http://dx.doi.org/10.1590/1678-4162-10210

Arq. Bras. Med. Vet. Zootec., **v.71, n.1, p.35-43, 2019**

Blood gas analysis in pigs submitted to different concentrations of nitrous oxide or oxygen, under different ventilatory modalities

[*Estudo hemogasométrico em suínos submetidos a diferentes concentrações de óxido nitroso ou oxigênio, sob diferentes modalidades ventilatórias*]

E.G.F. *Biteli*[1], N. *Nunes*[1], P.C.F. *Lopes*[2], P.E.S. *Silva*[1], C.K. *Ido*[1], H.R.A. *Silva*[1], M. *Horr*[1], R.L. *Carneiro*[1], T.F.V. *Bompadre*[3]

[1]Universidade Estadual Paulista - Jaboticabal, SP
[2]Faculdade Jaguariúna - Jaguariúna, SP
[3]Centro de Energia Nuclear na Agricultura - Piracicaba, SP

ABSTRACT

The effects of different concentrations of oxygen and nitrous oxide on blood gas parameters in pigs maintained under spontaneous or pressure-controlled ventilation, with or without positive end-expiratory pressure (PEEP), were compared. Forty-eight pigs were randomly divided into six groups, submitted to different concentrations of compressed air or N_2O, associated with different fractions of inspired oxygen (FiO_2). The group subject to 30% of compressed air (GA30) showed the closest proximity to the physiological range of partial pressure (PaO_2) expected for the species. For oxygen saturation (SaO_2), the values obtained were below the lower physiological limit in the group administered 30% N_2O (GN30). Use of PEEP positively interfered in $PaCO_2$ independent of FiO_2, however, its effectiveness can be compromised when complemented by N_2O-based anesthesia. For SaO_2, only GN30 showed values lower than adequate for maintaining tissue oxygenation. The pH, base deficit and bicarbonate in arterial blood were influenced by FiO_2 and N_2O. In conclusion, the use of compressed air maintains blood gas parameters at their most stable, especially GA30 and PEEP, which seemed to positively influence the experimental groups, with some interference from FiO_2 and N_2O.

Keywords**:** alkylphenol, atelectasis, pigs, respiration

RESUMO

Compararam-se os efeitos de diferentes concentrações do óxido nitroso ou oxigênio sobre variáveis hemogasométricas, em suínos mantidos em ventilação espontânea ou controlada à pressão, associada ou não à pressão expiratória final positiva (PEEP). Foram utilizados 48 porcos, distribuídos em seis grupos. Administraram-se diferentes concentrações de ar comprimido ou N_2O, associadas a diversas frações de oxigênio inspirado (FiO_2). O grupo sujeito a 30% de ar comprimido (GA30) mostrou maior proximidade do intervalo fisiológico da pressão parcial de oxigênio (PaO_2). Para a saturação de oxigênio (SaO_2), observaram-se valores aquém do limite inferior fisiológico no grupo administrado com 30% de N_2O (GN30). A utilização da PEEP é capaz de interferir positivamente na $PaCO_2$, independentemente da FiO_2, porém tem a efetividade comprometida quando há complemento da anestesia com o N_2O. Para a SaO_2, apenas o GN30 esboçou valores inferiores aos adequados para manutenção da oxigenação tecidual. O pH, o déficit base e o bicarbonato no sangue arterial foram influenciados pela FiO_2 e pelo N_2O. Concluiu-se que o uso do ar comprimido mantém os parâmetros hemogasométricos mais estáveis, com destaque para o GA30 e a PEEP, o que parece influenciar positivamente os grupos experimentais, mas com interferência da FiO_2 e do N_2O.

Palavras-chave: alquilfenol, atelectasia, porcos, respiração

Recebido em 28 de julho de 2017
Aceito em 9 de fevereiro de 2018
E-mail: lellygfaria@gmail.com

INTRODUCTION

Nitrous oxide is an anesthetic gas that emerged as an alternative for inducing analgesia, despite its inefficient potency, which is nonexistent in the pharmacological characteristics of propofol (Bueno *et al*., 2001). In addition, it promotes sedation and reduces the volume of anesthetics used under anesthesia (Heath *et al*., 1996).

The fraction of inspired oxygen (FiO_2) and inert gas solubility in the inspired mixture are determining factors for the rate of gas absorption in the alveoli. Thus, when the inspired gas contains oxygen and an inert gas, such as nitrous oxide, transfer of the mixture occurs faster and can accelerate the formation of alveolar collapse due to absorption (Joyce *et al*., 1993). The choice of mixture used in anesthesia assists in the prevention or aggravation of areas of alveolar collapse. Thus, questions arise regarding the best proportion of oxygen and nitrous oxide used to prevent oxygen deficiency occurring due to the formation of atelectatic airways. In addition, it is known that mechanical ventilation contributes to changes in pulmonary hematosis, requiring lower FiO_2 compared with spontaneous ventilation (Ashworth and Cordingley, 2003). A mechanical ventilation device that can assist in preventing atelectasis, positive end-expiratory pressure (PEEP), promotes distension and prevents alveolar collapse, thus allowing for a lower FiO_2. However, hemodynamic changes have been reported following its use (Benseñor and Auler, 2004).

