

The following studies received ethical approval by institutional and/or national review committees if appropriate.

Session 1

Anaesthetic technique, complications and outcome of 28 cases of adrenalectomies (2007-2015)

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Adrenalectomies are uncommon and challenging procedures in veterinary anaesthesia. Morbidity (up to 51 %) and mortality (13.5 % to 60 %) are usually high (Massari et al., Scavelli et al.) but little information is available about the anaesthetic management. Our aim was to describe the anaesthetic management, the complication rate and immediate outcome of these cases.

Data were collected retrospectively from the patients' records including demographics, invasion of the vena cava, premedication, induction and analgesic drugs and histological diagnosis. Complications recorded were arrhythmia, haemorrhage, hypertension, hypotension. Descriptive statistics were performed along t-tests and Chi-square tests where appropriate. Statistical significance was set at 0.05.

Twenty-eight cases were included. The mean age was 122 ± 28.7 months and the median body weight was 24.6 kg [5.3-69]. Carcinoma was the most common diagnosis (39.3 %). Premedication was most commonly achieved with methadone alone (75 %) IV. Propofol was the most common induction agent alone (39.2 %). An infusion of opioids (85.7 %) and an epidural injection of morphine (75 %) were the most common analgesic techniques. Hypotension was the most common complication observed (42.9 %) followed by hypertension (39.3 %), haemorrhage (21.4 %) and arrhythmia (17.9 %). The mortality rate was 10.7 % within the first 3 days post-surgery.

This study highlights difficulties with the anaesthetic management, the complications encountered and the outcome of the procedure.

Massari, F., Nicoli, S., Romanelli, G., Buracco, P. and Zini, E., 2011. Adrenalectomy in dogs with adrenal gland tumors: 52 cases (2002–2008). Journal of the American Veterinary Medical Association, 239(2), pp.216–221.

Scavelli, T.D., Peterson, M.E. and Matthiesen, D.T., 1986. Results of surgical treatment for hyperadrenocorticism caused by adrenocortical neoplasia in the dog: 25 cases (1980-1984). Journal of the American Veterinary Medical Association, 189(10), pp.1360–1364.

A pilot study comparing metabolic oxygen consumption via in-line gas analysis with results obtained via fick's equation applied to thermodilution cardiac output measurement

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Determination of metabolic oxygen consumption (VO_2) can be achieved using Fick's equation applied to oxygen but requires cardiac output (CO) determination ($\text{VO}_2 = \text{CO} * [\text{CaO}_2 - \text{CvO}_2]$). An alternative way to determine VO_2 using in-line gas analysis has been proposed in dogs ($\text{VO}_2 = V_E * [\text{FiO}_2 - \text{Fe}'\text{O}_2]$) (Borland & Clutton 2016).

We hypothesised that those two methods would provide similar results and offer the opportunity to estimate CO non-invasively.

Seven pigs were anaesthetised for another unrelated experimental procedure. At steady state when CO determination was required for the main procedure, an arterial and a mixed venous sample were taken for determination of the CaO_2 and CvO_2 and immediately analysed. VO_2 was determined from the in-line gas analysis equation ($\text{VO}_{2\text{in-line}}$) and Fick's principle ($\text{VO}_{2\text{true}}$) and indexed to body weight. A Bland-Altman analysis and Wilcoxon test were performed.

One measurement was available per pig. Median (min-max) indexed $\text{VO}_{2\text{in-line}}$ and $\text{VO}_{2\text{true}}$ were 15.05 (2.55 – 30.63) $\text{mL kg}^{-1} \text{min}^{-1}$ and 4.18 (2.1 – 6.4) $\text{mL kg}^{-1} \text{min}^{-1}$ respectively. The mean difference ($\pm$ SD) between indexed $\text{VO}_{2\text{true}}$ and indexed $\text{VO}_{2\text{in-line}}$ was -9.97 ± 8.51 (SE = 3.21) $\text{mL kg}^{-1} \text{min}^{-1}$ ($p = 0.028$), the lower limit of agreement was -26.65 (95 % confidence interval: -40.28; -13.02) $\text{mL kg}^{-1} \text{min}^{-1}$ and the upper limit of agreement 6.71 (95 % confidence interval: -6.92; 20.34) $\text{mL kg}^{-1} \text{min}^{-1}$.

These results suggest a lack of agreement between the two methods in this experimental setting. A higher sample size is needed to confirm these findings and understand the limitations of the technique.

References

Borland, K & Clutton, E 2016, 'A pilot study comparing Brody's formula and in-line gas analysis to determine metabolic oxygen consumption in anaesthetised dogs', AVA Spring Meeting, Lyon.

Agreement of high definition oscillometry (HDO) and conventional oscillometry (petMAP) with direct arterial blood pressure (ABP) measurement at different pressure ranges in awake and anesthetized beagle dogs

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The agreement of two non-invasive blood pressure devices with direct ABP measurements in normotensive, hypotensive and hypertensive awake and anesthetized dogs was investigated.

In a randomized, complete crossover study ABP was measured in seven beagle dogs. For petMAP and HDO oscillometric measurements cuffs were randomly placed around the forelimb, hindlimb or the base of the tail. Data were compared to invasive measurements from the dorsal metatarsal artery. To induce hypertension (MAP > 120 mmHg) or hypotension (MAP < 60 mmHg) dopamine (10-18 µg kg⁻¹ minute⁻¹ IV) was administered or FiSEVO increased, respectively. Corresponding cardiac output was determined by thermodilution and systemic vascular resistance (SVR) was calculated (Shoemaker and Parsa, 2000). Bland-Altman analysis was used to determine agreement of non-invasive and invasive measurements at different pressure and SVR ranges.

A total of 752 and 640 paired measurements were obtained for HDO and petMAP, respectively. High SVR impaired the agreement with ABP with both devices. Table 1 presents bias and limits of agreement at different MAP ranges.

Table 1:

	bias ± SD	limits of agreement	MAP	n
HDO	-1.0 ± 7.8	14 to -16	Hypotension	116
	-8.3 ± 11.8	15 to -31	Normotension	559
	-19.5 ± 19.5	19 to -58	Hypertension	77
petMAP	4.3 ± 8.3	20 to -12	Hypotension	110
	5.4 ± 16.6	38 to -27	Normotension	471
	1.3 ± 16.8	34 to -32	Hypertension	59

The HDO device obtained good agreement at hypo- and normotension, while hypertension was considerably underestimated. The petMAP overestimated ABP, particularly at normotensive and hypertensive ranges.

References

Shoemaker, W.C. & Parsa, M.H. 2000. Invasive and noninvasive Monitoring. In: Grenvik, A., Ayres, S.M., Halbrook, P.R. & Shoemaker, W.C. (eds.) Textbook of critical care. 4th ed. Pennsylvania, USA

Assessment of agreement between invasive blood pressure measured centrally and peripherally and the influence of different haemodynamic states – presentation of preliminary data.

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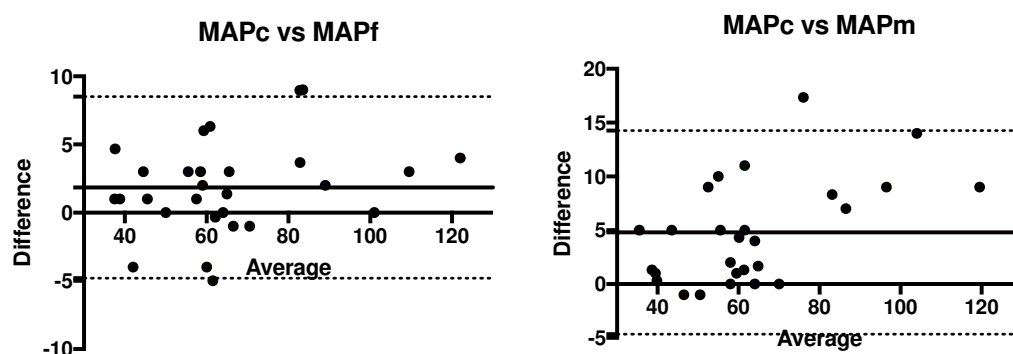
The aim of this study was to assess the agreement of blood pressure measured between peripheral and central sites across different haemodynamics states in horses. Seven horses were anaesthetised and positioned in dorsal recumbancy. Invasive blood pressure was measured simultaneously via catheters placed in the facial, metatarsal and carotid artery. Cardiovascular function and agreement between arteries was assessed before and during administration of phenylephrine and sodium nitroprusside (randomised order). Phenylephrine or sodium nitroprusside were administered until carotid mean pressure (MAPc) increased or decreased from baseline (65 ± 5 mmHg) to > 90 mmHg or < 50 mmHg, respectively. Data recorded at each sample time included SAP, DAP, MAP for carotid (c), facial (f) and metatarsal (m) artery. Bland Altman analysis was used to assess agreement between peripheral and central sites.

The largest difference was observed in SAPc and SAPm with a bias and limits of agreement (LOA) of 2 mmHg and $-16 - 20$ mmHg, respectively. The bias for MAPc and MAPf was 1.8 mmHg (LOA: $-5 - 9$ mmHg) and MAPc and MAPm 4.8 mmHg (LOA: $-5 - 14$ mmHg). Visual inspection of the Bland Altman Plots showed changing bias for MAPm across the spectrum of measurements compared to a consistent bias for MAPf (Figure 1). The best agreement for DAP was seen between DAPc and DAPf with bias of 1 mmHg (LOA: $-3 - 5$ mmHg)

The best agreement for SAP, MAP and DAP was found between the facial and carotid artery.

Figure 1 Bland Altman plots of MAP (mmHg)

Legend: Bias LOA



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Intraoperative evaluation of the parasympathetic tone activity (PTA) in dogs undergoing laparoscopic ovariectomy

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The objective was to evaluate the association between changes in Parasympathetic Tone Activity (PTA) and haemodynamic parameters during noxious stimuli in dogs. In this observational, prospective study 32 healthy dogs undergoing laparoscopic ovariectomy were premedicated with dexmedetomidine (0.004 mg kg^{-1}) and pethidine (4 mg kg^{-1}) IM. Anaesthesia was induced with propofol $2\text{--}4 \text{ mg kg}^{-1}$ IV and maintained with isoflurane in 50% oxygen. When HR or MAP increased more than 20%, end-tidal isoflurane was increased 0.2% or fentanyl 0.002 mg kg^{-1} was administered. PTA, HR, MAP and BIS were registered before and after pneumoperitoneum insufflation, introduction of trocars, removal of the left and right ovaries. Data before and after each stimulus were compared using a t-test or a Wilcoxon test. A Pearson correlation was performed between PTA and HR, MAP and BIS.

