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EVALUATION OF DIFFERENCES BETWEEN PARTIAL PRESSURE OF ARTERIAL AND END-TIDAL CARBON DIOXIDE IN RABBIT DURING MECHANICAL VENTILATION AND PNEUMOPERITONEUM

EVALUAREA DIFERENȚEI DINTRE PRESIUNEA PARȚIALĂ A DIOXIDULUI DE CARBON ARTERIAL ȘI CEL EXPIRAT LA IEPURI PE DURATA VENTILAȚIEI MECANICE ȘI PNEUMOPERITONEULUI

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ABSTRACT | REZUMAT

End tidal carbon dioxide (E_tCO_2) is a non-invasive and continuous mean of assessment of arterial partial pressure of carbon dioxide (P_aCO_2). However, high variability has been recorded between these parameters in patients with ventilation dysfunction. The present study was undertaken to evaluate the accuracy of E_tCO_2 monitoring for P_aCO_2 level estimation in rabbits and to assess whether arterial to end-tidal carbon dioxide ($P_{(a-Et)}CO_2$) gradient can predict lung function impairment. P_aCO_2 and E_tCO_2 relationship was evaluated in ten healthy rabbits subjected to three types of ventilation, as follows: spontaneous breathing (S), mechanical ventilation (MV) and mechanical ventilation during experimentally induced pneumoperitoneum (CO_2-PP). Arterial blood samples were drawn after each treatment and simultaneous E_tCO_2 reading was performed. Thirty E_tCO_2 and P_aCO_2 pairs were recorded. In S group, E_tCO_2 had a positive correlation with P_aCO_2 (R=0.752, p=0.012), with a 95% level of agreement between -4.2 and 12.72. In two rabbits a negative gradient was noted. End-tidal CO_2 registered higher values in the MV group (p=0.010) and CO_2-PP group (p=0.000) comparatively to S group but remained within the normal limits. Similar, P_aCO_2 had higher values in the MV group (Z=-2.805, p= 0.005) and CO_2-PP group (Z=-2.805, p=0.005), without correlation with E_tCO_2 level. The highest $P_{(a-Et)}CO_2$ gradient was recorded in CO_2-PP group (30.480 ± 19.830 mmHg), secondary to inefficient ventilation. In conclusion, both mechanical ventilation and pneumoperitoneum caused significant ventilation dysfunction demonstrated by an increased $P_{(a-Et)}CO_2$ gradient. End tidal CO_2 does not reliably predict P_aCO_2 in rabbits with compromised ventilation; hence it is recommended that blood gases be measured in these patients.

Keywords: capnography, gas exchange, pneumoperitoneum, arterial to end-tidal carbon dioxide gradient

Măsurarea dioxidului de carbon (E_tCO_2) expirat reprezintă o metodă non-invazivă și continuă de evaluare a presiunii parțiale arteriale (P_aCO_2) a acestui gaz. Cu toate acestea, studiile au raportat o variabilitate mare între acești parametrii, în special la pacienții cu disfuncții ventilatorii. În acest context, prin studiul de față se urmărește evaluarea preciziei E_tCO_2 în estimarea P_aCO_2 la iepuri anesteziați, precum și analiza gradientului P_aCO_2-E_tCO_2 ($P_{(a-Et)}CO_2$) ca parametru predictor al insuficienței ventilatorii. Relația P_aCO_2-E_tCO_2 a fost studiată la 10 iepuri supuși la trei tipuri de ventilație, după cum urmează: ventilație spontană (S), ventilație mecanică (MV) si ventilație mecanică cu pneumoperitoneu îndus experimental (CO_2-PP). Evaluarea P_aCO_2 s-a realizat prin analiza sângelui arterial, simultan cu înregistrarea valorii E_tCO_2 afișat de capnograf. În urma analizei a 30 de perechi P_aCO_2-E_tCO_2, s-a observat o corelare pozitivă între E_tCO_2 și P_aCO_2 la iepurii cu respirație spontană (R=0.752, p=0.012), gradul de concordanță la 95% fiind între -4.2 și 12.72. Pentru două animale, E_tCO_2 a avut o valoare mai mare decât P_aCO_2, rezultând un gradient negativ. Presiunea CO_2 la finalul expirului a înregistrat valori semnificativ mai mari în cazul loturilor MV (p= 0.010) și CO_2-PP (p=0.000) comparativ cu lotul S, menținându-se în valorile de referință. P_aCO_2 a înregistrat valori mai mari în loturile MV (Z=-2.805, p=0.005) și CO_2-PP (Z=-2.803, p=0.005), fără corelare cu E_tCO_2 corespondent lotului. Gradientul P_aCO_2-E_tCO_2 a înregistrat valoarea cea mai mare în cazul lotului CO_2-PP (30.480 ± 19.830 mmHg) consecutiv alterărilor de ventilație. În concluzie, atât ventilația mecanică, cât și pneumoperitoneul au cauzat alterări de ventilație alveolară sugerate de creșterea gradientului P_aCO_2- E_tCO_2.De asemenea, E_tCO_2 nu a dovedit precizie în estimarea P_aCO_2 la iepurii cu ventilație compromisă; prin urmare se recomandă analiza gazelor sangvine la această categorie de pacienți.

