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Comparison of Acid-base Status and Hemodynamic Stability during Propofol and Sevoflurane-based Anesthesia in Patients Undergoing One Lung Ventilation

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Abstract

Background: This study compared the effects of Propofol and Sevoflurane anesthesia on the stabilization of acid-base values and hemodynamic parameters during one lung ventilation (OLV).

Methods: Patients with OLV were randomized two groups: the Propofol group (Group P, n=23) and the Sevoflurane group (Group S, n=23). In Group P, patients were induced and maintained with Propofol. In Group S, patients were induced with Propofol and maintained with Sevoflurane. Blood samples were obtained one minute before OLV (t_1) and 1, 2 hours (t_2, t_3) after OLV. Hemodynamic values were recorded at patients entered operation room (T_1); one minute before intubation (T_2); 1, 3, and 5 minutes after intubation (T_3, T_4, T_5); one minute before OLV (T_6); and 1, 2 hours after OLV (T_7, T_8).

Results: There were significant differences between different time points in pH value, base excess, and bicarbonate (P<0.001). The values of pH, base excess and bicarbonate in two groups both tended to reduce progressively from t_1 to t_3. There were no significant differences between the groups at all of the time points. There were significant differences between the different time points in terms of mean arterial pressure and heart rate (P<0.001), more patients in Group P received Nicardipine for hypertension (P<0.001). However, there were no significant intergroup differences.

Conclusions: The duration of one lung ventilation, anesthesia and operation, rather than the anaesthetic used, are key factors in maintaining acid-base balance during OLV. Sevoflurane anesthesia is superior to Propofol anesthesia in avoiding the fluctuation of hemodynamic parameters.

Keywords: Acid-base; Hemodynamic; Propofol; Sevoflurane; One lung ventilation

Introduction

The One lung ventilation (OLV) allows for increasingly complex intrathoracic surgery and is required with the increased use of minimally invasive techniques. The One lung ventilation facilitates surgical exposure of the unventilated lung, and can prevent lung rupture and contamination. However, OLV significantly alters intra-thoracic lung volumes, and the normal relationship between functional residual capacity and closing capacity. These alterations may be associated with life-threatening impairment of gas exchange [1]. Blood flow through the unventilated lung cannot be oxygenated and contributes to arterial hypoxemia. In addition to hypoxemia, collapse of the non-ventilated lung, volutrauma of the ventilated lung and surgical manipulation may affect acid-base balance and hemodynamic homeostasis. Hypoxic pulmonary vasoconstriction (HPV), a homeostatic mechanism intrinsic to the pulmonary vasculature, plays an important role during OLV. Intrapulmonary arteries constrict in response to alveolar hypoxia, diverting blood to the better oxygenated lung segments, thereby improving ventilation-perfusion matching and systemic oxygen delivery [2,3].

During OLV, anesthesia is maintained by delivering an inhalation anesthetic, such as Sevoflurane, to the ventilated lung or by infusion of an intravenous anesthetic, for example, Propofol. Due to the distinct pharmacological properties of each anesthetic, the method chosen to maintain anesthesia may affect the patients' acid-base status and hemodynamic stability. As is well-known that Propofol may induce metabolic disturbances that occur primarily in intensive care patients with impaired oxygen delivery who receive prolonged infusions of high-dose Propofol [4,5]. However, metabolic disturbances have also been reported in surgical patients receiving low doses of Propofol [6,7]. Inhalation anesthetics (Sevoflurane) may impair HPV and increase intrapulmonary shunt and hypoxemia. Simultaneously, Sevoflurane anesthesia may result in arterial hypotension. Metabolic disturbances, hypoxemia, and hypotension may impair homeostasis, particularly during OLV. In this prospective randomized single blind study, we compared acid-base profiles and hemodynamic parameters in patients undergoing OLV for thoracic surgery under Propofol or Sevoflurane based general anesthesia. All other elements of standard anesthetic management were maintained as comparable as possible.