Significant changes were found during insufflation (68 ± 11 ; 78 ± 11), trocars (78 ± 11 ; 87 ± 13), left (86 ± 13 ; 94 ± 14) and right ovary (88 ± 13 ; 91 ± 12) for MAP; trocars (81 ± 12 ; 86 ± 10), left (84 ± 14 ; 90 ± 13) and right ovary (82 ± 14 ; 87 ± 12) for HR; insufflation (69 ($52\text{--}86$) ; 48 ($32\text{--}65$)) and trocars (52 ($38\text{--}72$); 44 ($37\text{--}55$)) for PTA. PTA and MAP showed a negative weak correlation (-0.192). BIS didn't change after stimuli. During adequate depth of anaesthesia, PTA showed significant changes after noxious stimuli in less occasions than MAP or HR. No correlations were found.

References

Jeanne M, Clement C, De Jonckheere J et al. (2012) Variations of the analgesia nociception index during general anaesthesia for laparoscopic abdominal surgery. J Clin Monit Comput 26, 289–94.

Gruenewald M, Ilies C., Herz J et al. (2013) Influence of nociceptive stimulation on analgesia nociception index (ANI) during propofol-remifentanyl anaesthesia. Br J Anaesth 110 (6), 1024–30.

Evaluation of the PTA (Parasympathetic Tone Activity) index to assess the analgesia/nociception balance in anaesthetized cats.

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The present study aimed to evaluate the performance of the Parasympathetic Tone Activity (PTA) index to assess the analgesia/nociception balance in anaesthetized cats undergoing surgery.

Female cats (n = 25) were anaesthetised for neutering procedures with a standardised protocol. Heart rate (HR), systolic arterial pressure (SAP), PTA were assessed before surgery (T_{StSt}), at nociceptive stimulations (T_{Clamp}, T_{Cut}, T_{ExtOv1}, T_{ExtOv2}, T_{Sut}) and at the end of anaesthesia (T_{EndIso}). An analysis of variance for repeated measures with, a posteriori, post-hoc Tukey tests was used to detect significant variations of PTA, HR and SAP within time. The performance of the dynamic variation of PTA over 1 minute (Δ PTA) to predict a haemodynamic reaction (increase by > 20% in HR and/or SAP within 3 to 5 minutes) was assessed by building Receiver Operating Characteristics (ROC) curves. A p-value < 0.05 was considered significant.

Significant increases in HR and/or SAP and PTA within 5 minutes were observed at T_{Clamp}, T_{Cut}, T_{ExtOv1}, T_{ExtOv2}, and T_{EndIso}, with an early significant increase in HR of $3,5 \pm 7,1\%$ after 1 min at T_{Cut}. In comparison, an early significant decrease in PTA was noticed after 1 minute at T_{ExtOv1} ($-7,4 \pm 19,1\%$) T_{ExtOv2} ($-11,0 \pm 28,6\%$) and T_{EndIso} ($-12,8 \pm 20,3\%$). The AUC of the ROC curve at 3 minutes was $0.63 \pm 0,05$ [95% CI 0,53 - 0,73] (p < 0,05) and non-significant at 5 minutes.

The performance of Δ PTA was poor to predict a haemodynamic variation in anaesthetised cats, the index needs to be further evaluated.

References

Mansour C, Merlin T, Bonnet-Garin JM et al. (2017) Evaluation of the Parasympathetic Tone Activity (PTA) index to assess the analgesia/nociception balance in anaesthetised dogs. Res Vet Sci. 2017 May 10;115:271-277

Session 2

Comparison of the effect of buprenorphine or butorphanol on quality of detomidine sedation for cheek tooth extraction and postoperative pain in horses

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The aim was to compare effects of buprenorphine or butorphanol on detomidine sedation in cheek tooth extraction and postoperative pain behaviour in horses.

Fourty horses were randomized into two groups. Horses were premedicated with meloxicam (0.6 mg kg^{-1}). Ten minutes after detomidine ($15 \text{ } \mu\text{g kg}^{-1} \text{ IV}$), a bolus of butorphanol ($0.05 \text{ mg kg}^{-1} \text{ IV}$) (BUT) or buprenorphine ($7.5 \text{ } \mu\text{g kg}^{-1} \text{ IV}$) (BUP) was administered and infusion of detomidine was started ($20 \text{ } \mu\text{g kg}^{-1} \text{ h}^{-1}$). Mandibular or maxillary blocks with mepivacaine (2%) were performed. Heart rate, respiratory rate and head height were measured. Resistance towards manipulation and ataxia were scored (1 to 5). Resistance score > 3 resulted in a bolus of detomidine ($3 \text{ } \mu\text{g kg}^{-1} \text{ IV}$) followed by an increase in detomidine infusion rate of $10 \text{ } \mu\text{g kg}^{-1} \text{ h}^{-1}$. Surgeon and anaesthetist were blinded to the protocol. The surgeon assessed quality of sedation and surgical conditions on a Numerical Rating Scale (NRS; 1-10). Postoperative pain was assessed by Composite-Pain-Scale (Bussieres et al. 2008), Horse-Grimace-Scale (Dalla Costa et al. 2014), EQUUS-COMPASS and EQUUS-FAP (van Loon and van Dierendonck 2015). Pedometers recorded locomotor activity. Data were analyzed by Wilcoxon-test ($p < 0.05$).

Quality of sedation (NRS) was significantly better in BUP ($p = 0.03$). There was no difference in required detomidine dose between groups ($p = 0.22$). Horses in BUP showed compulsive behaviour and increased locomotor activity, interfering with postoperative pain scoring.

Buprenorphine for cheek tooth extraction improved sedation, but undesirable side effects dominated postoperative behaviour at the dose used.

This study was supported by CP-Pharma.

Pharmacokinetics and Sedative Effects of Intramuscularly Administered Ketamine in Adult Standing Horses

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Ketamine has been administered IM to increase sedation in hyperexcitable horses, usually in combination with alpha-2 agonists. The objectives were to examine sedation and pharmacokinetics following IM ketamine alone or with detomidine.

Six horses received four treatments in random order:

A: 5 mL saline IV, 0.6 mg kg⁻¹ ketamine IM; B: 0.3 mg kg⁻¹ ketamine IV, 5 mL saline IM; C: 0.01 mg kg⁻¹ detomidine IV, 0.6 mg kg⁻¹ ketamine IM; D: 0.01 mg kg⁻¹ detomidine IV, 5 mL saline IM.

Venous blood samples were collected and sedation variables recorded blindly prior to drug administration, and at various times for 480 minutes. A global sedation score was calculated: 15 (no sedation) to 0 (profound sedation). Plasma ketamine concentration was determined using liquid chromatography-mass spectrometry. Data were compared using a paired Wilcoxon test and presented as median (range), with significance at $p < 0.05$.

Ketamine could be administered IM to horses, but did not produce adequate sedation. Ketamine IM with detomidine, and detomidine resulted in significant decreases in sedation score (lowest median scores of 4 (3 – 12) and 4 (2 – 8), respectively; these were not significantly different). Sensitivity to touch of the front limb was significantly reduced with detomidine/IM ketamine. Detomidine significantly increased the area under the plasma ketamine concentration curve from 539 (270 – 1247) to 14187 (12334 – 15316) ng min mL⁻¹.

Ketamine IM did not significantly increase detomidine induced sedation in horses, though it did increase tolerance to forelimb stimulation. Detomidine significantly influenced the disposition of ketamine.

This study was funded by the Center for Equine Health, University of California, Davis, USA

Protective effects of pharmacologic (dexmedetomidine) or ischaemic preconditioning on intestinal ischaemia-reperfusion injury in horses under general anaesthesia

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The aim was to evaluate protective effects of dexmedetomidine infusion and ischaemic preconditioning on ischaemia-reperfusion injury (IRI) of the small intestine. Fifteen Warmblood horses were randomized into three groups (control (C), ischaemic preconditioning (IPC), dexmedetomidine (DEX)). After induction of anaesthesia with guaifenesin, midazolam and ketamine, anaesthesia was maintained with isoflurane. In group DEX, dexmedetomidine was infused at $7 \mu\text{g kg}^{-1} \text{h}^{-1}$ additionally. In group IPC, 3 x brief periods (2 minutes) of ischaemia and reperfusion were implemented before prolonged ischaemia. Warm ischaemia of the small intestine was induced for 90 minutes, followed by 30 minutes reperfusion. Full-thickness jejunal biopsies were collected before ischaemia, at the end of ischaemia and at the end of reperfusion. Mucosal injury was scored by histopathology (0=normal; 5=complete loss of villi) (White et al. 1980, Chiu et al. 1970). Neutrophils were counted and the degree of apoptosis was assessed by cleaved-caspase-3 and TUNEL. Data were analysed by one-way-ANOVA, Wilcoxon-test and Mixed-Procedure ($p < 0.05$).

During ischaemia, mucosal injury was significantly more severe in DEX compared to C ($p = 0.0273$). After reperfusion, mucosal injury progressed in C ($p = 0.047$), whereas in IPC ($p = 0.089$) and DEX ($p = 0.008$) mucosal injury was less severe than during ischaemia. Neutrophil infiltration increased over time, but did not differ among groups. Apoptotic cells increased with ischaemia and reperfusion, but were lower in DEX compared to C and IPC at all time points.

Ischaemic and pharmacologic preconditioning with dexmedetomidine attenuated small intestinal ischaemia-reperfusion injury in horses.

Cardiopulmonary effects of high doses of racemic methadone and l-methadone-fenpipramide in ponies anaesthetized with isoflurane

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In horses, methadone can be used as racemic mixture or as a combination of L-methadone with fenpipramide (L-Polamivet). Fenpipramide may cause cardiovascular changes after IV administration. We evaluated changes in heart rate (HR) and mean arterial blood pressure (MAP) both after racemic methadone and L-Polamivet.

