

Acid-base balance during volatile and total intravenous anaesthesia in dogs

Hroje Capak¹, Zrinka Filipović-Genter², Višnja Nesek-Adam³,
Silvijo Vince⁴, Srećko Solina⁵, Damir Milas⁵, and Darko Capak^{6*}

¹Department of Radiology, Ultrasound Diagnostic and Physical Therapy, Faculty of Veterinary Medicine, University of Zagreb, Zagreb, Croatia

²Veterinary practice "Pets2Vets", Koprivnica, Croatia

³Department of Anaesthesiology, Resuscitation and Intensive Care, Sveti Duh General Hospital, Zagreb, Croatia

⁴Clinic of Obstetric and Reproduction, Faculty of Veterinary Medicine, University of Zagreb, Zagreb, Croatia

⁵PhD student, Faculty of Veterinary Medicine, University of Zagreb, Zagreb, Croatia

⁶Clinic of Surgery, Orthopaedics and Ophthalmology, Faculty of Veterinary Medicine, University of Zagreb, Zagreb, Croatia

CAPAK, H., Z. FILIPOVIĆ-GENTER, V. NESEK-ADAM, S. VINCE, S. SOLINA, D. MILAS, D. CAPAK: Acid-base balance during volatile and total intravenous anaesthesia in dogs. Vet. arhiv 87, 281-289, 2017.

ABSTRACT

The aim of this study was to compare the effects of two different anesthetic techniques on the acid base balance in bitches. Research was carried out on 20 bitches randomly divided into two groups. In group A general anaesthesia was induced by intravenous application of ketamine and diazepam, and maintained with an additional intravenous bolus of ketamine. In group B a combination of propofol and ketamine was used for induction of anaesthesia. General anaesthesia was maintained with N₂O and O₂ in a range of 1:1 in combination with 2% isoflurane. Animals in both groups were kept on spontaneous ventilation. Arterial blood for blood gas analysis was taken at two time points (3 and 45 min. after induction of anaesthesia, respectively). Group A had a significantly (P<0.05) higher pH value than Group B at 45 min. The pCO₂ was significantly (P<0.05) lower in group A than in group B at 3 and 45 min, respectively. There was also a significant difference in values of pO₂ between the groups at 3 and 45 min. The pO₂ was lower in group A than in group B. Group B had a significantly (P<0.05) higher HCO₃⁻ value than Group A at 45 min. Volatile anaesthesia minimally disturbs acid-base balance, and oxygen access capability is better.

Key words: acid-base balance, inhalation anaesthesia, total intravenous anaesthesia, dogs

*Corresponding author:

Darko Capak, PhD, Full Professor, Clinic of Surgery, Orthopaedics and Ophthalmology, Faculty of Veterinary Medicine, Heinzelova 55, 10000 Zagreb, Croatia, Phone: +385 1 2390 383; E-mail: dcapak@vef.hr

Introduction

Body fluids are dynamic compartments with various functions essential for physiological and biochemical processes. All life's processes are supported with body fluids in which electrolytes and proteins are dissolved. Electrolytes are essential cofactors in enzymatically maintained metabolic reactions. Regulation of pH involves the following: extracellular and intracellular buffering, alveolar ventilation and carbon dioxide concentration, and regulation of renal hydrogen excretion. The pH of body fluids is a control mechanism for the structure and function of proteins, and subsequently maintaining metabolic reactions in progression. Fluid and electrolyte balance is controlled by every organ system and *vice versa* every organ system is affected by fluid and electrolyte imbalances. Fluid and electrolyte imbalances can be caused by insufficient fluid intake, excessive fluid losses, inappropriate therapy and anaesthesia (CARLSON and BRUSS, 2008).