Cuvinte cheie: capnografie, schimb de gaze, pneumoperitoneu, presiunea parțială a dioxidului de carbon arterial și cel expirat

General anaesthesia, mechanical ventilation and pneumoperitoneum are common scenarios that impair pulmonary gas exchange and respiratory mechanics, even in the healthy patient. These effects result as a consequence of lung atelectasis development with subsequent shunting of pulmonary flow and improper gas exchange. Atelectasis of variable severity has been described in almost 90% of all anesthetised patients, and it is caused by a variety of factors, like drugs, patient position and fraction of inspired oxygen (12). Laparoscopic surgery has been proved to impair further the ventilation of the patient, due to an elevated intraperitoneal pressure and cranial shift of the diaphragm with reduced chest compliance. Andersson et al. (2005) demonstrated that carbon dioxide pneumoperitoneum can result in an increased surface of atelectasis up to

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66% and a 16% reduction in functional residual capacity (FRC)(3). In clinical settings, ventilatory status monitoring of the anaesthetized patient is done by invasive and non-invasive methods. The ideal evaluation of respiratory gas exchange is blood gas analysis; nevertheless, this technique requires arterial blood sampling, which is invasive and offers intermittent values (14). End-tidal carbon dioxide (E_tCO_2) monitoring is a non-invasive and continuous mean of assessment in patient ventilation, considered as the most useful monitoring technique in contemporary anaesthesia practice. Capnography is widely used for confirmation of endotracheal intubation, by displaying the level and waveform of CO_2 of exhaled air at the end of expiration (11). It is often referred as a substitute for arterial partial pressure of CO_2 (P_aCO_2); however, its clinical utility dependents on the gradient between these two variables. Arterial to end-tidal partial pressure gradient of CO_2 ($P_{(a-Et)}CO_2$) is defined as the difference between P_aCO_2 and E_tCO_2 and is a result of the relationship between ventilation airflow to the alveoli and perfusion flow to the capillaries (4). In human patients, a $P_{(a-Et)}CO_2<5$ mmHg is considered normal, but significant variability has been reported in mechanically ventilated patients (9) and patients undergoing laparoscopic surgeries (13). The E_tCO_2 and P_aCO_2 relationship is highly influenced by alterations in ventilation/perfusion matching, thus, limiting the ability to use E_tCO_2 for P_aCO_2 estimation. The physiological effect of mechanical ventilation and pneumoperitoneum may lead the clinician to question whether E_tCO_2 monitoring is adequate for assessing the ventilation of the patient. Therefore, the primary objective of the present study was to evaluate the accuracy of E_tCO_2 monitoring in anesthetised rabbits and secondarily, to assess whether $P_{(a-Et)}CO_2$ gradient can predict lung function impairment, starting from the assumption that both mechanical ventilation and pneumoperitoneum induce various degrees of ventilation dysfunction.