Six healthy adult Shetland ponies were anaesthetized twice (6 months apart) using different premedication in a non-randomized block design. Ten minutes prior to induction either IV romifidine 0.08 mg kg⁻¹ (group M) or detomidine 0.04 mg kg⁻¹ (group L) were administered. Additionally ponies in group L received IV detomidine 0.02 mg kg⁻¹ and butorphanol 0.01 mg kg⁻¹ 85 minutes prior to induction. At baseline = 15 minutes after connection to the circle system (isoflurane/oxygen) group M received IV racemic methadone 0.5 mg kg⁻¹, group L IV L-methadone 0.25 mg kg⁻¹ with fenpipramide 0.0125 mg kg⁻¹.

HR and MAP were recorded every 10 minutes and compared to baseline values before methadone administration using the Wilcoxon-signed rank test. Data are presented as median ± interquartile range.

In both protocols a significant, but transient increase in blood pressure was seen between baseline and t₁₀ (M: 72 ± 8.6 *versus* 91 ± 17 mmHg; p = 0.031; L: 85 ± 16 *versus* 100 ± 26 mmHg; p = 0.031). Simultaneously, heart rate increased slightly, but not statistically significantly (M: 26 ± 7 *versus* 30 ± 11; p = 0.181, L: 31 ± 4 *versus* 36 ± 8; p = 0.248).

Methadone increases MAP transiently after intravenous administration in anaesthetized ponies.

Cardiopulmonary effects of alfaxalone induction and total intravenous anesthesia with alfaxalone, dexmedetomidine and remifentanyl in foals for abdominal surgery.

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A novel combination of injectable drugs was investigated for cardiopulmonary effects in foals undergoing abdominal surgery for 80 minutes.

Six foals (8-33 days old) were sedated with dexmedetomidine ($3\text{--}7\ \mu\text{g kg}^{-1}\ \text{IV}$) to place a pulmonary balloon catheter. Anesthesia was induced with alfaxalone ($2\ \text{mg kg}^{-1}\ \text{IV}$) and maintained using alfaxalone ($3\ \text{mg kg}^{-1}\ \text{hr}^{-1}$), dexmedetomidine ($1\ \mu\text{g kg}^{-1}\ \text{hr}^{-1}$) and remifentanyl ($3\ \mu\text{g kg}^{-1}\ \text{hr}^{-1}$). Lungs were mechanically ventilated with oxygen. Measurements included: cardiac output (thermodilution), systemic, pulmonary arterial and pulmonary wedge pressure. Arterial and mixed venous blood were analyzed for blood gases, electrolyte and glucose concentrations. Calculated values included cardiac index (CI), systemic vascular resistance (SVR) and alveolar dead space to tidal volume ratio.

Data were compared to those obtained during sedation or 10 minutes postinduction (PI) using ANOVA for repeated measures with Dunnett's correction. $P < 0.05$.

Time from sedation to first measurement and induction was 17.5 ± 6.8 and 32.8 ± 4.5 minutes, respectively. The CI was significantly decreased 60 and 80 minutes PI (106.5 ± 30.9 and $86.9 \pm 21\ \text{ml kg}^{-1}\ \text{min}^{-1}$) compared to sedation (156.9 ± 32.9). The SVR was significantly increased 80 minutes PI ($1223 \pm 166\ \text{dynes second cm}^{-5}$) compared to 10 minutes PI (704 ± 247). Changes followed start of surgery. Glucose concentration was significantly decreased at 60 and 80 minutes PI (8.7 ± 2.8 , $7.7 \pm 2.5\ \text{mmol L}^{-1}$) compared to 10 minutes PI (11.5 ± 3.5).

This drug combination produced cardiopulmonary stability for abdominal surgery in neonatal foals.

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Comparison of alveolar recruitment in horses using heliox (an oxygen-helium-mixture) or pure oxygen as a carrier gas

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When ventilating with high pressures, heliox is associated with lower peak pressures and improved lung compliance. The aim was to evaluate the effects of heliox on pulmonary parameters during alveolar recruitment maneuver in horses.

In this *in vivo* randomized crossover study six isoflurane-anesthetized horses (mean $\pm$ SD bodyweights 585 ± 51 kg and ages 5 ± 1 years) were volume-limited ventilated using either heliox (group HO) or O₂ (group O2) as carrier gas. After 60 minutes, an incremental/decremental PEEP titration recruitment maneuver with steps of 5 cmH₂O every 5 minutes up to a PEEP of 30 cmH₂O was performed. During each step mean arterial blood pressure, heart rate, peak airway pressure (PIP), dynamic compliance (C_{dyn}) and arterial oxygen partial pressure (PaO₂) were measured. Indices of pulmonary O₂ exchange and alveolar dead space were calculated. Statistical analysis was performed using two-factorial variance analysis for repeated measurements and t-test for direct comparison ($p < 0.05$).

In both groups, alveolar recruitment produced significant increases in pulmonary O₂ exchange indices and C_{dyn}. The C_{dyn} was significantly higher (120 ± 8 vs. 85 ± 12 mL/cmH₂O) and the alveolar to arterial PO₂ gradient (38 ± 11 vs. 266 ± 88 mmHg) were significantly lower in group HO versus group O2. The other O₂ exchange indices were significantly higher in group HO during decremental PEEP titration.

We conclude that alveolar recruitment in isoflurane-anesthetized horses breathing heliox instead of O₂ as fresh gas is associated with significantly greater improvement of pulmonary O₂ exchange and respiratory mechanics

Session 3

Intra-observer and inter-observer variability of quantitative sensory testing with electronic von Frey and von Frey filaments in cats

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The Electronic von Frey Anaesthesiometer (EVF) and the von Frey filaments (VFF) enable quantitative measurement of sensory thresholds, and could represent complementary tools to behavioural pain scores. The aim of this study was to investigate the intra- and inter-observer variability, and the limits of agreement (LOA) between the EVF and the VFF, in 15 healthy cats.

Two investigators with different expertise in pain assessment carried out the measurements independently, over a two-day period. Application sites were the upper lip and the stifle. The inter- and intra-individual variability were assessed with either the Paired t-test or the Wilcoxon Signed Rank, and with the Bland Altman. The level of agreement between the EVF and the VFF was analyzed with the Bland Altman.

There were no statistically significant differences between the values obtained for paired measurements by the investigators (95% confidential interval (CI) = 166.55 to 243.54; P values min-max range: 0.11-0.93), and between the values recorded by the same investigator on day 1 and day 2 (95% CI = -7.48 to 30; P values min-max range: 0.13-0.96). Poor limits of agreement were found between EVF and VFF (95% CI = 24.69 to 68.46; LOA = -186.76, 280). The values obtained with the EVF showed less variation than those measured with the VFF.

Our findings indicate that intra- and inter-observer variability are low with EVF and VFF, regardless the experience of the investigators. The EVF may be regarded as a more reliable method than the VFF to measure sensory thresholds in cats.

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Repeatability and reliability of SMALGO (SMall animal ALGOmeter) to measure sensory thresholds in healthy cats and in cats with gingivo-stomatitis

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The SMALGO is designed to measure sensory thresholds to perform quantitative sensory testing (QST) in small mammals.

The main aim of this study was to evaluate intra- and inter-observer variability when the device is used to measure sensory thresholds in healthy cats and in cats with chronic gingivo-stomatitis (CSG).

Two investigators with different expertise in pain assessment carried out the measurements independently, on the upper lip of 30 cats (15 healthy and 15 with CSG), over a two-day period. A modified feline chronic gingivo-stomatitis veterinary surgeon's questionnaire (FVSQ) was used to grade the severity of the CSG.

Paired t-test or Mann-Whitney U test were used to assess intra- and inter-observer variability, and to detect differences between the sensory thresholds of healthy and diseased cats. The Pearson Correlation Coefficient was calculated to correlate the sensory thresholds to the FVSQ scores.

No statistically significant differences were found between the values recorded by the same investigator on day 1 and 2, and between the measurements obtained by the two investigators, in both healthy and CSG cats ($P > 0.05$). There were no statistically significant differences between sensory thresholds of healthy and diseased cats ($P > 0.05$). Poor correlation was found between SMALGO thresholds and FVSQ scores for both observers ($P > 0.05$).

Our findings show that intra- inter-observer variability is low for both healthy and diseased cats, regardless the experience of the investigator. The sensory thresholds measured with the SMALGO correlate neither with the modified FVSQ, nor with the severity of the CSG.

Effect of methadone on esophageal reflux, analgesia and sedation in comparison with morphine in dogs under anesthesia

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The present study compared the effect of methadone and morphine on gastroesophageal reflux (GER), regurgitation (REG) and postoperative analgesia in dogs undergoing ovariohysterectomy.

Dogs ($n = 66$) were randomly assigned into two groups: group MT received methadone 0.5 mg kg^{-1} and group MP morphine 0.5 mg kg^{-1} for premedication, both in combination with acepromazine 0.05 mg kg^{-1} IM. Anaesthesia was induced with propofol and maintained with isoflurane in oxygen. Carprofen (4 mg kg^{-1}) was administered SC after intubation. Three hours after premedication, a second dose of methadone 0.2 mg kg^{-1} IV (MT) or morphine 0.5 mg kg^{-1} IM (MP) was administered. Prior to recovery, oesophageal and oral pH were measured using a pH meter and pH strips. Sedation and postoperative analgesia (using a dynamic interactive visual analogue scale, the short form of the Glasgow composite pain scale (Reid et al. 2007), and mechanical wound threshold measurement) were assessed at 0.5, 1, 2, and 4 hours after extubation by one blinded observer. Data were analysed using Mann-Whitney and Fisher's exact tests ($p < 0.05$).

Regurgitation occurred in 3/36 (MT) and 1/28 dogs (MP; $p = 0.63$), GER in 3/36 (MT) and 1/28 dogs (MP; $p = 0.69$); rescue analgesia was required in four dogs (3 MT and 1 MP) with no significant difference between groups, neither in any of the pain or sedation scores.

We conclude that methadone does not increase the risk of GER nor REG compared to morphine and that the quality of sedation and analgesia is very similar.

