

## **Neck restraint in head and tail rope-assisted recovery method in horses: a retrospective case series**

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Anaesthetic mortality in horses commonly results from recovery problems including fractures and myopathy. The objective was to evaluate a case series using a novel method of restraint for rope-assisted recoveries in horses. We hypothesized that this method reduces fatal complications at recovery.

Horses recovered using the restraint technique following anaesthesia for a variety of elective and emergency procedures were included. After the horse was positioned in lateral recumbency for recovery, the neck was restrained manually against the recovery stall floor. A rope was passed around the neck and through 5 cm diameter hoops bolted to the floor. A foam pad was placed between the rope and neck to avoid compression damage. The restraint was released depending on subjective assessment by the observers and recovery was then assisted with head and tail ropes. Any problems encountered during the recovery period recorded on the anaesthetic record were assessed.

Anaesthetic records from 679 horses were assessed (331 elective surgeries, 210 colic and 138 non-colic emergency surgeries). All horses received xylazine 1 mg kg<sup>-1</sup> IV, followed by midazolam 0.1 mg kg<sup>-1</sup> and ketamine 2.2 mg kg<sup>-1</sup> IV and anaesthesia was maintained with isoflurane. Colic surgeries also received IV lidocaine, ketamine and morphine. Complications occurred during recovery in 10 cases: three fatal limb fractures (one mare after caesarean surgery; 2 after surgical fracture repair) and seven horses had non-fatal forelimb lameness. No other complications were recorded. Mortality rate was 0.4%. We highly recommend this alternative for recovery in horses.

This study was supported by Centro de rehabilitación y Hospital equino Kawell, Solís, Buenos Aires, Argentina.

## **Description of ultrasound-guided serratus plane block in dogs: cadaveric study**

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Ultrasound-guided serratus plane block (UGSPB) has been described in human medicine as an analgesic technique for thoracic wall procedures (Blanco et al. 2013; Madabushi et al. 2015; Lee et al. 2015). The aim of the study was to describe this technique in canine cadavers.

Nine canine beagle cadavers with a body weight of  $9.1 \pm 1$  kg were used. UGSPB was performed on both sides of thoracic wall in each cadaver by one investigator. A 10-14 MHz linear probe was placed perpendicular to the ribs at the level of the serratus muscle. A 1:1 mixture of Iohexol and methylene blue was injected between the ventral border of the serratus muscle and intercostal muscle at two penetration points on each thoracic wall side. The total volume administered was  $1.0 \text{ ml kg}^{-1}$ ; The volume was split evenly between each penetration point. Computed tomography (CT) was performed ten minutes later. The spread of the contrast agent on the CT images (width and depth) was analysed by a second investigator.

CT images revealed contrast agent at the level of the 1st, 2nd, 3rd, 4th, 5th and 6th intercostal space in 77.7%, 88.8%, 100%, 88.8%, 77.7% and 33.3% of cases respectively. Diffusion of contrast through the intercostal muscles towards the parietal pleura also occurred but varied depending on intercostal space.

UGSPB can be performed in dog cadavers and coverage of several intercostal spaces is possible using only two penetration points. Further studies are needed to evaluate its clinical efficacy.

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## **Stereoselective pharmacokinetics of a single IV bolus of methadone in isoflurane anaesthetised ponies**

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The stereoselective pharmacokinetics of methadone in anaesthetised ponies was investigated.

Six healthy ponies were anaesthetised with IV romifidine (0.08 mg kg<sup>-1</sup>), diazepam (0.05 mg kg<sup>-1</sup>), ketamine (2.2 mg kg<sup>-1</sup>) and maintained with isoflurane (FiO<sub>2</sub> 0.5, end-tidal 0.8-1.1%). After stabilization, racemic methadone (0.5 mg kg<sup>-1</sup>) was given IV. Arterial blood samples were collected at predetermined time points until 64 minutes after methadone administration. The concentration of methadone enantiomers in plasma was analysed with capillary electrophoresis using an assay similar to that developed for ketamine (Theurillat et al. 2016). Data for each enantiomer were analysed with a two compartment model and pharmacokinetic parameters were determined using Phoenix WinNonlin 6.4 software. Data were statistically compared with paired T-tests and presented as mean ± SD. Statistical significance was set at p < 0.05.

Clearance (mL min<sup>-1</sup> kg<sup>-1</sup>) was significantly lower for l-(-)methadone (14.95 ± 5.64) than d-(+)methadone (34.87 ± 10.14; p < 0.001). The area under the curve (min ng L<sup>-1</sup>) was significantly greater for l-(-)methadone (33.42 ± 11.13) compared with d-(+)methadone (13.32 ± 2.72; p = 0.003). Both, the terminal half-life (min) and the volume of distribution at steady state (L kg<sup>-1</sup>) were not significantly different (l-(-)methadone: 53.88 ± 17.08 and 0.95 ± 0.16, respectively; d-(+)methadone: 50.72 ± 28.72 and 1.81 ± 0.94, respectively). In 3/6 ponies muscle twitches of head and neck were observed after methadone administration that disappeared without further treatment. All ponies recovered uneventfully.

Results suggest stereoselective disposition of methadone in equines. Enantiomer-enantiomer interactions should be investigated in further studies.

### Reference

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## **Correlation between two scoring instruments for acute pain in cats undergoing ovariohysterectomy**

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The aim of this study was to evaluate the correlation between two pain scoring instruments in cats.

Fifty-two cats ( $3.0 \pm 0.7$  kg) were included in a randomized, prospective, blinded study. Anesthetic protocol included acepromazine-buprenorphine-propofol-isoflurane. Gabapentin group (GG,  $n = 19$ ) received gabapentin (50 mg PO). Positive (PG,  $n = 15$ ) and negative (NG,  $n = 18$ ) groups received placebo capsules. PG also received meloxicam ( $0.2 \text{ mg kg}^{-1}$  SC) before surgery. Following ovariohysterectomy, postoperative pain was evaluated using a composite pain scale (CPS) (Steagall et al. 2015) and the Glasgow feline pain scale (GPS) (Calvo et al. 2014) up to 8 hours. Rescue analgesia was provided if  $\text{CPS} \geq 6$ . A linear model was used for statistical analysis ( $p \leq 0.05$ ). Spearman's rank correlation (SRC) was evaluated. Percentage of disagreement between postoperative CPS and GPS scores for rescue analgesia (%DIRA; where one scale would indicate rescue, but not the other) was calculated.

Prevalence of rescue analgesia was not significantly different using CPS ( $p = 0.08$ ; GG,  $n = 5$ ; PG,  $n = 2$ ; NG,  $n = 9$ ), but it would have been significantly higher in NG ( $n = 14$ ) than GG ( $p = 0.003$ ;  $n = 5$ ) and PG ( $p = 0.005$ ;  $n = 4$ ) if GPS was used. The SRC indicated a strong association ( $r > 0.7$ ) for most time points. The %DIRA was 7.8%; outcome for rescue analgesia would have changed in 6.4%.

Despite strong association, outcome for rescue analgesia may differ when using the CPS and GPC.

### References

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Calvo G, Holden E, Reid J et al. (2014) Development of a behaviour-based measurement tool with defined intervention level for assessing acute pain in cats. *J Small Anim Pract* 55, 622-629.

Supported by Morris Animal Foundation and Fonds en santé des animaux de compagnie (FSAC), Université de Montréal.

## **Blood pressure measured at dorsal pedal, coccygeal, and auricular arteries compared to the pressure at abdominal aorta in isoflurane-anesthetized dogs.**

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This study compared SAP, MAP and DAP measured at the abdominal aorta with dorsal pedal (DP), coccygeal and auricular arteries.

8 beagles were premedicated with acepromazine 0.02 mg kg<sup>-1</sup>, induced with propofol (5 mg kg<sup>-1</sup>) with anesthesia maintained with 1.5% end-tidal isoflurane. Peripheral 22 gauge, 2.5 cm catheters were placed into DP, coccygeal and auricular arteries to measure SAP, MAP and DAP. An 18 gauge 15 cm catheter was placed in the abdominal aorta via the femoral artery. Blood pressure was measured simultaneously by two calibrated transducers, one dedicated to the aortic pressures (reference) and the other to the alternate sites. Measurements were performed at normotension (MAP 60 to 130 mmHg); catecholamine- induced hypertension (MAP >130 mmHg); and hypovolemic hypotension (MAP < 60 mmHg). Bland-Altman plots evaluated the agreement between peripheral and aortic pressures. A two-way ANOVA followed by Tukey's test were used to compare mean bias at each measurement site ( $p < 0.05$ ).

All sites underestimated MAP and DAP with the largest bias at the auricular artery ( $-14.1 \pm 7.0$  mmHg) for MAP and coccygeal artery ( $-11.4 \pm 4.3$  mmHg) for DAP and the smallest bias at DP for MAP ( $-2.6 \pm 5.7$  mmHg) and DAP ( $-2.1 \pm 4.2$  mmHg). Auricular ( $-32.5 \pm 15.6$  mmHg) and coccygeal arteries ( $-11.4 \pm 12.9$  mmHg) underestimated SAP, while DP overestimated ( $14.7 \pm 23.4$  mmHg).

Auricular arterial pressures should be interpreted with caution in anesthetized dogs; coccygeal and DP sites are preferred due to greater accuracy, especially for MAP.

## Joint pharmacokinetic modelling after subcutaneous, buccal or intravenous administration of a high-concentration formulation of buprenorphine in cats

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The aim of the study was to characterize joint pharmacokinetics of a high-concentration formulation of buprenorphine after subcutaneous (SC), buccal (B) or intravenous (IV) administration in cats.

Six healthy adult cats ( $4.9 \pm 0.7$  kg; 4 males and 2 females) were included in a prospective, randomized, blinded, experimental study. A high-concentration formulation of buprenorphine hydrochloride ( $1.8 \text{ mg mL}^{-1}$ ) was administered by the SC ( $0.24 \text{ mg kg}^{-1}$ ), IV ( $0.12 \text{ mg kg}^{-1}$ ) or B ( $0.12 \text{ mg kg}^{-1}$ ) route of administration. Blood samples were collected via jugular catheter at predetermined time points up to 72 hours. Plasma buprenorphine and norbuprenorphine concentrations were measured using liquid chromatography mass spectrometry (LCMS/MS). A bespoke bi-compartmental pharmacokinetic model simultaneously fitted data from two analytes and three administration routes.

The absolute buprenorphine clearance was  $0.98 \text{ L kg}^{-1} \text{ hour}^{-1}$  (CV 25%), the volume of distribution at steady state was  $7.9 \text{ L kg}^{-1}$  and the elimination-half-life was 12.3 hours.

Bioavailabilities for SC and B were 94% and 24%, respectively. Buccal absorption was rapid (half-life 0.48 hours); SC absorption was biphasic. An initial peak (0.08 hours) was followed by a slow (half-life 11.2 hours) and progressive (peak acceleration at 2.8 hours) uptake.

Plasma norbuprenorphine resulted from buprenorphine metabolism (conversion rate  $0.19 \text{ hour}^{-1}$ ) and, for B, first-pass absorption producing 1% of the dose as norbuprenorphine (half-life 1.1 hours). Norbuprenorphine clearance was  $0.42 \text{ L kg}^{-1} \text{ hour}^{-1}$  (CV 4.3%).

The SC administration of a high-concentration formulation of buprenorphine was characterized by prolonged absorption half-life and sustained plasma concentrations.

This study was funded by Zoetis.

## **Effects of metoclopramide on emesis in dogs premedicated with dexmedetomidine and morphine**

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Opioids and  $\alpha$ 2-agonists, used as premedication agents, can often result in emesis (Koh et al. 2014). The aim of this study is to assess the effect of metoclopramide on nausea and vomiting after morphine and dexmedetomidine administration.

Forty-five healthy dogs (ASA I-II) scheduled for elective surgery or diagnostic procedures, were included. Dogs were randomly assigned to three groups of 15 patients each. In all cases premedication consisted of dexmedetomidine  $3 \mu\text{g kg}^{-1}$  and morphine  $0.2 \text{ mg kg}^{-1}$  IM. Metoclopramide  $0.2 \text{ mg kg}^{-1}$  SC was administered 30 minutes before premedication in group A, and together with premedication in group B. Dogs in group C did not receive metoclopramide. Dogs were observed for 30 minutes after premedication to evaluate signs of nausea (lip-licking and sialorrhea) and evidence of emesis. Data were analysed with Kruskal-Wallis Test (age and weight) and Fisher Exact Test (others variables). Statistical significance was taken as  $p \leq 0,05$ .

Significant differences amongst groups for age and weight were not found. The incidence of lip-licking was significantly higher in group C than in group A ( $p = 0,0001$ ) and B ( $p = 0,0127$ ). The incidence of sialorrhea was significantly higher in group B ( $p = 0,0251$ ) and in group C ( $p = 0,004$ ) than in group A. The incidence of emesis was statistically higher in group B ( $p = 0,0498$ ) and C ( $p = 0,0003$ ) than in group A.

In conclusion, metoclopramide  $0.2 \text{ mg kg}^{-1}$  reduces morphine and dexmedetomidine induced emesis and nausea, if administered thirty minutes before premedication.

Koh RB, Isaza N, Xie H et al. (2014) Effects of maropitant, acepromazine, and electroacupuncture on vomiting associated with administration of morphine in dogs. *J Am Vet Med Assoc* 244, 820-829.

## **ANTI-NOCICEPTIVE EFFECTS OF TRANS-DERMAL LIDOCAINE OR LIDOCAINE WITH PRILOCAINE OR TETRACAINE IN HORSES**

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The aim of this study was to evaluate transdermal effectiveness of lidocaine or lidocaine combined with prilocaine or tetracaine in horses.

Five adult, healthy, warmblood horses were clipped at six locations (withers, cranial saddle area, caudal saddle area; each bilaterally). Nociceptive thermal thresholds (WTT2, Topcat Metrology Ltd) and mechanical superficial sensation (von Frey Filaments) were determined. After baseline measurements, a 5 % lidocaine patch (Versatis – 12 hour exposure), lidocaine/prilocaine (EMLA) and lidocaine/tetracaine (Pliaglis) cream were applied (both 2 hours exposure). At each location, the same product was applied bilaterally, but with prior epidermal micro-perforation (DRS Body Dermaroller, 1200 needles) on the right side. Measurements were performed at baseline, immediately after exposure and at 60, 120, 180 and 240 minutes. Statistical analysis was performed with one and two way ANOVA and Wilcoxon Sign Rank Test ( $p < 0.05$ ).

An increase in thermal thresholds was seen with all tested products after exposure and 60 minutes. With both creams cut-out of 55 °C was reached after exposure and 60 minutes, in 100% and 40% of measurements, respectively, whereas, cut-out with the lidocaine patch was reached only in 20% of measurements after exposure. Mechanical superficial sensation was decreased for EMLA and Versatis for 3 measurements (120 minutes). With Pliaglis a statistical reduction of mechanical superficial sensation was detected at all time points. Pre-treatment with microperforation did not affect results. The combination of lidocaine with either prilocaine or tetracaine led to a reduction in thermal nociception and mechanical sensation for 1 to 2 hours.