MATERIALS AND METHOD

This research was performed as a comprised part of a larger study on mechanical ventilation in rabbit with experimentally induced pneumoperitoneum (aut. no 204/12.03.2020) and complied with the European Directive 22.09.2010/63/EU, and Romanian national law 43/2014 for protection of animals used for scientific purposes. The working methodology was divided into two phases and all animals were part of each group, as follows: spontaneous ventilation group (S), mechanically ventilated group (MV) and mechanically ventilated with carbon dioxide pneumoperitoneum group (CO_2-PP).

Study protocol

Phase 1: Each rabbit was anesthetised by chamber induction with isoflurane (Isoflutek, 1000 mg/g, Laboratorios Karizoo, Barcelona, Spain) in oxygen for arterial and vein catheter placement. The rabbits were allowed to recover from the brief anaesthesia for a minimum of 2 h prior to following experimental treatment. The animals were given intravenously Midazolam 2 mg/kg (Midazolam Aguettant 1mg/ml, Laboratoire Aguettant, Lyon, Frace) and Propofol 10 mg/kg (Propofol-Lipuro 1%, B Braun, Melsungen, Germany). Tracheal intubation was facilitated by lidocaine 1% (Xilina 10 mg/ml, Zentiva, Bucharest, Romania) application on the larynx. The rabbits were placed in dorsal recumbency in a patient positioner (Pawsitioner, Avail Concepts, LLC, USA) and allowed to breathe room air. Anaesthesia was maintained with a constant rate infusion of midazolam (0.13 mg/kg/hr,) and propofol (1 mg/kg/hr). End expiratory CO_2 tension was measured by infrared mainstream capnography, part of a multiparameter monitor (Drager Infinity Delta, Drager, Germany) with the sensor attached to the endotracheal tube. The arterial blood samples were drawn after 10 minutes of stabilization in this position. During this time, computed tomography investigation was performed to exclude subclinical pulmonary lesions. If no lesions were identified, the rabbits were allowed to recover and were included in the second part of the study. The data obtained in this phase corresponded to group S.

Phase 2: After a washout period of 7 days, the rabbits were anaesthetized by intramuscular administration of xylazine 5 mg/kg (Xylazin Bio 2%, Bioveta, Ivanovice na Hane, Czech Republic) and ketamine 35 mg/kg (Narkamon Bio 100 mg/ml, Bioveta, Ivanovice na Hane, Czech Republic). After auricular artery and vein catheterization and endotracheal intubation, the animals were connected to a rebreathing circuit for anaesthesia maintenance with isoflurane in 100% oxygen. Rabbits were mechanically ventilated using a volume-control ventilation mode (Dräger Fabius Plus XL, Dräger, Lübeck, Germany), with the tidal volume set at 6 ml/kg bodyweight, zero positive end-expiratory pressure and the respiratory rate adjusted to maintain E_tCO_2 below 45 mmHg. After 10 minutes of mechanical ventilation, pneumoperitoneum was created by insufflation of CO_2 into the peritoneal cavity via a Veress needle until it reached a pressure of 8 mmHg (Karl Storz Endoflator, Karl Storz Endoscopy, Tuttlingen, Germany). Expired gases for measurement of E_tCO_2 were drawn from the T-connector and analysed with a side stream capnograph (Scio Four gas Module, Dräger, Lübeck, Germany)(Dräger Fabius Plus XL, Dräger, Lübeck, Germany). Blood analysis was performed in two-time points: after 10 minutes of mechanical ventilation and after 30 minutes of CO_2-PP. The data obtained during this phase corresponded to groups MV and CO_2-PP, respectively. The ear used for arterial catheterization was alternated between experiments to allow healing. All blood samples were collected following the manufacturer recommendations, in 2 ml heparinised syringes (Luer Slip Blood Gas Sampling system, Numbrecht, Germany). The E_tCO_2 was recorded every time the blood sample was drawn. After blood aspiration, air bubbles were expelled and the syringe was covered with a plastic cap. Blood gas tension measurement were performed within 1 to 3 minutes, with body temperature correction, using a point-of-care blood gas machine (Stat Profile Prime Plus® VET Critical Care Analyzer, Nova Biomedical, USA). For our study, the following measured and calculated parameters were evaluated: pH, P_aCO_2 (mmHg), RI (respiratory index), P_aO_2/F_iO_2 (ratio between arterial oxygen partial pressure and inspired oxygen concentration) (mmHg) and $P_{(a-Et)}CO_2$ (mmHg).