References

Reid J, Nolan AM, Hughes JML, et al. (2007) Development of the short-form Glasgow Composite Measure Pain Scale (CMPS-SF) and derivation of an analgesic intervention score. *Animal Welfare* 16, 97-104.

Comparison of the sevoflurane Minimal Alveolar Concentration (MAC) sparing effect of methadone and its enantiomer levomethadone at doses assumed to be equipotent in dogs

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The aim of this study was to determine the sevoflurane MAC sparing effect of methadone and levomethadone at two different doses assumed to be equipotent in dogs.

Six adult, healthy beagle dogs were used in a randomized, blinded, complete crossover study. Each dog received methadone ($0.4 \text{ mg kg}^{-1} \text{ IV}$, treatment M) and levomethadone ($0.2 \text{ mg kg}^{-1} \text{ IV}$, treatment L) with a minimal washout period of 1 week between treatments. Anaesthesia was induced with sevoflurane in 100 % oxygen via face mask. Sevoflurane concentrations were collected from the distal end of the endotracheal tube. Before and after treatment, MAC values were determined by transdermal constant current electrical stimulation (50 mA) via adhesive electrodes at a thoracic limb using the bracketing technique (Sonner, 2002). The study was performed at 57 m above sea level. Normally distributed quantitative parameters were analyzed by one-way analysis of covariance for paired measurements with consideration of duration between opioid application and MAC determination.

Baseline MAC was $2.3 \pm 0.1 \text{ Vol\%}$ in both groups. Methadone reduced the sevoflurane MAC by 33.3 % (to $1.5 \pm 0.2 \text{ Vol\%}$) and levomethadone by 34.8 % (to $1.5 \pm 0.1 \text{ Vol\%}$), without a group difference. Time between treatment and MAC determination was 113 ± 24 minutes in group M and 109 ± 18 minutes in group L and did not differ significantly between groups.

Methadone and levomethadone at the investigated doses have profound anaesthetic sparing effects and can be considered equipotent concerning their MAC reducing abilities for sevoflurane.

Sonner, J. M. 2002. Issues in the design and interpretation of minimum alveolar anesthetic concentration (MAC) studies. *Anesth Analg*, 95, 609-14, table of contents.

A comparison of the effect of propofol and alfaxalone on laryngeal motion and function in normal and brachycephalic dogs

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Anaesthetic agents preserving laryngeal function allow a more objective assessment when diagnosing dogs with laryngeal paralysis and are potentially safer in brachycephalic breeds by maintaining airway patency. Airway patency is maintained better with alfaxalone compared to propofol in humans (Monagle et al. 2015). The aim of this study was to compare the effect of propofol and alfaxalone on laryngeal function in twenty-four normal and twenty-four brachycephalic, client owned dogs, anaesthetised for non-emergency procedures.

This was a prospective, randomized, blinded clinical trial. Each dog received a standardised premedication of methadone (0.2 mg kg^{-1}) and acepromazine (0.01 mg kg^{-1}). Dogs were randomly assigned to receive increments of propofol ($1 - 4 \text{ mg kg}^{-1}$) or alfaxalone ($0.5 - 2 \text{ mg kg}^{-1}$). Laryngeal assessment was performed by a blinded assessor under a light plane of anaesthesia. The maintenance of laryngeal movement was simply assessed as 'Yes' when abduction of the laryngeal cartilages upon inspiration was present or 'No' when abduction was absent. Simultaneously, a sixty-second video was recorded. The same assessor and a separate assessor re-evaluated the videos one month later. Categorical comparisons were studied using Chi squared and Fisher's Exact tests where appropriate. Pair-wise evaluation of agreement between scorers was undertaken with the kappa statistic (κ).

There were no significant differences ($p > 0.05$) in laryngeal function between all dogs receiving propofol or alfaxalone, as well as when analysing normal and brachycephalic dogs separately. Agreement between assessors was excellent ($\kappa = 0.822$).

Afaxalone maintains laryngeal function similarly when compared to propofol in normal and brachycephalic dogs.

References

Monagle J, Siu L, Worrell J et al. (2015) A Phase 1c Trial Comparing the Efficacy and Safety of a New Aqueous Formulation of Alphaxalone with Propofol. *Anesthesia & Analgesia*, 121(4), 914–924.

The influence of melatonin on behaviour and propofol dose for anaesthesia induction in healthy dogs (ASA 1-2)

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Melatonin is used in human medicine as premedication drug which significantly reduces propofol dose for induction of anaesthesia (Naguib et al. 2006).

The aim of this prospective, randomized, double-blinded study was to investigate the influence of melatonin on behaviour and propofol dose for induction in dogs.

Dogs (8-33 kg) presented for elective surgery were included and divided into groups: Group M: 5 mg kg⁻¹ melatonin; Group P: placebo (sucrose), both administered orally prior to induction. Behaviour, handling, calming effect and vital parameters (*fr*, PR, blood pressure and body temperature) were evaluated before and after treatment. The propofol dose (mg kg⁻¹ IV) to allow endotracheal intubation and induction quality were documented.

50 dogs met inclusion criteria (Group M, n = 25; Group P, n = 25). Dogs were further subjectively characterized and divided in rather sceptical (Group MS, n = 10; Group PS, n = 8) or trustful (Group MT, n = 15; Group PT, n = 17) individuals.

Treatment Group MT needed significantly less propofol for induction than Group PT and Group MS (Table 1). The calming effect was significantly higher in Group MS compared to Group PS. Preliminary results showed no significant differences in other evaluated parameters. A general linear model was used.

Results show that melatonin may be used to reduce propofol dose for anaesthesia induction in trustful dogs.

Propofol dose (mg kg ⁻¹ IV)	Melatonin	Placebo
Trustful dogs	5.98 ± 0.96	7.04 ± 1.82
Sceptical dogs	9.48 ± 3.22	7.69 ± 2.71

Table 1: Propofol dose for induction

References

Naguib M, Samarkandi AH, Moniem MA et al. (2006). The effects of melatonin premedication on propofol and thiopental induction dose-response curves: A prospective, randomized, double-blind study. *Anesth Analg* 103, 1448-1452.

This project is funded by a scholarship of the VetmedUni Vienna, Austria.

Session 4

Effect of different synthetic colloids on refractometric reading of total solids in horse plasma

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Refractometry does not accurately reflect total solid (TS) of human serum albumine after addition of 6% hetastarch and 6% dextran in vitro (Bumpus et al., 1998). This effect has not been described in whole blood and not for other colloids. After owner consent, 60 mL blood was collected from ten healthy horses undergoing elective surgery. Each sample was divided into three parts. For each of these, ten dilutions with modified succinylated gelatin (GEL), 6% hydroxyethylstarch (VOL) and Hartmann's Solution (HTM) were performed (representing administration of 1 to 10 mL kg⁻¹ of each fluid to a 500-kg horse) and the TS/ total protein (TP) measured via refractometry and using the biuret method respectively. Separate statistical analyses were performed for each fluid using a mixed model with horse as random effect and measurement method, dilution and their interaction as fixed effects ($\alpha = 0.05$). Linear regression was performed to predict TP from TS. Refractometry consistently overestimated the biuret method (baseline difference 0.9 ± 0.21 g dL⁻¹, $p < 0.001$). A significant interaction between method and dilution was found for GEL and VOL: the difference between the methods increased with higher dilutions in the VOL group (difference at highest dilution 1.3 ± 0.18 g dL⁻¹, $p < 0.001$) and decreased with increasing dilutions in the GEL group (difference at highest dilution 0.7 ± 0.16 g dL⁻¹, $p = 0.045$). Equations to predict TP from TS were obtained. The administration of both colloids significantly affected refractometry readings.

References

Bumpus S.E., Haskins S.C., Kass P.H (1998) Effect of synthetic colloids on refractometric readings of total solids. Vet Emerg & Crit Care 8, 21 – 26.

Comparison of two intravenous infusion regimens for maintenance of anesthesia using alfaxalone in cats

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The aim of this study was to determine if a 3-step infusion regimen (3-step) would maintain a target plasma alfaxalone concentration better than a constant rate infusion (CRI) in cats. Six cats were used. A preserved formulation of alfaxalone (RD0327) was administered intravenously for 4 hours on two occasions in each cat. Previous pharmacokinetic data was used to calculate a loading dose (volume of the central compartment times target plasma concentration of 7.6 mg L⁻¹; 2 mg kg⁻¹) and CRI (clearance times target plasma concentration; 200 µg kg⁻¹ minute⁻¹ for 240 minutes) or a 3-step infusion through simulation (400 µg kg⁻¹ minute⁻¹ for 10 minutes, then 300 µg kg⁻¹ minute⁻¹ for 30 minutes, then 200 µg kg⁻¹ minute⁻¹ for 200 minutes) aiming at maintaining the same target plasma concentration, following the same loading dose. The order of treatments was randomized. Venous blood was collected prior to drug administration and 15, 30, 60, 120, 180, and 240 minutes after starting the drug infusion. Plasma alfaxalone concentration was determined using liquid chromatography/tandem mass spectrometry. The performance error was calculated as ((measured concentration – target concentration) / target concentration) x 100. Performance error in the two treatments was compared using the Wilcoxon test. Significance was set at p < 0.05.

Median (range) performance error (CRI: -14 (-48 – 14) %; 3-step: 0.6 (-20 – 87) %) was significantly different between treatments (p < 0.0001).

A 3-step intravenous infusion regimen was better able to maintain the target plasma alfaxalone concentration than a constant rate infusion in cats

The study was funded by Jurox Pty Ltd

Context-sensitive half-time of alfaxalone in cats

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Context-sensitive half-time is the time required for plasma drug concentration to decrease by 50 % after termination of intravenous drug infusions of a given duration (the context), and has been suggested to be more relevant to the prediction of duration of effect than terminal half-life (Hughes et al. 1992).

Six healthy 1 year old male neutered cats were used. A preserved formulation of alfaxalone (RD0327) was administered intravenously using a target-controlled infusion system, for 30, 60, or 240 minutes (2 cats for each duration). The target alfaxalone concentration was 7.6 µg mL⁻¹. Blood was sampled prior to drug administration, and at various times up to 8 hours after discontinuing the infusion. Plasma alfaxalone concentration was measured using liquid chromatography/tandem mass spectrometry. A 3-compartment model was fitted to the time-concentration data in each individual to predict the context-sensitive half-time. In addition, population analysis was performed to fit a single 3-compartment model to all datasets, and was used to predict time from discontinuation of drug administration to decrease in plasma concentration by 50 to 95%, using simulation.