## Effect of stomach filling on ventilation distribution in dorsally recumbent ponies measured by electrical impedance tomography

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Abdominal and thoracic compartments influence each other. Using electrical impedance tomography (EIT) we assessed the impact of stomach filling and decompression on ventilation distribution in dorsally recumbent ponies.

Anaesthesia was induced in six adult healthy ponies ( $138 \pm 26$  kg) using IV xylazine, midazolam, ketamine ( $1.1/0.05/2.2$  mg kg<sup>-1</sup>), maintenance with sevoflurane in oxygen (FIO<sub>2</sub> > 0.95, FE'Sevo 2.5-2.7) and mechanical ventilation to maintain PE'CO<sub>2</sub> around 40 mmHg. Settings were not changed after baseline measurements. At baseline, after stomach filling with 30 mL kg<sup>-1</sup> of physiological saline contained in a balloon, and after decompression EIT was recorded over a period of 5 minutes in triplicate. Post hoc, Centres of Ventilation (CoV) in % were calculated as the geometrical centre from right to left (R-L) and ventral to dorsal (V-D) direction of the functional image of ten consecutive breaths for each measurement period. Values below 50% indicate a CoV in the right as well as non-dependent (dorsal) lung region. Data were analysed using repeated measures ANOVA; alpha set to  $\leq 0.05$ .

At baseline CoV was R-L 43% ( $\pm 2.7$ ), V-D 52% ( $\pm 0.3$ ). Stomach filling significantly decreased CoV R-L to 39% ( $\pm 2.7$ ;  $p = 0.003^{-13}$ ), but not V-D with 51% ( $\pm 0.4$ ). Upon decompression CoV R-L and V-D returned to baseline with 42% ( $\pm 2.8$ );  $p = 0.001^{-6}$  for difference 'filled *versus* decompression'), 52% ( $\pm 0.4$ ), respectively.

Stomach filling reversibly moved ventilation towards the right lung, without changing ventro-dorsal distribution. Stomach decompression improves distribution of ventilation between right and left lung.

## Resting metabolic rate (RMR) measurements in general anaesthesia: Reduction provided by dexmedetomidine in dogs

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We aimed to verify the reduction in RMR (Vandarakis et al. 2013) comparing two anaesthetic protocols with dexmedetomidine.

Dogs were randomly divided into two groups: in Group DM (n = 5) the first metabolic measurement (MM1-DM) was performed 15 minutes after premedication (dexmedetomidine 5 µg kg<sup>-1</sup> and methadone 0.2 mg kg<sup>-1</sup> IM); a second measurement (MM2-DM) was carried out after induction with titrate-to-effect propofol; in Group M (n = 5), premedicated with methadone (0.2 mg kg<sup>-1</sup> IM), the first measurement (MM1-M) was performed after induction with propofol, whereas the second metabolic measurement (MM2-M) after intravenous dexmedetomidine administration (2 µg kg<sup>-1</sup>). HR and  $f_R$  were recorded every 5 minutes. RMR (Kcal die<sup>-1</sup>), EV (expiration-volume, L minute<sup>-1</sup>), FeO<sub>2</sub> (expired-oxygen-fraction, %), VO<sub>2</sub> (oxygen-consumption, mL minute<sup>-1</sup>), VO<sub>2</sub> kg<sup>-1</sup> (oxygen-consumption kg<sup>-1</sup>), mL minute<sup>-1</sup> kg<sup>-1</sup>) measurement were performed with an indirect calorimeter providing a canopy helmet (COSMED-FitMate™). Statistical analysis: ANOVA for repeated measurements (p < 0.05). HR was lower in each dog after any dexmedetomidine administration (p = 0.002). RMR was lower at MM1-DM (778 Kcal die<sup>-1</sup> ± 174,8) and MM2-DM (739 Kcal die<sup>-1</sup> ± 196,71) compared with MM1-M (999 Kcal die<sup>-1</sup> ± 158,76) (p = 0.0348 and 0.0254) and between MM2-M (771 Kcal die<sup>-1</sup> ± 65,83) and MM1-M (p = 0.009). Dexmedetomidine significantly diminished EV, VO<sub>2</sub>, but increased FeO<sub>2</sub> in any case and diminished VO<sub>2</sub> kg<sup>-1</sup> only after intravenous administration (M).

In methadone-premedicated dogs, dexmedetomidine and dexmedetomidine plus propofol at adopted doses results in a reduction in RMR and oxygen consumption compared to propofol alone.

### Reference

Vandarakis D, Salacinski AJ, Broeder CE. A comparison of COSMED metabolic systems for the determination of resting metabolic rate. Res Sports Med. 2013; 21(2):187-94.

## **Assessment of the efficacy of a rapid single bolus of dexmedetomidine in the treatment of emergence agitation in dogs.**

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The study aimed to assess the efficacy of a rapid single bolus of dexmedetomidine to treat Emergence Agitation (EA) (Kanaya 2015) compared with “titrate-to-effect” administration of propofol in dogs.

Treatment was randomly assigned to 14 dogs showing EA as evaluated with a modified Cole scale (Cole et al 2002) (threshold: 3/5): at T<sub>0</sub> group<sub>DEX</sub> (6 dogs) received a rapid IV bolus of dexmedetomidine (1 µg kg<sup>-1</sup>) and atipamezole (10 µg kg<sup>-1</sup>) 30 minutes after T<sub>0</sub>; group<sub>PPF</sub> (8 dogs) received IV propofol (1 mg kg<sup>-1</sup>) over 30 seconds, followed by “titrate-to-effect” administration. Sedation, sternal recumbency, and standing times were recorded. HR, f<sub>R</sub>, NIBP and temperature (°C) were recorded every five minutes. Statistical analysis: t-test for physiologic parameters and Mann Whitney U test for nonparametric data (p < 0.05).

Both groups were comparable for age, weight, temperature, pre-treatment HR, f<sub>R</sub>, NIBP and EA score. Group<sub>DEX</sub> showed a statistically significant shorter time to sedation (64.2 ± 7.9 versus 124.3 ± 74.1 seconds). No apnoea was detected in either group. The patient management was more demanding in group<sub>PPF</sub>. f<sub>R</sub> decreased in both groups (group DEX: p = 0.004; group PPF: p = 0.03); HR was lower in group<sub>DEX</sub> (50.81 ± 16.13 versus 109.16 ± 36.55 bpm; p = 0.0025). NIBP, sternal recumbency and standing time were not significantly different between groups.

Rapid sedation is crucial for patient and operator safety: a single rapid IV bolus of dexmedetomidine appears to be more effective than propofol for managing post-anaesthetic EA.

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## **Morphine vs Butorphanol: evaluation of two standing sedation protocols in horses undergoing bone scintigraphy**

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During equine scintigraphy, retakes are most commonly necessitated by motion artefacts. The aim of the study was to evaluate two sedative protocols (Muir 1981; Dodman 1980) in horses undergoing bone scintigraphy, focusing on immobility and sedation quality. Twenty-nine horses were enrolled in an observer blinded, randomized, prospective clinical pilot study. All received acepromazine  $0.03 \text{ mg kg}^{-1}$  IV followed 30 minutes later by detomidine  $0.01 \text{ mg kg}^{-1}$  IV. Five minutes later, morphine (MOR)  $0.25 \text{ mg kg}^{-1}$  (n=17) or butorphanol (BTF)  $0.01 \text{ mg kg}^{-1}$  (n=12) was administered IV; adjunctive boluses of detomidine were administered to maintain appropriate sedation. HR,  $f_R$ , temperature, and sedation score (Taylor et al. 2014) were assessed. The number of retakes needed to obtain excellent diagnostic image quality as evaluated by the same radiologist was recorded. Data were analysed using Student's t-test or Mann-Whitney test as appropriate ( $p < 0.05$ ). Between groups HR did not differ ( $p = 0.1$ ) but  $f_R$  was higher in BTF ( $p = 0.002$ ). Total detomidine used ( $p = 0.49$ ) and sedation score were not significantly different between groups ( $p = 0.4$ ). The number of retakes for each region investigated was greater in BTF ( $p = 0.01$ ). The ratio between the number of retakes and the scan acquisitions number for each group was 48% in MOR and 96 % in BTF. Both protocols appeared to demonstrate similar sedation quality but MOR achieved higher patient immobility. Further studies are needed to evaluate this protocol in other diagnostic imaging techniques that require standing sedation.

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## EFFECTIVENESS OF LIDOCAINE PERITONEAL LAVAGE FOR POST-OPERATIVE PAIN CONTROL IN DOGS UNDERGOING LAPAROTOMY: PRELIMINARY STUDY

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The study aimed to evaluate the efficacy of perioperative pain management using lidocaine for peritoneal lavage in dogs undergoing laparotomy.

Sixteen dogs, with owner consent, scheduled for laparotomy, premedicated with IM methadone (0.2 mg kg<sup>-1</sup>) and dexmedetomidine (5 µg kg<sup>-1</sup>), were randomly allocated to groupIPL (n=8) receiving peritoneal lavage with lidocaine (200 mg of lidocaine 2% diluted in 500 ml of NaCl 0.9%) left *in situ* for 3 minutes and removed before abdominal wall closure; or to control groupSAL (n=8) receiving peritoneal lavage with saline solution alone.

Postoperative pain assessment was carried out by a blinded observer using the Glasgow Composite Measure Pain Scale short form (Reid et al. 2007), from awakening time (T<sub>0</sub>) until 6 hours. Cut off for treatment failure and rescue analgesia administration (buprenorphine 15 µg kg<sup>-1</sup> IM) was set at 8/24. Statistical analysis: Mann-Whitney U test (p < 0.05).

There was no significant difference between groups regarding age, weight, surgical and anaesthetic duration or incision length. During evaluation, one dog in groupIPL required rescue analgesia (180 minutes after T<sub>0</sub>, score 8/24). In groupSAL, rescue analgesia was required in four dogs at 15 minutes from T<sub>0</sub> (median 11.5; range 8 - 14), in three dogs at 30 minutes (median 10; range 8 - 14) and in one dog at 45 minutes (score 10/24). The percentage treatment failure was 12.5% at 180 minutes in groupIPL but reached 100% in groupSAL (p = 0.0012), starting at 45 minutes.

Peritoneal lavage with lidocaine appeared effective in postoperative pain management.

## Impact of general anaesthesia on rotational thromboelastometry (ROTEM) parameters and standard plasmatic coagulation tests in healthy beagle dogs

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The unknown influence of general anaesthesia on rotational thromboelastometry (ROTEM) and standard coagulation testing was assessed in healthy dogs undergoing standardised anaesthesia for a magnetic resonance imaging study.

Ten healthy beagles received methadone (0.2 mg kg<sup>-1</sup>) IM 30 minutes prior to anaesthetic co-induction with midazolam (0.1 mg kg<sup>-1</sup>) and propofol (to effect) IV. Anaesthesia was maintained with sevoflurane to effect. Crystalloid fluid rate was 5 ml kg<sup>-1</sup> hour<sup>-1</sup>. Venous blood was sampled immediately before induction (T0) and 3.5 hours later (T3.5). ROTEM parameters (ExTEM, InTEM, FibTEM, ApTEM), standard plasmatic coagulation tests (prothrombin time [PT], activated partial thromboplastin time [aPTT], thrombin time [TT], fibrinogen concentration [Clauss]), complete blood count, pH and body temperature were compared over time with Students t - test or Wilcoxon signed rank test after normality testing ( $p \leq 0.05$  considered significant).

The pH, PT, aPTT, TT and ExTEM, InTEM and ApTEM parameters revealed no significant changes between T0 and T3.5. Haematocrit (49 [40 – 59] to 37 [30 – 41] %,  $p < 0.0001$ ), platelet count (314 [235 – 513] to 258 [207 – 333] 10<sup>3</sup>  $\mu\text{L}^{-1}$ ,  $p = 0.001$ ), body temperature (38.3 [37.7 – 38.7] to 34.9 [34.2 – 35.8] °Celsius,  $p < 0.0001$ ) and fibrinogen concentration decreased (2.2 [1.4 – 3.3] to 1.9 [1.1 – 3.1] gL<sup>-1</sup>,  $p = 0.002$ ). FibTEM maximum clot firmness increased from 4 (3 – 10) to 5 (3 – 12) mm ( $p = 0.03$ ).

General anaesthesia with concurrent haemodilution induced no clinically significant changes in coagulation. Measurements at 37 °Celsius did not reflect possible hypothermia-induced coagulopathy.

## **Evaluation of the effects of a perioperative ketamine infusion on perioperative pain and functional rehabilitation in dogs undergoing orthopaedic surgery**

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Based on human reports (Aveline et al., 2009), this study aimed to assess the effect of an infusion of ketamine on perioperative pain and postoperative functional rehabilitation in dogs undergoing orthopaedic surgeries.

Twenty two dogs, admitted for hindlimb surgery were anaesthetized following a standardized protocol. They were randomly assigned to 2 groups: group F received a continuous rate infusion of fentanyl ( $0.005 \text{ mg kg}^{-1} \text{ h}^{-1} \text{ IV}$ ) for the duration of the surgery, whereas group FK received in addition ketamine ( $0.6 \text{ mg kg}^{-1} \text{ h}^{-1}$ ). Physiological variables, volatile anaesthetic requirement and amount of rescue analgesia were recorded during anaesthesia. During hospitalisation, postoperative pain and lameness were evaluated using a 4A-Vet pain scale and gait analysis (GAITRite®), respectively. A quality of life form was given to the owners to estimate comfort of their animal at 3, 7, 11 days after surgery. Finally, gait analysis was re-assessed 15 days after surgery. Data were analyzed using a Friedman, Wilcoxon and Mann-Whitney tests; ( $p < 0.05$ ).

Animals of group FK required less isoflurane (1,3% [0,9-2,0] vs 1,7% [1,6-2,3]  $p = 0,04$ ). On day 0, group FK showed a significantly increased support duration than group F ( $p = 0,03$ ). No significant difference was found between groups after hospitalisation.

These results support a positive effect of perioperative infusion of ketamine on immediate functional rehabilitation after orthopaedic surgery, but further work is warranted.

### Reference:

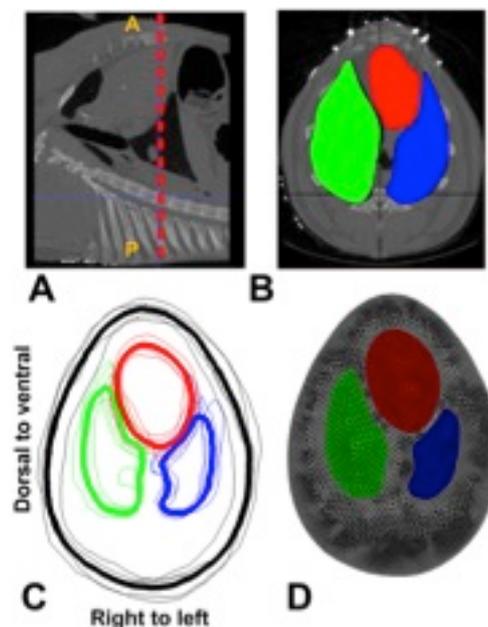
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## Best belt position and construction of a robust pony model for electrical impedance tomography applications

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Belt position impacts the information on ventilation given by Electrical impedance tomography (EIT). Using computer tomography (CT) we aimed to find the best-belt position and construct an average finite element model (FE) for EIT reconstruction. Based on a pilot CT scan of an anaesthetised dorsally recumbent pony the internal maximum lung field was selected to determine the “best-belt position”. Thus, the position between smallest possible heart contour and one CT slice before the diaphragm appeared was selected. This was matched with external palpable anatomical landmarks: the 7<sup>th</sup> intercostal space and the end of the last sternbrae (Fig. 1 A). CT scans were then performed during inspiratory hold with the belt placed over the thorax in 5 ponies. In the CT slices at the height of the belt heart, lungs and thorax contours were segmented by ITK-SNAP (Fig. 1B). Thereafter Matlab was used to align, calculate and average contours from all ponies (Fig. 1C) to generate the corresponding averaged FE model for further use (Fig.1D).



