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Effects of end tidal CO_2 and venous CO^2 levels on postoperative nausea and vomiting in paediatric patients

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Abstract. – OBJECTIVE: Postoperative nausea and vomiting (PONV) is a common complaint of paediatric surgical patients. The aim of this prospective study was to compare the effects of end tidal CO_2 ($PeCO_2$) and venous CO_2 ($PvCO_2$) in laryngeal mask (LMA) and face mask (FM) ventilation on the occurrence of PONV in paediatric patients with surgical interventions in the inguinal region. To date, no data regarding these parameters on PONV are available.

PATIENTS AND METHODS: Ninety children were randomized using the sealed-envelope method. Group 1 consisted of 45 patients whose airway was managed with LMA; Group 2 consisted of 45 patients whose airway was managed with FM. Induction of anaesthesia was performed via administration of 8% sevoflurane in a mixture of air/oxygen in all patients. In both groups, manually controlled ventilation was applied. Five (t1) and fifteen (t2) min after the start of surgery, venous blood samples were obtained and $PeCO_2$ was determined.

RESULTS: $PeCO_2$ (t2) and $PvCO_2$ (t2) levels and the occurrence of PONV were significantly increased in Group 2 compared to Group 1 ($p < 0.005$ for all). In both groups, the occurrence of PONV was positively correlated with BMI, $PeCO_2$ (t2), and $PvCO_2$ (t2) levels ($p < 0.05$ for all), whereas it was inversely correlated with SpO_2 levels ($p < 0.05$ for all) in a bivariate analysis. We found that the $PeCO_2$ (t2) and $PvCO_2$ (t2) levels were independently associated with the occurrence of PONV in both groups.

CONCLUSIONS: Our results showed that elevated levels of $PeCO_2$ (t2) and $PvCO_2$ (t2) are independent risk factors for PONV, and these parameters may be used as adjunctive tools to assess the occurrence of PONV.

Key words:
Children, Complication, Carbondioxide.

Introduction

Modern anesthetic techniques have attempted to limit post-anesthesic problems. However, postoperative nausea and vomiting (PONV) is the most frequent side effect after general anesthesia[1]. PONV may decrease patient and parent satisfaction and increase the use of drugs, and can affect nursing care, intravenous fluids, and duration of discharge. Moreover, in outpatient treatment, PONV is a common undesirable reaction. PONV is one of the common complaints from parents of paediatric surgical patients[2]. Severe vomiting is unpleasant and a leading cause of delayed discharge and unplanned readmission after surgery[3-5]. In addition, one of the most stressful situations in paediatric patients is PONV, and the etiology is multifactorial[3].

Factors that cause PONV may or may not be under the control of the anesthesiologist. Although age, sex, and previous history of PONV or motion sickness are independent of anesthesia and the anesthesiologist, selection and management of the anesthetic technique to be applied to the patient, preoperative sedation, choice of intraoperative anaesthetic drugs, and postoperative pain management are variable. This study focused on anesthesiologist factors related to the choice of anesthesia administered to patients.

In the paediatric age group, the number of surgical interventions in the inguinal region is increasing each year. However, the majority of surgical procedures do not require neuromuscular blockade and endotracheal intubation. Thus, laryngeal mask airway (LMA) and face mask (FM) are used to provide safe airways during these types of surgery. The LMA is an available supraglottic airway device for airway maintenance during elective surgical procedures in paediatric patients for many years. FM is one of the airway managements used for short-term surgical procedures. FM is typically used for manually controlled ventilation in anesthetised patients, but skill is required to maintain effective ventilation with the face mask. Compared

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with FM, LMA provides safe and hands-free airway management for longer periods because LMA allows the anesthesiologist to perform other tasks, such as patient follow-up, drug administration, and record keeping. LMA decreases the respiratory dead space/tidal volume ratio compared with the FM[6]. End tidal CO_2 ($PeCO_2$) and venous pCO_2 ($PvCO_2$) are considered safe and effective methods to evalaute oxygenation during general anaesthetic procedures[6]. However, to the best of our knowledge, reports on the affect of $PeCO_2$ and $PvCO_2$ on the appearance of PONV in paediatric patients are not yet available.