Context-sensitive half-times were 2 and 8, 6 and 9, and 18 and 20 minutes for the 30, 60, and 240 minutes (2 cats each), respectively. Median decrease in plasma concentration from end of infusion to standing was 88%; time for that decrease was predicted to range from 8 to 118 minutes following a bolus to an 8 hours infusion.

Recovery time from alfaxalone in cats is predicted to be influenced by the duration of infusion.

References

Hughes MA, Glass PS, Jacobs JR (1992) Context-sensitive half-time in multicompartment pharmacokinetic models for intravenous anesthetic drugs. *Anesthesiology* 76, 334-341.

This study was funded by Jurox Pty Ltd.

Comparison of dexmedetomidine-ketamine and medetomidine-ketamine immobilization in free-ranging and captive african lions (panthera leo)

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Dexmedetomidine-ketamine and medetomidine-ketamine combinations were evaluated for immobilisation of lions (*Panthera leo*).

Twenty-five anaesthetic events in 8 free-ranging and 17 captive lions (50 - 190 kg) were studied. Lions were darted intramuscularly: 0.077 ± 0.04 mg kg⁻¹ medetomidine and 2.2 ± 0.5 mg kg⁻¹ ketamine (MK, n = 13); 0.013 ± 0.005 mg kg⁻¹ dexmedetomidine and 2.6 ± 1 mg kg⁻¹ ketamine (DK, n = 12). Physiological variables and anaesthetic scores (Wenger et al. 2010) were recorded. Procedures were divided into phases "T" and "TO2". In TO2 intranasal oxygen (5 l/minute) was administered. Haemogasanalysis were performed in 13 lions at T and TO2. Atipamezole was administered intramuscularly (0.07 ± 0.05 mg kg⁻¹ MK; 0.11 ± 0.04 mg kg⁻¹ DK). Statistical analysis included Student's t-test and Mann-Whitney U-test.

Both protocols produced similar cardio-respiratory and blood gas effects. Six lions developed hypoxaemia, but oxygen delivery significantly increased PaO₂ (T = 78 ± 13 , TO2 = 171 ± 56 mmHg) and oxygen saturation (T = $87\% \pm 5$, TO2 = $98\% \pm 2$). Scores were significantly better in DK than MK: induction 1 (1 – 2) versus 2 (1 - 4), recovery 2 (1 – 3) versus 4 (2 - 4), immobilization 5 (2 – 5) versus 3 (2 - 5). Recumbency and recovery times (minutes) were significantly shorter in DK (8.2 ± 3.7 and 15.2 ± 10) than MK (13.4 ± 6.9 and 100 ± 100.8).

At the investigated doses, DK provided more reliable immobilisation in lions than MK. Intranasal oxygen administration is advisable.

The authors thank IDEXX Laboratories, Inc. (Italy) for the donation of the VetStat Electrolytes and Blood Gas Analyzer and cartridges.

Ketamine and dexmedetomidine infusion for the treatment of super-refractory status epilepticus in dogs: a case series

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Super-Refractory Status Epilepticus (SRSE) is a life-threatening condition that requires a prompt and aggressive approach (Serrano et al. 2006).

We report the effectiveness of ketamine (KET) and dexmedetomidine (DEX) combination for SRSE treatment in dogs.

Five dogs of different breed, gender and weight, with idiopathic epilepsy, presented for status epilepticus, were treated, unsuccessfully, with 0.5 mg kg⁻¹ transrectal diazepam. A 12-hours propofol total intravenous anaesthesia (TIVA) was administered at 0.2 – 0.4 mg kg⁻¹ minute⁻¹. All animals were intubated. Three out of five dogs required mechanical ventilation because of respiratory depression. When propofol TIVA was discontinued, seizures recurred in all dogs. All patients then received a bolus of KET (1 mg kg⁻¹ IV) followed by a bolus of DEX (3 µg kg⁻¹ IV) both administered over 5 minutes and maintained as Constant Rate Infusion (CRI) for 12 hours (KET 1 mg kg⁻¹ hour⁻¹ and DEX 3 µg kg⁻¹ hour⁻¹). Non invasive blood pressure (NIBP), HR, f_R , and ECG were recorded during KET-DEX CRI; values of NIBP (mean 89 ± 9.6 mmHg), HR (77.5 ± 4.5 beats minute⁻¹) and f_R (11.41 ± 2.1) remained within physiological range. No arrhythmias were recorded. Endotracheal intubation was unnecessary during KET-DEX CRI (PaCO₂ and PaO₂ within normal range). All dogs recovered uneventfully over the next 48 hours after treatment discontinuation. After a 72-hours seizures-free period, dogs were discharged with long-term antiepileptic therapy (phenobarbital – levetiracetam).

In conclusion, 12 hours of KET-DEX CRI provides a complete recovery from SRSE without significant cardiorespiratory or haemodynamic effects in this series.

References

Serrano S, Hughes D, Chandler K (2006) Use of Ketamine for the Management of Refractory Status Epilepticus in a Dog. J Vet Intern Med 20, 194 – 197.

How much atipamezole to reverse the effect of an α_2 -agonist? A regression analysis study in dogs

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As there is no dose range of atipamezole to reverse the sedative effect of the α_2 -agonists, the purpose of this study was to define the dose of atipamezole after the use of dexmedetomidine or medetomidine.

Twenty-two dogs admitted for sedation were randomly allocated into two groups. In group A (n = 11), dexmedetomidine was administered at 175 - 375 $\mu\text{g m}^{-2}$, while in group B (n = 11) medetomidine was administered at 10 - 15 $\mu\text{g kg}^{-1}$, intramuscularly. At the end of the procedure, atipamezole was given intramuscularly, in a dose based on the time elapsed after the administration of the α_2 -agonist and clinical measurements of the patient, using a sedation scoring system. Correlation and linear regression models were used for the statistical analysis.

All dogs were fully alert, a few minutes after the administration of atipamezole. Regression analysis revealed these formulas: in group A, atipamezole ($\mu\text{g kg}^{-1}$) = dexmedetomidine ($\mu\text{g kg}^{-1}$) $\times$ 6.23 (p < 0.005) – time elapsed (minutes) $\times$ 0.29 (p < 0.005) ($r^2 = 0.907$), while in group B, atipamezole ($\mu\text{g kg}^{-1}$) = 18.6 (p = 0.150) + medetomidine ($\mu\text{g kg}^{-1}$) $\times$ 2 (p < 0.005) – time elapsed (minutes) $\times$ 0.23 (p < 0.005) ($r^2 = 0.650$).

The regression models were highly significant and therefore, they could be applied in clinical practice for the reversal of the sedation of these α_2 -agonists, in dogs.

Session 5

Questionnaire based evaluation of pet owners' anxiety and desire for information regarding general anaesthesia and surgery at a referral university hospital: a pilot study

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In people, anaesthesia is a source of concern that can lead to increased perioperative anxiety. In veterinary medicine, the same assumption is made but no data is available. We designed a questionnaire aimed at quantifying owner's anxiety regarding anaesthesia and their information desire.

A questionnaire was designed and divided in two sections, one regarding owner's and patient's demographics and anaesthetic background, the second trying to quantify the anxiety and the information desire with the Amsterdam Preoperative Anxiety and Information Scale (APAIS) (Moerman et al. 1996). Closed and semi open questions about the preferred interlocutor and the need for a preoperative consultation were also asked. The questionnaire was given to owners at the beginning of the consultation. Results are presented as descriptive statistics and were analysed using Chi-squared tests.

Seventy questionnaires were collected. APAIS scores are reported in table 1. These results were not influenced by the demographic data of the responders ($p > 0.05$). Examination of the patient by a specialist anaesthetist before giving consent for GA was deemed very important (median score of 5/5 (1-5)). A specialised nurse in anaesthesia (65.6 %) would be the preferred interlocutor. Delaying an elective surgery to meet with an anaesthetist was acceptable to 44.1 % of the responders.

These results provide some evidence of owner's anaesthesia-related anxiety and a strong desire for information.

	Anaesthesia related anxiety score (/10)	Surgery related anxiety score (/10)	Combined anxiety component (/20)
Median	5	6	12
Minimum	2	2	4
Maximum	10	10	20

Table 1 - APAIS scores

Moerman, N. et al., 1996. The Amsterdam Preoperative Anxiety and Information Scale (APAIS). *Anesthesia & Analgesia*, 82(3), pp.445–451.

Survey of Veterinary Professionals into the use of Locoregional Anaesthetic Techniques

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Local anaesthetic techniques are commonly recommended as perioperative analgesia for orthopaedic procedures. Here we aimed to determine the prevalence of use of these techniques amongst veterinary anaesthetists.

Veterinary anaesthetists were contacted via an email (ACVA-list) containing a link to an online survey. The survey consisted of 4 parts; demographics, technique choice for a specific hind limb surgery (tibial osteotomy), drug choices and adverse effects.

The survey was fully completed by 112 respondents. Peripheral nerve blocks and epidural techniques were the preferred techniques of 46% and 38% of respondents respectively. Of the respondents, 96 had experience of femoral/sciatic peripheral nerve blocks and answered the following questions. For femoral nerve blockade, blind, ultrasound guided or nerve stimulator based techniques were used by 5%, 23%, and 72% of respondents respectively. The most common site for blockade was at the femoral triangle. For the sciatic nerve the most common sites were lateral/transgluteal with the nerve stimulator and as per Campoy et. al (2010) with ultrasound. The majority of respondents used bupivacaine (71%) and thirty seven percent of respondents used an adjuvant in addition to local anaesthetic; most commonly an alpha-2 agonist. Respondents claimed a cumulative experience of over 15,000 procedures with 50% reporting having observed no adverse effects. Severe adverse effects were reported by 11 respondents. More experienced anaesthetists (> 100 blocks performed) were more likely to have seen adverse effects ($p < 0.001$, Chi-Squared).

Peripheral nerve blocks are commonly utilised by anaesthetists for hind limb orthopaedic surgery, with severe complications apparently reported uncommonly.

