Influence of capnoperitoneum on intraocular pressure in spontaneously breathing dogs undergoing ovariectomy

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ABSTRACT: The objective of this study was to evaluate potential changes in intraocular pressure in spontaneously breathing dogs undergoing laparoscopic ovariectomy with capnoperitoneum. Twenty bitches undergoing laparoscopic ovariectomy were enrolled in a prospective clinical trial. The dogs were under general anaesthesia and were breathing spontaneously throughout the entire period of the procedure. Capnoperitoneum was then established with an intra-abdominal pressure setting of 10 mmHg. Collected data included intraocular pressure, pupil size, heart rate, respiratory frequency, systolic and diastolic arterial pressure, end-tidal CO_2, oxygen saturation of haemoglobin and tidal volume. Data were recorded 5 min before starting CO_2-insufflation (baseline), after capnoperitoneum establishment (T0), and at further 5-min intervals (T5, T10, T15, T20, T25, T30). Compared to baseline, pupil size was increased at T30 ($P = 0.03$) and respiratory frequency at T25 ($P < 0.01$) and T30 ($P = 0.02$). No other significant changes were found regarding intraocular pressure. Our data show that the induction of an intra-abdominal pressure of 10 mmHg for a 30-min laparoscopy with the use of medetomidine-butorfanol-propofol-isoflurane in spontaneously breathing dogs in the horizontal position does not result in any important changes in intraocular pressure or end-tidal CO_2.

Keywords: laparoscopy; veterinary ophthalmology; pupil size; heart rate, respiratory frequency; systolic and diastolic arterial pressure; oxygen saturation of haemoglobin; tidal volume; end-tidal CO_2

List of abbreviations

DAP = diastolic arterial pressure, **EtCO$_2$** = end-tidal CO_2, f_R = respiratory frequency, **HR** = heart rate, **IOP** = intraocular pressure, **PS** = pupil size, **SAP** = systolic arterial pressure, **SpO$_2$** = oxygen saturation of haemoglobin, **V$_T$** = tidal volume

Intraocular pressure (IOP), defined as the pressure of intraocular aqueous humour on the eye's fibrous layer, is approximately 10–25 mmHg in healthy dogs (Renwick 2002). Intraocular pressure can be altered by numerous mechanisms, including changes in the relative volumes of aqueous and vitreous humour, rigidity of the sclera and tone of extraocular muscles, as well as external pressure on the globe, pupil size, eyelid or extraocular muscles (Gelatt and Brooks 1999; Almeida et al. 2004; Rauser et al. 2012). Intraocular pressure is also influenced by ocular haemodynamics. Changes in

arterial blood pressure affect IOP. A sudden increase in systolic blood pressure produces a transient acute rise in IOP and, whilst moderate decreases in blood pressure have little effect, at a mean arterial pressure of below 90 mmHg, a marked reduction in IOP occurs (Cunningham and Barry 1986). An increase in central venous pressure also alters intraocular vascular diameter, which in turn affects venous outflow and drainage of aqueous humour, thus raising IOP (Verbruggen et al. 2000). Intraocular vascular tone is also markedly influenced by arterial partial pressure of carbon dioxide (P_aCO_2). An increase in P_aCO_2 causes vasodilatation, resulting in an increase of choroidal blood volume and consequently an increase of IOP (Hvidberg et al. 1981).

The advantages of laparoscopic ovariectomy include the limited manipulation of other abdominal organs, improved visualisation, fewer wound complications, decreased postoperative discomfort and an overall decrease in morbidity (Shariati et al. 2014). Nevertheless, abdominal distension due to CO_2 insufflation (capnoperitoneum) can alter the patient's cardiovascular and respiratory functions (Weil 2009). Carbon dioxide in the abdominal cavity is absorbed into the circulation and increased CO_2 levels (hypercapnia) can lead to an increase of heart rate, arterial blood pressure, cardiac output and IOP (Hvidberg et al. 1981). Increased intra-abdominal pressure causes decreased tidal volume and hypoventilation further increasing P_aCO_2 (Nunn 1990). This decrease becomes marked when intra-abdominal pressure exceeds 16 mmHg, while no significant changes are observed when the pressure is approximately 10 mmHg (Ishizaki et al. 1993; Luz et al. 1994). Intra-abdominal insufflation pressures of higher than 15 mmHg should be avoided in dogs (Duke et al. 1996; Bailey and Pablo 1999).