Statistical analysis

Statistically, the Gaussian distribution of the raw data was analysed by Shapiro-Wilks normality test (p<0.05)

Table 1

Ventilator and clinical variables in rabbits

Variables	S	MV	CO_2-PP
	n=10	n=10	n=10
F_iO_2 (%)	21	100	100
PIP (cmH_2O)		9 ± 0.29	14.8 ± 0.56
PEEP (cmH2O)		1	1
RR	50 ±12.22	31.5 ± 2.41	37 ± 2.58
pH	7.517 ± 0.059	7.408 ± 0.079	7.324 ± 0.061
E_tCO_2 (mmHg)	29.600 ± 5.967	37.400 ± 4.695	41.600 ± 5.481
P_aCO_2(mmHg)	33.860 ± 6.266	49.750 (47.3, 51.4)[b]	72.080 ± 16.340
Respiratory index	0.557 ± 0.506[a]	0.550 (0.3,1.9)[b]	0.450 (0.2,1.0)[b]
PO_2/FiO_2 ratio	316.957 ± 74.081[a]	356.950 ± 137.972	415.050 ± 166.686
a/A	0.714 ± 0.219[a]	0.610 ± 0.233	0.700 ± 0.258
$P_{(a-Et)}CO_2$	4.260 ± 4.316	9.1 (8.3,17.4) [b]	30.480 ± 19.830

F_iO_2 indicates fraction of inspired oxygen; PIP, positive inspiratory pressure; PEEP, positive end expiratory pressure; RR, respiratory rate, E_tCO_2, end-tidal carbon dioxide, P_aCO_2, partial pressure of arterial carbon dioxide; PO_2/F_iO_2, ratio between arterial oxygen partial pressure and inspired oxygen concentration, a/A, arterial-alveolar ratio; $P_{(a-Et)}CO_2$, arterial to end tidal carbon dioxide gradient; a indicates 7 samples out of 10; b, median value (IQR)

and by visual analysis of graphic Q-Q plot. Characterization of the data (means, standard deviation (SD) or medians and IQR (Inter Quartile Range)) is showed in Table 1. For each group, the correlations between E_tCO_2 and P_aCO_2, RI and $P_{(a-Et)}CO_2$ and between RI and P_aO_2/F_iO_2, was analysed using Pearson or Spearman correlation depending on the approximate distribution of data.

Depending on the approximate data distribution, one-way ANOVA or Friedman were performed to assess the existence of statistically significant difference on mean values or medians between groups for investigated variables. To compare differences in means, a Bonferroni post hoc analysis was used (statistical significance at $p<0.05$), whereas differences in medians were compared using a Wilcoxon signed-rank test after applying the Bonferroni correction at a level of $p<0.017$.

Bland Altman analysis was used to evaluate the level of agreement between E_tCO_2 and P_aCO_2 values. Statistical analysis was performed using SPSS version 20 software.

RESULTS AND DISCUSSIONS

There were 30 paired E_tCO_2-P_aCO_2 values from 10 rabbits (Fig 1). All of the paired measurements were taken simultaneously. This study included male rabbits, with a mean bodyweight of 3.25 (±0.305) kg, of 7 months old.

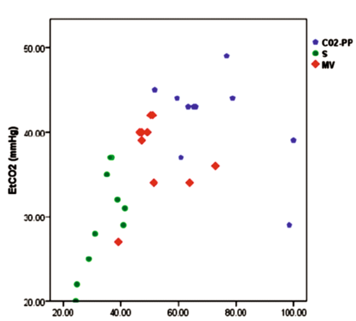

Fig. 1. Regression analysis comparing E_tCO_2 and P_aCO_2 by studied groups (S- spontaneous breathing group; MV-mechanical ventilation group; CO_2-PP – pneumoperitoneum group)

In group S, after analysis of 10 pairs, a strong positive correlation between E_tCO_2 and P_aCO_2 was noted (R=0.752, p=0.012). The 95% level of agreement between parameters ranged from -4.200 and 12.720, with a significant difference between values (p=0.012) (Fig. 2).