Reference

Campoy L, Bezuidenhout AJ, Gleed RD et al. (2010) Ultrasounds-guided approach for axillary brachial plexus, femoral nerve, and sciatic nerve blocks in dogs. *Veterinary Anaesthesia and Analgesia* Vol. 37, 144-153.

Evaluation of topical ropivacaine delivered via absorbable gelatin sponge for postoperative analgesia following enucleation in dogs

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Preoperative ophthalmic regional anesthesia may be contraindicated in orbital infection and neoplasia. The goal of this study was to evaluate the analgesia produced by ropivacaine delivered via absorbable gelatin sponge (gelfoam) following enucleation in dogs.

Twenty client-owned dogs scheduled for enucleation were recruited in this randomized, masked, controlled clinical trial. Premedication included methadone ($0.5\text{--}1\text{ mg kg}^{-1}$) IM and maintenance included remifentanyl infusion ($30\text{ }\mu\text{g kg}^{-1}\text{ hour}^{-1}$). Dogs were randomly assigned to receive an intra-orbital gelfoam soaked with 2 mg kg^{-1} ropivacaine 1% (ROP; $n = 10$) or an equivalent volume of saline 0.9% (SAL; $n = 10$). Carprofen was administered SC following extubation, and was continued orally for 5 days. Pain was assessed before premedication (baseline), at extubation, and 1, 2, and 4 hours afterwards using modified short form Glasgow composite pain scale (CMPS-SF; 0-20). Methadone (0.25 mg kg^{-1}) was administered IV for rescue analgesia if score was ≥ 5 . Analysis was performed using Fischer exact test and Mann-Whitney U test. Significance was set at $p \leq 0.05$.

At extubation the median (range) CMPS-SF score was significantly higher in the SAL group, 8 (2-14), than in the ROP group, 3 (1-7), and significantly more dogs were administered methadone in the SAL group (7 versus 1). The mean time to first methadone administration was significantly shorter in the SAL group (13 versus 110 minutes). No complications were observed 14 days following surgery.

Deposition of orbital ropivacaine via gelfoam was not related with side-effects, and provided superior analgesia following enucleation.

A comparison of an infraorbital or maxillary block using a lidocaine/bupivacaine mixture in dogs

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This study aimed to determine onset and duration of effect of lidocaine/bupivacaine (LB) administered via the infraorbital canal or a lateral maxillary approach.

Six healthy adult intact female hound dogs were anesthetized with IV propofol and maintained with isoflurane in oxygen, ventilated to maintain a mean $PE\dot{V}CO_2$ between 21-41 mmHg at normothermia (37.9 ± 0.3 °C). Insulated gingival stimulating needles were inserted lateral to both maxillary canine teeth and the fourth premolar and second molar teeth and the hard palate (random allocation of sides). The applied current was adjusted to achieve a maximum digastricus reflex (DR) for each site. Three baseline recordings at 10-minute intervals were averaged. Lidocaine (2%) and bupivacaine (0.5%) (1 mL of each solution) were then administered via the infraorbital canal using a 4.5 cm catheter or via a lateral approach to the maxillary nerve using a 4 cm insulated needle. Recordings were made at 5, 10, 15, 30, 45 and 60 minutes, then every 20 minutes for up to 6 hours. The areas (duration x amplitude) were normalized using the DR for the unblocked canine tooth. Anything <15% of baseline was considered a successful block.

6/6 and 3/6 canine, all premolar, 4/6 molar teeth and 2/6 and 4/6 palatine nerves were blocked by infraorbital and maxillary injections, respectively. The onset and duration of the premolar blocks was not different.

The maxillary block was less successful for the canine teeth than the infraorbital block but there was little difference in onset or duration for the premolars.

This study was funded by the Center for Companion Animal Health at the School of Veterinary Medicine, University of California, Davis.

Session 6

Evaluation of dexmedetomidine, midazolam and buprenorphine as premedication for neutering surgery in pet rabbits.

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Dexmedetomidine and midazolam have already been described for sedation in rabbits (Bellini et al. 2014). The aim of this study is to evaluate the effect of this combination with buprenorphine on intraoperative respiratory and cardiovascular variables in 20 pet rabbits undergoing elective neutering under isoflurane anaesthesia.

Dexmedetomidine 50 µg kg⁻¹ and midazolam 0,4 mg kg⁻¹ were administered IM. Following the loss of righting reflex, buprenorphine 50 µg kg⁻¹ was injected IV and airways secured with a laryngeal mask (LMA n=10) or an endotracheal tube (ET n=10) connected to a circle breathing system. Dose of propofol used for anaesthesia induction, PR, non-invasive MAP, SpO₂, fR, PE'CO₂ and end-tidal isoflurane concentration were recorded. A repeated generalized linear mixed model and a Bonferroni post hoc test were used to analyse the variables over time. P < 0.05 was considered statistically significant.

During surgery rabbits had a mean PR, MAP, fR and PE'CO₂ of 194 ± 14 beats minute⁻¹, 60 ± 10 mmHg, 27 ± 12 breaths minute⁻¹ and 51 ± 12 mmHg respectively. Airway devices presented a significant effect on MAP. End-tidal isoflurane to maintain a surgical anaesthetic plane was increased after skin incision and maintained intraoperatively at a median value of 0.6% (0% - 2.5%). Mean extubation time was 7 ± 3 minutes and all animals were able to walk spontaneously within 1 hour after the end of surgery.

The premedication evaluated provided sedation and analgesia with minimal cardiovascular and respiratory changes in rabbits for elective neutering.

References

Bellini L, Banzato T, Contiero B, et al. (2014) Evaluation of sedation and clinical effects of midazolam with ketamine or dexmedetomidine in pet rabbits. Vet Rec 175, 372.

Tricaine Methane Sulfonate (MS-222) anesthesia in fishes: Relationship to Thermal Divergence

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The objective was to evaluate if acclimation temperature and acute temperature divergence either above or below the animal's acclimation temperature influenced MS-222 induced anesthesia in the goldfish.

Ninety-nine goldfish (*Carassius auratus*) were divided into a nine-cell treatment matrix consisting of three separate acclimation temperature groups (AC10, AC20, and AC30 °C) versus three acute temperature treatments (A10, A20, and A30 °C) (N=11 per treatment). Following a 30 day temperature acclimation period (± 1 °C) individual fish were exposed to un-dosed water (2 l) at the desired acute temperature for 50 minutes followed by scotaxic stress evaluation at the same temperature for 10 min. Using the acute temperature and a buffered 80 mg L⁻¹ MS-222 (2 L) fish were anesthetized and following times recorded: time to sedation, partial loss of equilibrium, complete loss of equilibrium and surgical plane of anesthesia for a maximum of 30 minutes. Data were analyzed using ANOVA with a Tukeys post-hoc test followed by survival analysis with Bonferroni post hoc comparisons ($p < 0.05$).

Most notably fish at AC10:A10 and AC20:A20 °C exhibited identical times to surgical depth anesthesia (median 768 seconds (420 – 1792 seconds) vs 1067 seconds (601 – 1320 seconds)) while AC30:A30 °C never attained surgical depth. The AC10:A30 °C treatment reached surgical plane anesthesia rapidly (median 65 seconds (12 – 152 seconds) while the AC30:A10 °C group reached surgical plane as determined by loss of reflexes without use of MS-222.

Acclimation and divergent water temperatures dramatically influenced MS-222 anesthesia as a function of complex adaptive changes.

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Ultrasound-guided transversus abdominis plane (TAP) block in calves: a cadaveric study

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Transversus abdominis plane (TAP) block has been described in humans and dogs. Our aims were to assess the feasibility of two ultrasound-guided TAP block approaches in calves and evaluate the spread of 2 different volumes of solution. Sixteen calves' cadavers weighting 47 ± 11 kg were used. With the animal in dorsal recumbency, lateral and subcostal ultrasound guided injections (0.2 or 0.4 ml kg^{-1} of a solution containing saline, 1% toluidine blue solution containing 1% borax and iodine-based contrast medium in a 2:1:1 ratio), were performed. Then, computed tomography scan and anatomical dissection were carried out to evaluate the spread of the solution. Accidental intra-spinal solution spread and percentage of thoracic (T) and lumbar (L) nerves stained more than 1 cm were recorded. Techniques feasibility was evaluated. With both techniques no intra-spinal spread was observed. With the lateral approach, using 0.2 ml kg^{-1} , 47%, 88%, 29% of T13, L1, L2 and using 0.4 ml kg^{-1} , 75%, 83%, 25% of T13, L1, L2 were stained, respectively. With the subcostal approach, using 0.2 ml kg^{-1} , 67%, 83%, 67%, 67%, 50% of T8, T9, T10, T11, T12 and using 0.4 ml kg^{-1} , 75%, 100%, 87%, 87%, 50% of T8, T9, T10, T11, T12 were stained, respectively. Feasibility score was excellent for both approaches in the majority of the cases. Ultrasound guided lateral and subcostal TAP blocks are feasible and safe in calves. A combination of the two techniques is recommended to obtain an optimal spread.

Intraoperative haemodynamic changes in sheep undergoing experimental spinal surgery: comparison of three opioid-based regimens.

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Opioids may decrease the cardiovascular response due to surgical stimulation. This study evaluates the efficacy of three opioid-based analgesic protocols to prevent a 20% increase in HR or MAP during experimental spinal surgery.

Eighteen female Brogna sheep weighing 47 ± 8 kg undergoing lumbar transpedicular intervertebral disk nucleotomy were sedated with medetomidine; anaesthesia was induced with propofol and maintained with an end-tidal isoflurane (FE'ISO) concentration of $1.5 \pm 0.1\%$. The animals were evenly distributed in three groups receiving IV: methadone 0.3 mg kg^{-1} , group M; fentanyl $2 \mu\text{g kg}^{-1}$ followed by $10 \mu\text{g kg}^{-1} \text{ h}^{-1}$, group F; buprenorphine $10 \mu\text{g kg}^{-1}$ and 30 minutes later ketamine 1 mg kg^{-1} followed by $5 \text{ mg kg}^{-1} \text{ h}^{-1}$, group BK. If during surgery HR and/or MAP increased more than 20% compared to the value measured at the previous 5 minutes, IV fentanyl $2 \mu\text{g kg}^{-1}$ was administered. Variables were analysed with Kruskal-Wallis test and a Two-way ANOVA.