It is believed that using LMA may decrease $PeCO_2$ and $PvCO_2$ compared to FM and lead to lower rates of PONV in paediatric patients. Therefore, we compared the effects of $PeCO_2$ and $PvCO_2$ in LMA and FM ventilation on the incidence of PONV in paediatric patients with surgical interventions in the inguinal region.

Patients and Methods

This prospective study was performed in the Department of Anesthesiology and Reanimation at Harran University Research Hospital between October 2013 and September 2014 after obtaining approval of the local Ethics Committee (ID number: B.30.2.HRÜ.0.20.05.00.050.01.04/91), and written informed consent was obtained from the parents of children undergoing elective inguinal region surgery. A total of 90 children with ASA physical status was I and II were randomzed using the sealed-envelope method. Group 1 consisted of 45 patients whose airway was managed with LMA (The Laryngeal Mask Company Limited, Le Rocher, Victoria, Mahe, Seychelles); Group 2 consisted of 45 patients whose airway was managed with FM (Intersurgical, Wokingham, UK). Children were kept fasting for 4 h and premedicated with oral midazolam (0.5 mg/kg, Miloz® 5 mg, Novell Pharmaceutical Laboratories, Bocor, Indonesia) 30 min prior to induction. Patients at risk of aspiration, history of gastroesophageal reflux, symptoms of upper respiratory tract infection, morbid obesity, history of bronchial asthma, and potential difficult airways were excluded from the study. After the patients were transferred into the operating room, peripheral oxygen saturation, non-invasive blood pressure, and electrocardiogram monitoring were performed. The CO_2 analyzer was calibrated before each patient was tested, according to the manufacturer's instructions. Induction of anaesthesia was performed via administration of 8% sevoflurane (Sevorane® Liquid 100%, Aesica Queenborough Ltd., Queenborough, Kent ME11 5EL, UK) in a mixture of air/oxygen for all patients. Manual ventilation was performed until loss of the eyelash reflex, followed by i.v. remifentanil 1 mcg/kg (Ultiva® 2 mg, GlaxoSmithKline Manufacturing S.p.A., Torrile, PR, Italy) administration with secured vascular access; neuromuscular blockade agents were not used. In Group 1 (LMA group), after controlling the adequacy of the depth of anaesthesia with loss of motor response to jaw thrust manoeuvre, LMA that was chosen according to the manufacturer's recommendations and was placed with the index finger method in the sniffing position by an experienced anaesthesiologist. LMA was completely deflated and lubricated with a water-based gel before insertion. After LMA insertion, the airway device was inflated until the cuff pressure reached 60 mmHg, and the airway device was connected to the breathing circuit. Failed airway device placement was defined as being unable to observe a smooth shaped end tidal CO_2 wave, inadequate ventilation (failure to provide a tidal volume of at least 8-10 ml/kg), or findings of airway obstruction (SpO_2 being below 90%, abnormal thoracoabdominal movement, or no rise of the chest). The number of attempts to place the airway device was recorded and patients on whom three trials were performed with failure were intubated and excluded from the study. While placing the airway device, we applied maneuvers in the order of replacement of the airway device upwards and downwards, jaw lift-jaw thrust, and head extension-neck flexion. In Group 2 (face mask group), proper oropharyngeal airway was placed into the oral cavity. Inadequate ventilation (inadequate to provide a tidal volume of at least 8-10 ml/kg) was defined as being unable to observe a smooth-shaped end-tidal CO_2 wave.

In both groups, manually controlled ventilation was applied with a tidal volume of 8-10 ml/kg and fresh gas flow of 4-6 L/min using a nonrebreathing circle system. The respiratory rate was changed between 15 and 25 min according to the patient's age. Peak airway pressure was maintained below 20 cmH_2O to prevent gas leaks around the LMA. Tidal volume was measured at the expiratory limb. Peak airway pressure was measured at the proximal end of the inspiratory limb of the breathing circuit attached to the anaesthesia machine. Anaesthesia was maintained by a mixture of 50% O_2 and 50% air and with sevoflurane at an end-tidal concentration of 2.5 %, and additional opioids if necessary. With the last skin suture, the sevoflurane and air were turned off and 100% O_2 was started. The LMA was removed while the patients were under deep anaesthesia and spontaneous breathing was adequate. Standard monitoring was used throughout the study, including peripheral oxygen saturation (SpO_2), noninvasive blood pressure, and electrocardiogram monitoring recorded before induction, immediately after LMA insertion or airway, after 1 min, and perioperatively every 5 min.