Partial pressure of carbon dioxide ($p\text{CO}_2$) is the most frequently used index of the respiratory system's response to general anesthetics. The respiratory pattern may be altered by the induction and deepening of anaesthesia. When the depth of anaesthesia is inadequate, the respiratory pattern may vary from hyperventilation to an apneustic respiratory pattern. Hyperventilation can be defined as increased alveolar ventilation, and the common cause is too light anaesthesia. Hyperventilation causes respiratory alkalosis. However, an inhalant anesthetic may also depress alveolar ventilation and increase CO_2 in a dose dependent manner (STEFFEY and MAMA, 2007). Hypoventilation causes carbon dioxide retention and respiratory acidosis. Animals suffering from gastrointestinal tract obstruction, or renal and respiratory disease have a mixed acid-base disorder of metabolic alkalosis with respiratory acidosis (HA et al., 2013).

The choice of anesthetic agent should therefore be adjusted, depending on its pharmacokinetic and pharmacological actions, in addition to the patient's underlying condition.

Medetomidine is an α_2 adrenergic receptor agonist, potential sedative and analgesic (CONGDON et al., 2011). Ketamine is a partially water- and high lipid-soluble dissociative anesthetic, with potent analgesic properties and with minimal production of respiratory depression (EILERS, 2007). This theory is supported by other authors (KENNEDY and SMITH, 2015). Propofol is rapidly metabolized in the liver and extracted by the kidney. It decreases cerebral blood flow and intracranial and intraocular pressure. It may cause metabolic acidosis, which can be attributed to respiratory depression (EILERS, 2007) and increasing bicarbonate ions (HCO_3^-) (ALMEIDA et al., 2007). Propofol produces a decrease in blood pressure due to vasodilatation in the arterial and venous circulation, and consequently reduces cardiac preload and afterload. It also inhibits the baroreflex response thus causing a hypotensive effect and bradycardia. The induction dose of propofol can vary

often cause apnea and consequently hypoxia and hypercapnia. Unexpected tachycardia may occur during propofol anaesthesia, which requires prompt attention with acid-base balance electrolytes assessment (EILERS, 2007).

The minimum alveolar concentration (MAC) of inhaled anesthetics increases with age and electrolyte concentration, especially hypernatremia, whereas, MAC decreases with propofol, ketamine and benzodiazepines (McKAY et al., 2007). Isoflurane is generally considered the most widely used inhalant anesthetic in veterinary medicine (STEFFEY and MAMA, 2007).

The purpose of the current study was to determine the metabolic effects of anesthetics and also to determine the best combination of drugs to carry out surgical procedures successfully.

Materials and methods

Twenty bitches between the ages of 6 months and 5 years were included in the study and divided into two groups. According to physical examination and blood work all the animals were considered healthy and assigned to the American Society of Anesthesiologists (ASA) category 1.

The study was approved by the Ethical Committee of the Veterinary Faculty and the owners' consent was obtained. The bitches underwent ovariohysterectomy, performed by ventral midline laparotomy, according to routine methods. All surgical procedures were done by the same surgeon. All animals were premedicated with medetomidine (Domitor[®], Pfizer Animal Health, USA) in doses of 0.01 mg/kg and metadone (Heptanon[®], Pliva, Croatia) in doses of 0.2 mg/kg applied intramuscularly. The induction of anaesthesia was performed 15 minutes after i/m administration of premedication in all animals.

In group A general anaesthesia was induced with ketamine (Ketaminol[®], Vetoquinol, Switzerland) in a dose of 8 mg/kg i/v, and diazepam in a dose of 0.20 mg/kg i/v. Endotracheal intubation was performed, in case animal stopped breathing and immediate ventilation was necessary. In order to maintain general anaesthesia ketamine was applied if needed in a dose of 3 mg/kg i/v.

In group B a combination was used of diazepam in a dose of 0.20 mg/kg i/v, propofol (Propofol[®], 1%, Fresenius Cabi, Austria) in dose of 2 mg/kg i/v and ketamine (Ketaminol[®], Vetoquinol, Switzerland) in dose of 1 mg/kg i/v for endotracheal intubation. Following endotracheal intubation anaesthesia was maintained with N₂O and O₂ in ratio of 1:1, in combination with 2% isoflurane (Forane[®], Abbott, UK) with nitrous oxide and oxygen flow 1 L/min totally.