Intra-abdominal insufflation of CO_2 and redundant delivery of CO_2 increases P_aCO_2. To maintain proper ventilation and prevent pathological hypercapnia, artificial ventilation is required. The relationship between IOP and P_aCO_2 has been described (Cooper et al. 1979).

Intraocular pressure may decrease due to a reduction in the formation of aqueous humour, as well as due to choroidal vessel constriction or by the action of carbonic anhydrase under the influence of P_aCO_2 (Samuel and Beaugie 1974). The increase of IOP under the influence of an elevation of P_aCO_2 results from choroidal vasodilatation, elevation of central venous pressure or both (Hvidberg et al. 1981).

Thus, the aim of the present study was to investigate and describe changes in IOP occurring in spontaneously breathing dogs undergoing standard laparoscopic ovariectomy.

MATERIAL AND METHODS

The study protocol was adopted and amended from previous studies comparing the influence of sedatives and anaesthetic drugs on IOP in dogs (Rauser et al. 2012; Rauser et al. 2016). All procedures were carried out with the consent of the Animal Welfare Ethics Committee of the University of Veterinary and Pharmaceutical Sciences, Brno, and all owners signed an informed consent before study enrolment.

Animals. Twenty adult client-owned female dogs of different breeds scheduled for elective laparoscopic ovariectomy were enrolled in this study. All dogs were fasted overnight prior to anaesthesia, but had free access to water.

Only dogs with American Society of Anesthesiologists physical status I or II were included. An ophthalmic examination consisting of observation of eyelids and conjunctiva, slit lamp biomicroscopy of cornea, anterior chamber, lens and vitreous inspection and applanation tonometry (without pupil dilatation) was performed. Only dogs with IOP within the physiological range of 10–25 mmHg (Renwick 2002) were included. Dogs with health problems, ocular pathologies or IOP outside the physiological range were excluded.

Study protocol. A prospective clinical trial was performed. After ophthalmic examination and IOP measurement, intravenous catheterisation of the cephalic vein was performed. Premedication consisted of *i.v.* 0.01 mg/kg medetomidine (Domitor, Orion Pharma, Finland) and *i.v.* 0.2 mg/kg butorphanol (Butomidor; Richter Pharma AG, Austria). Anaesthesia was induced with *i.v.* 1–2 mg/kg propofol (Norofol 10 mg/ml, Norbrook, Northern Ireland) after which dogs were orotracheally intubated and connected to an anaesthetic machine (Venar, Chirana, Slovak Republic). Anaesthesia was maintained with isoflurane (1.5–2.0 vol. % inspiratory concentration, Isofluran, Torrex Chiesi, Austria) vaporised in an oxygen air mixture (1–2 l/min, semi-closed rebreathing circle system, fraction of inspired oxygen (FIO_2) was 0.6). All dogs were breathing spontaneously during surgery.

Surgery. All surgeries were performed by the same surgeon who was experienced in laparoscopic procedures. Dogs were positioned in dorsal recumbency with the table in a strictly horizontal position (no Trendelenburg). A standard ventral midline laparoscopic approach was performed using three ports (Lhermette and Sobel 2008). A Veress needle was placed for CO_2 insufflation, pneumoperitoneum was created to an intra-abdominal pressure of 10 mmHg, and automatically maintained at the same pressure level (Lapflow 40, Smith and Nephew, Germany). Three trocars (two 5-mm and one 10-mm) were placed and a 5-mm telescope was introduced for abdominal inspection. Two grasping forceps were used to locate and manipulate the ovarian bursa. Both ovaries were removed with an ultrasonic device (Harmonic Blade Endo-Surgery, Ethicon, Germany). At the end of surgery, CO_2 was evacuated from the abdomen through the ports and the portal incisions were closed in a routine manner.