The purpose of this study was to compare the effects of different concentrations of oxygen and nitrous oxide on blood gas analysis in pigs anesthetized with propofol and maintained under spontaneous or controlled ventilation, with or without PEEP.

MATERIAL AND METHODS

The study was approved by the Ethics Committee for the Use of Animals (CEUA) of the Faculty of Agricultural and Veterinary Sciences of São Paulo State University (FCAV/UNESP), under protocol n°. 026519 Forty-eight male and female, Large White pigs, aged roughly seven weeks old and weighing between 18 and 20kg, were randomly assigned to six groups and administered concentrations of 10, 30 and 50% compressed air (GA10, GA30 and GA50) or N_2O (GN10, GN30 and GN50), associated with fractions of inspired oxygen (FiO_2) of 0.9, 0.7 and 0.5, respectively.

Prior to the procedure, the pigs were deprived of feed for 12h and water for 2h (fasted). Each pig underwent intramuscular administration of azaperone (Destress®, DES-VET, São Paulo, SP, Brazil) at a dose of 2mg/kg, as preanesthetic medication. Once sedation was established, the right and left atrial veins were catheterized to allow administration of the drugs.

Anesthetic induction was performed with intravenously (iv) propofol (Propovan®, Cristália, Brazil) at the required dose (14.4±2.8mL) for loss of laryngotracheal reflex, immediately followed by orotracheal intubation (Magill tube: 6.0mm). The tube was coupled to the inhalation anesthesia device and included an anesthetic circuit with partial gas rebreathing (SAT 500, K. Takaoka Ind. e Com. Ltda., Brazil), equipped with a volumetric/pressure gauge, installed in line with the valve filter to supply the gas mixtures at the concentrations determined for each group. Readings for O_2 and N_2O concentrations were verified on a multiparameter monitor (Dixtal DX-2020D-C, Dixtal Biomédica Ind. Com. Ltda., Brazil), in which the gas analyzer sensor was adapted to the proximal end of the tube following orotracheal intubation. The pigs were then positioned in the right lateral decubitus, on an active thermal mattress, with continuous infusion of propofol 0.5mg/kg/min by infusion pump (ST 1000 PLUS, Samtronic®, Brazil).

Next, the inner side of the right thigh was trichotomized and prepared for aseptic intervention, femoral artery puncture with flexible polyethylene catheter and collection of blood samples (0.7mL) for arterial blood gas analysis, using a heparinized syringe connected to the three-way tap. After 125min (T0) of anesthesia induction, rocuronium (rocuronium bromide, Eurofarma, Brazil) was administered iv at a dose of 0.6mg/kg. From this point and throughout the experimental period, continuous infusion of the muscle relaxant was maintained at a dose of 0.6mg/kg/h, administered by infusion pump. Next, time-cycled pressure-controlled ventilation ($15cmH_2O$) was initiated, adjusting the total flow of the inhaled gas

between 30 and 50mL/Kg/min in relation to inspiration/expiration and a respiratory rate of 20mpm. Once adjusted, these parameters remained unaltered throughout the experimental protocol. Sixty minutes after the onset of continuous infusion of the muscle relaxant and after collecting blood samples (T60), PEEP was applied at 5cmH_2O. The third evaluation was initiated at 215min post-anesthesia induction and after PEEP application of 5cmH_2O (T75), followed by two further evaluations at 15-min intervals (T90 and T105).

Two-way ANOVA was used to detect differences in the means between the groups, followed by the Bonferroni test. Time points were analyzed by one-way ANOVA for repeated measurements, followed by the Bonferroni test. Differences were considered statistically significant when $P< 0.05$.

RESULTS

Intergroup analysis showed arterial oxygen partial pressure (PaO_2) was higher for GA10 over the experimental period, except compared with GA30. The latter was higher than groups administered N_2O and for GA50. PaO_2 of GA50 was lower than that of GN10 and higher than GN50 under spontaneous ventilation and under mechanical ventilation (MV) with PEEP, but lower than GN30 under MV, with and without PEEP. GA30 and GN10 increased at T60 and GA30 showed increased PaO_2 when PEEP was used (Table 1).

GA10 showed the lowest $PaCO_2$ value over time. GA30 showed the lowest tendency for hypercapnia over the experimental period, except compared with GA50 at T0. Under spontaneous and pressure-controlled ventilation with and without PEEP, values closest to the expected physiological range were observed for GA50 compared with the groups administered N_2O. Spontaneous ventilation generated significant hypercapnia in all groups administered N_2O and in GA30. MV appeared to contribute to $PaCO_2$ maintenance in GA50 (Table 1).