After the induction of anaesthesia, a solution of 0.9% sodium chloride was infused continuously at a rate of 10 mL/kg/h in both groups. A blood gas sample for acid-base

assessment was taken intraoperatively from both groups at 3 and 45 minutes after induction of anaesthesia. Samples were collected from the metatarsal artery into a 2 mL commercial preheparinized syringe (BD Vacutainer® Eclipse™ Arterial Blood Syringe, UK). Immediately after collection, cooled blood samples were delivered to laboratory, and all blood gas analyses were done in 30 minutes after blood sampling. Statistical analyses were performed using SAS 9.3 software (2002-2010 SAS Institute Inc., Cary, NC, USA). The generalized linear mixed model (proc glimmix) was used to analyze the pH and blood gas parameters. The statistical model included the fixed effects of group, time of blood sampling and their interactions, as well as animal age and body weight as covariates. The animal effects on repeated measures over time were included in the model by random statement, with residual option and simple structure. A multiple comparison test of least-squares means with Tukey correction was performed using the slice option to compare each level of group within each level of blood sampling time and conversely. Results are expressed as least squares means and a 95% confidence interval (lsm and 95% CI). To analyze the correlations between variables, corr procedure was used. The level of statistical significance was set at $P < 0.05$.

Results

According to the blood gas analysis, a gradual increase in pH was observed during experimental protocol. The value of pH was significantly higher in group A than in group B (7.32; 7.30-7.34 vs. 7.29; 7.27-7.31) at 45 min after induction of anaesthesia (Fig. 1.).

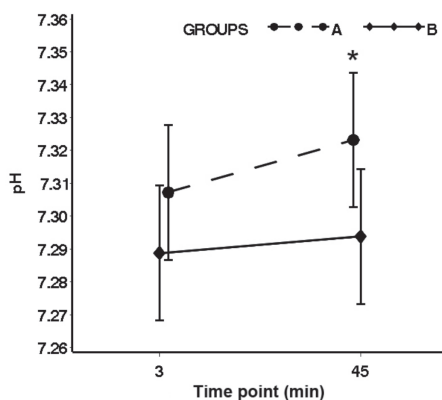


Fig. 1. Least squares means and 95% confidence interval of pH in bitches with total intravenous anaesthesia (TIVA) - group A, and anaesthetized with volatile anesthetic - group B at two time points

No statistically significant differences were observed in $p\text{CO}_2$ at 3 and 45 min following anaesthesia in either group. The $p\text{CO}_2$ was significantly lower in group A than in group B at 3 (5.09; 4.41-5.77 v. 6.26; 5.58-6.93) and 45 minutes following induction of anaesthesia (4.99; 4.32-5.67 v. 6.28; 5.61-6.96) (Fig. 2).

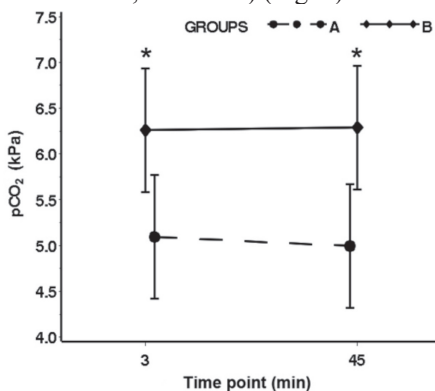


Fig. 2. Least squares means and 95% confidence interval of serum $p\text{CO}_2$ in bitches with total intravenous anaesthesia (TIVA) - group A, and anaesthetized with volatile anesthetic - group B at two time points

In group B statistically significant differences in $p\text{O}_2$ were noted between 3 and 45 minutes (19.26; 16.14-22.39 and 24.79; 21.66-27.91) ($P < 0.05$). There were also statistically significant differences between groups A and B, at 3 (19.26; 16.14-22.39 v. 7.95; 4.83-11.07) and 45 minutes (24.79; 21.66-27.91 v. 9.25; 6.13-12.37) ($P < 0.05$) (Fig. 3).