The stable of acid-base status during the anesthesia has been widely concerned and studied in many kinds of surgeries such as brain, heart catheter. However, until now, few researches have been focused on that of the OLV in the thoracic surgery. Here, we supposed that the acid-base status would be changed despite undergoing less than 2 hours OLV even in ASA I - II patients. The aim of this study is to compare the effects of Propofol and Sevoflurane anesthesia on the stabilization of acid-base values and hemodynamic parameters during one lung

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ventilation (OLV) via measurements of arterial blood gas indexes, mean arterial pressure (MAP), and heart rate (HR).

Methods

Subjects and allocation

This study was approved by the Institutional Medical Ethics Committee of First Affiliated Hospital of Anhui Medical University, and was in accordance with the approved guidelines. Informed consent was obtained from all subjects. Patients ranged in age from 18 to 65 years, had an American Society of Anesthesiology (ASA) physical status I or II, and were undergoing OLV for thoracic surgery. Forty-six of fifty qualified patients (2 patients refused and 2 operations not qualified) were enrolled, the sealed envelope method was used for randomization, and the patients were divided into two groups (Sevoflurane: Group S, n=23 and Propofol: Group P, n=23) (Figure 1). Patients with ASA physical status greater than II, diabetes, uncontrolled hypertension, severe metabolic, renal, pulmonary, or hepatic disease, or OLV less than or greater than 120 ± 30 minutes were excluded from the study.

Anesthesia and data collection

All patients were sedated with midazolam (0.03-0.05 mg/kg) intramuscularly 30 minutes before the operation. In the operating room, oxygen saturation, electrocardiogram, invasive arterial blood pressure, and the bispectral index (BIS) value were continuously monitored and mean arterial pressure (MAP), and heart rate (HR), were recorded (T_1). Propofol (1.5-2.5 mg/kg) in Group S and Propofol (target controlled infusion, 1-3 μg/ml) in Group P were used for induction of anesthesia. After administration of Sufentanil (0.4-0.6 μg/kg) and Vecuronium (0.08-0.12 mg/kg) and when the BIS value was between 40 and 60, patients were intubated with a double lumen endotracheal tube. Hemodynamic parameters, mean arterial pressure (MAP), and heart rate (HR), were recorded before intubation (T_2), and 1, 3, and 5 minutes after intubation (T_3, T_4, T_5). After intubation, and before OLV, arterial samples for blood gas analysis were obtained (t_1) and hemodynamic parameters were recorded (T_6). 1 and 2 hours after the onset of one lung ventilation, the second and the third blood gas samples were obtained (t_2, t_3) and the hemodynamic parameters were again recorded (T_7, T_8).

In Group S, anesthesia was maintained to achieve a BIS value between 45 and 60 with Sevoflurane (1-3%) and Remifentanil (0.1-0.5 μg/kg/min). In Group P, anesthesia was maintained to achieve a BIS value between 40 and 60 with total intravenous anesthesia using Propofol (target controlled infusion, 1-3.5 μg/ml) and Remifentanil (0.1-0.5 μg/kg/min). In both groups, Vecuronium (0.01-0.05 mg/kg) was used for muscle relaxation. Based on surgical events and the BIS value, the dosage of Remifentanil (0.1 μg/kg/min), Propofol (0.5 μg/mL), or Sevoflurane (0.5%) was adjusted in a step-wise fashion. Vasoactive drugs were used to maintain mean arterial blood pressure (MAP) between 60 and 90 mmHg and heart rate between 50 and 90 beats/min. In both groups, hypertensive and/or tachycardic episodes of more than 10 minutes were treated with an intravenous bolus of Nicardipine (0.1 mg) or Esmolol (0.5 mg/kg). Hypotension was treated with an intravenous bolus of ephedrine (4-6 mg) or phenylephrine (20-40 μg) and bradycardia with atropine (0.3-0.5 mg). Ventilation was mechanically controlled and OLV was performed using a tidal volume of 6-8 mL/kg, respiratory rate of 12-20 respirations/min, and fraction of inspired oxygen of 100%. Ventilation was adjusted to maintain carbon dioxide levels between 35-45 mmHg. Sodium (Na), potassium (K), bicarbonate (HCO_3), chloride (Cl), pH, and lactate were measured, and base excess (BE) and anion gap (AG) were calculated.