Regarding SaO2 during PEEP, pigs administered compressed air obtained higher means than those administered N_2O, while SaO_2 in GN30 was lower than that of GN10 and GN50. Individually, the SaO_2 of groups administered N_2O decreased during PEEP (Table 1).

Regarding base deficit (BD), GA30 showed a lower BD than GN10 under spontaneous ventilation. During PEEP, GA10 showed a lower BD than GN10, but higher than GA30 and GN30. These last two groups showed lower BD than GA50, GN10 and GN50 while using PEEP. In the individual group assessments, the mean at T60 was smaller in GN10 than for the remaining time points. For GN30, the mean at T75 was lower than at T0, T60 and T105, while for GN50, the mean at T60 was significantly lower than at T75 and T90.

Regarding bicarbonate (HCO_3^-), under spontaneous and controlled ventilation, HCO_3^- for GN10 was higher than the remaining groups for most time points. Even under spontaneous ventilation, GN30 showed a higher mean than GA30. During PEEP for GA10, HCO_3^- was higher than GA30 and GN30 and the mean for GA30 was lower than GN10, GN50 and GA50. GA50 showed a lower value than GN10, but higher than GN30, while GN30 was even lower than GN10 and GN50. In individual group assessments, HCO_3^- for GN10 was lower at T60 than the remaining time points. For GN30, this parameter was higher at T0 compared with the remaining time points (Table 1).

Even under spontaneous ventilation, pH for all groups administered compressed air showed higher means than GN10 and GN50. For the same time point, GN10 showed a lower mean than the remaining groups administered N_2O and GN30 showed a higher mean than GN50. After establishing MV, GA30 showed a lower mean than GA10, GA50 and GN50. For GA50, pH was higher than for GN10 and GN30. While using PEEP, GA10 showed higher pH than GN10 and GN50. For GA50, pH was higher than in all N_2O groups. GA10 showed a lower pH while using PEEP compared with spontaneous ventilation. For GA30 at T60, the mean was lower than for all remaining time points. GA50 and GN10 showed lower pH under spontaneous ventilation and a lower mean was observed for GN10 at T60 compared with T90. For GN30, the mean was lower at T60 than at T0, T90 and T105. Finally, pH was lowest for GN50 at T0 (Table 1).

Table 1. Mean and standard deviation (x±SD) of oxygen and carbon dioxide partial pressure, oxygen saturation, base deficit, bicarbonate and pH, in pigs (n= 48) anesthetized with propofol, under spontaneous or pressure-controlled breathing associated with positive end-expiratory pressure, administered oxygen plus compressed air or nitrous oxide (90%+10%; 70%+30%; 50%+50%), respectively, GA10, GN10, GA30, GN30, GA50 and GN50