Contours of thorax shape at the selected best-belt position were similar in all five animals. Right and left lung varied in the ventral non-dependent parts. The size of the heart differed substantially between the individuals. The selected best-belt position was easily reproducible based on the above described landmarks. Further studies and calculations are suggested to validate the contours in other ponies and to characterize the differences between an averaged and an intra-individual model and their influence on the reconstructed EIT images.

## **Effect of dexmedetomidine on the minimum alveolar concentration of isoflurane in rabbits**

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This study aimed to determine the plasma concentration dependent effect of dexmedetomidine on isoflurane MAC in rabbits.

Six healthy adult female New Zealand white rabbits ( $3.6 \pm 0.3$  kg) were anesthetized with isoflurane in oxygen. Body temperature was maintained between 38.5 and 39.5 °C. Based on previously obtained pharmacokinetics, dexmedetomidine was administered IV to achieve 8 target plasma concentrations, 0.125, 0.25, 0.5, 1, 2, 5, 10, and 20 ng mL<sup>-1</sup>. At each target concentration, MAC was determined using the bracketing technique and a supramaximal electrical stimulus. Data were analyzed by repeated measures ANOVA followed by Dunnett's multiple pairwise comparisons to baseline.

Isoflurane MAC was reduced by targeted dexmedetomidine plasma concentrations of 0.5 ng mL<sup>-1</sup> and above. At the highest targeted concentration (20 ng mL<sup>-1</sup>) isoflurane MAC was reduced from  $1.95 \pm 0.22$  % to  $0.23 \pm 0.06$  % ( $p < 0.0001$ ), PE'CO<sub>2</sub> increased from  $32 \pm 3$  to  $50 \pm 3$  mmHg ( $p < 0.0001$ ), MAP increased from  $50 \pm 5$  to  $78 \pm 8$  mmHg ( $p < 0.0001$ ), and HR decreased from  $251 \pm 13$  to  $105 \pm 7$  beats per minute ( $p < 0.0001$ ), when compared to isoflurane alone.

Targeted plasma dexmedetomidine concentrations of 20 ng mL<sup>-1</sup> reduced isoflurane requirements by close to 90 %. Although associated with an increase in MAP, additional studies evaluating cardiac output are required to determine the suitability of dexmedetomidine for balanced anesthesia in rabbits.

Funded by Center for Companion Animal Health, University of California, Davis

## **The effect of different volumes of injectate on the infraorbital block using lidocaine/bupivacaine in dogs**

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Infraorbital nerve blocks (IO) are commonly performed but little clinical information is available. We evaluated 1, 2 or 3 mL of a 50:50 mixture of 2% lidocaine and 0.5% bupivacaine on the onset, duration and spread of the block.

Six adult female dogs weighing 19-30 kg were used. Anesthesia was induced using propofol and maintained with isoflurane in oxygen. Dogs were in dorsal recumbency and normocapnia and euthermia were maintained. Stimulating electrodes were inserted into the aboral gingival tissue of maxillary canine (MC), 4<sup>th</sup> premolar (MPM4) and 2<sup>nd</sup> molar (MM2) teeth and into the palatal mucosa (P) on the test injection side and MC contralaterally to serve as control. Digastricus muscle recording electrodes were inserted to obtain the reflex evoked motor potential (REMP) associated with electrical stimulation (20 x 1Hz). After recording three control values at 10 minute intervals, dogs received each injectate volume in randomized order and recordings obtained at 5, 10, 15, 30, 45, 60 and then 20 minute intervals for 5 hours or until the block regressed. A Friedman test was used to analyze the non-parametric data.

For the 1, 2 and 3 mL volumes, 4/6, 6/6 and 5/6 MC, 6/6, 6/6 and 5/6 MPM4, 2/6, 5/6 and 2/6 MM2 and 1/6 for all P were blocked, respectively. Onset ranged from 5-120 minutes and duration from 5-395 minutes. There were no significant volume related differences in the duration of blocks.

A higher volume used for IO was not associated with faster onset, greater extent or longer duration.

## Relation between tracheal diameter and morphometric parameters for tracheal tube size and cuff inflation volume choice in cats

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The aims of this study were to find morphometric parameters correlated to tracheal diameter in cats and inflation volumes for the endotracheal tube (ETT) cuff.

Sixty-one cats (36 females and 25 males), requiring endotracheal intubation during anaesthesia, were enrolled. Body weight, body condition score (5 point scale), occipito-coccygeal length, thoracic and carpal circumference and height at withers were recorded. After induction the tracheal transvers diameter was measured by ultrasound at the level of the second tracheal ring and the size of the ETT decided. After intubation the cuff was inflated at 25 cm H<sub>2</sub>O of pressure with a 1 or 2 mL syringe connected to a 3-way stopcock and to a manometer; the injected volume was recorded. A correlation test of Pearson or Spearman for parametric or nonparametric data was used, respectively. P values <0.05 were considered significant.

Injected volume and tracheal diameter are reported in the table below. A correlation between tracheal diameter and thoracic circumference ( $r = 0.46$ ;  $p = 0.02$ ) resulted only in males. The explored morphometric parameters seem not to be useful for ETT size choice.

<b>ETT internal diameter (mm)</b>	<b>n. cases</b>	<b>Injected volume median (range) (mL)</b>	<b>Mean tracheal diameter (mm)</b>
3.5	7	0.37 (0.25-0.5)	0.57 ± 0.02
4	13	0.35 (0.3-0.4)	0.62 ± 0.04
4.5	20	0.42 (0.25-0.65)	0.64 ± 0.03
5	19	0.8 (0.5-0.7)	0.71 ± 0.06
5.5	2	1.8 (1.7-1.9)	0.75 ± 0.01

Table: injected volume and tracheal diameter.

## **Partial neuromuscular block (NMB) impairs laryngeal abduction and ventilation during hypercarbic challenge in anesthetized dogs**

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Residual NMB impairs the ability to increase ventilation and is associated with a higher incidence of post-anesthetic hypoxia and upper-airway obstruction in humans. We evaluated the effect of partial NMB on the ability to increase ventilation and arytenoid abduction in response to a hypercarbic challenge in anesthetized dogs.

Six healthy adult beagles were anesthetized with propofol and dexmedetomidine infusions; the dogs breathed spontaneously. A laryngeal mask airway was inserted and videolaryngoscopy was used to visualize and measure the normalized glottal gap area (NGGA). Atracurium was infused to obtain the desired level of NMB measured with acceleromyography. The NGGA and  $V_T$  in response to 10%  $CO_2$  (administered for one minute) was measured at baseline (no NMB), at train-of-four (TOF) ratio 0.4-0.6, at TOF ratio 0.7-0.9, and 30 minutes after TOF ratio  $\geq 0.9$ . Both variables were compared with baseline values using paired t-tests.

Compared with baseline, hypercarbic-induced NGGA decreased by  $18\% \pm 0.2$  and  $17\% \pm 0.2$  at TOF ratios 0.4-0.6 and 0.7-0.9, respectively (both  $p \leq 0.03$ ), while hypercarbic-induced  $V_T$  decreased by  $40\% \pm 0.2$  and  $48\% \pm 0.3$ , respectively (both  $p \leq 0.008$ ). Thirty minutes after TOF ratio  $\geq 0.9$ , both variables were indistinguishable from baseline.

Mild residual NMB might be associated with an impaired ability to increase ventilation and glottal gap area in response to hypercarbia, even at TOF ratio values that are typically considered indicative of adequate return of neuromuscular function.

## Evaluation of the PTA (Parasympathetic Tone Activity) Index to predict hypotension in anaesthetized horses.

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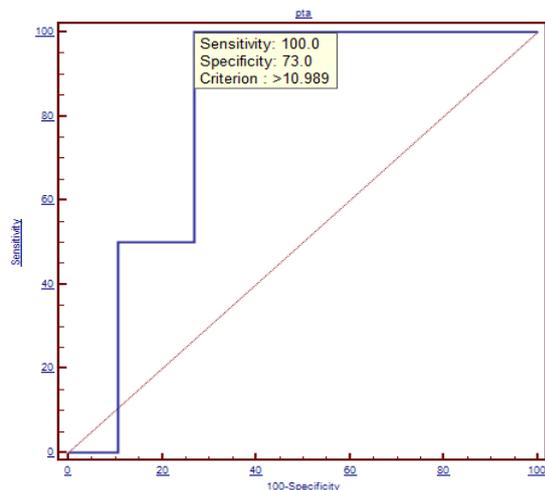
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Recently, an index derived from heart rate variability has been launched in veterinary medicine. It is called Parasympathetic Tone Activity (PTA) (MDolorisMedicalSystems, Lille, France) and reflects the relative parasympathetic tone of the animal. This study aimed to evaluate the performance of the dynamic variations of PTA ( $\Delta$ PTA), to predict hypotension in anesthetized horses, a complication associated with an increased mortality in horses (Johnston et al., 2002).

Fifteen healthy horses, admitted for elective surgery, were anaesthetized following a standardized protocol. Horses were artificially ventilated with continuous monitoring of cardiovascular parameters and PTA. Dobutamine ( $2 \mu\text{g kg}^{-1}\text{min}^{-1}$  IV) was administered in case of hypotension, defined as MAP < 70mmHg.  $T_{-1\text{min}}$ ,  $T_{-2\text{min}}$ ,  $T_{-3\text{min}}$  were retrospective times 1, 2 and 3 minutes before the time of dobutamine administration ( $T_{\text{Dobut}}$ ).  $\Delta$ PTA was calculated as followed:  $\Delta\text{PTA} = [(PTA_{-2\text{min}} - PTA_{-3\text{min}}) / (PTA_{-2\text{min}} + PTA_{-3\text{min}}) / 2]$ . A ROC curve analysis was performed to assess the performance of  $\Delta$ PTA to predict hypotension. The threshold for  $\Delta$ PTA providing the optimal sensitivity and specificity was calculated using the Youden index. A p-value < 0.05 was considered significant.

Based on the ROC analysis, a  $\Delta$ PTA > 11% was associated with a sensitivity of 100% and a specificity of 73 % to predict hypotension (AUC ROC [95% CI] = 0.81 [0.63 to 0.83], p < 0.001 (Figure 1).

In horses,  $\Delta$ PTA showed a good ability to predict intraoperative hypotension. This index could optimize arterial pressure monitoring by anticipating its variation. This should be confirmed by further study.



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This work was supported by the VetAgro Sup - Veterinary Campus of Lyon, University of Lyon, France

## **Comparison of preoperative robenacoxib or meloxicam on analgesic effects after ovariohysterectomy in dogs.**

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The perioperative use of NSAIDs in ovariohysterectomy has been supported previously in other studies (Leece et al 2005; Lascelles et al. 1998).

A prospective, randomized, blinded, clinical study was performed to compare the analgesic effects of robenacoxib and meloxicam. Thirty client owned dogs undergoing elective ovariohysterectomy were randomly assigned to receive pre-operative subcutaneous injection robenacoxib  $2 \text{ mg kg}^{-1}$  (RG, n = 11), meloxicam  $0.2 \text{ mg kg}^{-1}$  (MG, n = 10) or saline  $0.04 \text{ ml kg}^{-1}$  (PG, n = 9) 30 min prior to surgery and post-operatively for 3 days orally. Pre-anaesthetic medication included intravenous acepromazine ( $0.025 \text{ mg kg}^{-1}$ ) and buprenorphine ( $0.02 \text{ mg kg}^{-1}$ ). Anaesthesia was induced with propofol, and maintained with isoflurane. Pain scores were assessed using the modified Glasgow Composite Pain Scale 2, 4, 6, 12, 24, 48 and 72 hours after pre-anaesthetic medication by one observer, blinded to the treatment. Scores exceeding 6/24 (5/20 in non ambulatory dogs) received rescue analgesia (buprenorphine  $0.02 \text{ mg kg}^{-1}$  IV). Differences between groups were analysed using one-way analysis of variance and Kruskal-Wallis test. Groups were compared using Friedman tests and Mann-Whitney U-test where appropriate.  $P < 0.05$  was considered significant.

There were no significant differences in pain scores between the robenacoxib and meloxicam treatments over time. A high incidence ( $p < 0.05$ ) of treatment failure was observed in PG, 6/9 dogs (RG; 2/11, MG; 1/10).

This study suggests that, both meloxicam and robenacoxib administered pre-operatively provide similar and adequate postoperative analgesia in healthy dogs undergoing ovariohysterectomy.

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## Is Xenon a suitable euthanasia agent for mice?

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Carbon dioxide as a euthanasia agent for laboratory mice is considered to be noxious and aversive. Xenon has been suggested as an alternative euthanasia agent (Hawkins et al., 2006). This study investigated the viability of xenon as an alternative agent.

Adult male C57/Bl6j mice were chronically instrumented for unrestrained EEG recording and randomised into CO<sub>2</sub> (n = 6) or Xe (n = 6) groups. After 7 days of postoperative recovery, animals were placed individually into an airtight 15L chamber. A 5-minute baseline in air was recorded before CO<sub>2</sub> or Xe was injected into the chamber at 4L min<sup>-1</sup>. Measured variables were EEG, locomotor activity (assessed by video tracking software) in the first 30s of exposure, number of aversive jumps and grimace score. Parametric data was analysed by Students T-test and non-parametric by one-way ANOVA, with p < 0.05 considered significant.

Grimace score was significantly less for Xe exposure (0 (0-1)) compared to CO<sub>2</sub> (4 (4-5) p < 0.005), as was locomotor activity (17.1 ± 2.4 cm, CO<sub>2</sub> 33.9 ± 10.4 cm p < 0.049). No jumps were seen with Xe whereas all mice exposed to CO<sub>2</sub> jumped (3 (1-4)). Time to brain death was significantly longer for Xe (321 ± 58 s, CO<sub>2</sub> 62.2 ± 31.6 s, p < 0.0047).

Xenon exposure resulted in reduced aversive behaviour and no nociception compared to carbon dioxide. However, the prolonged duration to brain death makes it less suitable as a single gas agent.

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Work funded by the Bundesamt für Lebensmittelsicherheit und Veterinärwesen, Switzerland

## **Does age influence acute pain or stress following disbudding in calves under balanced analgesia?**

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Calf disbudding is an invasive husbandry procedure. This study aims to compare the occurrence of acute pain and stress following early (5-7 days) and late (28-30 days) disbudding/sham disbudding.