Statistics

Data are expressed as mean ± standard deviation (SD). Data were analyzed using the independent samples t-test (t test) and repeated measures ANOVA. Numerical data are expressed as absolute number and were compared using Fisher exact test. A p value <0.05 was considered statistically significant.

Results

In the work, the total 46 cases were selected form 50 cases. The reason is described as following: 2 cases were discarded because those who declined to participate before operation, case 1 was excluded due to OLV time less than 1 h, the case 2 was given up for massive hemorrhage. Demographic data and characteristics of surgery were comparable between groups (Table 1; Figure 1). There were no significant differences in age, weight, height, sex, body mass index (BMI), urine volume, or volume of fluid input. The dose of Sufentanil, Remifentanil and Vecuronium, the length of surgery, and the duration of the one lung ventilation procedure were not different between groups. All operations were successful without adverse events or complications.

Acid-base balance

In blood gas analyses, there were no significant differences between two groups in terms of pH, base excess (BE), blood lactate (Lac), anion gap (AG), bicarbonate (HCO_3), however, there were significant differences between different time points in terms of PH, BE, HCO_3 in group S and group P respectively, and the mean values of the three terms present a progressive falling tendency (Table 2; Figure 2).

Hemodynamic parameters

There were no significant differences between the two groups in the term of mean arterial pressures and heart rate comparing at the same

Index	Group P	Group S	P or Fisher P
Age (years)	64.4 ± 8.1	61.0 ± 7.8	0.752
Weight (kg)	63.4 ± 10.5	60.1 ± 7.6	0.068
Height (cm)	168 ± 6.8	169 ± 4.9	0.270
BMI	22.3 ± 2.5	20.7 ± 2.0	0.283
Gender (men) (n)	20	20	1
Vecuronium (mg)	15.5 ± 4.3	14.6 ± 3.3	0.347
Sufentanil (mg)	67.2 ± 12.3	65.9 ± 17.8	0.077
Remifentanil (mg)	2.8 ± 0.9	2.2 ± 0.9	0.627
Length of operation procedure(minutes)	208.8 ± 55.5	209.1 ± 74.0	0.566
Length of OLV procedure (minutes)	159.5 ± 43.5	158.3 ± 56.5	0.452
Volume of urine (ml)	511.9 ± 193.6	387.5 ± 213.9	0.316
Volume of transfusion (ml)	1908.7 ± 694.7	2090.9 ± 645.8	0.930

Table 1: Demographic characteristics of patients in the group P (n=23) and in the group S (n=23), and also the results of statistical comparison. *BMI: Body Mass Index; OLV: One Lung Ventilation.

Index	Group	N	t_1	t_2	t_3	P_{time}	P_{group}
pH	Group P	23	7.44 ± 0.03	7.39 ± 0.05	7.38 ± 0.05	0	0.699
	Group S	23	7.43 ± 0.03	7.40 ± 0.06	7.37 ± 0.05		
BE	Group P	23	1.94 ± 1.23	0.60 ± 1.75	-0.43 ± 1.80	0	0.68
	Group S	23	2.26 ± 1.80	0.61 ± 2.58	-0.08 ± 2.22		
Lac	Group P	23	1.57 ± 0.85	1.62 ± 0.82	1.65 ± 0.81	0.556	0.328
	Group S	23	1.35 ± 0.45	1.44 ± 0.66	1.52 ± 0.48		
AG	Group P	23	9.20 ± 1.57	9.63 ± 1.59	10.47 ± 2.4	0.054	0.973
	Group S	23	9.25 ± 2.15	10.13 ± 2.48	9.96 ± 2.00		
HCO_3^-	Group P	23	26.30 ± 1.22	25.80 ± 2.40	25.07 ± 2.63	0	0.847
	Group S	23	26.74 ± 1.84	25.66 ± 2.39	25.10 ± 1.94		