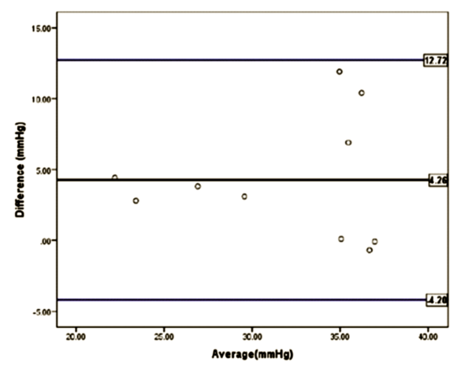

Fig. 2. Bland-Altman plot in S group ($EtCO_2$-$PaCO_2$) (pairs=10) with the representation of the limit of agreement, from -4.200 to 12.72

As regard E_tCO_2, there was a significant difference between the S group and MV group (p=0.010), as well as between S and CO_2-PP group (p=0.000). Similar to E_tCO_2, Wilcoxon signed-rank test for P_aCO_2 demonstrated a significant difference between medians of S and MV group (Z= -2.805, p= 0.005), as well as between S and CO2-PP group (Z=-2.803, p=0.005). The partial pressure of CO_2 registered lower values than E_tCO_2 in 2 rabbits, being referred as a negative $P_{(a-Et)}CO_2$ gradient. For 3 animals, RI, PO_2/F_iO_2 and a/A values were not determined. In the MV group, after analysis of 10 pairs, the mean ±SD $P_{(a-Et)}CO_2$ gradient was 14.5±10.528mmHg, with a significant difference between values (p=0.002). The 95% limits of agreement ranged from 35.136 and -6.135. Notably, 70% of the pairs had a smaller difference value than the mean (Fig 3).

In CO_2-PP group, after analysis of 10 pairs, no correlation between E_tCO_2 and P_aCO_2 was noted. Bland Altman correlation showed a 95% level of agreement from 69.347 and -8.387 mmHg, with a significant difference between gradient values (p=0.001) (Fig. 4).

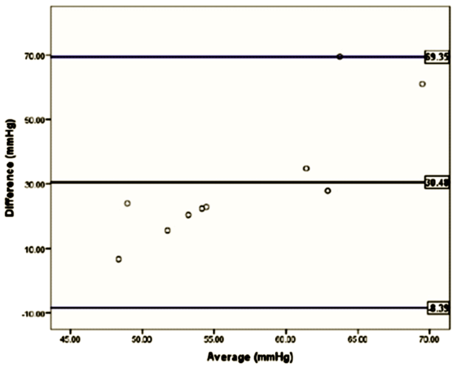

Fig. 3. Bland-Altman plot in MV group ($EtCO_2$-$PaCO_2$) (pairs=10) with the representation of the limit of agreement, from -6.14 to 35.14

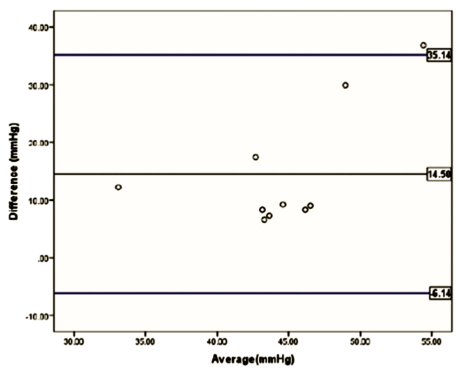

Fig. 4. Bland-Altman plot in CO_2-PP group ($EtCO_2$-$PaCO_2$) (pairs=10) with the representation of the limit of agreement, from -8.39 to 69.35

Further analysis was conducted to identify correlations between RI and $P_{(a-Et)}$+CO_2 gradient, as well as between RI and PO_2/F_iO_2 pressure. Spearman's correlation demonstrated a significant strong positive correlation between RI and $P_{(a-Et)}CO_2$ gradient in CO_2-PP group (ρ= 0.767, p=0.01). RI and PO_2/F_iO_2, strong negative correlations were demonstrated in S group (ρ=-0.955, p=0.001), MV group (ρ=-0.991, sig< 0.000) and CO_2-PP group (ρ=-0.930, sig<0.000).