Secure venous cannulation in two different extremities was performed in all patients after premedication. While one of them was used for intravenous fluid and drug administation, the other was used to obtain venous blood samples by measuring $PvCO_2$ 5 (t1) and 15 min (t2) after the start of surgery. In addition, $PeCO_2$ was simultaneously measured at the proximal connector end of each extratracheal airway using a side-stream infrared CO_2 analyser with a constant sampling rate of 200 ml/min. Patients were observed in the postoperative care unit for the occurrence of PONV and were visited twice on the ward within the 24-h observation period. Both patients and the nursing staff were asked whether PONV was present and analgesic drug consumption was recorded. Our study design is compliant with the CONSORT recommendations.

Intraoperative complications such as laryngospasm, bronchospasm, hypoxia (SpO_2 being below 90%), cough, hiccup, and postoperative complications such as blood on the airway device after removal and signs of trauma on the tongue, teeth, and lips were recorded.

Statistical Analysis

Statistical analysis was performed using the SPSS 20 computer software (SPSS® for Windows 16.0, Chicago, IL, USA). Continuous variables were expressed as means ± SD. The normality of distributions was evaluated with the one-sample Kolmogorov-Smirnov test, revealing a uniform distribution. Comparisons of categorical and continuous variables between the groups were performed using the chi-squared (χ^2) test and independent samples *t*-test, respectively.

The correlation between occurrence of PONV and clinical characteristics and laboratory parameters was assessed using Pearson's correlation test. Standardised β-regression coefficients and their significance from multiple linear regression analysis were reported. A two-tailed $p < 0.05$ was considered statistically significant. The power of the study was calculated using *post hoc* power analysis.

Results

After screening, 90 patients were randomly allocated into one of the intervention groups, as the flow chart shows in accordance with the CONSORT guidelines (Figure 1). LMA devices were successfully placed in all patients in Group 1. FM ventilation was performed safely and effectively with the oropharyngeal airway in Group 2. Demographic characteristics of both groups are shown in Table I. Each group's mean ages were 9.28 ±1.89 years (range 7 to 13 years) and 9.75±1.64 years (range 7 to 13 years), respectively, and there was no statistically significant difference between the two groups. No significant differences were observed in the female/male ratio, BMI and analgesic drug consumption between the two groups ($p > 0.05$). However, during the same period, there was no statistically significant difference between the groups based on haemodynamic parameters. $PeCO_2$ (t2) and $PvCO_2$ (t2) levels were significantly higher in Group 2 compared to Group 1 ($p < 0.001$ for all) (Figure 2). $PeCO_2$ (t2) levels of the Group 1 were hypocapnia, close to normocapnia. In addition, the appearance of PONV was significantly higher in Group 2 compared to Group 1 ($p = 0.006$).

In both groups, the prevalence of PONV was positively correlated with BMI, $PeCO_2$ (t2), and $PvCO_2$ (t2) levels ($p < 0.05$ for all), but inversely correlated with SpO_2 levels ($p < 0.05$ for all) in a bivariate analysis. The relationship between prevalence of PONV, clinical characteristics, and laboratory parameters in Groups 1 and 2 are presented in Tables 2 and 3. In a multiple regression analysis, we found that the $PeCO_2$ (t2) and $PvCO_2$ (t2) levels were independently associated with the occurence of PONV in Group 1 (β = 0.239, p = 0.017; β = 0.875, $p < 0.001$) and Group 2 (β = 0.340, p = 0.014; β = 0.475, p = 0.001), respectively (Tables II and III). There were no intraoperative and postoperative complications in both groups. The power of the study was calculated to be 96.3%.