No sheep but one in group B required a fentanyl bolus. During surgery, FE'ISO and percentage change in HR and MAP showed no difference among groups. All opioid protocols studied maintained the percentage change in HR and MAP between -4% and 7%. Mean value of MAP was higher in group B compared to group M and F ($102 \pm 6 \text{ mmHg}$ vs. $77 \pm 3 \text{ mmHg}$ and $86 \pm 8 \text{ mmHg}$; $p = 0.033$).

In sheep undergoing spinal surgery, the hemodynamic response to surgical stimulation was minimized by all the opioid protocols tested.

Session 7

Preventive analgesic effect of peripheral nerve blocks in dogs undergoing tibial plateau levelling osteotomy

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Postoperative analgesic effects of peripheral nerve blocks (PNBs) or a fentanyl target controlled infusion (fTCI) have not been investigated in dogs undergoing a tibial plateau levelling osteotomy (TPLO).

Thirty-nine dogs undergoing unilateral TPLO, in whom anaesthesia was induced with propofol and maintained with isoflurane 30 minutes after IM acepromazine (0.02 mg kg^{-1}) and methadone (0.2 mg kg^{-1}), were randomly allocated to receive fTCI (plasma target 1 ng ml^{-1}) or a stimulator guided femoral (Portela et al. 2013) and sciatic (Campoy et al. 2008) block (1 mg kg^{-1} and 0.5 mg kg^{-1} of levobupivacaine, respectively). Postoperatively, methadone (0.2 mg kg^{-1}) was administered IM when the Short Form Composite Measure Pain Score $\geq 6 / 24$ (Reid et al. 2007), with bihourly assessments for 24 hours. Data (Table 1) were analysed using Mann - Whitney U test, unpaired Student *t* test and Fisher's exact test as appropriate, considering $p < 0.05$ significant.

Results are presented in Table 1.

The postoperative analgesic effect provided by PNBs was greater than fTCI, suggesting a preventive analgesic effect.

	PNBs (n = 20)	fTCI (n = 19)
End Tidal Isoflurane (%)	1.16 ± 0.01	1.17 ± 0.01
Dogs requiring postoperative methadone (n)*	8	18
Postoperative methadone doses (n)*	0 (0 - 2)	2 (0 - 6)
Food intake (%)*	95.4 ± 2.3	75.1 ± 6.9

Table 1. Information recorded and results obtained in dogs undergoing tibial plateau levelling osteotomy in groups peripheral nerve blocks (PNB) and fentanyl target control infusion (fTCI). * indicates $p < 0.05$.

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Ultrasound-guided cervical plexus block in the dog: a cadaveric preliminary study

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Ultrasound-guided cervical plexus block (U-CPB) is part of multimodal anaesthetic management of elective (Mariappan et al. 2015) and emergency surgeries (Herring et al. 2012) of the neck region in human patients. The aim of this study was to assess its feasibility in dog cadavers.

Six dogs cadavers, two small (up to 10 kg), two medium (11 to 24 kg) and two large (over 25 kg) size, were used. With the cadavers in lateral recumbency, the neck was clipped from the transverse process of the atlas (C1) to the cranial edge of the scapula. A linear probe set at 12 MHz was positioned to obtain a transverse scanning plane from the C1 transverse process and moved in a cranio-caudal direction, until the transverse process of the fourth cervical vertebra (C4) was identified. A 22G, 70 mm spinal needle was inserted *in-plane*, oriented in a dorso-ventral direction. Methylene blue 15% at 5, 10 and 20 ml for the small-, medium- and large-size cadavers respectively, was injected bilaterally: half of the volume over the cervical fascia and half under it. Anatomical dissection was performed to evaluate dye deposition.

The anatomical landmarks were easily identified. The spread of methylene blue was homogeneous and the nerve roots of C2, C3 and C4 were stained. In the small-breed subjects, dye infiltration was noted up to C1.

In conclusion, U-CPB seems feasible in dogs; dosages might be reduced in small size animals. Further studies are warranted to assess its clinical effectiveness.

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The effect of hindlimb positioning on the distance between the dorsal lumbosacral laminae in dogs: a cadaveric computed tomography study.

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Epidural injections in dogs may be performed in sternal or lateral recumbency. Extending the hindlimbs cranially to increase the size of the lumbosacral space has been recommended (Jones, 2001), but supportive data are lacking.

Donated canine cadavers of any size and age were included. Dogs with lumbosacral abnormality were excluded. Computed tomography of the lumbosacral junction was performed in four positions: sternal and lateral recumbency, with hindlimbs extended cranially or not. Scan sequence was randomised. The distance between the dorsal laminae of L7 (caudal margin) and S1 (cranial margin) was measured for each position by two blinded, independent assessors. Mean distances in each position were compared using a paired t-test, corrected for multiple comparisons.

For n = 19 cadavers (7 female, median age 9 years (range 0.3 – 16), median weight 20.4 kg (range 1.0 – 34.0), cranial extension of the hindlimbs significantly increased the distance between the dorsal lumbosacral laminae, compared to control, in both sternal (9.2 ± 2.2 mm vs 3.1 ± 1.3 mm, $P < 0.0001$) and lateral recumbency (8.2 ± 1.9 mm vs 4.9 ± 1.5 mm, $P < 0.0001$).

Cranial extension of the hindlimbs in both sternal and lateral recumbency increases the distance between the dorsal lumbosacral laminae to an extent that is both statistically and clinically significant. Conversely, the small (1 mm) difference between cranial hindlimb extension in sternal versus lateral recumbency is unlikely to be clinically significant. Cranial extension of the hindlimbs in either sternal or lateral recumbency would be expected to facilitate epidural injection.

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Evaluation of the effects of intravenous dexmedetomidine infusion on spinal block using a hyperbaric solution of bupivacaine and morphine in dogs undergoing hind limb surgery.

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Dexmedetomidine has been found to prolong sensory spinal block, when administered as an intraoperative constant rate infusion in humans (Abdallah et al. 2013), however this effect has never been proven in dogs.

Anaesthesia was induced with propofol in 39 unpremedicated dogs randomly assigned for maintenance of anaesthesia with isoflurane (Group C) or isoflurane + 1 mcg kg⁻¹ h⁻¹ of dexmedetomidine (Group D). Spinal anaesthesia was then performed with a hyperbaric solution of bupivacaine 0.5% and morphine 1% at the L5-6 interspace. Intraoperative rescue analgesia (iRA) was provided with Fentanyl (1 µg kg⁻¹ IV) when either the HR or MAP increased by 30% above the pre-stimulation value and recorded as analgesic failure event. All dogs received Meloxicam (0.2 mg kg⁻¹ SC). The postoperative rescue analgesia was Methadone (0.2 mg kg⁻¹ IM). The iRA probability related to time between Groups was analyzed (Kaplan-Meier curve).

In Group C and D respectively hypotension incidence was 11/17 (65%) and 2/22 (9%), ($p = 0.0004$) and bradycardia 3/17 (18%) and 6/22 (27%) ($p = 0.7042$). In three dogs dexmedetomidine infusion was stopped due to severe bradycardia and excluded from iRA evaluation. The mean time at which iRA was required (minute) in Group C and D was respectively 77.4 ± 3.2 and 112.2 ± 8.6 ($p = 0.039$). Ability to walk 5 hours from intrathecal injection was recorded in 14/14 (100%) and 13/14 (93%) respectively in Group C and D.

Dexmedetomidine infusion is useful for increasing the duration of spinal anesthesia and reducing the incidence of hypotension.

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Abdallah FW, Abrishami A and Brull R. (2013) The facilitatory effects of intravenous dexmedetomidine on the duration of spinal anesthesia: a systematic review and meta-analysis. *Anesth Analg.* 117: 271–8.

Clinical efficacy of the addition of dexmedetomidine to lidocaine for the femoral and sciatic nerves block in dogs undergoing Tibial Tuberosity Advancement surgery

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Alpha 2 agonists have been proven to have a local anesthetic effect (Marhofer D. et al 2013). The aim of this study was to test the effects of the addition of dexmedetomidine to lidocaine for the sciatic and femoral nerves block in dogs undergoing knee surgery. Thirty dogs anesthetized with acepromazine, propofol and isoflurane in oxygen received a femoral and sciatic nerves block with the aid of a nerve stimulator. All dogs received 2.97 mg kg⁻¹ of a 2% solution of lidocaine alone (L, n = 10), in combination with 0.15 µg kg⁻¹ of dexmedetomidine administered locally (LDloc, n = 10) or with 0.3 µg kg⁻¹ of dexmedetomidine IM (LDsist, n = 10). After extubation every 30 minutes for 8 hours were monitored the return of touch sensibility of the femoral and sciatic dermatomes, proprioception, and reaction to the manipulation of the surgical site. Data were compared between the groups with the ANOVA test ($P < 0.05$).

The sensory block of the sciatic and femoral dermatomes last significantly longer in the LDloc (319.3 ± 16.2 minutes) and LDsist (214.6 ± 32.3 minutes) compared to the L (141.1 ± 27.3 minutes). Proprioception and the reaction to the manipulation returned later in the LDloc (306.2 ± 32.6 and 296.6 ± 50.5 minutes) as compared to the L (203.2 ± 63.7 and 180.5 ± 62.8 minutes).

Systemic and local dexmedetomidine is able to prolong the sensory block produced by lidocaine at the level of the sciatic and femoral nerves in dogs.

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Session 8

MAC-sparing effect of nitrous oxide in sevoflurane anaesthetised sheep and its reversal with systemic atipamezole administration

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Nitrous oxide (N₂O) reduces the minimum alveolar concentration (MAC) for volatile anaesthetics which may be related to α_2 -adrenoreceptor activity. We hypothesized that the MAC-sparing effect of 70% N₂O in sheep can be reversed with atipamezole.