Parameters	Groups	Time points				
		T0	T60	T75	T90	T105
		Spontaneous ventilation	Mechanical ventilation	Positive end-expiratory pressure (PEEP)		
PaO_2 (mmHg)	GA10	315.4±6.4^{A}	308.3±17.3^{A}	313.6±22.3^{A}	282.7±47.5^{A}	290.9±38.9^{A}
	GN10	245.9±45.2^{Bab}	256.6±13.4^{Ba}	224.1±0.1^{Bab}	215.1±0.3^{Bb}	243.7±0.3^{Bab}
	GA30	256.8±85.5^{Bb}	301.0±23.7^{Aa}	253.8±36.7^{Bb}	282.7±3.2^{Aab}	265.7±0.9^{ABab}
	GN30	214.0±2.1^{BCb}	237.3±24.9^{Bab}	256.1±58.8^{Ba}	217.8±38.7^{Bab}	247.1±29.8^{Bab}
	GA50	172.3±23.1^{C}	158.7±34.9^{C}	169.9±0.3^{C}	164.6±11.4^{C}	183.5±0.2^{C}
	GN50	117.7±17.8^{D}	119.6±23.3^{C}	124.4±3.2^{D}	125.4±0.9^{C}	127.3±1.1^{D}
$PaCO_2$ (mmHg)	GA10	57.1±8.4^{Ca}	38.1±3.5^{Bb}	48.5±0.9^{ABab}	47.9±1.8^{Bab}	46.8±1.3^{ABab}
	GN10	111.2±19.5^{Aa}	67.0±19.6^{Ab}	57.7±0.9^{Ab}	56.6±5.3^{ABb}	58.9±2.1^{Ab}
	GA30	79.5±17.8^{Ba}	37.8±7.4^{Bb}	45.8±15.1^{ABb}	47.2±10.1^{Bb}	42.2±6.4^{Bb}
	GN30	123.6±22.1^{Aa}	56.7±5.2^{Ab}	56.7±7.6^{ABb}	63.8±1.7^{Ab}	56.3±1.2^{Ab}
	GA50	61.1±4.8^{Ca}	42.7±5.2^{Bb}	44.3±4.5^{Bb}	44.7±2.0^{Bb}	50.0±1.0^{ABa}
	GN50	76.2±8.0^{Ba}	61.0±7.6^{Ab}	54.8±3.2^{ABb}	57.1±1.6^{ABb}	52.5±0.2^{ABb}
SaO_2 (%)	GA10	99.9±0.1	99.6±0.5	99.9±0.1^{A}	98.7±1.3^{A}	99.1±0.9^{A}
	GN10	99.5±0.2^{a}	99.4±0.8^{a}	87.6±1.3^{Bb}	88.6±1.3^{Bb}	88.6±0.8^{Bb}
	GA30	100.0±0.1	100.0±0.0	99.9±0.1^{A}	99.8±0.2^{A}	99.9±0.1^{A}
	GN30	98.8±0.6^{a}	100.0±0.0^{a}	81.4±6.6^{Cb}	80.1±8.9^{Cb}	83.1±7.2^{Cb}
	GA50	99.2±0.4	99.1±0.8	99.6±0.0^{A}	99.4±0.2^{A}	99.6±0.1^{A}
	GN50	97.2±1.1^{a}	98.2±1.2^{a}	88.3±0.7^{Bb}	87.2±1.2^{Bb}	89.2±0.2^{Bb}
BD (mEq/L)	GA10	3.1±2.1^{AB}	3.1±2.9	5.8±0.5^{A}	4.1±2.5^{AB}	4.3±1.7^{ABC}
	GN10	6.7±0.2^{Aa}	0.1±5.0^{b}	7.5±0.1^{Aa}	8.4±0.4^{Aa}	8.5±0.2^{Aa}
	GA30	-0.6±3.7^{B}	1.7±6.1	0.8±4.3^{BC}	1.1±3.2^{B}	-0.3±2.8^{C}
	GN30	3.6±2.5^{ABa}	1.4±1.2^{a}	-3.4±1.4^{Cb}	0.7±4.7^{Bab}	1.9±5.1^{BCa}
	GA50	3.5±2.7^{AB}	2.2±3.3	4.2±3.5^{AB}	5.2±4.3^{AB}	5.4±3.7^{AB}
	GN50	2.8±1.3^{ABab}	0.0±2.4^{b}	5.1±2.8^{ABa}	6.2±2.7^{Aa}	4.0±4.4^{ABCab}
HCO_3^- (mEq/L)	GA10	29.6±2.8^{BC}	28.8±2.7	30.9±0.3^{AB}	29.3±2.2^{BC}	29.3±1.1^{B}
	GN10	37.8±1.1^{Aa}	25.9±6.0^{b}	34.7±0.3^{Aa}	35.5±1.3^{Aa}	35.9±1.1^{Aa}
	GA30	27.9±1.4^{C}	26.4±3.8	25.8±5.1^{CD}	26.4±3.5^{C}	24.8±2.8^{C}
	GN30	33.7±3.0^{ABa}	28.8±2.3^{b}	23.0±1.3^{Dc}	26.8±4.4^{Cbc}	28.2±5.3^{BCb}
	GA50	30.3±2.1^{BC}	27.1±3.5	28.7±3.7^{BC}	29.5±4.0^{BC}	30.6±3.2^{B}
	GN50	30.8±1.8^{BC}	26.0±1.7	31.6±1.9^{AB}	32.6±1.7^{AB}	30.2±3.5^{B}
pH	GA10	7.337±0.020^{Ab}	7.357±0.073^{ABab}	7.418±0.006^{ABa}	7.398±0.027^{ABab}	7.425±0.042^{Aa}
	GN10	7.149±0.000^{Cc}	7.288±0.064^{BCb}	7.337±0.046^{Cab}	7.370± 0.040^{ABa}	7.308±0.037^{Cab}
	GA30	7.380±0.057^{Aa}	7.263±0.074^{Cb}	7.413±0.048^{ABCa}	7.417±0.038^{ABa}	7.401±0.036^{ABa}
	GN30	7.389± 0.016^{Aa}	7.300±0.093^{BCb}	7.354±0.020^{BCab}	7.399±0.062^{ABa}	7.418±0.059^{Aa}
	GA50	7.321± 0.065^{Ab}	7.398±0.069^{Aa}	7.434±0.012^{Aa}	7.441±0.039^{Aa}	7.409±0.053^{Aa}
	GN50	7.233±0.021^{Bb}	7.350±0.073^{ABa}	7.343±0.071^{BCa}	7.344±0.077^{Ba}	7.327±0.077^{BCa}

PaO_2, arterial oxygen partial pressure; $PaCO_2$, arterial carbon dioxide partial pressure; SaO_2, oxygen saturation; BD, base deficit; HCO_3^-, bicarbonate; PEEP, positive end-expiratory pressure.
Means followed by different capital letters in the columns differ from each other, P< 0.05.
Means followed by different lowercase letters along the rows differ from each other, P< 0.05.