Thirty-three bull calves were included in a prospective randomized cross-over experimental trial and allocated in three groups: ED (early disbudding/late sham), LD (early sham/late disbudding) and SH (sham/sham). Baseline sensory (mechanical nociceptive and Von Frey filaments) thresholds, cortisol and beta-endorphins plasma concentrations were recorded. Following intramuscular xylazine (0.1 mg kg<sup>-1</sup>) and cornual nerve block with lidocaine (4 mg kg<sup>-1</sup>), cautery/sham disbudding was performed; meloxicam (0.5 mg kg<sup>-1</sup>) was then injected intravenously. Outcome parameters were re-measured at several time points until 24 hours post disbudding/sham. Differences within groups over time and among groups at several time points were tested with ANOVA on ranks for repeated measures and ANOVA on ranks, respectively; differences between two time points were measured with Mann-Whitney Rank Sum test.  $p \leq 0.05$  was considered significant. Median and inter-quartile-ranges are presented.

Twenty-four hours after disbudding, in both ED and LD, sensory thresholds were significantly lower than baseline and Von Frey thresholds were significantly lower than SH. Cortisol and beta-endorphin, independently from the group, had significantly higher values at 5-7 days compared to 28-30 days [cortisol (ng ml<sup>-1</sup>): 6.30 (5.29-8.59) and 2.37 (1.9-2.8); beta-endorphin (pg ml<sup>-1</sup>): 12.08 (9.72-21.85) and 7.72 (6.29-8.69)], but did not increase significantly over time during disbudding/sham.

Sensory thresholds suggest sensitization in both ED and LD, despite analgesia. Cortisol and beta-endorphins suggest higher stress in younger calves.

## **Evaluation of sedative effects of different intramuscular premedication mixtures of alfaxalone, methadone and dexmedetomidine in healthy cats**

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This randomized, clinical study evaluates the sedative effects of different intramuscular drug mixtures in cats.

Sixty ASA I cats were divided in four groups of 15 animals each: group A (alfaxalone 2.5 mg kg<sup>-1</sup>), group AHM (alfaxalone 2.5 mg kg<sup>-1</sup> and methadone 0.3 mg kg<sup>-1</sup>), group ALM (alfaxalone 1.5 mg kg<sup>-1</sup> and methadone 0.3 mg kg<sup>-1</sup>), group DM (dexmedetomidine 5 µg kg<sup>-1</sup> and methadone 0.3 mg kg<sup>-1</sup>). A composite sedation score (0 to 16; Tamura et al. 2015) was used. Values for sedation (evaluated at each time point prior to further manipulations), HR and *fR* were recorded at baseline and every 5 minutes post intramuscular injection.

Excitatory side effects were recorded. Catheter Placement Score (CPS) was evaluated with a scale from 0 (very difficult) to 3 (very easy) (Bortolami et al. 2013). Non-parametric data were analysed with Kruskal-Wallis test with a post-hoc Dunn's test. Repeated measures within groups were analysed with a Friedman test with a post-hoc Dunn's test or with a one-way ANOVA and a Tukey post-hoc.

No significant differences were found between groups for sedation score whereas CPS was significantly different in group A [0 (0-2)] vs groups AHM [2 (0-3)] and DM [2 (0-3)]. Of the 45 cats that received alfaxalone, 40 showed excitatory effects, mostly elicited by manipulation. Sedation was not sufficiently reliable over all groups to allow a comfortable IV catheterisation in all individuals. The use of alfaxalone at low dose can be recommended only at 2.5 mg kg<sup>-1</sup> and in combination with methadone.

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## The effect of romifidine, MK-467, a peripheral alpha-2-adrenoceptor antagonist, and their combination on plasma glucose concentration in horses.

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Alpha-2-adrenoceptor agonists are known to induce hyperglycaemia. Our aim was to investigate the effects of an  $\alpha_2$ -adrenoceptor agonist romifidine and MK-467, a peripheral  $\alpha_2$ -adrenoceptor antagonist, on plasma glucose concentration in horses.

According to a blinded Latin square design with a minimum washout period of six days, seven horses received IV injections of: romifidine ( $80 \mu\text{g kg}^{-1}$ , ROM), MK-467 ( $200 \mu\text{g kg}^{-1}$ , MK), and their combination (ROM+MK). Venous blood samples were collected before (baseline) and 15, 30, 60, 90 and 120 minutes after medication. Plasma glucose concentrations were analyzed with the photometric glucose hexokinase 2 reagent method (Konelab™ Glucose HK). Friedman's test was used to compare glucose concentrations to baseline; comparison between treatments was performed with the Kruskal-Wallis test and ANOVA.

Results are presented in Table 1. Glucose concentration was highest after ROM and lowest after MK. Compared to baseline, plasma glucose concentration increased after both ROM and ROM+MK.

As a conclusion, romifidine altered glucose homeostasis of horses in this study by inducing hyperglycaemia, which MK-467 partially prevented.

Table 1. Plasma glucose concentrations ( $\text{mmol L}^{-1}$ , mean and standard deviation)

Time (minutes)	ROM	ROM+MK	MK
baseline	5.10 (0.48)	4.74 (0.19)	4.94 (0.34)
15	5.33 (0.57)	5.11 (0.33)	4.69 (0.34)
30 <sup>†‡</sup>	6.69 (0.82)	5.79 (0.51) <sup>§</sup>	4.33 (0.22)
60 <sup>*†‡</sup>	8.87 (1.43) <sup>§</sup>	5.77 (0.55) <sup>§</sup>	4.37 (0.26)
120 min <sup>*‡</sup>	9.33 (1.43) <sup>§</sup>	5.73 (0.70) <sup>§</sup>	4.86 (0.40)

Significant difference ( $P < 0.05$ ) between \*ROM and ROM+MK, <sup>†</sup>ROM+MK and MK and <sup>‡</sup>ROM and MK. <sup>§</sup>Significant difference ( $P < 0.05$ ) from baseline.

## **Impact of the Trendelenburg and reverse Trendelenburg position on respiratory and cardiovascular function in the anaesthetized horse**

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This randomized, crossover study describes the cardiorespiratory effects of changes in the table position in anaesthetized horses.

Six horses were anaesthetized twice and positioned in dorsal recumbency, either during 90 minutes in Trendelenburg (T) followed by 90 minutes in reverse Trendelenburg (RT) position, or in the inverse order, during mechanical ventilation. Cardiorespiratory monitoring included ECG, pulse oximetry, arterial, pulmonary arterial, right atrial pressure and cardiac output measurements, volumetric capnography and blood gas analysis. Statistical analysis consisted of a mixed model with horse as random effect and part, period, time and position as fixed effects ( $\alpha = 0,05$ ).

During the first 90 minutes, HR increased gradually in both groups, while MAP was lower in position RT ( $76.1 \pm 18.8$  vs  $81.4 \pm 14.7$  mmHg). In the second part, HR was higher in position RT ( $37.4 \pm 5.1$  vs  $36.1 \pm 4.8$  beats/minute<sup>-1</sup>). The PaO<sub>2</sub> ( $155.8 \pm 90.2$  vs  $118.6 \pm 112.1$  mmHg) and arterial oxygen content ( $15 \pm 2.5$  vs  $13 \pm 1.4$  ml/dl) were higher in position RT during the first part of the anaesthesia and remained higher also after changing position. The opposite evolution was observed for venous admixture. The right atrial ( $6.3 \pm 3.2$  vs  $11.2 \pm 4.4$  mmHg) and mean pulmonary arterial pressure ( $22.9 \pm 6.8$  vs  $26.7 \pm 7$  mmHg) were lower in position RT in both parts of the anaesthesia.

The reverse Trendelenburg position ameliorated gas exchange when applied from the start of anaesthesia.

## **The effects of ketamine or midazolam on the intubation dose of alfaxalone, hemodynamic function, glucose and insulin levels in healthy dogs.**

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We hypothesized that ketamine or midazolam added to alfaxalone would reduce the dose required for endotracheal intubation and that alfaxalone administration would not change serum glucose and insulin concentrations.

This was a randomized, prospective, blinded clinical study. Fifty-two healthy, client owned dogs (2 - 8 years, 15 - 50 kg) were included. After premedication with acepromazine (0.02 mg kg<sup>-1</sup>) and hydromorphone (0.1 mg kg<sup>-1</sup>) IM, alfaxalone (0.25 mg kg<sup>-1</sup>) was administered IV, followed immediately by 0.9% saline (AS), midazolam (0.3 mg kg<sup>-1</sup>; AM), ketamine (1 mg kg<sup>-1</sup>; AK1), or ketamine (2 mg kg<sup>-1</sup>; AK2) IV. Additional alfaxalone (0.25 mg kg<sup>-1</sup>) was administered as required to permit intubation. Time from intubation until spontaneous blinking or movement was recorded. Cardiorespiratory function was assessed before premedication, before induction, after intubation and 2, 5, 10 and 15 minutes thereafter. Blood was collected for measurement of serum glucose and insulin, prior to induction and at similar times as above. Data were analyzed by split plot ANOVA.

Intubation required  $1.0 \pm 0.4$ ,  $0.38 \pm 0.19$ ,  $0.54 \pm 0.33$  and  $0.52 \pm 0.35$  mg kg<sup>-1</sup> alfaxalone in the AS, AM, AK1 and AK2 groups respectively ( $p = 0.0005$ ). Most variables did not differ significantly between groups. Heart rate decreased in the AS group; in other groups, it increased transiently post-intubation. Midazolam significantly prolonged time from intubation until spontaneous movement ( $p < 0.002$ ).

Both midazolam and ketamine reduce the intubation dose of alfaxalone. Serum glucose and insulin concentrations are not influenced by alfaxalone administration.

## Minimum Anesthetic Concentration (MAC) of Isoflurane and Sevoflurane in Magellanic Penguins (*Spheniscus magellanicus*)

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The aim of this study was to establish the MAC of isoflurane (MAC<sub>iso</sub>) and sevoflurane (MAC<sub>sevo</sub>) in Magellanic penguins, due to the importance of inhalant anesthesia during penguin management and rehabilitation.

Determination of MAC was based on the “up-and-down” method (four crossovers), using nine animals for MAC<sub>iso</sub> and thirteen animals for MAC<sub>sevo</sub>, all healthy, of both genders and weighing  $3.6 \pm 0.3$  kg. Anesthesia induction was performed with isoflurane (5 V%) or sevoflurane (8 V%) in oxygen 100% with a non-rebreathing system and a face mask. After induction, animals were intubated and maintained under mechanical ventilation ( $f_R = 12$ ; 10 cmH<sub>2</sub>O; inspiratory-expiratory ratio 1:2) in a pre-determined expiratory fraction. F<sub>E</sub>-CO<sub>2</sub> was kept between 30 and 37 mmHg and cloacal temperature between 39 and 40 °C. An electrical stimulus (50 Hz, 65 mA, 6 milliseconds) was applied into the SC of the medial surface of the hindlimb. According to a positive or negative response, initial expired fractions of isoflurane (1.8 V%) and sevoflurane (3.5 V%) were increased or decreased in 0.1 V% in subsequent animals, respectively. The MAC values were established by arithmetic mean (Monteiro et al., 2016) and logic regression (Escobar et al., 2016).

Values obtained for isoflurane by arithmetic mean were  $1.93 \pm 0.10$  V% and by logistic regression  $1.87 \pm 0.10$  V%, and sevoflurane  $3.38 \pm 0.36$  V% and  $3.49 \pm 0.13$  V%, respectively.

The MAC<sub>sevo</sub> and MAC<sub>iso</sub> established in this study might be used as reference for inhalant anesthesia in this species.

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Supported by FAPESP 2013/19796-0

## **Sedative and antinociceptive effects of morphine and butorphanol in green iguana (*Iguana iguana*)**

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The aim of this study was to evaluate the sedative and antinociceptive effects of morphine and butorphanol in green iguanas (*Iguana iguana*).

Ten healthy iguanas ( $160 \pm 46$  grams) were given five treatments: saline (0.3 mL, CON), morphine  $5 \text{ mg kg}^{-1}$  (MOR<sub>5</sub>),  $10 \text{ mg kg}^{-1}$  (MOR<sub>10</sub>), butorphanol  $5 \text{ mg kg}^{-1}$  (BUT<sub>5</sub>), and  $10 \text{ mg kg}^{-1}$  (BUT<sub>10</sub>) IM, in a blinded and randomized study. Sedation was evaluated by forced swimming test (Slattery & Cryan 2012) for 120 seconds before treatment (baseline) and 0.5, 1, 2, 3, 4, 6, 12 and 24 hours after treatment. Latency of limb withdrawal reflex (LWR) to thermal stimulus (Sladky & Mans 2012) was evaluated at baseline and 0.25, 1, 2, 4, 6, 12 and 24 hours after treatment. Statistical analysis included two-way ANOVA followed by Bonferroni's post hoc test. A  $p < 0.05$  was considered significant.

Time of swimming decreased in MOR<sub>10</sub> from baseline ( $80.7 \pm 25.4$  seconds) from 0.5 hour ( $49.9 \pm 21.8$  seconds) to 2 hours ( $46.9 \pm 20.2$  seconds), in BUT<sub>5</sub> from baseline ( $76.9 \pm 25$  seconds) from 0.5 hour ( $40.4 \pm 18.3$  seconds) to 2 hours ( $48.3 \pm 19.5$  seconds), and in BUT<sub>10</sub> from baseline ( $75.1 \pm 22.6$  seconds) from 0.5 hour ( $42.7 \pm 22.6$  seconds) to 12 hours ( $39.6 \pm 30.6$  seconds). All groups decreased the swimming at 12 hours after treatment. None of the treatments increased the LWR.

Butorphanol and the higher dose of morphine promoted sedation, but antinociception was not detected in any of the treatments in healthy iguanas.

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Supported by FAPESP 2014/10452-9 and FAPESP 2014/09529-7

## **A comparison of cardiovascular effects, recovery quality and total doses required for total intravenous anaesthesia with alfaxalone versus an alfaxalone-fentanyl combination in dogs**

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The anaesthetic and cardiovascular effects of alfaxalone alone or in combination with a fentanyl constant rate infusion (CRI) for total intravenous anaesthesia (TIVA) were compared in dogs.