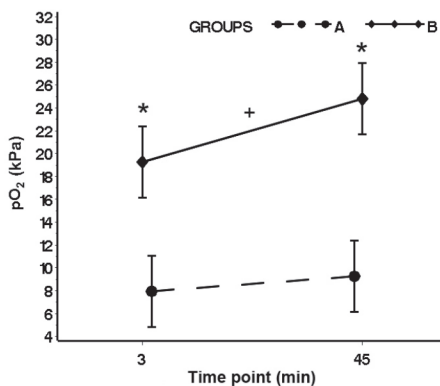


Fig. 3. Least squares means and 95% confidence interval of $p\text{O}_2$ levels in bitches with total intravenous anaesthesia (TIVA) - group A, and anaesthetized with volatile anesthetic - group B at two time points

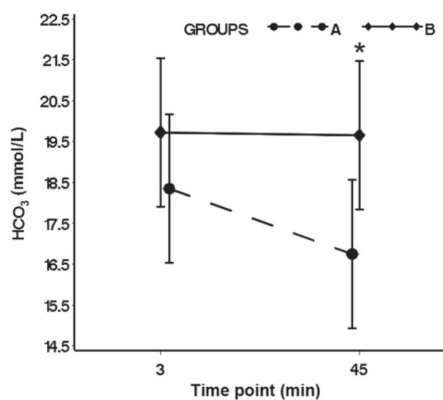


Fig. 4. Least squares means and 95% confidence interval of HCO₃⁻ in bitches with total intravenous anaesthesia (TIVA) - group A, and anesthetized with volatile anesthetic - group B at two time points

No statistical difference was found in HCO₃⁻ in the groups and between the groups at 3 min after induction, but in Group A a decrease in HCO₃⁻ was observed at 45 min compared to group B (19.65; 17.83-21.47 v. 16.74; 14.92-18.56) (P>0.05). (Fig. 4).

Correlation factors between measured blood gases are presented in Table 1. and Fig. 5.

Table 1. Correlation between different parameters

	Body weight	pH	pO ₂	pCO ₂	HCO ₃ ⁻
Body weight	1				
pH	-0.11	1			
pO ₂	0.30	-0.37 *	1		
pCO ₂	0.11	-0.36 *	0.54 ***	1	
HCO ₃ ⁻	0.16	-0.39 *	0.42 **	0.74 ***	1

*P<0.05; ** P<0.01; *** P<0.001

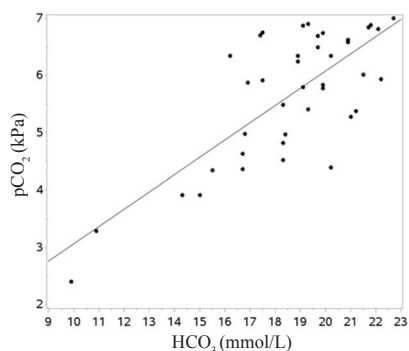


Fig. 5. Correlation between different parameters

Discussion

The concentration of hydrogen and bicarbonate ions in plasma have to be in physiological ranges in order to optimize enzyme activity, hemoglobin saturation with oxygen, myocardial contractility and other chemical reactions within a cell. The alpha-2 agonist, medetomidine was used for premedication in both groups in the same dose. Arterial blood pH, pO₂ and pCO₂ values were not altered regardless of the infusion rate of Ringers Lactate solution, at rates of 0, 10, 20 or 30 mL/kg/h in healthy dogs anesthetized with alpha-2 agonist and isoflurane (MUIR et al., 2011). In the current study, the infusion rate of 0.9% saline solution was 10 mL/kg/h in both groups, and is unlikely to affect pH, pO₂ and pCO₂. All anesthetic drugs (except ketamine and nitrous oxide) cause a dose-dependent reduction in respiratory minute volume. This can be due to a reduction in the respiratory rate (e.g. opioids), a reduction in the tidal volume (e.g. volatile anesthetics) or both (e.g. propofol). As we mentioned before, ketamine induces minimal respiratory depression (EILERS, 2007).