DISCUSSION

Gianotti (2010) reported a mean arterial oxygen partial pressure between 341mmHg and 379mmHg with 80% FiO_2, when anesthetizing pigs under controlled-pressure ventilation. Since arterial PaO_2 is directly related to oxygen supply, it was expected that groups submitted higher oxygen supply would show higher PaO_2 values. Corroborating this assertion, the group administered 10% compressed air (GA10) showed higher mean values compared with the other groups over time, except GA30 at certain time points. Similarly, the group administered 30% compressed air (GA30) showed higher mean values compared with groups administered 30% nitrous oxide (GN30) and 50% compressed air (GA50) or nitrous oxide (GN50) at certain time points.

Observation verified that nitrous oxide use seemed to negatively influence pulmonary oxygenation efficiency, not only in GN30 compared with GA30, but in GN50 compared with GA50 under spontaneous or pressure-controlled ventilation plus PEEP. These findings suggest that groups administered oxygen and nitrous oxide at the concentrations described above showed alterations in oxygenation, and this seems to be due to the formation of areas of atelectasis. Thus, it seems reasonable to conclude that such nitrous oxide concentrations are not ideal for maintaining PaO_2 in pig species.

Despite the addition of PEEP to reduce gas exchange disorders, allowing for administration of a lower FiO_2, PEEP seemed to have no influence on preventing changes in oxygenation in the groups administered nitrous oxide, except for GN10.

It is worth emphasizing that even though GA50 presented higher values than GN50, both presented mean values lower than expected for this species. Regardless of the ventilatory mode, GN10 and GN30 showed better pulmonary oxygenation compared with GN50. Thus, an increase in nitrous oxide supply leads to reduced ventilation efficiency, regardless of PEEP or the ventilatory mode used, indicating that PEEP is beneficial when patients are administered different mixtures of oxygen and compressed air or up to 10% nitrous oxide.

Among all groups, GA30 seemed to show he closest physiological range of PaO_2 expected for this species. According to Lopes *et al*. (2007), when alveolar oxygen pressure is calculated, oxygen deficiency and tissue perfusion paradoxically occur at high concentrations present in the alveoli. Thus, proportionally lower oxygen levels in the alveoli are more effective at promoting the passage of the molecule into the bloodstream, reflecting in optimal blood pressures. This assertion corroborates the findings of GA30 compared with GA10.

Carbon dioxide partial pressure ($PaCO_2$) (Table 1), the amount of blood-transported carbon dioxide, was assessed since it is directly influenced by the elimination rate of carbon dioxide present in the organism and is related to the patient's ventilatory and hemodynamic state (Yamamoto, 2008). When anesthetizing pigs with propofol and isoflurane, maintained under positive pressure mechanical ventilation and submitted to different FiO_2 (0.8, 0.6 and 0.4%), Gianotti (2010) reported respective mean values of 40, 39 and 40MmHg for $PaCO_2$. These values are less than the results obtained in this study.

According to Lumb (2003), under anesthesia, a decrease in pulmonary ventilation occurs due to CNS depression and, consequently, in spontaneous ventilation, resulting in hypercapnia. This is verified by correlating hypercapnia in the groups under spontaneous ventilation. In a study on dogs anesthetized with propofol under spontaneous ventilation, Nunes *et al*. (2008) affirmed that the increase in mean $PaCO_2$ values occurred due to the increase in the FiO_2 level, and that hypercapnia may have been caused by atelectasis. However, in this work, hypercapnia is not correlated with the different supply levels of FiO_2, since significant differences were observed in groups in which the same FiO_2 was used, modifying only the association of compressed air or nitrous oxide. Therefore, the different FiO_2 levels that the pigs were exposed did not influence circulating CO_2 levels. In addition, GA10 and GA50 presented better pulmonary functionality, corroborating Gianotti (2010).

Under mechanical ventilation, groups submitted to compressed air presented values within the physiological limits of the species. The addition of PEEP showed no interference on the

ventilatory status of GA10 and GA50. In the other groups, both the introduction of MV and the addition of PEEP promoted improvements in $PaCO_2$ values.

It should be noted that even though improvements occurred in $PaCO_2$ following MV and PEEP, for the experimental groups where nitrous oxide was administered, hypercapnia was still observed. Moreover, Warner *et al*. (1998) reported that nitrous oxide can cause dose-dependent respiratory depression due to the likely decrease in diaphragmatic contractility promoted by changes in the distribution and regulation of skeletal muscle nerve impulses, thus promoting hypercapnia. The same is not observed under compressed air when using MV and PEEP. Confirming this hypothesis, Fialho *et al*. (1993) observed an increase in $PaCO_2$ in equines, while administering a 1:1 ratio of oxygen and nitrous oxide.