Twelve intact female dogs were anaesthetized in this prospective, blinded, randomized, experimental study for a duration of 210 minutes. Following intramuscular dexmedetomidine ( $10 \mu\text{g kg}^{-1}$ ) and methadone ( $0.1 \text{ mg kg}^{-1}$ ) administration, anaesthesia was induced with alfaxalone ( $2 \text{ mg kg}^{-1}$ ; Group AP) or alfaxalone ( $2 \text{ mg kg}^{-1}$ ) preceded by fentanyl ( $2 \mu\text{g kg}^{-1}$ ) (Group AF). Anaesthetic maintenance was obtained with an alfaxalone variable rate infusion (VRI) started at  $0.15 \text{ mg kg}^{-1} \text{ minute}^{-1}$  (Group AP) or an alfaxalone VRI (similar starting rate) combined with a fentanyl CRI ( $10 \mu\text{g kg}^{-1} \text{ hour}^{-1}$ ) (Group AF). The alfaxalone VRI was adjusted every 5 minutes, based on clinical assessment. Cardiovascular parameters and recovery characteristics (using a numerical rating scale) were compared. A mixed model statistical approach was used to compare the mean CRI alfaxalone dose and cardiovascular parameters between groups; recovery scores were analyzed with the Wilcoxon Rank Sum Test ( $\alpha = 0.05$ ). The mean CRI alfaxalone maintenance dose was significantly higher in group AP compared to group AF (respectively,  $0.16 \pm 0.01 \text{ mg kg}^{-1} \text{ minute}^{-1}$ ;  $0.13 \pm 0.01 \text{ mg kg}^{-1} \text{ minute}^{-1}$ ). Overall HR, SAP, MAP and DAP were significantly lower in Group AF. Quality of recovery was poor and did not differ between groups.

When combined with a fentanyl CRI, an alfaxalone TIVA is effective for anaesthetic maintenance in dogs and resulted in a significant alfaxalone dose reduction.

## **Rapid fill carbon dioxide reduces aversive behaviour but not nociception in mice undergoing euthanasia.**

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Guidelines for carbon dioxide euthanasia of mice suggests using 10-30% vol<sub>chamber</sub> min<sup>-1</sup> flow rate. However, this is extrapolated from rats (Greenacre, 2013). This study investigated which flow rate was least stressful for mice undergoing euthanasia.

Adult C57/Bl6j mice were chronically instrumented for unrestrained EEG recording. After 7 days of postoperative recovery, animals were placed individually into an airtight chamber (15L capacity). A 5-minute baseline in air was recorded before carbon dioxide was injected into the chamber at either 4L min<sup>-1</sup> (gradual (G), n = 13) or 12L min<sup>-1</sup> (rapid (R), n = 16). Measured variables were EEG, locomotor activity (measured by video-tracking) in the first 30s of exposure, number of aversive jumps and grimace-score. Parametric data was analysed by Students T-test with p < 0.05 considered significant.

Activation of the EEG (theta:delta ratio) was increased from baseline equally in both groups (G 1.35 ± 0.31, R 1.19 ± 0.10, p = 0.045). Loss of consciousness occurred faster in R (G 69.8 ± 7.5 s, R 45.4 ± 6.5 s, p < 0.001) and aversive jumps were fewer (G 6(1-12), R 3(0-5) p = 0.025). Locomotor distance was increased in G (G 34.9 ± 4.9 cm, R 24.2 ± 5.8 cm, p = 0.047). There was no significant difference in grimace score between groups (G 4(3-5), R(4(3-6))).

Carbon dioxide exposure causes behavioural excitation in mice. Whilst nociception was equal in both groups, rapid-fill reduced the amount of aversive behaviour. Gradual-fill carbon dioxide is not beneficial to rapid-fill as a method of euthanasia for mice.

### Reference

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Funding provided by Bundesamt für Lebensmittelsicherheit und Veterinärwesen

## **Evaluation of the use of midazolam as a co-induction agent with ketamine for anaesthesia in healthy, sedated ponies undergoing field castration**

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There are limited investigations in horses comparing ketamine to a ketamine-midazolam anaesthetic co-induction. This study's aim was to determine if ketamine-midazolam improved induction quality compared to ketamine alone.

After IV detomidine ( $20 \mu\text{g kg}^{-1}$ ) forty ponies received either  $0.06 \text{ mg kg}^{-1}$  ( $0.6 \text{ ml kg}^{-1}$ ) midazolam (group M) or  $0.6 \text{ ml kg}^{-1}$  placebo (group P) with  $2.2 \text{ mg kg}^{-1}$  ketamine IV for induction. Quality of induction, endotracheal intubation, surgical relaxation and recovery were scored using combinations of simple descriptive (SDS) and visual analogue scales (VAS). Time of sedation, induction, start of endotracheal intubation, first movement, sternal recumbency and standing were recorded, as were time, number and total quantity of additional IV detomidine and ketamine injections. Cardiorespiratory variables were assessed every 5 minutes. Adverse effects were documented. Data were tested for normality and analysed with a mixed model ANOVA, unpaired Students' t-test and Wilcoxon Rank-sum test;  $p < 0.05$  was considered significant.

Group M had better scores (VAS) for induction (M: 90 (38 – 96) P: 74 (29 – 94),  $p = 0.005$ ), intubation (M: 91 (58 – 97) P: 55 (15 – 99),  $p < 0.001$ ) and SDS for surgical relaxation ( $p < 0.001$ ). Time (minutes) from induction to first movement ( $p < 0.001$ ), sternal recumbency ( $p = 0.001$ ) and standing was significantly longer ( $p = 0.01$ ) in group M. Recoveries were uneventful with no significant difference in quality between groups ( $p = 0.78$ ).

Midazolam-ketamine co-induction compared to ketamine alone improved quality of induction, ease of intubation and muscle relaxation without impacting recovery quality or cardiopulmonary function.

Funding was provided by Regivet BV.

## **The effect of lidocaine application on the ovarian pedicle on heart rate variability in dogs undergoing ovariohysterectomy**

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During ovariohysterectomy (OHE), nociceptive inputs may induce sympathetic stimulation. We hypothesised that lidocaine would reduce heart rate variability (HRV) caused by inadequate analgesia.

Twenty dogs admitted for OHE (weight 6 - 25 kg, age 0.5 - 10 years) were premedicated with acepromazine ( $0.1 \text{ mg kg}^{-1}$ , IM) and butorphanol ( $0.1 \text{ mg kg}^{-1}$ , IM). Anaesthesia was induced with propofol and maintained with isoflurane. In 10 dogs, lidocaine ( $2 \text{ mg kg}^{-1}$ ) was applied with a gauze on the ovarian pedicle (group L). In the rest 10 dogs Normal Saline solution was applied likewise (group C). Three 5-minute intervals of invasive arterial blood pressure waveforms were recorded: baseline (before surgical stimulation, T1), treatment (application of lidocaine or normal saline, T2), ligation of the ovary (T3). HRV was calculated according to the Task Force (1996). For the statistical analysis, a general linear model for repeated measurements was used.

There was a significant ( $p = 0.028$ ) increase in HR in group C, from T1 ( $96.7 \pm 17.7$ ) to T3 ( $109.1 \pm 12.3$ ). No significant ( $p = 0.145$ ) increase was seen in group L ( $95.2 \pm 21.4$  in T1,  $103.1 \pm 11.6$  in T3). Low frequency (LF) increased significantly ( $p = 0.008$ ) in group L from T1 ( $3.2 \pm 2.6$ ) to T3 ( $15.4 \pm 12.4$ ), whereas no significant increase ( $p = 0.567$ ) was detected in group C ( $22.7 \pm 12.4$  in T1,  $20.4 \pm 14.6$  in T3).

It seems that lidocaine may not suppress SNS activation during ovary ligation, even though heart rate is not increased.

Task Force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology (1996) Heart rate variability. *Eur Heart J* 17, 354–381.

## The Effect of Limb Position on Respiratory Mechanics in Pigs

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Lung function is greater during sternal recumbency in anaesthetized pigs (Mutoh et al., 1992). In sternal recumbency, there are four options for symmetrical & parallel limb positioning: forward: F; backward: B; outwards: O; inwards: I. These may affect respiratory mechanics.

Peak inspiratory pressure (PIP), plateau inspiratory pressure (PIIP), mean intrathoracic pressure (MITP), airway resistance (TAR) and compliance (dV/dP) were measured after the randomized imposition of B, F, O, I in 10 anaesthetized, sternally – positioned pigs whose lungs were ventilated using different VTs applied in the sequence: 8; 10; 12; 6; and 8 mL kg<sup>-1</sup>. At each VT, *f<sub>r</sub>* was altered to maintain FeCO<sub>2</sub> at 5.3 kPa. Measurements were recorded after > 20 minutes in each leg position. A Generalized Linear Mixed Effect Model with Poisson errors was used for statistical analysis.

Most limb positions exerted significant effects on dV/dP but were VT dependent. In F, O and I, VT and dV/dP showed strong negative correlation ( $p = 0.0387$ ,  $0.0459$ , and  $0.0000375$ , respectively), being the greatest in I (decline:  $- 0.05$ ). In B, VT had no effect on compliance. VT exerted statistically significant differences on all variables. Individual variation was most pronounced with TAR.

Respiratory mechanics in pigs in sternal recumbency are affected by limb position in a VT - dependent manner except for dV/dP in B. Position B is associated with optimum dV/dP. Position I has greatest adverse effects on respiratory mechanics. Studies involving blood gas analysis are required to establish definitive effects of limb position on lung function in anaesthetized pigs.

Mutoh, T., Guest, R. J., Lamm, W. J. & Albert, R. K. (1992) Prone position alters the effect of volume overload on regional pleural pressures and improves hypoxemia in pigs in vivo. *Am Rev Respir Dis*, 146, 300-6.

## **Evaluation of respiratory physiologic dead space variability during general anaesthesia in dogs**

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The aim of the study was to measure the variability of respiratory physiologic dead space in anesthetized dogs and evaluate any differences between dolichocephalic and brachycephalic breeds.

Nineteen adult dogs, 10 dolichocephalic (group A) and 9 mixed breed – brachycephalic dogs (group B), submitted for non-thoracic/non-abdominal operations were studied. All dogs were pre-medicated with intramuscular administration of dexmedetomidine ( $175 \mu\text{g m}^{-2}$ ) and butorphanol ( $0.1 \text{ mg kg}^{-1}$ ). Anaesthesia was induced with propofol and maintained with isoflurane. Three arterial blood samples were collected once every thirty minutes, the first sample taken immediately after intubation.  $\text{PaCO}_2$ ,  $\text{PaO}_2$ , pH, haemoglobin concentration and haemoglobin saturation ( $\text{SaO}_2$ ) were measured. These parameters were then used to calculate anatomical and alveolar dead space, as well as physiologic dead space ratio ( $\text{Vd/Vt}$ ), with the NICO monitor (Novamatrix Medical Systems, Wallingford, CT). For the statistical analysis, a general linear model for repeated measurements was used.

$\text{Vd/Vt}$  was  $65.5 \pm 13.2\%$  (group A) and  $67.2 \pm 9.68\%$  (group B) in the first time point,  $64.5 \pm 15.17\%$  (group A) and  $63.1 \pm 13.5\%$  (group B) in the second, and  $68.2 \pm 16\%$  (group A) and  $62.3 \pm 12.4\%$  (group B) in the last. No statistically significant effect of time or breed on  $\text{Vd/Vt}$  was detected.

The present study provides information on the physiologic dead space during anaesthesia in dogs. It seems that, despite the anatomical differences between dolichocephalic and brachycephalic breeds, dead space values are similar. Moreover, through this study, it appears that this respiratory variable does not change over time.

## **Cardiovascular Effects of Low and High doses of Fentanyl in the Isoflurane-Anaesthetised Dog With and Without Correction of Bradycardia**

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This study aimed to compare cardiovascular effects of two doses of fentanyl at equipotent levels of isoflurane in dogs in the presence or absence of bradycardia.

8 beagles were anaesthetised with isoflurane on two occasions (low or high dose), in a prospective, randomised cross-over trial. In each experimental day, cardiovascular parameters were recorded at 1.3 MAC of isoflurane (T1), and isoflurane with each fentanyl infusion (T2) (low dose [LD], 30  $\mu\text{g kg}^{-1}$  loading dose, 0.2  $\mu\text{g kg}^{-1} \text{ minute}^{-1}$ ; or high dose [HD], 90  $\mu\text{g kg}^{-1}$  loading dose, 0.8  $\mu\text{g kg}^{-1} \text{ minute}^{-1}$ ), and after receiving glycopyrrolate (0.01 mg  $\text{kg}^{-1}$ ) with HR between 80-100 beats  $\text{minute}^{-1}$  (T3). A 7-day washout period was observed.

Data were analysed using mixed-model ANOVA and Bonferroni correction, with  $\alpha$  level set at 0.05.

At T2, cardiac index (CI) decreased with both LD ( $2.34 \pm 0.67$  vs  $3.31 \pm 0.80$  L  $\text{minute}^{-1} \text{ m}^{-2}$ ) and HD ( $1.8 \pm 0.49$  vs  $3.12 \pm 0.97$  L  $\text{minute}^{-1} \text{ m}^{-2}$ ), despite increased MAP with HD ( $85 \pm 17.3$  vs  $72 \pm 15.5$  mmHg). Fentanyl caused severe bradycardia with HD compared to LD ( $42 \pm 6.8$  vs  $57 \pm 14.7$  beats  $\text{minute}^{-1}$ ). After glycopyrrolate (T3), CI was increased versus T1 with HD only ( $4.03 \pm 0.46$  vs  $3.12 \pm 0.97$  L  $\text{minute}^{-1} \text{ m}^{-2}$ ), as well as MAP ( $100 \pm 16.1$  mmHg). In dogs anaesthetised with fentanyl-isoflurane, MAP may not be an accurate indicator of adequate cardiovascular function, especially with bradycardia. This suggests that bradycardia should be treated to optimise cardiovascular function in these animals.

Funding for this study was supplied by the Veterinary Memorial Fund at the Virginia-Maryland College of Veterinary Medicine

## **A novel technique for ultrasound-guided paravertebral brachial plexus block in dogs: cadaveric study**

PM Monticelli, EF Fitzgerald, JV Viscasillas.

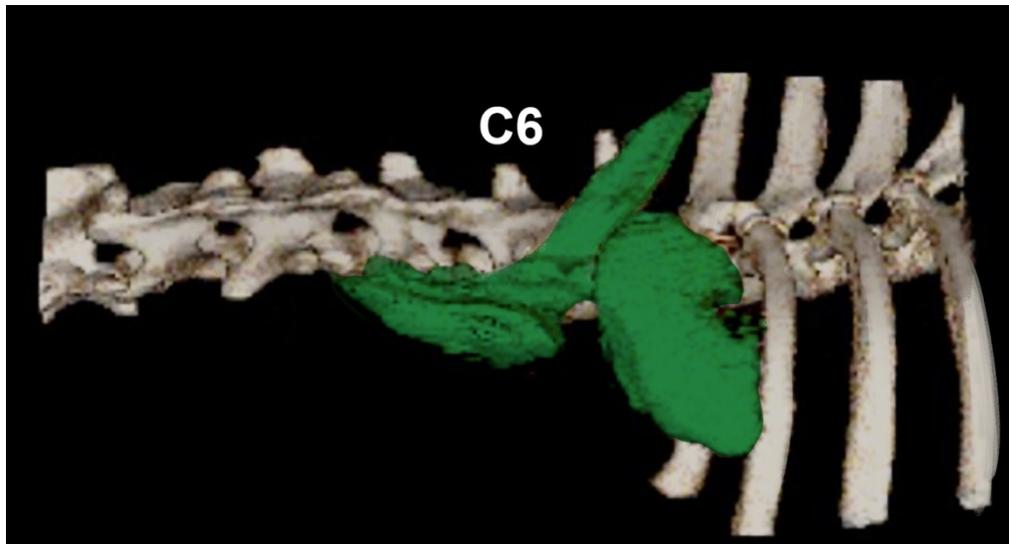
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Ultrasound-guided paravertebral brachial plexus block has been described in dogs (Bagshaw et al. 2009; Rioja et al, 2012). However, some limitations were found in both studies. The aim of this study was to describe a novel in-plane ultrasound-guided approach to the C6 to T1 nerves.