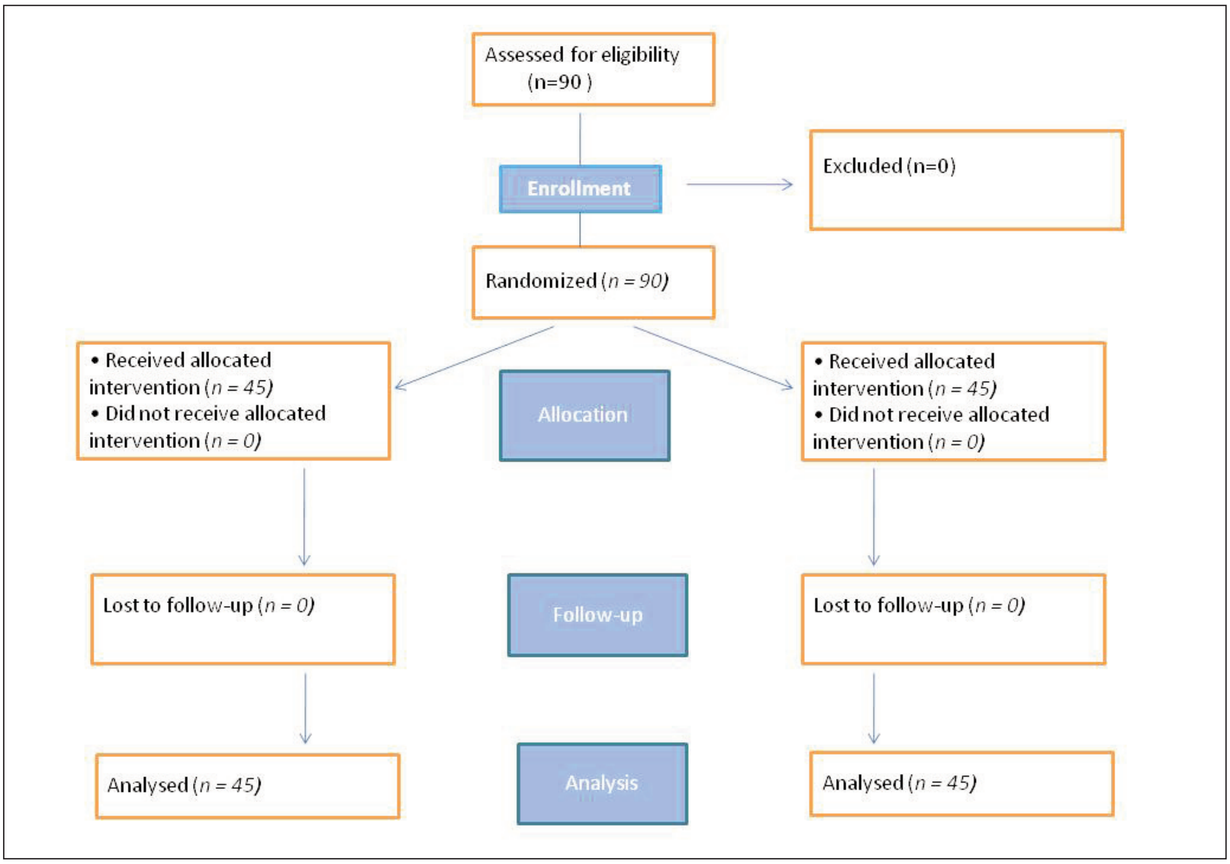

Figure 1. Study flow chart.

Discussion

In this study, we compared the effects of PeCO_2 and PvCO_2 in LMA and FM ventilation on the occurrence of PONV in paediatric patients with surgical interventions in the inguinal region. The main findings of this study are as follows. First, PeCO_2 (t2) and PvCO_2 (t2) levels were significantly higher in Group 2 compared to Group 1. Second, the occurrence of PONV was significantly higher in Group 2 compared to Group 1. Third, the incidence of PONV was positively correlated with BMI, PeCO_2 (t2), and PvCO_2 (t2) levels, and inversely correlated with SpO_2 levels in both groups. Last, PeCO_2 (t2) and PvCO_2 (t2) levels were independently associated with the occurrence of PONV in both groups. This is the

Table I. Demographic characteristics of the both groups.

	Group 1 (laryngeal mask)	Group 2 (face mask)	p-value
Age	9.28±1.89	9.75±1.64	0.861
Gender (female/male)	18/27	11/34	0.114
BMI	19.31±2.44	19.88±1.42	0.876
PONV	17	30	0.006
PeCO_2 (t1)	26.71±1.19	30.46±0.84	<0.001
PeCO_2 (t2)	28.37±1.17	31.15±0.70	<0.001
PvCO_2 (t1)	40.86±0.78	43.24±0.71	<0.001
PvCO_2 (t2)	44.46±0.86	46.17±1.09	<0.001

BMI, Body mass index; PONV, Postoperative nause and vomiting; PeCO_2, End tidal carbondioxide; PvCO_2, Venous carbondioxide values are given in mmHg; t1, 5 min after skin incision; t2, 15 min after skin incision.