When administering PEEP under VM, GA50 showed a more adequate $PaCO_2$ than GN10. In addition, while under PEEP, pigs administered different concentrations of compressed air showed more adequate $PaCO_2$ compared with those administered nitrous oxide. This indicates that the use of PEEP positively interferes with $PaCO_2$ in pigs, independent of FiO_2, but its effectiveness is compromised when nitrous oxide anesthesia is present.

Regarding oxygen saturation (SaO_2) in anesthetized patients administered oxygen, this should be maintained between 96 and 100% to ensure adequate tissue oxygenation (McDonell and Kerr, 2007). No statistically significant variations occurred under spontaneous ventilation, and as soon as positive pressure MV was introduced, the values remained above the expected physiological range for the proposed anesthetic conditions at the same time points, indicating adequate tissue oxygenation. However, when PEEP was initiated, pigs administered a mixture of oxygen and nitrous oxide presented lower values than those administered a mixture of oxygen and compressed air, reinforcing the idea proposed during PaO_2 analyses that the use of anesthetic gas seems to negatively influence the efficiency of pulmonary oxygenation and, consequently, tissue oxygenation (Table 1).

It is important to clarify that the pigs submitted to PEEP had been under the anesthetic effect for a prolonged period and that PEEP plus nitrous oxide likely contributed to the decrease in SaO_2. Finally, it is worth highlighted that when analyzing SaO_2 in the groups that presented statistically significant differences, only GN30 showed values lower than those considered adequate to maintain tissue oxygenation.

The base deficit is the amount of base needed to titrate one liter of total arterial blood to a pH of 7.40, with the sample completely saturated with oxygen at 37ºC and a $PaCO_2$ of 40mmHg (Kovacic, 2009). The BD is obtained by determining blood pH and $PaCO_2$ (Kovacic, 2009); however, it is important to note that values like arterial blood oxygen concentration are usually lower in pigs, most likely because the species has a lower hemoglobin concentration, together with a higher body temperature. In addition, pH and bicarbonate are significantly higher in pigs compared with humans (Hannon *et al*., 1990). This explains the more expressive values of BD in the species studied.

While analyzing arterial blood samples of awake pigs, Gianotti (2010) observed a mean of 7.57±2.86mEq/L for this parameter. In comparison, Marques *et al*. (1995) analyzed the BD of pigs administered a combination of flunitrazepam and droperidol, recording a mean of -1.01±8.13mEq/L. It is evident that in relation to pigs, there is no consensus regarding a standardized BD, particularly pigs administered anesthesia with propofol, submitted to different FiO_2 levels in association with compressed air or nitrous oxide.

Regarding GN10, BD decreased under spontaneous ventilation and PEEP use. In contrast, GN30 resulted in a similarly low mean when PEEP was introduced compared with the mean values under spontaneous and pressure-controlled ventilation and final time point using PEEP. Similar to GN10, GN50 also showed a lower mean under MV for this parameter compared with means while using PEEP. This behavior in groups administered nitrous oxide can be explained by the tendency toward acidemia and hypercapnia, observed mainly under spontaneous ventilation.

While under spontaneous ventilation, GA30 presented a lower mean than GN10. This result is explained by the presence of hypercapnia and a tendency toward acidemia in GN10 under spontaneous ventilation. In contrast, when MV was initiated, no significant differences were observed between the groups. When analyzing the groups during PEEP use, GA10 showed a lower BD compared with GN10, but higher than GA30 and GN30. This reinforces the hypothesis that nitrous oxide negatively influences respiratory dynamics (GN10); however, a high FiO_2 level (GA10) also generates oxygen deficiency and tissue perfusion, paradoxically at high concentrations in the alveoli (Suter *et al*., 1975), indirectly intervening in BD maintenance. High FiO_2 levels and higher concentrations of nitrous oxide can impair the maintenance of blood gas parameters, and analysis of the results obtained indicate that among the groups submitted to nitrous oxide during PEEP, GN30 is important because it presents the lowest BD values.

Regarding bicarbonate (HCO_3^-) (Table 1), Gianotti (2010) reported mean values between 27.8 and 36.6mEq/L in awake pigs, while Marques *et al*. (1995) verified values between 20 and 23mEq/L when administering a combination of flunitrazepam and droperidol to pigs. The data obtained herein are in agreement with those reported by Gianotti (2010). Similar to that observed for BD, only GN10 showed a strong decrease in bicarbonate compared with values obtained under spontaneous ventilation and PEEP use. In GN30, PEEP appeared to positively influence the maintenance of this parameter.