Our data reveal that E_tCO_2 shows an excellent relationship with P_aCO_2, providing a valid estimate of gas exchange in spontaneous breathing rabbits with no lung disease. For levels of P_aCO_2 of 35 mmHg or less, E_tCO_2 showed a higher level of accuracy to predict P_aCO_2 than for levels above 35 mmHg, to the extent of becoming a substitute of P_aCO_2. The average $P_{(a-Et)}CO_2$ gradient was reported to be lower compared to other studies (7). In the paper conducted by Eatwell et al. (2013), E_tCO_2 measured on conscious rabbits through a nasal probe provided lower values, as most of the rabbits were hyperventilating (5). To address this problem, in our study anaesthesia was used to reduce the stress of handling, while allowing the patients to adopt a dorsal position, as well as endotracheal intubation; moreover, the protocol used did not alter the respiratory function. As would be expected, P_aCO_2 was greater than E_tCO_2 in most cases; nevertheless, in two rabbits a negative gradient was registered. Negative values have been previously observed during anaesthesia in infant human patients, being attributed to the low ratio of tidal volume to dead space, high sampling rates by analysers and high ventilator rates with high fresh gas flows. In mechanically ventilated children, the negative gradient has been observed with higher-than-normal tidal volumes and better ventilation of dependent well-perfused alveoli (8). In our study, the most likely cause was an increased anatomic dead space due to the mainstream capnograph sensor, which caused a CO_2 rebreathing, as suggested by Rich et al. (1990) (15).

In mechanically ventilated patients, P_aCO_2, E_tCO_2 and $P_{(a-Et)}CO_2$ gradient registered higher values compared to spontaneous breathing rabbits, and no correlation was found between these variables. These findings do not corroborate with the study performed by Rich et al. (1990) in ventilated rabbits. According to them, P_aCO_2 decreased during mechanical ventilation, but the $P_{(a-Et)}CO_2$ gradient showed high variability. However, their study protocol consisted of higher volumes for lung ventilation, higher flow rates and an unmentioned inspired fraction of oxygen (F_iO_2), which could explain the differences among results (15). Ventilation of the lungs with pure oxygen can result in the appearance of the atelectasis in less than 6 minutes (6). Horr et al. (2019) observed high P_aCO_2 values in rabbits anaesthetized with isoflurane and maintained on 100% O_2, attributing this change to the occurrence of atelectasis (7). Studies suggest that the collapsed alveoli occur faster in dependent lung regions. This mechanism is even more pronounced during mechanical ventilation, due to a redistribution of inspired gas away from dependent to non-dependent lung regions (6). The resulted atelectasis reduces the lung ability to remove CO_2, expressed through an increased $P_{(a-Et)}CO_2$ gradient, as seen in our study. This supposition is sustained by Yamaouchi et al. (2011) which demonstrated that $P_{(a-Et)}CO_2$ in anaesthetized patients is dependent on F_iO_2 (19). In addition, Strang et al. (2009) showed a significant correlation between the magnitude of lung atelectasis and $P_{(a-Et)}CO_2$ in a porcine model (17). Based on these results, we can assume that mechanical ventilation with high F_iO_2 had a significant effect on gas exchange in our rabbits. Another theory raised by Rich et al. (1990) which could explain the high $P_{(a-Et)}CO_2$ gradient was about the differences between E_tCO_2 measured at different sites of the endotracheal tube. In their study it was noted that, in small animals, expired CO_2 sampled at the distal port can be diluted by fresh gas flow, underestimating P_aCO_2 (15). This situation could explain as well the high gradient registered in the present study, given the fact that the ventilation was performed using a human anaesthesia machine, not suited for use in very small animals. Insufflation of CO_2 inside the peritoneal cavity elevated further the $P_{(a-Et)}CO_2$ gradient. In general, the $P_{(a-Et)}CO_2$ can increase either because of increased P_aCO_2, either because a decrease in E_tCO_2. The first situation occurs most commonly with an increase in pulmonary shunt, whereas the second situation is related to a high dead space fraction (16, 17). In the current study, an increase in pulmonary shunt was reflected through a high P_aCO_2 measurement and subsequent increased $P_{(a-Et)}CO_2$, a positive correlation between $P_{(a-Et)}CO_2$ gradient and RI and a negative correlation between RI and PO_2/F_iO_2. Shunting is defined as blood passing from the right heart to the left heart without being oxygenated. The relationship between shunt fraction and arterial P_aCO_2 is nonlinear, but when the shunt is very high, arterial P_aCO_2 can rise very fast, in the absence of ventilation compensation (18). Respiratory index (RI = alveolar-arterial oxygen gradient normalized by partial pressure of arterial O_2) is a scale that reflects the difference between alveoli oxygen and arterial blood oxygen and is frequently used in the evaluation of respiratory function (7). Laghi et al. (1989) have suggested that RI is a more specific quantifier of lung dysfunction, correlating closely with the shunt, as was demonstrated in patients with post-traumatic acute respiratory distress syndrome, being used as a mortality predictor (10). It might be suggested that during CO_2-PP elevated $P_{(a-Et)}CO_2$ ratio results as a consequence of high CO_2 load and secondary hypercapnia. Both P_aCO_2 and E_tCO_2 variables would move in the same directions, thus maintaining a fairly constant gradient, which was not observed in the present study.