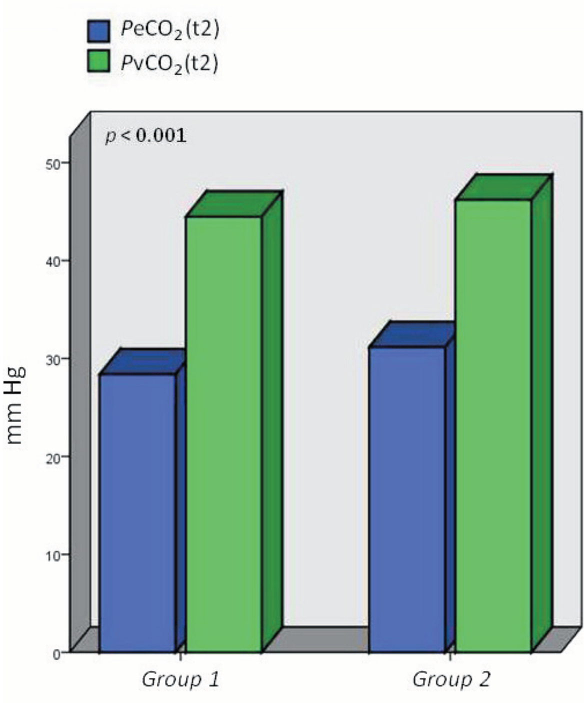

Figure 2. $PeCO_2$ (t2) and $PvCO_2$ (t2) levels in both groups.

first report to reveal the prevalence of PONV in paediatric patients to be significantly different between the FM and LMA group. We believe these favourable results were caused by the positive effect of LMA on oxygenation.

Ideal end-tidal CO_2 levels for adult patients undergoing general anesthesia are still controversial. Saghaei et al[7] showed that the beneficial effect of hypercapnia on PONV in adult patients might be related to enhanced global perfusion and oxygenation and its effects on cerebral and gastrointestinal tissues, with the accompanying improvement in gastrointestinal or neurological functions (the main effector sites for PONV). However, it is believed that children differ from adults both physiologically and metabolically, and have low tolerance to changes in physiological limits. In our study, the lower prevalence of PONV in Group 1 paediatric patients may be due to the positive effect of hypocapnia close to normocapnia.

A variety of anesthetic, non-anesthetic, and postoperative factors are thought to be associated with the occurrence of PONV[2,8]. Approximately 30% of patients who take general anesthesia experienced PONV. The etiology of PONV is multifactorial and includes factors such as the type of surgery, the patient's age, anesthetic applications, analgesic drugs, pain, and anxiety, and is a major complaint from parents of paediatric surgical patients[2]. For these reasons, it continues to be a common and unpleasant postoperative occurrence. Paediatric patients are more likely to develop PONV than adults[9], with rates of more than half associated with strabismus surgery, ton-

Table II. Relationship between PONV and clinical characteristics and laboratory parameters in group 1.

	Pearson's correlation coefficient	*p*-value	β regression coefficient*	*p*-value
BMI	0.527	0.041		
SpO_2 (t2)	–0,776	0.034		
$PeCO_2$ (t2)	0.378	0.010	0.239	0.017
$PvCO_2$ (t2)	0.706	<0.001	0.875	<0.001

*From multiple linear regression.
BMI, Body mass index; SpO_2, Subcutaneous peripheral oxygenation; $PeCO_2$, End tidal carbondioxide; $PvCO_2$, Venous carbondioxide; t2, 15 min after skin incision.

Table III. Relationship between PONV and clinical characteristics and laboratory parameters in group 2.