A scientific paper confirmed that healthy Beagle dogs anesthetized with ketamine had minimal respiratory impairment compared with a group anesthetized with ketamine and propofol. Significant changes in respiratory parameter values were attributed to propofol (KENNEDY and SMITH, 2015). In the current research, in group A lower pCO₂, however within the physiological range, was noted owing to tachypnea during spontaneous breathing. The cause of tachypnea could be pain produced by the surgical procedure (especially during suspensory ligament stretching during ovariohysterectomy) or discomfort.

Rabbits premedicated with alpha-2 agonist xylazine and general anaesthesia maintained with isoflurane, showed similar results to the current study, that is slight acidemia and increased pCO₂ (BENATO et al., 2013). A reason for hypercapnia may be

alveolar hypoventilation as a direct impact of anesthetic drug depression of the respiratory center, a presurgical respiratory disease or body positioning.

The value of $p\text{CO}_2$ increased in spontaneously breathing dogs anesthetized with isoflurane and the increase depends on the dose of isoflurane. The lowest increase of $p\text{CO}_2$ was noted with methoxyflurane and enflurane anaesthesia and in dogs in comparison to other species (McDONELL and KERR, 2007).

In one study CONGDON et al. (2011) reported that in dogs premedicated with the α_2 adrenergic receptor agonist dexmedetomidine, with or without atropine, there was no significant effect on pH, $p_a\text{CO}_2$, HCO_3^- and $p_a\text{O}_2$ at any time point in either group and also, there were no differences in comparison with the baseline and physiological values. Only the respiratory rate decreased after 15 minutes of application of the α_2 adrenergic receptor agonist.

HCO_3^- effects the systemic acid-base status and is an important determinant of glomerular filtration rate and skeletal health during aging in humans (TABATABAI et al., 2015)

In conclusion, TIVA with adequate analgesia is acceptable for ovariohysterectomy, although volatile anaesthesia is a better choice because it minimally disturbs the acid-base balance and oxygen access capability.

References

- ALMEIDA, T. F., D. T. FANTONI, S. MASTROCINQUE, A. C. TATARUNS, W. H. IMAGAWA (2007): Epidural anesthesia with bupivacaine, bupivacaine and fentanyl, or bupivacaine and sufentanyl during intravenous administration of propofol for ovariohysterectomy in dogs. *J. Am. Vet. Med. Assoc.* 230, 45-51.
- BENATO, L., M. CHESNEL, K. EATWELL, A. MEREDITH (2013): Arterial blood gas parameters in pet rabbits using a combination of fentanyl-fluanisone-midazolam-isoflurane. *J. Small Anim. Pract.* 54, 343-346.
- CARLSON, G. P., M. BRUSS (2008): Fluid, Electrolyte, and Acid-Base Balance. In: *Clinical Biochemistry of Domestic Animals*. 6th ed. (Kaneko, J. J., Ed.), Academic press, Burlington, pp. 529-559.
- CONGDON, J. M., M. MARQUEZ, S. NIYOM, P. BOSCAN (2011): Evaluation of the sedative and cardiovascular effects of intramuscular administration of dexmedetomidine with and without concurrent atropine administration in dogs. *J. Am. Vet. Med. Assoc.* 239, 81-89.
- EILERS, H. (2007): Intravenous anesthetics. In: *Basics of Anesthesia*. 4th ed. (Stoelting, R. K., R. D. Miller, Eds.), Churchill Livingstone Elsevier, Philadelphia, pp. 97-111.
- HA, Y. S., K. HOPPER, S. E. EPSTEIN (2013): Incidence, nature, and etiology of metabolic alkalosis in dogs and cats. *J. Vet. Intern. Med.* 27, 847-853.
- KENNEDY, M. J., L. J. SMITH (2015): A comparison of cardiopulmonary function, recovery quality, and total dosages required for induction and total intravenous anesthesia with propofol versus a propofol-ketamine combination in healthy beagle dogs. *Vet. Anest. Analg.* 42, 350-359.