It has been reported that the aggravation of atelectasis caused by pneumoperitoneum is not paralleled by an increase in shunt or impaired oxygenation (17).

Furthermore, Andersson et al. (2002) demonstrated on patients undergoing laparoscopic cholecystectomy that pneumoperitoneum reduces the intrapulmonary shunt and improves the oxygenation (2). This seeming paradox derives from a redistribution of blood flow away from atelectatic lung, which times both ventilation and perfusion shift away from caudal regions along the horizontal axis, thus maintaining a good ventilation/perfusion matching.

Several conclusions can be drawn from the present study. First, the combination of midazolam and propofol offered a reliable anaesthesia protocol for short term and painless investigations,such as computer tomography imaging, maintaining a good respiratory function. Anaesthesia induction and patient intubation required a higher dose of propofol;however, it was lower in comparison with the dose used by Allweiler et al. (2010) (1). Despite this, no complications such as respiratory depression or arrest were noticed throughout the procedure. End-tidal CO_2 measurement showed to be well correlated with $PaCO_2$, proving validity for gas exchange monitoring in rabbits with spontaneous respiration, and without lung function impairment. Mechanical ventilation with high F_iO_2 and CO_2-PP negatively affected ventilation and gas exchange, which was not demonstrated by E_tCO_2 monitoring. The change in $P_{(a-Et)}CO_2$ gradient was directly proportional to the degree of ventilation/perfusion mismatch; therefore, it should be introduced as a monitoring parameter in rabbit patient during mechanical ventilation and laparoscopic surgery.In the present study, the ventilation pattern was not changed, which induced hypercapnia in all animals. In clinical settings, the authors recommend adjusting the minute ventilation and the application of higher positive end-expiratory pressure, in order to maintain normocarbia. However, the magnitude of $P_aCO_2$should always be investigated trough arterial blood gas analysis. Limitations of the study include the small number of patients, the absence of a group with spontaneous ventilation on high F_iO_2 and the confirmation of the atelectasis through computer tomography measurements.

CONCLUSIONS

Both mechanical ventilation and pneumoperitoneum caused significant ventilation dysfunction demonstrated by an increased $P_{(a-Et)}CO_2$ gradient. End tidal CO_2 does not reliably predict P_aCO_2 in rabbits with compromised ventilation; it is recommended that blood gases be measured in these patients.

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