Six canine Beagle cadavers weighing  $9.5 \pm 1$  kg, were included. Dogs were positioned in lateral recumbency. A 10MHz linear probe was positioned lateral to the sixth cervical vertebra. A volume of 0.05 ml/kg of a 50:50 mixture of iohexol and methylene blue was injected cranioventral and caudoventral to the transverse process. The probe was moved caudally to identify the cranial costal fovea of T1 and 0.1 ml/kg of the mixture was injected cranial and lateral to the first rib. All injections were performed by the same operator. Computed tomography verified proximity of contrast to C6, C7, C8 and T1 nerves. Contamination of vasculature, vertebral canal, mediastinum or pleural was recorded. Staining of the phrenic nerve was assessed by dissection.

At all sites (12/12), the C6, C7 and C8 nerves were in contact with contrast material. For T1 nerve, contrast was demonstrated medial to the first rib in 11/12 sites. Mediastinal, epidural and intravascular contamination were observed in 6/6, 4/6 and 2/6 cadavers, respectively. The phrenic nerve was stained in 2/12 of sides.

This study showed a successful and repeatable technique. Further studies are needed to assess the clinical effectiveness of this block.



Contrast distribution after performing the ultrasound-guided paravertebral brachial plexus block

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## **Influence of tidal volume and PEEP on ventilation distribution measured by EIT in anaesthetized horses in lateral recumbency – preliminary results**

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Differences in VT and positive end-expiratory pressure (PEEP) might alter the regional distribution of ventilation. The parameter center of ventilation (CoV) indicates well-ventilated region of lung. The influence of different VT and PEEP on CoV was assessed.

Five horses (weighting 531±71kg) were anaesthetised in lateral recumbency. Nine ventilation modes with VT of 8, 10, and 12 ml kg<sup>-1</sup> combined with PEEP of 0, 10, 20 cmH<sub>2</sub>O were scheduled in random order, each lasting 4 minutes. Between modes, 4 minutes baseline ventilation (VT 15 ml kg<sup>-1</sup>, PEEP 0) was applied. Respiratory function was monitored with electrical impedance tomography (EIT) (Dixtal, Corp.). The last two minutes of each treatment were analysed post hoc. CoV given in percent was calculated as the geometrical center from right to left and ventral to dorsal direction of the functional image.

Values below 50% indicate the CoV in the left and non-dependent lung. Data were analysed using descriptive statistics only. Results are given in percentage related to baseline.

Ventilation modes with PEEP 0 resulted in a CoV between 22.3% (baseline) and 22.0, 22.7, and 22.2% for VT 8, 10 and 12 ml, respectively. Adding PEEP shifts the CoV in the direction of dependent lung with the exception of VT 8/PEEP10. PEEP20 e.g. shifts ventilation to 30.5 (VT 8), 33.4 (VT 10) and 35.7% (VT 12) of baseline in the direction of dependent lung.

The shift of distribution of ventilation to more dependent lung regions is depending on PEEP with the effect being greater with higher VT.

## **Correlation between Visual Analog, Glasgow, Colorado and Melbourne Scales in the evaluation of postoperative pain in dogs undergoing total unilateral mastectomy**

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The aim of this study was to report the need for postoperative analgesic rescue determined by Visual Analog Scale (VAS), Glasgow Composite Measure Pain Scale (GCMPS), Colorado State University Canine Acute Pain Scale (CSU-CAPS) and University of Melbourne Pain Scale (UMPS), in dogs undergoing total unilateral mastectomy. 24 healthy dogs were used. Animal pain scores were evaluated preoperatively (24 hours, Baseline) and postoperatively (1, 2, 4, 6, 8, 12 and 24 hours). Dogs were pre-medicated with morphine and acepromazine (0.5 and 0.02 mg Kg<sup>-1</sup>) IM, anesthesia was induced with propofol (4 mg Kg<sup>-1</sup>) and maintained by isoflurane 1.4% delivered in 100% oxygen. The analgesia during surgery was maintained with ketamine (10 µg Kg<sup>-1</sup> minute) and fentanyl (10 µg Kg<sup>-1</sup> hour). Animals scoring 5, 6, 2, 9 or higher on the VAS, GCMPS, CSU-CAPS or UMPS respectively received rescue analgesia with morphine IM at 0.5 mg kg<sup>-1</sup>. Wilcoxon's test used for non-parametric analysis ( $p < 0.05$ ).

Pain scores higher than the pre-surgical value were seen in VAS (16.6% of the dogs, 4/24) and UMPS (12.5% of the dogs, 3/24) at 6 hours, in CSU-CAPS (45.8% of the dogs, 11/24) at 4 hours, and in GCMPS (70.8% of the dogs, 17/24) at 1 hour postoperatively. The best correlation between the scales was 0.775 between GCMPS and CSU-CAPS.

We concluded that the GCMPS scale was more sensitive to detect the need for postoperative analgesic rescue in dogs undergoing total unilateral mastectomy.

## Assessment of cardiac troponin I in dogs sedated with medetomidine or anaesthetized with propofol and sevoflurane with or without premedication with medetomidine

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This study aimed to establish whether medetomidine may induce myocardial hypoxic injury, indicated by increased serum cardiac troponin I (cTnI) concentration.

The dogs were sedated with medetomidine 0.04 mg kg<sup>-1</sup> IV (group M; n = 20) or anaesthetized with propofol 6 to 8 mg kg<sup>-1</sup> IV and sevoflurane (group P+S; n = 20) or with medetomidine 0.04 mg kg<sup>-1</sup> IV, propofol 1 to 3 mg kg<sup>-1</sup> and sevoflurane (group M+P+S; n = 26), respectively. Group M was breathing air while the latter two groups were breathing oxygen during procedure. After 35 minutes, medetomidine was reversed with atipamezole 0.1 mg kg<sup>-1</sup> IM. Blood samples for cTnI determination were taken before sedation/anaesthesia, 6 and 12 hours and 4 days thereafter. Serum cTnI concentrations were measured with Architect STAT Troponin-I assay. Data were analyzed with Friedman and Kruskal Wallis tests with post-hoc pairwise multiple comparisons (p < 0.05).

Results are presented in Table 1.

Oxygenation during anaesthesia and reduction of propofol and sevoflurane dose due to medetomidine sparing effect alleviated myocardial hypoxic injury (less severe and short-lived increase of cTnI in M+P+S group).

Table 1 Serum cTnI concentration (mean ± SD; ng mL<sup>-1</sup>)

	Basal	6 hours	12 hours	4 days
M	0.014 ± 0.033	0.04 ± 0.057*	0.121 ± 0.143* <sup>‡</sup>	0.071 ± 0.104*
P+S	0.007 ± 0.002	0.018 ± 0.019*	0.052 ± 0.050* <sup>‡</sup>	0.011 ± 0.007
M+P+S	0.007 ± 0.003	0.050 ± 0.173*	0.013 ± 0.008*	0.012 ± 0.007

\* significantly higher comparing to basal values

<sup>‡</sup> significantly higher comparing to M+P+S group

This work was supported by the Slovenian Research Agency (P4-0053).

## **Evaluation of sedative and antinociceptive effects of dexmedetomidine and midazolam, isolated or in combination, in tegus (*Salvator merianae*)**

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The aim of this study was to evaluate antinociceptive and sedative properties of dexmedetomidine, midazolam and dexmedetomidine-midazolam in tegus (*Salvator merianae*).

Six healthy tegus ( $1.6 \pm 0.3$  kg) were given saline (0.5 mL; Control), dexmedetomidine ( $0.2 \text{ mg kg}^{-1}$ ; DX), midazolam ( $1 \text{ mg kg}^{-1}$ ; MZ) and dexmedetomidine-midazolam (same doses; DM), IM. Sedation scores (0 - 18) were recorded according to resistance to physical restraint, posture and response to noxious stimulus, before treatment (baseline) and 5, 10, 15, 30 minutes, 1, 2, 4, 6, 8, 12 and 24 hours after treatment. Latency of limb withdrawal reflex (LWR) to thermal stimulus was recorded at baseline and 15 minutes, 1, 2, 4, 8, 12 and 24 hours after treatment. Sedation was analyzed by Kruskal-Wallis' test with Dunn post hoc test and LWR by ANOVA followed by Bonferroni's post hoc test (within treatments) or Tukey's post hoc test (among treatments) ( $p < 0.05$ ).

Sedation scores increased from baseline [1 (0.8 - 1.3)] from 10 minutes [11 (10.3 - 11)] to 1.5 hour [9 (5.5 - 11)] in MZ, and from 10 minutes [14 (12.5 - 14.8)] to 3 hours [9.5 (6.8 - 12.8)] in DM. LWR increased from baseline ( $11.0 \pm 2.2$  seconds) from 15 minutes ( $18.5 \pm 2.2$  seconds) until 8 hours ( $20.1 \pm 0.5$  seconds) in DX and from 15 minutes ( $20.1 \pm 0.5$  seconds) until 12 hours ( $16.5 \pm 3.5$  seconds) in DM.

Midazolam provided sedation without antinociception, and dexmedetomidine provided antinociception without sedation in tegus. Dexmedetomidine-midazolam combination enhanced both effects.

Supported by FAPESP n° 2014/10452-9, FAPESP n° 2014/19765-0.

## Effects of azaperone and xylazine combination in captive red brockets (*Mazama americana*)

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The aim of this study was to establish a sedation protocol that allows common handling procedures for captive red brockets (*Mazama americana*).

Six adult animals, weighing  $38.4 \pm 5$  kg, were sedated with  $1 \text{ mg kg}^{-1}$  azaperone and  $0.5 \text{ mg kg}^{-1}$  xylazine (AX0.5) IM, and with  $1 \text{ mg kg}^{-1}$  azaperone and  $1 \text{ mg kg}^{-1}$  xylazine (AX1.0) IM.

The onset time of sternal recumbency, safe handling and unsafe handling were recorded.

The HR,  $f_R$ , MAP and body temperature were recorded for up to 60 minutes. Arterial blood gas analysis (pH, PaCO<sub>2</sub>, PaO<sub>2</sub>, SaO<sub>2</sub>, bicarbonate, sodium and potassium) was assessed at 10, 30 and 60 minutes, and lactate was assessed at 30 and 60 minutes. Statistical analysis included paired t-test, and a two-way ANOVA followed Bonferroni's or Tukey's post hoc test. A p value < 0.05 was considered significant.

Sternal recumbency was faster in AX1.0 ( $5.6 \pm 3.0$  minutes) than AX0.5 ( $11.9 \pm 6$  minutes).

No differences in safe handling (AX1.0 =  $11.6 \pm 5.2$  minutes; AX0.5 =  $13.7 \pm 4.5$  minutes)

and in unsafe handling (AX1.0 =  $85.0 \pm 6.7$  minutes; AX0.5 =  $74.6 \pm 12.3$  minutes) were observed. The other parameters remained within its physiological range throughout, except PaO<sub>2</sub> at 30 minutes in both groups (AX1.0 =  $74 \pm 11.6$  mmHg; AX0.5 =  $79 \pm 12.8$  mmHg).

Both protocols led to adequate sedation. Despite no alterations in physiological parameters being detected in any group, oxygen therapy is recommended for the first 30 minutes of chemical restraint in this species.

## **Influence of premedication with Butorphanol or Methadone on the passage of an endoscope through the canine pyloric sphincter**

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Opioid premedication is said to affect gastroduodenal motility and sphincter tone. This blinded clinical study investigated whether premedication with butorphanol or methadone affects ease of passing a duodenal endoscope.

After obtaining owner consent, 20 dogs were randomly assigned to two treatment groups. Intravenous premedication was with butorphanol (0.4 mg kg<sup>-1</sup>) Group B, or methadone (0.3 mg kg<sup>-1</sup>) Group M. General anaesthesia was induced with propofol to effect, and maintained with isoflurane in 100% oxygen. Sedation score was assessed 20 minutes after administering premedication. Induction dose of propofol was recorded. Every five minutes HR, MAP, SpO<sub>2</sub>, fR and Fe'iso were recorded. Spontaneous lower oesophageal and pyloric sphincter opening, presence of oesophageal and duodenal reflux, antral movement and response to endoscopy were recorded as Yes / No. Ease of entering the duodenum (ED) was graded on a four point scale (Matz et al. 1991). Time (seconds) from start of intubation to successful gastroduodenal intubation was recorded. Data were statistically analysed using t-test, Mann-Whitney U test and Fisher Exact test where appropriate. Significance =  $p < 0.05$ .

Median ED score ( $2.5 \pm 1.1$  B,  $4.0 \pm 1.0$  M,  $p = 0.035$ ), time ( $65 \pm 35.5$  s B,  $120 \pm 38.1$  s M,  $p = 0.028$ ) and spontaneous pyloric sphincter opening (7/10 B, 2/10 M,  $p = 0.035$ ) significantly differed between groups with greater ease, shorter time and more frequent spontaneous opening in group B. No other significant differences were found.

In conclusion, duodenal endoscopy was easier after butorphanol premedication in these clinical cases.

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## Sevoflurane effects on NET1 gene expression in canine mammary tumor cells after a 6-hour exposure: preliminary results

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Anaesthetics may promote metastasis via interaction with the neuroepithelial transforming gene 1 (NET1; Shen et al. 2001). The effects of sevoflurane on NET1 expression on canine tumor cells have not been studied previously.

Primary and metastatic canine mammary tumor cell lines were incubated in triplicate with and without sevoflurane (1 – 4 mM) for six hours. Sevoflurane was supplemented hourly to counteract evaporation (Ecimovic et al. 2013). Thereafter, cells were lysed and RNA isolated. Gene expression was analysed with quantitative PCR following a previously described technique (Ecimovic et al. 2011) and reported using a relative quantification assay (comparative cycle threshold method; Ct). Delta Cts were compared using a 3-way ANOVA. Data are presented as changes in the % of mean values between treated cell cultures and baseline. A  $p < 0.05$  was considered significant.

Sevoflurane significantly decreased (-10.2%) or increased (+7.91%) NET1 expression in metastatic tumor cells at 1 mM and 4 mM, respectively. No significant changes were observed in the primary tumor cell line.

In canine mammary tumor cells, sevoflurane significantly influenced NET1 expression with divergent effects depending on the concentration. While this study provides valuable data on the effect of sevoflurane *in vitro*, additional studies with canine patients with mammary tumors are required to elucidate the potential clinical relevance of this phenomenon.