	Pearson's correlation coefficient	*p*-value	β regression coefficient*	*p*-value
BMI	0.655	0.024		
SpO2 (t2)	–0.812	0.037		
PeCO2 (t2)	0.631	<0.001	0.340	0.014
PvCO2 (t2)	0.683	<0.001	0.475	0.001

*From multiple linear regression.
BMI, Body mass index; SpO_2, Subcutaneous peripheral oxygenation; $PeCO_2$, End tidal carbondioxide; $PvCO_2$, Venous carbondioxide; t2, 15 min after skin incision.

sillectomy/adenoidectomy, orchidopexy, and hernia repair[7,10,11]. Previous reports have shown that 5-hydroxytryptamine (serotonin) secretion is involved in a cascade of events including both the central nervous system and gastro-intestinal tract, and may play a role in the pathogenesis of PONV[12,13]. In addition, the appearance of emesis in the youngest age group was unexpected since it was believed that (within the paediatric population) the prevalence of PONV increases with age[2,8]. Numerous studies have been performed on PONV assessment in paediatric patients. Bourdaud et al[14] identified five independent risk factors for PONV in children: age, predisposition to PONV, surgery at risk, duration of anesthesia > 45 min, and multiple opioid doses. This evaluation was called VPOP scoring. In another study, Kranke et al[15] described four independent risk factors for prediction and validation of PONV in children: duration of surgery > 30 min, age > 3 yr, strabismus surgery, and a positive history of PONV in the children or PONV in relatives (mother, father, or siblings). This evaluation was called POVOC scoring. Common criteria between this scoring and the current study were age, duration of anesthesia, and surgery. However, $P\mathrm{eCO_2}$ and $P\mathrm{vCO_2}$ were not risk factors for VPOP and POVOC scoring systems. In our study, we preferred the same age groups, similar duration and types of operations, and the same anesthetic drugs for both groups. Therefore, we believe that better assessment of the effects of $P\mathrm{eCO_2}$ and $P\mathrm{vCO_2}$ on the occurence of PONV could be obtained.

Intra-abdominal pressure is higher in patients with a high BMI index in the supine position[16]; these patients perform abdominal breathing. Thus, intra-abdominal pressure is higher than intrathoracic pressure. Consequently, nausea and vomiting may be more common than in other patients. In our study, a positive correlation between the BMI and PONV could be explained by this physiological mechanism.

Various studies have demonstrated that the larger $P\mathrm{eCO_2}$ values observed during FM ventilation are probably due to a greater dilution of the alveolar gases before they reach the CO_2 sampler. In fact, while LMA bypasses part of the upper airways, the FM adds its own dead space volume to the anatomical dead space. This situation could reduce the predictive value of $P\mathrm{eCO_2}$ readings during FM ventilation. $P\mathrm{eCO_2}$ with the LMA is comparable with that measured when a tracheal tube is used, although some concerns have been reported regarding *P*eCO2 monitoring and manually controlling ventilation. Different breathing systems have been described to increase the accuracy of $P\mathrm{eCO_2}$ measurement during FM ventilation using a nasopharyngeal cannula[17,18]. In the current study, we performed FM ventilation using the oropharyngeal airway. $P\mathrm{eCO_2}$ measurements were higher during FM ventilation than LMA, which is consistent with previous reports.

Our study has several limitations. First, there is no objective test to evaluate PONV. Therefore, we evaluated the presence or absence of PONV. Second, we used venous blood gas analysis instead of arterial blood gas analysis to evaluate oxygenation since it is a less invasive method. Third, a limited number of patients were included in the study.

Conclusions

We observed markedly higher $P\mathrm{eCO_2}$ (t2) and $P\mathrm{vCO_2}$ (t2) levels, and an increased occurence of PONV in Group 2. Additionally, the occurence of PONV was positively correlated with BMI, $P\mathrm{eCO_2}$ (t2), and $P\mathrm{vCO_2}$ (t2) levels, and inversely correlated with $\mathrm{SpO_2}$ levels in both groups. Multiple regression analysis showed that $P\mathrm{eCO_2}$ (t2) and $P\mathrm{vCO_2}$ (t2) levels were independently associated with the occurence of PONV. Therefore, the elevated levels of $P\mathrm{eCO_2}$ (t2) and $P\mathrm{vCO_2}$ (t2) are independent risk factors for PONV, and these parameters may be used as adjunctive tools to assess the occurence of PONV. The findings of this study demonstrate for the first time the relationship between $P\mathrm{eCO_2}$ (t2) and $P\mathrm{vCO_2}$ (t2) levels and the occurence of PONV in paediatric patients. Further prospective randomized clinical studies with larger sample sizes are required to determine whether these alterations are consistent and clinically relevant.

Conflict of interest

The Authors declare that they have no conflict of interests.

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