Under spontaneous ventilation, the groups administered a mixture of compressed air performed better regarding bicarbonate maintenance. When PEEP was introduced, groups administered nitrous oxide showed larger means than those obtained from pigs administered a mixture of oxygen and compressed air. GA30 seemed to adapt more favorably to the proposed methodology than GA10 and GA50.

It is important to highlight that both pH and bicarbonate are appreciably higher in pigs than in humans (Hannon, *et al*., 1990). In their study on pigs under the effect of flunitrazepam and droperidol, Marques *et al*. (1995) showed means between 7.43 and 7.44 for pH. Later, while standardizing physiological parameters of awake pigs, Gianotti (2010) verified means between 7.45 and 7.54. Under spontaneous ventilation, significantly lower values were observed, together with a tendency toward acidemia, particularly among pigs administered nitrous oxide. This parameter was not significant only for GN30; however, in absolute values, even this group showed a tendency toward acidemia.

Several factors can influence the acid-base balance, leading to acidemia. According to Marques *et al*. (1995), researchers must take into account numerous characteristics that can directly influence blood gas parameters, including sex, age, climatic conditions, time of day, breed and stress. Among these factors, stress evidently influenced pH, since even the use of preanesthetic medication was insufficient to induce decubitus in the pigs and handling them for venoclysis. Add to this the standard practice of prolonged food and water fasting, complementary to the immediate stress, and the acid-base ratio becomes imbalanced (Luna, 2010).

Given all the factors that appear to influence the onset of acidemia, it is important to correlate this data with the tissue perfusion rate, which when incorrectly performed can also cause this alteration (Groeneveld *et al*., 1991). This became clear when analyzing previous parameters, such as PaO_2 and $PaCO_2$. The values obtained herein indicate compromised pulmonary and tissue perfusion, which causes not only metabolic acidosis, but also respiratory acidosis.

Having established pressure-controlled ventilation, GA30 showed the lowest tendency toward pH maintenance, while GA50 showed the highest tendency. Carvalho *et al*. (2007) described the use of MV in respiratory insufficiency, indicating that ventilation support allowed for a number of clinical improvements: improved ventilation/perfusion ratio, resulting in better PaO_2; increased alveolar ventilation, resulting in better pH and $PaCO_2$; increased lung volume by preventing or treating atelectasis; optimized pulmonary residual capacity; reduced respiratory muscle work, with decreased systemic and myocardial oxygen consumption; decreased intracranial pressure; and stabilization

of the chest wall. Corroborating this assertion, the groups presented improvement in pH following the onset of MV, except for GA30. However, this improvement was insufficient to significantly change the level of acidemia in the pigs. Based on analysis of the absolute values, once PEEP was initiated, the groups administered compressed air showed decreased levels of acidemia. Among pigs administered nitrous oxide, only GN50 continued to show a clinical level of acidemia. This observation once again reinforces the suggestion that nitrous oxide negatively influences blood gas parameters, even while using PEEP. No less important, a marked improvement in pH observed in GN30 compared with pigs administered 10% nitrous oxide confirms the theory that higher oxygen rates can paradoxically influence poor pulmonary and tissue oxygenation, resulting in or maintaining acidemia.

Briefly, the pH of GA10 was not positively influenced by the maintenance of MV or PEEP use, possibly due to the high FiO_2 supplied, which seems to impair tissue oxygenation. In GA30 and GN30, this parameter was positively influenced by PEEP, but not by MV alone. GA50 and GN10 were benefitted by PEEP.

Thus, for pigs anesthetized with propofol and submitted to different levels of FiO_2 associated with compressed air or nitrous oxide, under spontaneous or pressure-controlled ventilation, and with the addition of PEEP, pH, BD and bicarbonate were directly influenced by the fraction of inspired oxygen and nitrous oxide.

CONCLUSIONS

In conclusion, the use of nitrous oxide at concentrations higher than 10% compromises tissue oxygenation and PEEP is unable to attenuate this alteration. Nitrous oxide is therefore contraindicated for pig under the experimental conditions proposed. Nitrous oxide concentrations in excess of 10% and a high fraction of inspired oxygen are not feasible for use in pigs in a range of experimental or routine procedures, because they compromise the maintenance of oxygen saturation, base deficit, pH and bicarbonate. Pressure mechanical ventilation helps to maintain blood gas parameters, but its association with positive end-expiratory pressure is dispensable in pigs under certain nitrous oxide concentrations. The group administered 30% compressed air showed the best performance among the blood gas parameters.

ACKNOWLEDGMENT

To the Foundation for Research Support of the State of São Paulo (FAPESP) for the support granted in the form of project financing (process 2013/25655-0).

REFERENCES

ASHWORTH, S.F.; CORDINGLEY, J.J. New Modes of Ventilation. *Crit. Care*, v.14, p.90-99, 2003.

