscopy and endosurgery* (2nd edn). Lehrmette P, Sobel D (eds), British Small Animal Veterinary Association. pp. 42–72. UK.
- Hammas B, Hvarfner A, Thörn SE, Wattwil M (1998) Propofol sedation and gastric emptying in volunteers. *Acta Anaesthesiol Scand* 42, 102–105.
- Hammond R, England G (1994) The effect of medetomidine premedication upon propofol induction and infusion anaesthesia in the dog. *Vet Anaesth Analg* 21, 24–28.
- Happe R, Ivd Gaag (1983) Endoscopic examination of esophagus, stomach, and duodenum in the dog. *J Am Anim Hosp Assoc* 19, 197–206.
- Inada T, Asai T, Yamada M, Shingu K (2004) Propofol and midazolam inhibit gastric emptying and gastrointestinal transit in mice. *Anesth Analg* 99, 1102–1106.
- Kuusela E, Raekallio M, Anttila M et al. (2000) Clinical effects and pharmacokinetics of medetomidine and its enantiomers in dogs. *J Vet Pharmacol Ther* 23, 15–20.
- Lee TL, Ang SB, Dambisya YM et al. (1999) The effect of propofol on human gastric and colonic muscle contractions. *Anesth Analg* 89, 1246–1249.
- Leib M, Clutton E, Zajac A (1990) The effects of volatile anesthetics on endoscopic intubation of the duodenum of dogs. *J Vet Intern Med* 4, 123.
- Li Y, Wang Y, Chang H et al. (2021) Inhibitory Effects of dexmedetomidine and propofol on gastrointestinal tract motility involving impaired enteric glia Ca²⁺ response in mice. *Neurochem Res* 46, 1410–1422.
- Matz M, Leib M, Monroe W et al. (1991) Evaluation of atropine, glucagon, and metoclopramide for facilitation of endoscopic intubation of the duodenum in dogs. *Am J Vet Res* 52, 1948–1950.
- McFadzean WJ, Hall EJ, van Oostrom H (2017) Effect of premedication with butorphanol or methadone on ease of endoscopic duodenal intubation in dogs. *Vet Anaesth Analg* 44, 1296–1302.
- Murrell JC, Hellebrekers LJ (2005) Medetomidine and dexmedetomidine: a review of cardiovascular effects and antinociceptive properties in the dog. *Vet Anaesth Analg* 32, 117–127.
- Salla KM, Lepajoe J, Candido MV et al. (2020) Comparison of the effects of methadone and butorphanol combined with acepromazine for canine gastroduodenoscopy. *Vet Anaesth Analg* 47, 748–756.
- Sap R, Hellebrekers L (1993) Medetomidine/propofol anaesthesia for gastroduodenal endoscopy in dogs. *J Vet Anaesth* 20, 100–102.
- Schurizek B, Willacy L, Kraglund K et al. (1989a) Effects of general anaesthesia with enflurane on antroduodenal motility, pH and gastric emptying rate in man. *Eur J Anaesthesiol* 6, 265–279.
- Schurizek B, Willacy L, Kraglund K et al. (1989b) Effects of general anaesthesia with halothane on antroduodenal motility, pH and gastric emptying rate in man. *Br J Anaesth* 62, 129–137.

- Simpson JW (2005) Gastrointestinal endoscopy. In: BSAVA Manual of Canine and Feline Gastroenterology (2 edn). Hall Edward, Simpson James, Williams D (eds). British Small Animal Veterinary Association, UK. pp. 34–49.
- Steffey E, Howland D Jr. (1977) Isoflurane potency in the dog and cat. *Am J Vet Res* 38, 1833–1836.
- Thrushfield M (2018). In: *Veterinary Epidemiology* (4th edn). John Wiley & Sons, USA. pp. 251–269.
- Torjman MC, Joseph JI, Munsick C et al. (2005) Effects of isoflurane on gastrointestinal motility after brief exposure in rats. *Int J Pharm* 294, 65–71.
- Yamashita K, Iwasaki Y, Umar MA, Itami T (2009) Effect of age on minimum alveolar concentration (MAC) of sevoflurane in dogs. *J Vet Med Sci* 71, 1509–1512.

- Zoran DL (2001) Gastroduodenoscopy in the dog and cat. *Vet Clin North Am Small Anim Pract* 31, 631–656 vii.

Received 17 January 2022; accepted 10 September 2022.

Available online xxx

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.vaa.2022.09.035>.