Monitoring. Collected data included intraocular pressure (IOP), pupil size (PS), heart rate (HR), respiratory frequency (f_R), systolic and diastolic arterial pressure (SAP, DAP), end-expiratory partial pressure of carbon dioxide ($EtCO_2$), oxygen saturation of haemoglobin (SpO_2) and tidal volume (V_T).

The IOP was measured using applanation tonometry (TonoPen XL, Medtronic, Jacksonville, USA). Prior to measurements in each new patient, the rubber cover was replaced and the tonometer was calibrated. During measurement of IOP, each dog was positioned in dorsal horizontal recumbency, with the head maintained in a relaxed fashion at the level of the thorax. The dog's head was not below the level of the body in order to avoid both fixation and compression in the cervical area or the globe itself. In all dogs, IOP was measured on the left eye. The globe was gently fixed in a central position using the conjunctiva and anatomical forceps. Pupil size was measured using a pupil gauge placed on the cornea.

Heart rate was monitored using 3-lead electrocardiography, leads were applied on both front and left hind limbs. Respiratory frequency was detected with the use of side-stream capnography, arterial blood pressure was measured non-invasively using a cuff applied to the front limb and a blood pressure monitor (Cardel 9401, Midmark, UK). Heart rate, respiratory frequency, $EtCO_2$ and SpO_2 were measured using vital sign monitors (Datex Cardiocap II, Datex-Ohmeda, Finland). Oxygen saturation of haemoglobin was measured using a sensor applied to the tip of the patients' tongue. Tidal volume was measured using a spirometric module attached to the end of the patients' endotracheal tube (Pitot's tube, along with $EtCO_2$) and connected to an inhalation anaesthetic machine (Venar, Chirana, Slovakia). A single investigator obtained all the measurements.

In all dogs, IOP, PS, HR, f_R, SAP, DAP, $EtCO_2$, SpO_2 and V_T were measured and recorded 5 min before CO_2 insufflation (baseline). After establishing a 10 mmHg capnoperitoneum the same parameters were measured in 5-min intervals (T0, T5, T10, T15, T20, T25 and T30).

Statistical analysis. Statistical analysis was performed using Minitab software (Minitab 16 Statistical Software 2010, State College, USA) and Microsoft Excel (Microsoft, Czech Republic). Data are reported as mean ± SD (range). Anderson-Darling and Bartlett's tests were used to confirm normal distribution of data and homogeneity of variance, respectively. For multiple comparison of IOP, PS, HR, f_R, SAP, DAP, SpO_2, V_T and $EtCO_2$ between time points (T0, T5, T10, T15, T20, T25, T30 versus baseline) within the studied group, Dunnett's test was used. Differences were considered significant at $P < 0.05$.

RESULTS

Twenty adult healthy female dogs of eight different breeds were enrolled in this study: Golden or Labrador retriever (4), mixed breed dogs (4), Rhodesian ridgeback (4), Border collie (2), German shepherd dog (2), Pointer (2), English cocker spaniel (1) and Rottweiler (1). Median age was 2.0 years (range 1.0–11.0 years), median weight was 30.5 kg (range 12.0–40.0 kg).

Ocular parameters

Intraocular pressure after induction of anaesthesia (at baseline) was higher compared to pre-anaesthetic values; however, without statistical difference. Likewise, IOP values after capnoperitoneum induction were not significantly different from baseline values. Intraocular pressure after capnoperitoneum induction was not statistically different between T0 and T30 (Table 1).

An almost identical situation was noted in PS. After anaesthesia induction, PS decreased non-

significantly. After the establishment of capnoperitoneum, PS remained similar to baseline until T25. At T30, a significant increase was noted (baseline, 3 mm versus T30, 5 mm; *P* = 0.03; Table 1).

Cardiovascular parameters

There were no significant differences in cardiovascular parameters – HR, SAP, DAP and SpO_2 – at any time points.