BENSEÑOR, F.E.M.; AULER, J.O.C. $P_{ET}CO_2$ e SpO_2 permitem ajuste ventilatório adequado em pacientes obesos mórbidos . *Rev. Bras. Anestesiol*., v.54, p.542-552, 2004.

BUENO, R.; POMPERMAYER, L.G.; ANTUNES, F.; SOUZA, A.P. Influência do óxido nitroso na anestesia pela associaç ão tiletamina-zolazepam, em cães. *Rev. Bras. Cienc. Vet.*, v.8, p.100-104, 2001.

CARVALHO, C.R.R.; TOUFEN JUNIOR , C.; FRANCA, S.A. Ventilação mecânica: princípios, análise gráfica e modalidades ventilatórias . *J. Bras. Pneumol*., v.33, p.54-70, 2007.

FIALHO, S.A.; SILVA, A.M.; CAMPELLO, R.A. *et al*. Anestesia inalatória em equinos com halotano e óxido nitroso : efeitos sobre os gases sanguíneos e equilíbrio ácido -base. *Arq. Bras. Med. Vet. Zootec*., v.45, p.199-211, 1993.

GIANOTTI, G.C. *Dinâmica cardiorrespiratória de suínos sedados e submetidos a diferentes frações inspiradas de oxigênio em ventilação mecânica volume versus pressão controlada*. 2010. 72f. Dissertação (Mestrado em Medicina Veterinária) – Faculdade de Veterinária, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS.

GROENEVELD, A.B.J.; VERMEIJ, C.G.; THIJS, L.G.M.D. Arterial and mixed venous blood acid-base balance during hypoperfusion with incremental positive end-expiratory pressure in the pig. *Anesth. Analg.*, v.73, p.576-582, 1991.

HANNON, P.J.; BOSSONE, C.A.; WADE, C.E. Normal physiological values for conscious pigs used in biomedical research. *Lab. Anim. Sci.*, v.40, p.293-298, 1990.

HEATH, K.J.; SADLER, P.; WINN, J.H.; MCFADZEAN, W.A. Nitrous oxide reduces the cost of intravenous anaesthesia. *Eur. J. Anaesth.*, v.13, p.369-372, 1996.

JOYCE, C.J.; BAKER, A.B.; KENNEDY, R.R. Gas uptake from an unventilated area of lung: computer model of absorption atelectasis. *J. Appl. Physiol.*, v.74, p.1107-1116, 1993.

KOVACIC, J.P. Acid-base disturbances. In: SILVERSTEIN, D.C.; HOPPER, K. *Small animal critical care medicine.* St Louis: Saunders Elsevier, 2009. p.249-257.

LOPES, P.C.F.; NUNES, N.; PAULA, D.P. *et al*. Biespectral index in dogs at three intravenous infusion rates of propofol. *Vet. Anesth. Analg.*, v.35, p.228-231, 2007.

LUMB, A.B. *Nunn's applied respiratory physiology*. 5.ed. Edinburgh: Butterworth - Heinamann, 2003. 687p.

LUNA, S.P.L. Equilíbrio ácido -basico. In: FANTONI, D.T.; CORTOPASSI, S.R.G. *Anestesia em cães e gatos* . 2.ed. São Paulo : Roca, 2010. p.147-156.

MARQUES, J.A.; MORAES, F.C.Y.; MARQUES, L.C. *et al*. Emprego da associação flunitrazepam/droperidol na tranquilização de suínos. *Ciênc. Rural*, v.25, p.71-74, 1995.

McDONELL, W.; KERR C.L. Respiratory system. In: TRANQUILLI, W.J.; THURMON, J.C.; GRIMM, K.A. *Lumb & Jones' veterinary anesthesia*. 4.ed. Oxford: Blackwell Publishing, 2007. p.117-151.

NUNES, N.; LOPES, P.C.F.; SANTOS, P.S.P. *et al*. Hemodinâmica de diferentes frações inspiradas de oxigênio em cães submetidos à infusão contínua de propofol sob ventilação espontânea. *Ciênc. Rural*, v.38, p.729-735, 2008.

SUTER, P.M.; FAIRLEY, H.B.; SCHLOBOHM, R.M. Shunt, lung volume and perfusion during short periods of ventilation with oxygen. *Anesthesiology*, v.43, p.617-627, 1975.

WARNER, D.O.; WARNER, M.A.; JOYNER, M.J. *et al*. The effect of nitrous oxide on chest wall function in humans and dogs. *Anesth. Analg*., v.86, p.1058-1064, 1998.

YAMAMOTO, E.Y. Noções básicas de equilíbrio ácido-básico – hemogasometria e eletrólitos. In: SANTOS, M.M.; FRAGATA, F.S. *Emergência e terapia intensiva veterinária em pequenos animais* – bases para o atendimento hospitalar. São Paulo: Roca, 2008, p.105-114.