Table 2: Blood gas index of patients in the group P (n=23) and in the group S (n=23), and also the results of statistical comparison between groups. *BE: Base Excess; Lac: Lactate; AG: Anion Gap.

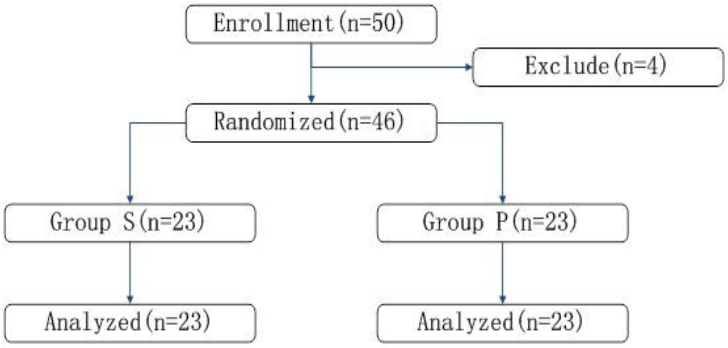

Figure 1: Flow diagram of the study.

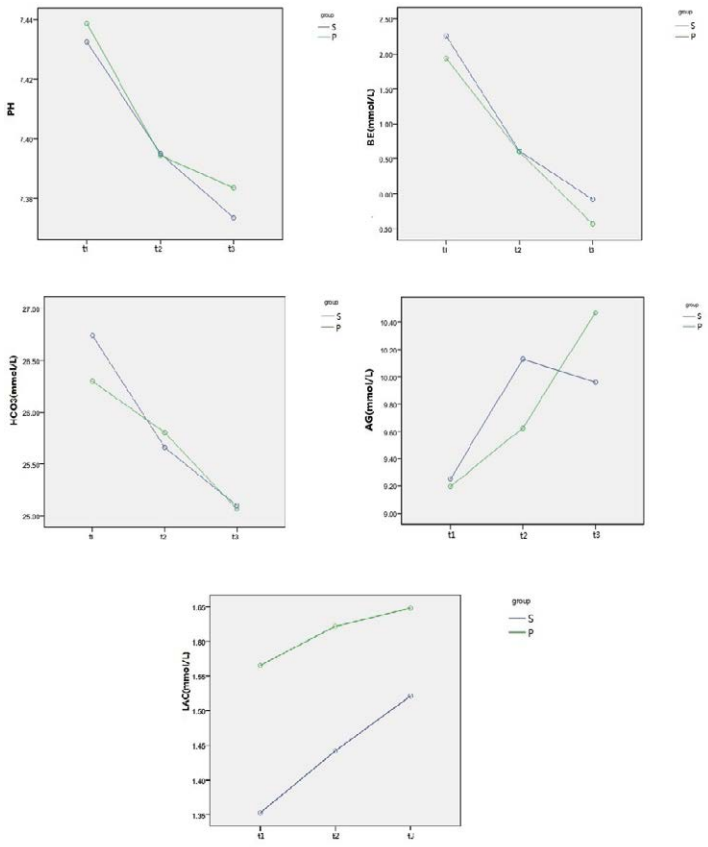

Figure 2: Profile plots of blood gas index at t1, t2, t3. In blood gas analyses, there are similar tendency of two groups. pH, BE, HCO3 perform down trends and Lac and AG, Lac show rising trends.