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## Effects of propofol on canine mammary tumor cells NET1 gene expression: a preliminary study for the evaluation of possible antimetastatic properties

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Neuroepithelial transforming gene 1 (NET1) has been associated with malignant behaviors and metastasis potential (Shen et al. 2001). Propofol reduces NET1 expression in human tumor cells (Ecimovic et al. 2014). Its effects on canine tumor cells are unknown. Primary and metastatic canine mammary tumor cell lines were incubated with propofol (1 and 10  $\mu\text{g ml}^{-1}$ ) or culture media alone, each in triplicate. Cells were lysed and RNA isolated without (baseline) or after 12, 24 and 36 hours of propofol exposure. Quantitative PCR was performed and gene expression analysed using a relative quantification assay corresponding to the comparative cycle threshold (Ct) method (Ecimovic et al. 2011). Delta Cts ( $\Delta\text{Ct}$ ) were analysed using a 3-way ANOVA. Significance was set at  $p < 0.05$ . Data are presented as increases or decreases % of mean  $\Delta\text{Ct}$  values compared with mean baseline values.

Results are presented in Table 1.

Both propofol treatments decreased NET1 expression. However, longer exposures showed negligible or no effects. The reported differences may be considered relatively small compared to previous results in human tumor cells (Ecimovic et al. 2014). Further studies are warranted to better understand this phenomenon and the potential clinical implications.

Table 1 – Expression of neuroepithelial transforming gene 1 in primary and metastatic canine tumor cells exposed to propofol compared with baseline (\* =  $p < 0.05$ ).

Time (hours)	Cell line	Propofol	
		1 $\mu\text{g ml}^{-1}$	10 $\mu\text{g ml}^{-1}$
12	Primary	-15.65%*	-19.00%*
	Metastatic	-6.02%*	-6.30%
24	Primary	-22.86%*	-16.61%*
	Metastatic	-1.40%	-2.06%
48	Primary	-7.67%	+18.19%
	Metastatic	-2.23%	+0.66%

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## **A comparison between methadone and buprenorphine for peri-operative analgesia in dogs undergoing ovariohysterectomy**

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This study investigated whether pre-operative methadone provided superior peri-operative analgesia compared to buprenorphine in dogs undergoing ovariohysterectomy. Eighty dogs were recruited for an assessor-blinded, randomised, clinical trial. Dogs received a premedication of 0.05 mg kg<sup>-1</sup> acepromazine (acp) or 10 µg kg<sup>-1</sup> medetomidine (med) combined with either 0.3 mg kg<sup>-1</sup> methadone (MET) or 20 µg kg<sup>-1</sup> buprenorphine (BUP) intramuscularly. Anaesthesia was induced with propofol and maintained with isoflurane in oxygen. Pain was assessed using a dynamic interactive visual analogue (DIVAS) and short form of the Glasgow Composite Pain (GCPS) scale. Assessments were completed prior to premedication, 30 minutes later and every hour for eight hours after premedication. If indicated by the GCPS, rescue analgesia was provided with methadone. If rescue analgesia was not given within 5 hours of premedication, a second dose of test opioid was administered. Meloxicam was administered after the last assessment. Differences in GCPS between groups were compared using a two way repeated measures ANOVA and requirement for rescue analgesia was compared using a Chi-squared test. Data are presented as mean ± SD.

Both groups premedicated with buprenorphine (acpBUP 3.1 ± 0.95, medBUP 3.4 ± 0.95) had significantly higher GCPS scores than those premedicated with methadone (acpMET 2.2 ± 0.95, medMET 2.1 ± 0.95) over time ( $p < 0.001$ ). Rescue analgesia was required by significantly more dogs premedicated with buprenorphine (55%) compared to methadone (20%) ( $p = 0.001$ ).

Methadone produced superior post-operative analgesia compared to buprenorphine in dogs undergoing ovariohysterectomy.

The authors would like to thank Dechra Pharmaceutical Ltd for funding the postgraduate Masters of Meera D. Shah for the duration of this clinical study. They would also like to thank the staff at the Greater Manchester RSPCA hospital for assistance.

## **The analgesic and cardiovascular effects of a constant rate infusion of medetomidine during thoracolumbar hemilaminectomy in dogs: a pilot study**

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The administration of a medetomidine constant rate infusion during hemilaminectomy in dogs was evaluated.

Twelve client-owned dogs randomly received placebo (saline) (PLA group, n = 6) or medetomidine  $1 \mu\text{g kg}^{-1}$  loading dose, followed by  $1.7 \mu\text{g kg}^{-1} \text{hour}^{-1}$  started 10 – 20 minutes before surgical incision (MED group, n = 6). All dogs were premedicated with methadone  $0.2 \text{mg kg}^{-1}$  and acepromazine  $0.01 \text{mg kg}^{-1}$  intravenously, maintained with isoflurane, and received ketamine  $10 \mu\text{g kg}^{-1} \text{min}^{-1}$  intravenously during surgery and morphine  $0.1 \text{mg kg}^{-1}$  epidurally. Invasive arterial blood pressures, HR, ECG and  $\text{SpO}_2$  were monitored. The same investigator, unaware of the treatment, evaluated pain scores for 24 hours postoperatively. Rescue analgesia was provided with fentanyl intraoperatively if invasive SAP increased by  $\geq 20\%$ , or with methadone postoperatively if Glasgow pain score was  $\geq 5/20$ . Nonparametric methods including Mann-Whitney and Bartlett's tests were used for statistical analysis.

There were no statistically significant differences between groups for the median total dose of fentanyl [MED and PLA groups  $0.007 (0 - 0.03) \mu\text{g kg}^{-1} \text{min}^{-1}$  and  $0.12 (0.03 - 0.23) \mu\text{g kg}^{-1} \text{min}^{-1}$  respectively,  $p = 0.139$ ], lag times for intra- and postoperative rescue analgesia, postoperative pain scores or amount of methadone for 24 hours. No differences were found for the cardiovascular data collected.

Taking into account the small sample size as a given, both protocols produced similar analgesia and rescue drug requirement. A larger study (22 animals per group for 80% power) to reach statistical significance for the intraoperative fentanyl requirement is needed.

## Is methadone administration every four hours needed after uncomplicated Tibial Plateau Levelling Osteotomy in dogs?

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Efficacy and side effects of postoperative methadone administered according to pain scoring (PS) or every four hours (Q4) after Tibial Plateau Levelling Osteotomy (TPLO) have not been compared in dogs.

Complete clinical records of dogs that underwent a unilateral uncomplicated TPLO in 2015, and in which a peripheral nerve block (PNB) was performed, were retrieved and assigned to group Q4 or PS, if the short-form of the Glasgow Composite Measure Pain Scale (Reid et al. 2007) was used to monitor analgesia. Frequency of side effects ascribable to methadone was recorded (Table 1); median pain scores and food intake were calculated. Fisher's exact test or Mann Whitney U test were used, considering  $p < 0.05$  significant.

The files retrieved were 148: 94 were assigned to group PS, 54 to group Q4. Results are presented in Table 1.

Administration of methadone Q4 may cause more side effects compared to administration according to PS without providing superior analgesia in the population examined.

	Methadone following pain scoring	Methadone every four hours	$p$ value
Food intake (%)	88 (0 – 100)	50 (0 – 100)	0.0016
Unsettled (%)	37	37	1
Vocalisation (%)	13	35	0.0038
Vomiting (%)	0	17	0.0006
Reacting to wound palpation (%)	48	32	0.0551
Painful (%)	6	18	0.044
Pain score 0 – 12 hours	2.5 (0 – 8)	2 (1 – 8)	0.25
Pain score 12 – 24 hours	2.5 (1 – 6)	2 (0 – 6)	0.54

Table 1. Median (range) of food intake and pain scores, % of side effects recorded in the two groups.

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## Hemodynamic effects of MK-467 in combination with dexmedetomidine following IM administration in cats

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The hemodynamic effects of the peripheral alpha-2 adrenoceptor antagonist MK-467 in combination with dexmedetomidine, were evaluated following IM administration in five cats anesthetized with isoflurane in oxygen. Instrumentation included venous, carotid, and pulmonary arterial catheters and ECG. All cats received dexmedetomidine (25 µg kg<sup>-1</sup>) IM, with or without MK-467 (600 µg kg<sup>-1</sup> IM). Hemodynamic variables, arterial and mixed venous blood were obtained prior to, and at various times for 6 hours following, drug administration. Data were analyzed by repeated measures ANOVA followed by Dunnett's and paired t-tests where appropriate. Selected results are summarized (mean ± SD) below.

Time (minutes)	Dexmedetomidine			Dexmedetomidine + MK-467		
	-15	10	30	-15	10	30
Heart rate (bpm)	186 ± 75	130 ± 28*	135 ± 27	166 ± 16	146 ± 11	143 ± 11
Mean arterial pressure (mm Hg)	88 ± 20	171 ± 14*	155 ± 14*	96 ± 34	98 ± 9 <sup>†</sup>	73 ± 5 <sup>†</sup>
Cardiac index (L min <sup>-1</sup> BW <sup>-0.67</sup> )	0.23 ± 0.08	0.12 ± 0.04*	0.12 ± 0.04*	0.20 ± 0.05	0.18 ± 0.05	0.19 ± 0.03
Systemic vascular resistance index (dynes sec cm <sup>-5</sup> BW <sup>-0.67</sup> )	27,926 ± 5,854	119,432 ± 40,423*	104,251 ± 42,941*	36,504 ± 13,136	41,479 ± 7,908 <sup>†</sup>	28,254 ± 4,090 <sup>†</sup>
Oxygen delivery index (mL min <sup>-1</sup> BW <sup>-0.67</sup> )	30 ± 11	22 ± 9	21 ± 9	27 ± 14	24 ± 6	18 ± 10

\* and <sup>†</sup> significantly (p < 0.05) different from -15 minutes and dexmedetomidine at that time point, respectively.

MK-467 minimized the vasoconstrictive effect of dexmedetomidine.

This study was funded by the Winn Feline Foundation and the Center for Companion Animal Health (CAAH) at the UC Davis School of Veterinary Medicine.

## **Monitoring acute equine head-related pain with the Equine Utrecht University Scale for Facial Assessment of Pain (EQUUS-FAP)**

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Several studies have shown the usefulness of facial expression to assess pain in horses after castration (Dalla Costa et al. 2014) and in acute colic (Van Loon and Van-Dierendonck 2015).

The current study presents the validation of a recently described pain scale, the Equine Utrecht University Scale for Facial Assessment of Pain (EQUUS-FAP), in horses with acute or postoperative pain originating from the head (dental, ocular pain or trauma to the skull). A cohort follow-up study using 46 adult horses ( $n = 23$  patients with head-related pain, 9 of these presented with acute pain and 20 comprised the postoperative pain group,  $n = 23$  healthy control animals) was performed for validation of the EQUUS-FAP scale for this type of pain. Pain scores were acquired by two independent observers. Inter-observer reliability was assessed using Intraclass Correlation Coefficients (ICC). Differences in scores between controls and patients were analyzed using Kruskal-Wallis test, with post-hoc Mann-Whitney tests with Bonferroni correction for multiple comparisons. Statistical significance was accepted at  $P < 0.05$ .

Significant differences between control horses (2 (2-5)) (median (range)) and horses with acute (6 (3-14)) or postoperative pain (5 (1-11)) were found ( $P < 0.001$ ) and pain scores after surgery decreased significantly ( $P < 0.001$ ). The scale showed good inter-observer reliability (ICC = 0.92) and good sensitivity and specificity (80% and 78% respectively). The results of this study show that EQUUS-FAP can be used for reliable and reproducible pain assessment in horses with acute and postoperative pain originating from the head.

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This study was partly funded by Boehringer Ingelheim BV, Alkmaar, The Netherlands.

## **Isoflurane MAC-Sparing Effects of Fentanyl in the Dog**

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The ability of fentanyl to decrease anaesthetic requirements has been incompletely characterised in dogs. We aimed to describe the isoflurane (ISO) MAC-sparing effect in this species.

8 purpose-bred beagle dogs were anaesthetised using ISO alone and MAC was determined in duplicate by the bracketing method via the use of electrical stimulus applied to the dorsal surface of the pes. Animals then randomly received a low dose ( $30 \mu\text{g kg}^{-1}$  loading dose,  $0.2 \mu\text{g kg}^{-1} \text{ minute}^{-1}$ ) or high dose ( $90 \mu\text{g kg}^{-1}$  loading dose,  $0.6 \mu\text{g kg}^{-1} \text{ minute}^{-1}$ ) of fentanyl (Murphy & Hug 1982) in a cross-over design and MAC re-determined after one hour of infusion. Results were analysed for normality by inspection of normal quantiles, which showed all data was normally distributed. Isoflurane MAC values were analysed by one-way ANOVA for repeated measures with Tukey's test for multiple comparisons. Percentage MAC reduction data was evaluated by t-test. Changes were considered significant with  $p \leq 0.05$ . Isoflurane MAC was  $1.30 \pm 0.20\%$ , which was decreased to  $0.75 \pm 0.22\%$  and  $0.29 \pm 0.11\%$  with the low and high dose, respectively. This correlated to a MAC reduction of  $43 \pm 9\%$  and  $78 \pm 7\%$ , respectively, with the low dose showing less MAC reduction than the high dose. There was no difference in initial MAC between experiments. Fentanyl in both dose groups reduced MAC, with the higher dose showing greater efficacy than the lower.

### Reference

Murphy MR & Hug CC Jr. (1982) The anesthetic potency of fentanyl in terms of its reduction of enflurane MAC. *Anesthesiology* 57, 485-488.

Funding for this study was supplied by the Veterinary Memorial Fund at the Virginia-Maryland College of Veterinary Medicine

## Effects of low-dose intramuscular alfaxalone in dogs

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Alfaxalone provides dose-dependent sedation and anesthesia in dogs at doses between 2.5 and 10 mg kg<sup>-1</sup> IM (Tamura et al. 2015; Tamura et al. 2016). This study describes the effects of alfaxalone at 1 and 2 mg kg<sup>-1</sup> IM in dogs.

Ten adult mixed-breed dogs were assigned to receive one of three injections [saline 0.1 mL kg<sup>-1</sup> (S), alfaxalone 1 mg kg<sup>-1</sup> (A1), or alfaxalone 2 mg kg<sup>-1</sup> (A2)] using a randomized crossover design. Heart rate, *fR*, and sedation score (modified from Hofmeister et al. 2010) were assessed before injection (T0) and at 5 (T5), 10 (T10), 15 (T15), 20 (T20), 30 (T30), 45 (T45), and 60 (T60) minutes post-injection. A Friedman test and Dunn's multiple comparisons test evaluated differences in non-parametric data. A one-way repeated-measures ANOVA evaluated differences in parametric data. Adverse effects were recorded. There were no differences between or within groups in HR or *fR*. Sedation score [median (range)] was higher in the A2 group at T15 [5.5 (-1-13)] and T30 [5.5 (-1-13)] compared to the S group at T15 [0 (-3-4)] ( $p = 0.042$ ) and T30 [1 (-2-4)] ( $p = 0.042$ ). Adverse effects were observed in both A1 and A2 groups. These included ataxia (17/20), auditory hyperesthesia (5/20), visual disturbance (5/20), pacing (4/20), and tremor (3/20).

While alfaxalone at 2 mg kg<sup>-1</sup> IM resulted in greater median sedation scores compared to saline, the range was high and adverse effects frequent. Neither protocol alone can be recommended for providing sedation in healthy dogs.