Respiratory parameters

Respiratory frequency after induction of anaesthesia (at baseline) was similar to pre-anaesthetic values. After capnoperitoneum induction, respiratory frequency slightly increased between T0 and T20, without differing significantly from baseline values, however. The respiratory frequency was, however, significantly increased compared to baseline at T25 (baseline, 10 breaths/min vs T25, 15 breaths/min; *P* < 0.01) and at T30 (baseline, 10 breaths/min vs T25, 14 breaths/min; *P* = 0.02; Table 1).

There were no significant differences in the other respiratory parameters – V_T or $EtCO_2$ – at any time points compared to values before capnoperitoneum induction.

DISCUSSION

In the current study, we did not detect any effect of a 10-mmHg capnoperitoneum of 30 min duration on the IOP in spontaneously breathing dogs.

Several factors can influence the IOP and should therefore be considered when evaluating the effect of the capnoperitoneum on IOP. An important factor is the patient's body position. Marked changes in IOP during pneumoperitoneum were described in human patients undergoing Trendelenburg tilt (Hvidberg et al. 1981). This abnormal position pro-

Table 1. Changes in intraocular pressure (IOP), pupil size (PS), heart rate (HR), respiratory frequency (f_R), systolic and diastolic arterial pressure (SAP, DAP), end-tidal CO_2 ($EtCO_2$), oxygen saturation of haemoglobin (SpO_2) and tidal volume (V_T) in dogs undergoing laparoscopy for selected periods of time. Data are expressed as mean ± standard deviation (range)

Parameter	Before anaesthesia	Time (min)							
		baseline	T0	T5	T10	T15	T20	T25	T30
IOP (mmHg)	20 ± 6 (11–25)	25 ± 6 (14–32)	26 ± 7 (14–34)	23 ± 6 (13–33)	23 ± 5 (14–30)	26 ± 6 (17–35)	27 ± 8 (13–36)	24 ± 8 (14–35)	29 ± 12 (13–38)
PS (mm)	7 ± 2 (3–8)	3 ± 1 (2–3)	3 ± 1 (2–4)	3 ± 1 (2–4)	3 ± 1 (2–3)	3 ± 1 (2–4)	4 ± 1 (3–4)	4 ± 1 (2–6)	5 ± 1* (3–6)
HR (beats/min)	128 ± 27 (85–174)	66 ± 14 (51–98)	71 ± 23 (34–102)	69 ± 16 (49–59)	73 ± 12 (48–86)	74 ± 17 (39–101)	68 ± 12 (44–82)	77 ± 17 (54–97)	80 ± 12 (70–99)
SAP (mmHg)	155 ± 34 (112–208)	119 ± 20 (96–152)	116 ± 22 (91–168)	117 ± 20 (89–163)	120 ± 16 (93–142)	130 ± 31 (99–204)	121 ± 19 (96–157)	114 ± 23 (78–137)	121 ± 29 (78–153)
DAP (mmHg)	93 ± 25 (47–125)	75 ± 23 (53–119)	70 ± 17 (56–111)	75 ± 20 (48–123)	73 ± 12 (55–93)	87 ± 39 (57–185)	79 ± 25 (55–137)	73 ± 11 (57–96)	79 ± 16 (57–98)
SpO_2 (%)	NA	98 ± 2 (94–99)	97 ± 2 (91–99)	96 ± 3 (92–99)	98 ± 2 (93–99)	98 ± 1 (95–99)	96 ± 4 (91–99)	97 ± 2 (95–99)	98 ± 2 (94–99)
f_R (breaths/min)	10 ± 3 (5–15)	10 ± 3 (5–15)	12 ± 5 (6–22)	13 ± 5 (9–29)	12 ± 3 (6–18)	12 ± 3 (6–18)	12 ± 4 (4–22)	15 ± 4*** (10–22)	14 ± 3** (11–19)
V_T (ml/kg)	NA	13 ± 5 (8–28)	12 ± 6 (8–26)	12 ± 4 (8–24)	12 ± 5 (7–28)	13 ± 5 (8–28)	13 ± 6 (8–30)	11 ± 3 (8–16)	12 ± 3 (9–18)
$EtCO_2$ (mmHg)	NA	52 ± 3 (47–55)	52 ± 4 (45–58)	53 ± 3 (45–59)	50 ± 8 (35–59)	52 ± 7 (43–62)	53 ± 6 (44–62)	47 ± 8 (37–56)	47 ± 5 (42–56)