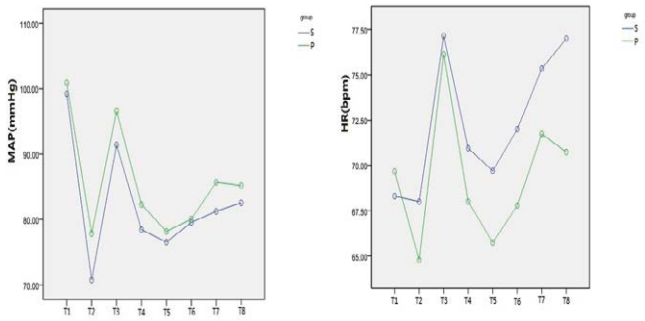

Figure 3: Profile plots of hemodynamic parameters at T1, T2, T3, T4, T5, T6, T7, T8. In hemodynamic parameters, they show the similar volatility in the general tendency.

Index	Group	T_1	T_2	T_3	T_4	T_5	T_6	T_7	T_8	P_{time}	P_{group}
MAP	Group P	101 ± 14	78 ± 11	97 ± 13	82 ± 10	78±8	80 ± 13	86 ± 10	85 ± 11	0.000	0.164
	Group S	99 ± 12	71 ± 8	91 ± 16	78 ± 9	77±10	80 ± 8	81 ± 7	83 ± 11		
HR	Group P	70 ± 10	65 ± 8	76 ± 12	68 ± 10	66±7	68 ± 9	72 ± 11	71 ± 9	0.000	0.272
	Group S	68 ± 14	68 ± 12	77 ± 14	71 ± 11	70 ± 12	72 ± 10	75 ± 11	77 ± 15		

Table 3: Hemodynamic Parameters of Patients in the group P (n=23) and in the group S (n=23), and also the results of statistical comparison between groups. *MAP: mean arterial pressure; HR: Heart Rate.

Agent	Group P	Group S	X^2	p
Nicardipine	16	3	15.154	0.000
Esmolol	1	1	0	1
Atropine	2	3	0	1
Phenylephrine	3	1	0.274	0.601
Ephedrine	8	12	0.789	0.375

Table 4: Use of Vasoactive Drugs of Patients in the Group P (n=23) and in the Group S (n=23), and also the results of statistical comparison between groups.

time point. However, there were significant differences between the different time points and they show the similar volatility in the general tendency (Table 3; Figure 3).

Vasoactive agent

There were significant differences between two groups in terms of Nicardipine and more patients in the Propofol group received Nicardipine for hemodynamic evaluation (Table 4; Figure 3).

Discussion and Conclusion

Respiration involves the acquisition of oxygen, the removal of carbon dioxide, and the control of acid-base balance [8]. Ventilation is controlled by neural and chemical inputs. One-lung ventilation, a standard practice in thoracic surgery, may result in manipulation of the airway, tissue damage, significant ventilation-perfusion mismatching, and hypoxia [9]. During OLV, blood flow through the unventilated lung is not oxygenated, contributing to arterial hypoxemia. Although the occurrence of hypoxemia has decreased, it may occur in about 10% of cases [10]. Hypoxia results in increased lactate production and excretion due to changes in the mitochondrial redox status caused by reduced oxygen availability [11,12]. Hypoxia may result in acid-base various disturbances ranging from alkalosis to acidosis. Hypoxia can affect non-genomic and genomic systems, in part via altered hypoxia-inducible factor (HIF) metabolism. Severe hypoxia can result in metabolic and hypercapnic acidosis, increased lactate formation, and decreased arterial pH. Metabolic and respiratory acidosis, generally considered deleterious to cell function, may provide cytoprotection. Hypoxia-induced anti-inflammatory, antioxidant, and anti-apoptotic mechanisms limit the hypoxic or ischemia/reperfusion injuries. The use of alkalinizing agents and re-oxygenation, to correct the hypoxia and acidosis may be ill advised. A better understanding of the "pH paradox" or permissive acidosis, may offer therapeutic possibilities [13]. With hypoxia, changes in bicarbonate are matched by changes in lactate, indicating that anaerobic glycolysis is a key factor determining the metabolic alterations and overall acid-base status [14]. Our study is consistent with previous studies that describe a decrease in BE bicarbonate, and pH in one lung ventilation for thoracic surgery.