- McDONELL, W. N., C. L. KERR (2007): Respiratory system. In: Lumb Jones' Veterinary Anesthesia and Analgesia. 4th ed. (Tranquilli, W. J., J. C. Thurmon, K. A. Grimm, Eds.), Blackwell publishing, Iowa, pp. 117-151.
- McKAY, R. E., J. SONNER, W. R. McKAY (2007): Inhaled anesthetics. In: Basics of Anesthesia. 4th ed. (Stoelting, R. K., R. D. Miller, Eds.), Churchill Livingstone Elsevier, Philadelphia, pp. 77-96.
- MUIR, W. W., A. KIJTAWORNAT, Y. UEYAMA, S. V. RADECKI, R. L. HAMLIN (2011): Effects of intravenous administration of lactated Ringer's solution on hematologic, serum biochemical, rheological, hemodynamic, and renal measurements in healthy isoflurane-anesthetized dogs. *J. Am. Vet. Med. Assoc.* 239, 630-637.
- STEFFEY, E. P., K. R. MAMA (2007): Inhalation anesthetics. In: Lumb Jones' Veterinary Anesthesia and Analgesia. 4th ed. (Tranquilli, W. J., J. C. Thurmon, K. A. Grimm, Eds.), Blackwell publishing, Iowa, pp. 355-393.
- TABATABAI, L. S., S. R. CUMMINGS, F. A. TYLAVSKY, D. C. BAUER, J. A. CAULEY, S. B. KRITCHEVSKY, A. NEWMAN, E. M. SIMONSICK, T. B. HARRIS, A. SEBASTIAN, D. E. SELLMAYER (2015): Arterialized venous bicarbonate is associated with lower bone mineral density and an increased rate of bone loss in older men and women. *J. Clin. Endocrinol. Metab.* 100, 1343-1349.

Received: 9 May 2016

Accepted: 23 November 2016

CAPAK, H., Z. FILIPOVIĆ-GENTER, V. NESEK-ADAM, S. VINCE, S. SOLINA, D. MILAS, D. CAPAK: Acido-bazni status u pasa tijekom inhalacijske i intravenske anestezije. *Vet. arhiv* 87, 281-289, 2017.

SAŽETAK

Cilj je rada usporediti učinke dvaju različitih anestezioloških protokola na acidobaznu ravnotežu. Istraživanje je provedeno na 20 kuja nasumično podijeljenih u dvije skupine. U skupini A indukcija u opću anesteziju učinjena je s ketaminom i diazepamom primijenjenim intravenski te je anestezija održavana bolusima ketamina. U skupini B indukcija prije endotrahealne intubacije učinjena je propofolom i ketaminom. Opća anestezija održavana je s N₂O i O₂ u omjeru 1:1 u kombinaciji s 2% izoflurana. U obje skupine životinje su disale samostalno. Uzorci arterijske krvi uzeti su dva puta, u trećoj i četrdesetpetoj minuti od indukcije. Kod skupine A primijećen je značajno viši pH nego kod skupine B u 45. minuti. Razina pCO₂ bila je značajno niža u skupini A nego u skupini B u oba mjerenja (3. i 45. minuta). Zabilježena je i značajna razlika u pO₂ među istraživanim skupinama u 3. i 45. minuti. Razina O₂ bila je niža u A skupini u odnosu na skupinu B. Skupina B imala je značajno višu vrijednost HCO₃ u odnosu na A skupinu u 45. minuti. Rezultati mjerenja plinova u krvi pokazuju da inhalacijska anestezija minimalno utječe na acidobaznu ravnotežu.

Ključne riječi: acido-bazni status, inhalacijska anestezija, opća intravenska anestezija, pas