NA = not available

*Significant increase of pupil size compared to values before capnoperitoneum establishment (*P* = 0.03)

**Significant increase of respiratory frequency compared to values before capnoperitoneum establishment (*P* = 0.02)

***Significant increase of respiratory frequency compared to values before capnoperitoneum establishment (*P* < 0.01)

duced IOP elevations in 80% of the human patients. It was even concluded that the patient's position during surgery represented a stronger risk factor for IOP increase than pneumoperitoneum-related intra-abdominal pressure (Grosso et al. 2013). A significant decrease of IOP after induction of anaesthesia with an alfentanil-propofol-atracurium-isoflurane anaesthetic combination in women undergoing gynaecological laparoscopy was reported by Lentschener et al. (1996). Subsequently, the IOP remained stable after a pneumoperitoneum of up to 15 mmHg had been created. Intraocular pressure did increase significantly with head-down tilt (Trendelenburg position), but never reached pre-induction values. To avoid any concurrent effect of the body position, the dogs in our study were positioned in dorsal recumbency with the table in a strictly horizontal position (no Trendelenburg).

Another contributing factor is that, due to their influence on the cardiovascular system, most drugs used for anaesthesia will change the IOP. Ketamine increases IOP due to contraction of extraocular muscles, and morphine and hydromorphone may increase IOP due to the induction of vomiting (Thomson 2007). In this study, medetomidine in combination with butorphanol was used for sedation. Previously, this combination of drugs has been shown to cause a transient increase in IOP (Rauser et al. 2012). Volatile anaesthetics, like isoflurane used in this study, either slightly reduce, or have no effect on IOP in dogs (Thomson 2007). Thus, this protocol was also chosen because the effect on IOP has been previously documented, allowing the isolated evaluation of the effect of the capnoperitoneum in the current study.

Pupil size is another important factor that can affect IOP. The *i.v.* administration of medetomidine has been shown to cause miosis in dogs (Verbruggen et al. 2000). Miosis is known to reduce IOP by increasing the outflow of aqueous humour (Gelatt and Brooks 1999). Measurement of PS revealed smaller sizes compared to pre-anaesthetic values (from 7 mm to 3 mm). At T30, pupil size started to return to pre-anaesthetic values. Since this timeframe fits the half-life of medetomidine, we attribute the changes in PS to the use of medetomidine (Verbruggen et al. 2000). It is, therefore, possible that the resulting miosis and increased outflow of aqueous humour partly negated any increase in IOP that may have been caused by capnoperitoneum.

In human medicine, studies in children without ocular pathologies revealed no effect of premedication, anaesthesia technique or ventilation method in eliciting IOP variations, but surgical technique (laparoscopy) and position (Trendelenburg) were observed to cause changes (Astuto et al. 2011). The results describe a significant IOP increase in the Trendelenburg position after pneumoperitoneum introduction, which returned to baseline values in the supine position after pneumoperitoneum evacuation. In their study on adult humans, Adisa et al. (2016) observed a mild increase in IOP after pneumoperitoneum induction, with a mean difference of +2.85 mmHg in the reverse Trendelenburg and +0.40 mmHg in the Trendelenburg group. Also, Grosso et al. (2013) found that standard pneumoperitoneum pressures (≤ 14 mmHg) led to mild and reversible IOP increases. The current study could, however, not detect any difference in IOP (no significant increase compared to baseline). This can hypothetically be attributed to the intra-abdominal pressures used in the current study. When Ece et al. (2015) studied the IOP in artificially ventilated humans undergoing laparoscopy, three different intra-abdominal pressures (9, 12 and 15 mmHg) were used. Ventilation was maintained by f_R 10–12/min, V_T 8–20 ml/kg, PEEP 3 cmH_2O and $EtCO_2$ 35 to 40 mmHg. Intraocular pressure was only increased in groups with an intra-abdominal pressure of 12 mmHg or more. The current study used an intra-abdominal pressure of 10 mmHg. This value was chosen so as to remain below the threshold of 15 mmHg at which dangerous cardiovascular changes occur in dogs (Ishizaki et al. 1993). On the other hand, it was well above 6 mmHg, which is the most effective intraabdominal pressure with regard to the pressure-volume curve, to allow the detection of capnoperitoneum-related changes (Dorn et al. 2017).