In this study, there were no significant differences in blood gas values between two groups. Previous studies comparing Sevoflurane and Propofol reported variable results [15]. Metabolic acidosis has been reported in pediatric patients undergoing cardiac catheterization anesthetized with Propofol, but not Sevoflurane [16]. Propofol for total intravenous anesthesia in OLV may be safer than Sevoflurane and may have a lower risk of direct damage from anesthetic metabolites [17]. However, Sevoflurane may offer better protection against reperfusion injury after OLV [18]. The bispectral index Bispectral index, a technique which has been scientifically validated, is commercially available to monitor the depth of for anesthesia [19]. It was used to titrate anesthetic dose, and the optimum range of BIS values for adequate anesthesia is between 40 and 60. Risk factors for metabolic disorders related with Propofol are cardiac disease, pediatric patients, patient with metabolic acidosis, and overuse of Propofol [20,21]. However, in our study, patients in both groups were ASA category I or II, and considered relatively healthy and low risk for anesthetic complications. Intrapulmonary arteries constrict in response to alveolar hypoxia, hypoxic pulmonary vasoconstriction (HPV), diverting blood to better-oxygenated lung segments and optimizing ventilation-perfusion matching and systemic oxygen delivery. Inhibition of HPV, in a dose dependent fashion, was noted with older inhaled anesthetic agents, including halothane and nitrous oxide. Newer agents, for example Desflurane and Sevoflurane, do not appear to inhibit HPV. A study in anesthetized piglets demonstrated that Sevoflurane, at a clinically relevant concentration, had no significant effect on HPV [22]. Additionally, both tend-tidal carbon dioxide and oxygen saturation were controlled in the ideal range

throughout the procedure. Therefore, arterial blood gas measurements remained in the acceptable range despite there were statistic difference over time. However, it is unknown whether similar acid-base responses would be seen in patients with an ASA of greater than II or OLV of greater duration.

Our study shows that less Nicardipine are required in the Sevoflurane group when compared to the Propofol group. Simultaneously, the results implied that depressurization of Sevoflurane are greater than Propofol. Our findings are in agreement with Sneyd et al. work demonstrating increased frequency of hypotensive events in the Sevoflurane group, and these patients required a greater total dose of ephedrine [23]. These authors reported that both Sevoflurane and Propofol, in combination with Remifentanil, are satisfactory agents for maintenance of anesthesia for neurosurgery.

In our randomized prospective study, there are three main findings: Firstly, base excess, bicarbonate, and pH significantly decreased across t_1, t_2, and t_3; however, there were no differences between groups. Secondly, the one lung ventilation and the duration of OLV play a major role in acid-base balance. Propofol and Sevoflurane are both safety profiles for thoracic surgery. Thirdly, more hypertensive events requiring Nicardipine were observed in the Propofol group. Sevoflurane anesthesia did not have a higher risk of arterial hypotension.

There are several limitations of this study. We only focus on acid-base disturbances and hemodynamic changes for two hours during OLV for One lung ventilation is rarely used for more than two hours in thoracic surgical procedures. In addition, recovery and postoperative data were not recorded. Further studies will be needed in the future.

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Implication Statement

This article is an original work, has not been published before and is not being considered for publication elsewhere in its final form either in printed or electronic form.

Ethical Adherence

Ethical approval was provided by the Ethical Committee Anhui Medical University, Hefei, Anhui, China in July, 2013. All patients provided informed consent and all procedures were conducted according to the Declaration of Helsinki.

Conflicts of Interest

None of the authors have any conflicts of interest.

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