Sevoflurane (SEVO) MAC (MAC_{SEVO}) was determined in 14 Sardinian milk sheep (mean weight 34.4 kg, age 2-8 years) by electrical tetanic stimulation to the metacarpus for 1 minute or until gross purposeful movement was observed. Thereafter, 70% N₂O was added to the inspired gas and MAC_{SN} determined. A subgroup of sheep (n = 6) were anaesthetised with SEVO/N₂O for re-determination of MAC_{SN}, after which atipamezole (0.2 mg kg⁻¹) was injected intravenously and MAC_{SNA} determined. Another subgroup of sheep (n = 6) were anaesthetised with SEVO/O₂ to re-determine MAC_{SEVO}, atipamezole (0.2 mg kg⁻¹) was injected and MAC_{SA} determined. Shapiro-Wilk test was employed to determine normality; student's t test was performed to determine statistical significance for parametric variables, *p-value* < 0.05.

The MAC_{SEVO} was, mean (SD), 2.7 (0.3) %. Addition of 70% N₂O resulted in a 37% reduction of MAC_{SEVO} to MAC_{SN}, 1.7 (0.2) % (*p* < 0.0001). Atipamezole reversed this effect, producing MAC_{SNA} of 3.1 (0.7) %, which did not differ from MAC_{SEVO} (*p* = 0.12). MAC_{SEVO} did not differ from MAC_{SA} (*p* = 0.69).

Nitrous oxide produces significant MAC_{SEVO}-reduction in sheep that is completely reversed by intravenous atipamezole. This confirms the involvement of α_2 -adrenoreceptors in the antinociceptive and hence MAC-sparing action of N₂O.

This work was supported by the Centro di Ricerca di Chirurgia Comparata (CRCC), Università degli Studi di Sassari and a contribution of the Fondazione Banco di Sardegna as well as the Regione Autonoma della Sardegna. Some essential equipment was acquired

Haemodynamic effects of MK-467, a peripherally acting alpha2-adrenoceptor antagonist, in sevoflurane-anaesthetized sheep receiving dexmedetomidine

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Dexmedetomidine induces haemodynamic changes in sevoflurane-anaesthetized sheep (Kästner et al. 2005, 2007) and we hypothesized that MK-467 could prevent them.

Seven sheep were treated twice in a cross-over study with a 20-day washout period. Anaesthesia was induced with propofol and maintained with sevoflurane (3% end-tidal) in oxygen and air (0.5 FiO₂). Sheep were mechanically ventilated and positive end-expiratory pressure was set at 5 cmH₂O. The treatments were: 150 µg kg⁻¹ MK-467 (MK+DEX) or saline IV 10 minutes (T-10) before IV dexmedetomidine (3 µg kg⁻¹, DEX) (T0). Heart rate (HR), cardiac output (CO) and MAP were recorded at baseline, 3 minutes after treatment (T-7), and 5 and 25 minutes after DEX (T5 and T25). Data were analyzed with repeated measures ANOVA and T-test.

Results (mean ± standard deviation) are presented in the following table:

	Treatment	Baseline	T-7	T5	T25
HR (beats min ⁻¹)	DEX	84 ± 16	84 ± 16	74 ± 9	76 ± 11
	MK+DEX	82 ± 8	85 ± 6	76 ± 9	73 ± 9
CO (L min ⁻¹)	DEX	2.87 ± 0.78	3.15 ± 0.72	2.82 ± 0.52	3.37 ± 0.25
	MK+DEX	2.77 ± 0.26	3.63 ± 0.69*	3.25 ± 0.68	3.15 ± 0.44
MAP (mmHg)	DEX	92 ± 17	95 ± 13	100 ± 8*	81 ± 6†
	MK+DEX	94 ± 10	90 ± 8	96 ± 4	69 ± 5*

*Significant difference from baseline, †significant difference between treatments (p < 0.05)

DEX did not induce clinically relevant changes in haemodynamics; MK+DEX decreased MAP below the baseline.

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MK-467, a peripherally acting alpha2-adrenoceptor antagonist, alleviates dexmedetomidine-induced pulmonary changes in sevoflurane-anaesthetised sheep

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Dexmedetomidine-induced pulmonary alterations have been described in sevoflurane-anaesthetised sheep (Kästner et al. 2005, 2007) and we hypothesised that MK-467 could prevent them.

Seven sheep received two treatments in a crossover study with a 20-day washout period. Anaesthesia was induced with propofol and maintained with sevoflurane (3% end-tidal) in oxygen and air (0.5 FiO₂). The sheep were ventilated with pressure-regulated volume-controlled mode and positive end-expiratory pressure of 5 cmH₂O. Peak inspiratory pressure (PIP) was set at 20 cmH₂O and altered as required to achieve normocapnia (P_{E'}CO₂ 35 – 45 mmHg). The treatments were: 150 µg kg⁻¹ MK-467 (MK+DEX) or saline IV 10 minutes (T-10) before IV dexmedetomidine (3 µg kg⁻¹, DEX) (T0). PaO₂, PIP and dynamic compliance (C_{dyn}) were recorded at baseline and 5, 15 and 25 minutes after DEX (T5, T15 and T25). Data were analysed with repeated measures ANOVA.

Results (mean ± SD):

	Treatment	Baseline	T5	T15	T25
PaO ₂ (mmHg)	DEX	289 ± 23	196 ± 86*†	213 ± 78*†	259 ± 37
	MK+DEX	280 ± 36	289 ± 23	289 ± 19	291 ± 16
PIP (cmH ₂ O)	DEX	20 ± 2.3	24 ± 4.3*†	24 ± 3.2*†	24 ± 5.4*†
	MK+DEX	20 ± 2.1	19 ± 2.6	19 ± 2.6	19 ± 2.6
C _{dyn} (ml cmH ₂ O ⁻¹)	DEX	46 ± 8.5	30 ± 11.8*†	33 ± 9*†	37 ± 13
	MK+DEX	47 ± 7	47 ± 6	49 ± 2.6	41 ± 6.7

*Significantly different from baseline; †significant difference between treatments.

MK-467 prevented significant changes in PaO₂, PIP and C_{dyn}.

References

Kästner SBR, Kull S, Kutter APN et al. (2005) Cardiopulmonary effects of dexmedetomidine in sevoflurane-anesthetized sheep with and without nitric oxide inhalation. Am J Vet Res 66, 1496-1502.

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Intramuscular use of a peripherally acting alpha2-adrenoceptor antagonist MK-467 with medetomidine and butorphanol in dogs – a prospective, randomized clinical trial

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Our aim was to investigate the clinical usefulness of MK-467 in dogs sedated for diagnostic imaging with medetomidine-butorphanol. We hypothesized that MK-467 would alleviate the bradycardia, hasten drug absorption and thus intensify the early-stage sedation.

In this prospective, randomized, blinded clinical trial, dogs received IM:

1. medetomidine 0.5 mg (m²)⁻¹ + butorphanol 0.1 mg kg⁻¹ (MED) (n = 29) or
2. medetomidine 0.5 mg (m²)⁻¹ + MK-467 10 mg (m²)⁻¹ + butorphanol 0.1 mg kg⁻¹ (MK) (n = 27)

Visual sedation scores and HR were recorded at intervals. Plasma drug concentrations were analyzed with liquid chromatography tandem mass spectrometry from samples obtained at 10 minutes. Additional sedation (50 % of original dose IM) and atipamezole for reversal (if unable to walk) was given as needed. Independent samples T-test, Mann-Whitney U-test and Fishers exact test were used when appropriate.

Data are presented in Table 1. Sedation scores were significantly higher after MK during the first 30 minutes (P < 0.001). With MK, more dogs required additional sedation after 30 minutes (p = 0.023) and fewer needed atipamezole (p < 0.001). All the procedures were successfully completed.

MK-467 intensified the early-stage sedation, shortened its duration and alleviated the bradycardia in healthy dogs receiving medetomidine-butorphanol.

Table 1. Data expressed as mean ± standard deviation.

	MED	MK
HR at 20 minutes (beats minute ⁻¹)	38.7 ± 9.2	57.0 ± 17.6*
Medetomidine (ng mL ⁻¹)	9 ± 3	13 ± 4*
Butorphanol (ng mL ⁻¹)	16 ± 7	35 ± 15*

*Significantly different from MED (p < 0.05)

This research has been funded by Vetcare Ltd Finland.

The effects of MK-467, a peripheral α_2 -adrenergic receptor antagonist, on the plasma drug concentrations and sedation in dogs receiving atipamezole to reverse medetomidine-induced sedation

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We studied the effects of MK-467 in dogs receiving medetomidine and later atipamezole, hypothesizing that MK-467 would decrease plasma drug concentrations and the duration of sedation.

Eight healthy adult beagles received intramuscular (IM) medetomidine [$20 \mu\text{g kg}^{-1}$ (MED)] with or without MK-467 [$400 \mu\text{g kg}^{-1}$ (MEDMK)], followed by IM atipamezole [$100 \mu\text{g kg}^{-1}$ (ATI)] 30 minutes later in a prospective, randomized, experimental cross-over study. Sedation scores were determined at intervals. Drug concentrations in plasma were analyzed with liquid chromatography tandem mass spectrometry. Differences between treatments were evaluated with Wilcoxon signed rank sum tests (sedation) and paired t-tests with Bonferroni corrections (drug concentrations).

Dogs became markedly sedated after both MED and MEDMK prior to ATI. Significant differences in sedation scores were observed between MED and MEDMK at 60 and 90 minutes after ATI (Table 1). MK-467 decreased plasma dexmedetomidine concentrations after ATI, which was associated with faster recoveries.

Atipamezole effectively reversed the sedation in dogs receiving medetomidine and MK-467 without adverse drug interactions. MK-467 decreased drug plasma concentrations and prevented resedation.

Table 1: Data presented as median (range) or mean $\pm$ standard deviation.

Time after atipamezole	60 minutes		90 minutes	
Treatment	MED	MEDMK	MED	MEDMK
Sedation score (0-20)	8 (0-17)	3 (0-8)*	7 (5-16)	3 (0-5)*
Dexmedetomidine (ng mL^{-1})	2.4 ± 0.5	$0.79 \pm 0.1^*$	1.8 ± 0.5	$0.45 \pm 0.09^*$
Atipamezole (ng mL^{-1})	14.1 ± 3.7	11.2 ± 1.6	9.8 ± 2	$7.5 \pm 1.4^*$

*Significantly different from MED ($p < 0.05$)

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