The results of our study contradict those in Uno et al. (1994). They reported slight but significant increases in IOP and peak airway pressure when the abdominal CO_2 insufflation was started. The study was performed on people undergoing mechanical ventilation and in head-down position. They speculated that the increases were due to the effect of increased central venous pressure with abdominal CO_2 insufflation and postural change on the IOP. Central venous pressure was not measured in the current study in clinical patients. Moreover, no significant changes in systolic or diastolic arterial

pressure and $EtCO_2$ after abdominal CO_2 insufflation were detected, as in the cases presented by Uno et al. (1994).

Capnoperitoneum induction results in cardiovascular alterations (Weil 2009), hypoventilation and increased $EtCO_2$ (Nunn 1990). Elevated CO_2 tension should entail, in patients without eye diseases, an increase in the IOP (Hvidberg et al. 1981). In Rhesus monkeys, increasing the $PaCO_2$ from 2.66 to 10.24 kPa (approx. 20–77 mmHg) resulted in a similar increase in IOP (Smith et al. 1981). This study protocol used spontaneous breathing instead of artificial ventilation to exaggerate the effects of the capnoperitoneum. Myint et al. (1995) reported that $EtCO_2$ levels during laparoscopy were significantly higher when dogs were breathing spontaneously compared to when they were artificially ventilated. End-tidal CO_2 concentrations ranging between 35–45 mmHg are considered normal in anaesthetised dogs (Moens and Coppens 2007). The dogs in this study had $ETCO_2$ values ranging from 47–53 mmHg and were therefore only slightly hypercapnic. Furthermore, these values remained stable during the 30-min evaluation period of the study. Our $EtCO_2$ values were probably only slightly increased because of the adequate breathing of the patients (minimal changes of f_R and V_T) during capnoperitoneum in the neutral position (no Trendelenburg).

Changes in $PaCO_2$ are the driving force behind cardiovascular (heart rate, blood pressure) and IOP changes. In our study, $PaCO_2$ was not measured because of its complicated analysis and related costs. We measured $EtCO_2$ values, which are, in healthy animals, closely related to $PaCO_2$ values (Moens and Coppens 2007). Slight increases in $EtCO_2$ were insufficient to generate any significant changes in IOP, heart rate or systemic arterial pressure. This is confirmed by a study in anaesthetised horses, under neuromuscular blockade and receiving artificial ventilation, where the effects of different $PaCO_2$ levels (40, 60 and 80 mmHg) on IOP were evaluated (Cullen et al. 1990). At the highest $PaCO_2$ level, the systemic arterial pressure was increased; however, heart rate and IOP did not change.

Adisha et al. (2016) reported the reversion of mild pneumoperitoneum-induced IOP changes after evacuation of pneumoperitoneum. Future studies should, therefore, evaluate the selected variables until evacuation of the pneumoperitoneum, instead of stopping before this time point like in the current study.

We suggest that the significant increases in pupil size and respiratory frequency at T20 and T30 are due to the loss of the medetomidine effect.

In conclusion, based on our results, we conclude that laparoscopic ovariectomy at an intra-abdominal pressure of 10 mmHg with dogs in horizontal body position, with an anaesthetic protocol using medetomidine-butorphanol-propofol-isoflurane and spontaneous breathing lasting 30 min results in no significant changes to IOP. In this study, we also found that at 10 mmHg intra-abdominal pressure and with the table in neutral body position dogs did not require artificial ventilation for laparoscopic ovariectomy. Further and more extensive studies would be necessary to confirm and validate the above in cases of dogs with abnormalities in intraocular homeostasis or head-down tilt.

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