### References

Tamura J, Ishizuka T, Fukui S et al. (2015) The pharmacological effects of the anesthetic alfaxalone after intramuscular administration to dogs. *J Vet Med Sci* 77, 289-296.

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## **Assessment of the sedative and gastrointestinal effects of different combinations of detomidine and methadone in standing horses**

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This blinded, randomised, cross-over, prospective study assessed sedation and gastrointestinal motility (GIM) after different combinations of detomidine and methadone in horses.

Eight horses received IV saline (SAL), 5 µg kg<sup>-1</sup> detomidine (DET), 0.2 mg kg<sup>-1</sup> methadone alone (MET), or combined with 2.5 (MLD), 5 (MMD) or 10 (MHD) µg kg<sup>-1</sup> detomidine. Head height above ground (HHAG) (cm) was measured and a visual analogue scale for ataxia, responses to tactile and audiovisual stimuli and GIM scored at 5/15/30/45/60/75/90/120/180 minutes (GIM not at 5). Mixed-model ANOVA was used for HHAG and GIM and Kruskal-Wallis for remaining data ( $p < 0.05$ ).

Minimal HHAG values were: SAL (96 ± 6), MET (102 ± 7), DET (49 ± 26), MLD (94 ± 16), MMD (68 ± 22) and MHD (41 ± 29) at 15 minutes. Compared to baseline, HHAG was only lower after DET and MMD for 30 minutes and after MHD for 45. Between treatments, after DET, HHAG was lower than SAL, MET and MLD for 30 minutes. After MMD, HHAG was lower than SAL and MLD for 15 minutes and MET for 30. After MHD, HHAG was lower than SAL, MET, MLD and MMD for 45 minutes. Concerning the other sedation parameters only lower responses to tactile stimuli after MHD than DET at 15 and 45 minutes occurred. GIM was reduced for 75 minutes in MHD and for 30 in all other groups.

Methadone did not potentiate detomidine-induced sedation. MMD produced shorter, less evident sedation than MHD, minimizing associated GIM side-effects.

Source of funding: São Paulo Research Foundation (FAPESP). Process 2014/00474-5 and 2010/08967-0

## **A novel approach for regional anaesthesia of the ear in horses: a descriptive clinical study**

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The aim of this study was to evaluate the efficacy and safety of a novel approach for regional anaesthesia of the ear in horses, previously described in a cadaver study (Cerasoli et al. 2015).

Regional anaesthesia of both ears was performed in eight healthy experimental horses, using 12 mL of either lidocaine 2% (L) or mepivacaine 2% (M) on 2 different occasions (randomized order). All horses were sedated using a constant rate infusion of detomidine (0,008 mg kg<sup>-1</sup> IV; 0,006 mg kg<sup>-1</sup> hour<sup>-1</sup>). Before and at prefixed timepoints after injection of the local anaesthetic, mechanical stimulation with forceps, electrical stimulation, and stylet insertion in the ear canal were applied. The reactions were recorded until baseline conditions were restored. The presence of side effects was monitored and recorded daily during two weeks.

In both groups the pinna was partially unresponsive to forceps stimulation in 100% of the horses. No response to electrical stimulation (> 2 times the baseline threshold) was seen in 37,5 and 25% of the horses in group L for respectively the right and left ears, and in 75% in group M, for both ears. Stylet insertion was possible in 25% and 62,5% of the horses in group L and M respectively. No adverse events were noted.

Lidocaine 2% resulted in a less reliable regional block compared to mepivacaine 2%. Although a complete desensitization of the region is not guaranteed, this technique can safely be used in a multimodal analgesic approach of the auricular region of horses.

### References

Cerasoli I, Cornillie P., Gasthuys F. et al. (2015) "A novel approach for the internal and lateral auricular branch of the facial nerve and the caudal and great auricular nerve in horses: an anatomical study" Proceedings WCVA meeting Kyoto, pg 155.

## Cardiopulmonary effects of MK-467, a peripheral alpha<sub>2</sub>-adrenoceptor antagonist, in sheep receiving medetomidine-ketamine

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MK-467 attenuates the peripheral effects of various alpha<sub>2</sub>-agonists in many animal species. We investigated the cardiopulmonary effects of MK-467 administered IM with medetomidine-ketamine in sheep.

Nine adult healthy female sheep received two treatments in a randomized, assessor-blinded, cross-over design: medetomidine 30 µg kg<sup>-1</sup> and ketamine 1 mg kg<sup>-1</sup> (MED) and MED with MK-467 300 µg kg<sup>-1</sup> (MMK). Drugs were administered IM in the same syringe. Systemic hemodynamics and arterial oxygen tensions were measured before treatments and at intervals thereafter. Sedation was assessed subjectively. Data were analyzed with repeated measures ANOVA and post hoc Bonferroni tests with P < 0.05 considered as significant. Hemodynamic data are summarized in Table 1. Both treatments produced deep sedation. We conclude that MK-467 attenuated the adverse cardiopulmonary influences, such as a decrease in PaO<sub>2</sub> and bradycardia induced by medetomidine-ketamine in sheep, without significantly affecting sedation quality.

Table 1.

	Treatment	Time (minutes)		
		Baseline	15	45
HR (beats min <sup>-1</sup> )	MED	74.7 ± 8.8	55.2 ± 9.5 <sup>†</sup>	54.1 ± 6.7 <sup>†</sup>
	MMK	76.3 ± 13.6	62.7 ± 10.2	76.7 ± 19.8 <sup>*</sup>
MAP (mmHg)	MED	103.1 ± 5.6	116.8 ± 11.2	106.0 ± 19.4
	MMK	105.3 ± 10.4	107.0 ± 6.8	77.4 ± 13.9 <sup>†*</sup>
CO (L min <sup>-1</sup> )	MED	4.4 ± 0.8	3.7 ± 1.3	3.9 ± 1.0
	MMK	4.9 ± 0.9	4.6 ± 1.6	4.1 ± 0.6
PaO <sub>2</sub> (mmHg)	MED	97.2 ± 7.8	70.2 ± 11.7 <sup>†</sup>	74.9 ± 10.0 <sup>†</sup>
	MMK	99.5 ± 2.1	79.2 ± 11.8 <sup>†</sup>	92.9 ± 8.0 <sup>*</sup>

<sup>†</sup>within treatment, significantly different from baseline; <sup>\*</sup> within time-point, significant difference between treatments.

Supported by Vetcare, Ltd, Finland

## Effective plasma alfaxalone concentration in cats

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Alfaxalone is widely used in feline anesthesia. However, its effective plasma concentration has not been determined.

Sixteen healthy adult male neutered cats were used. Catheters were placed in a jugular and medial saphenous vein under isoflurane anesthesia the day prior to the study. Cats were administered alfaxalone (alfaxalone in cyclodextrin, RD0327 preserved formulation) via the medial saphenous catheter, using a target-controlled infusion (TCI) system, for 32 minutes, starting at time 0. The pharmacokinetic parameters used for TCI were obtained from a previous study in 24 cats using the same formulation (Jurox Ltd, unpublished data). The cat's tail was clamped at time 30 minutes for 1 minute, or until movement was observed, whichever occurred first. Target concentration was 5  $\mu\text{g mL}^{-1}$  in the first cat and was adjusted by 1  $\mu\text{g mL}^{-1}$  in subsequent cats, based on the response of the previous cat. Blood samples (2 mL) were collected from the jugular catheter prior to drug administration, and at times 15 and 32 minutes. The plasma was separated and frozen at  $-80^{\circ}\text{C}$  until analysis. Plasma alfaxalone concentrations were determined using liquid chromatography/tandem mass spectrometry. Logistic regression was applied to the concentration-response data. The plasma alfaxalone concentrations corresponding to a 50 and 99% probability of prevention of movement ( $\text{EC}_{50}$  and  $\text{EC}_{99}$ , respectively), and their 95% Wald confidence intervals were calculated.

The alfaxalone  $\text{EC}_{50}$  and  $\text{EC}_{99}$  were 3.7 (2.4-4.9) and 7.6 (5.5-9.7)  $\mu\text{g mL}^{-1}$ , respectively. The effective plasma alfaxalone concentration was determined in cats and can be used to establish appropriate dosing.

This study was funded by Jurox Ltd.

## Cardiopulmonary effects of anaesthesia maintained by propofol infusion versus isoflurane inhalation in cheetah (*Acinonyx jubatus*)

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This study compared cardiopulmonary function in cheetah (*Acinonyx jubatus*) undergoing propofol total intravenous anaesthesia (TIVA) to isoflurane maintenance to evaluate feasibility for field use.

Twenty-four adult cheetah were immobilised with zoletil (1.2 mg kg<sup>-1</sup>) and medetomidine (40 µg kg<sup>-1</sup>) IM by darting. A maintenance protocol of propofol TIVA (Group-P) or isoflurane inhalation (Group-I) was randomly assigned to each cheetah. Anaesthesia was maintained for at least 60 minutes. Cardiopulmonary parameters were recorded at five minute intervals and three arterial blood gas samples analysed. Following maintenance, atipamezole was administered (100 µg kg<sup>-1</sup> IM) and recovery observed. Data is reported as mean ± SD; variables over time were compared using a linear mixed model (fixed: time, treatment; random: cheetah).

Lack of response to manipulations was maintained in all cases (end tidal isoflurane 1.1 ± 0.1%, propofol rate maintained at 0.1 mg kg<sup>-1</sup> minute<sup>-1</sup>). The HR and fR were 82 ± 10 beats minute<sup>-1</sup> and 14 ± 4 breaths minute<sup>-1</sup>, respectively. The P<sub>E'</sub>CO<sub>2</sub> increased slowly (44.0 ± 5.0 mmHg) with no differences between groups. All cheetah were initially markedly hypertensive (invasive MAP 163.3 ± 17 mmHg); MAP normalised for Group-I (125 ± 30 mmHg) but remained high for Group-P (161.0 ± 17 mmHg) (p < 0.001). The PaCO<sub>2</sub> (48.9 ± 14.6 mmHg) never differed between groups. Recovery time was 10.8 ± 5.0 and 51.9 ± 23.5 minutes for Group-I and Group-P, respectively.

Both protocols provided acceptable cardiopulmonary values. Propofol may be an alternative to isoflurane for field use, but the prolonged recovery requires investigation.

The authors wish to thank HW-SETA and the Department of Companion Animals, University of Pretoria for funding.

## Comparison of intramuscular butorphanol and buprenorphine combined with dexmedetomidine for sedation in cats

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Sedation following butorphanol or buprenorphine combined with dexmedetomidine has not been compared in cats.

Using a prospective, randomized, blinded design, dexmedetomidine (0.01 mg kg<sup>-1</sup>) combined with either butorphanol (0.4 mg kg<sup>-1</sup>) or buprenorphine (0.02 mg kg<sup>-1</sup>) was compared after IM injection in 40 client-owned adult cats requiring sedation for IV catheterisation. Sedation was scored before (0) and 5, 10, 15 and 20 minutes afterwards (10 = maximum sedation) (Santos et al. 2010). Alfaxalone (1.5 mg kg<sup>-1</sup>) was administered IM at T20 if IV catheterisation was unachievable. Adverse events were recorded. Friedman two-way ANOVA analysed sedation scores within groups. Mann-Whitney Rank Sum test compared sedation scores between groups; Fisher Exact test analysed frequency of alfaxalone administration and adverse events.  $p < 0.05$  was considered significant. Data from 37 cats (18 butorphanol, 19 buprenorphine) were analysed, three were excluded. Results are shown in table 1.

At these doses, IM butorphanol-dexmedetomidine provides superior sedation to buprenorphine-dexmedetomidine in cats with a lower incidence of vomiting.

Time (minutes)	0	5	10	15	20	Alfaxalone (n)	Vomiting (n)
Butorphanol (n = 18)	2 (0-5) ace	5 (2-10) bd*	7 (3-10) a*	8 (3-10) bc*	8 (4-10) de*	2	1*
Buprenorphine (n = 19)	1 (0-5) ace	2 (0-6) bd*	5 (0-8) a*	6 (3-8) bc*	7 (3-9) de*	5	11*

Table 1. Sedation scores [median (range)], number (n) of cats requiring alfaxalone and vomiting after butorphanol-dexmedetomidine or buprenorphine-dexmedetomidine.

Within same line, same letters indicate  $p < 0.05$ .

Within same column (\*) indicates  $p < 0.01$ .

### Reference

Santos LCP, Ludders JW, Erb HN et al. (2010) Sedative and cardiorespiratory effects of dexmedetomidine and buprenorphine administered to cats via oral transmucosal or intramuscular route. *Vet Anaesth Analg*: 37, 417-424.

## Single dose analgesic efficacy of butorphanol, morphine, lidocaine, bupivacaine or carprofen after periodontal treatment in dogs: A clinical, randomized, double blind, placebo-controlled study

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Effectiveness of analgesics after periodontal treatment was investigated. Eighty-four dogs were allocated into groups (n = 14): SAL (saline 0.02 ml kg<sup>-1</sup> IM), BUT (butorphanol 0.2 mg kg<sup>-1</sup> IM), MOR (morphine 0.3 mg kg<sup>-1</sup> IM), CAR (carprofen 4 mg kg<sup>-1</sup> IM), LID (lidocaine 2 mg kg<sup>-1</sup> maxillary and mandibular blocks) or BUP (bupivacaine 1 mg kg<sup>-1</sup> maxillary and mandibular blocks). Pain was assessed 2 hours after treatment using a Visual Analog Scale (VAS) and a modified University of Melbourne Pain Score (UMPS); blood glucose and cortisol concentrations were measured before and 2 hours after treatment. Rescue analgesia was provided when VAS > 50 mm or UMPS > 14 points. For statistical analysis ANOVA and Mann-Whitney U-test were used. Rescue analgesia was necessary in 1 MOR and 1 CAR.

Table: Post treatment values

	VAS	UMPS	Glucose (mmol l <sup>-1</sup> )	Cortisol (nmol l <sup>-1</sup> )
SAL	29 (24 – 40)	4 (3 – 7)	6.3 (4.1 – 8.2)	103.0 (71.2 – 180.0)
BUT	22 (15 – 31)*	4 (2 – 7)	6.1 (5.8 – 7.9)	81.5 (37.6 – 255.0)
MOR	21 (9 – 55)	3 (0 – 11)	6.7 (5.8 – 11.9)	156.0 (45.8 – 601.0)
LID	29 (20 – 40)	4 (2 – 11)	7.4 (5.0 – 10.0)	172.0 (108.0 – 518.0)^
BPU	18 (2 – 26)*†	2 (0 – 4)*†‡	6.5 (4.4 – 10.1)	75.0 (27.6 – 460.0)
CAR	23 (5 – 52)†	2 (1 – 7)*†	6.8 (5.4 – 8.7)	134.0 (45.1 – 368.0)

\*lower than SAL; †lower than LID; ‡lower than BUT; ^higher than SAL, BUP and CAR; p < 0.05

Carprofen IM or a bupivacaine block produced better analgesia than butorphanol, morphine or lidocaine.

This work was supported by the Ministry of Education, Youth and Sports of the Czech Republic (Research Project IGA VFU No. 60/2012/FVL).