Oxygen reserve index guided oxygen titration in one lung ventilation with low fresh gas flow

Abstract

Background/aim: Continuous oxygen reserve index (ORI) measurement with multiple wave pulse co-oximetry is a noninvasive measurement. The decrease in the ORI trend provides a prediction for the development of hypoxemia and provides information on hyperoxia. Our aim is to determine the effect of ORI-guided oxygen titration on hyperoxemia-mediated morbidity.

Materials and methods: Consecutive 120 ASA I-III patients, 18-70 years of age, without severe obstruction or restriction, undergoing one lung ventilation (OLV), were included in the study. Patients were divided into 4 groups. Oxygen titration without ORI monitoring with low-flow anesthesia (1 L/min, Group 1, n=25) and high-flow anesthesia (4 L/min, Group 2, n=28). Oxygen titration by ORI monitoring with low flow anesthesia (1 L/min, Group 3, n=25) and high flow anesthesia (4 L/min, Group 4, n=25). FiO_2 increased up to 100% if necessary. OLV time, duration of surgery and anesthesia, FiO_2 applied during OLV, oxygen application time (T) over 60%, vital signs, hospital and ICU stay time and complications were recorded.

Results: There was a statistically significant difference in terms of FiO_2 used during OLV ($p< 0.05$). There was no difference in ORI values ($p <0.05$). In Group 3, both PaO_2 and SpO_2 were significantly lower than the others both before and during OLV. There was no significant difference in terms of ORI parameters between low flow and high flow anesthesia groups. There was a strong, positive correlation between the duration of hospital stay and FiO_2 used above 80% during OLV.

Conclusion: We concluded that ORI-guided thoracic anesthesia may reduce hospital stay and increase patient safety.

Key words: Oxygen reserve index, thoracic surgery, one lung ventilation, low flow anesthesia

1. Introduction

Oxygen saturation (SpO_2) is measured by pulse oximetry during intraoperative period. Unless there is a significant decrease in PaO_2 (arterial oxygen partial pressure), SpO_2 may not always adequately reflect the reduction in oxygenation. Multi-wave pulse co-oximeter (Masimo, Irvine, CA, USA) and oxygen reserve index (ORI) measurement offers a noninvasive way of providing real-time visibility to oxygenation status in moderate hyperoxic range (PaO_2 of approximately 100 to 200 mm Hg) [1]. ORI provides additional data on hyperoxia when SpO_2 is greater than 98% [2]. The harmful effects of hyperoxemia include the formation of reactive oxygen compounds, cell damage, inflammatory pathway activation and cell death [3]. Absorption atelectasis, prolongation of hospital stay and poor neurological activity in discharge have been reported previously [4].

One lung ventilation (OLV) is a technique used for single lung isolation to facilitate a wide variety of procedures on ipsilateral thoracic or mediastinal structures as well as to provide lung isolation. In the studies conducted to date, the importance of intraoperative hypoventilation, hypoxemia, ventilation perfusion disorders that may occur during OLV has been mentioned [5,6]. Immediately after the onset of OLV, arterial oxygenation and saturation decrease. Accordingly, hypoxic pulmonary vasoconstriction (HPV) occurs. In order to keep SpO_2 over 90% during this process, 100% oxygen (O_2) is recommended [7]. Therefore, the patients are exposed to hyperoxemia.

This study aims to protect patients from the harmful effects of hyperoxemia with a noninvasive probe during OLV. The primary outcome of this study is to compare the mean FiO_2 (the fraction of inspired oxygen) values in patients undergoing thoracic surgery with and without ORI monitoring. The secondary outcome is to compare the duration of 100% O_2 use.

2. Materials and Methods

The study was approved by the Human Research Ethics Committee of our University Medical School. Written informed consent was obtained from every patient during the preoperative visit. The study was registered in UMIN Clinical Trials Registry (UMIN000038068). This prospective, randomized, cross-sectional study included patients with lung tumors between September 2018 and September 2019. Inclusion criteria were age between 18 and 80 year old patients undergoing elective thoracic surgery requiring OLV. Exclusion criteria were the refusal to participate and a history of pulmonary resection.

Patients were divided into 4 groups. Oxygen titration in the absence of ORI monitoring with low-flow anesthesia (1 L/min, Group 1, n=25) and normal-flow anesthesia (3-4 L/min, Group 2, n=28). Oxygen titration by ORI monitoring with low flow anesthesia (1 L/min, Group 3, n=25) and normal flow anesthesia with ORI monitoring (3-4 L/min, Group 4, n=25). Randomization was performed by opaque sealed envelopes.

After the patients were admitted to the operating theatre, SpO_2, Electrocardiogram (ECG) and noninvasive blood pressure were measured routinely. Anesthesia was induced with propofol, 2-3 mg/kg, rocuronium, 0.6 mg/kg, and fentanyl, 2 to 3 mcg/kg. A 20 G, radial artery catheter was placed and connected to a disposable pressure transducer following

the induction of anesthesia. Tracheal intubation was performed using a left Robertshaw double lumen tube. We confirmed the position by a flexible 4.2 mm fiberoptic bronchoscope. Anesthesia maintenance was achieved with sevoflurane or desflurane, and remifentanil 0.25 mcg/kg/h.

In addition to standard follow-up parameters, ORI, Noninvasive and Continuous Hemoglobin (SpHb), Peak Variable Index (PVI), Perfusion Index (PI) and SpOc (oxygen contusion) were continuously monitored in Group 3 and Group 4. Patients' SpO_2, arterial oxygen partial pressure (PaO_2), ORI, PVI, PI, SpOc values were recorded and the correlation between them were determined on the continuous graphs. ORI values were measured with the Rainbow R1 25-L probe (Irvine, CA, USA). Patients were monitored with the Masimo Low Noise Cabled Sensors (M-LNCS) probe, which is attached to the Radical-7 Pulse CO-Oximeter device for the measurement of PVI. The duration of surgery, anesthesia, OLV and total 100% oxygen application time were recorded. The titration of oxygen was performed manually according to the SpO_2 and PaO_2 values in Group 1 and 2.

In the study groups oxygen titration was performed according to PaO_2, SpO_2, ORI and SpOc values. Routine blood gas follow-ups were taken before achieving OLV, at the 15th minute of OLV, 45th minute of OLV. Routinely, patients were ventilated with 50% FiO_2 (50% oxygen + 50% air mixture, 1 liter / minute fresh gas flow) after induction. FiO_2 was increased to 60% when OLV is applied. Afterwards FiO_2 was increased to 70%, 80% and 100% concentration if necessary. Hemodynamic variables were recorded including heart rate and blood pressure. The incidence of thromboembolic complications, arrhythmia, pneumonia, the duration of hospital and intensive care unit stay were recorded.

Data analysis

Study data was processed using IBM SPSS Statistics for Windows, Version 22.0 Armonk, NY: IBM Corp. The distribution of the variables were analyzed using the Kolmogorov–Smirnov test. The Mann-Whitney U test was used to investigate the qualitative data. The Spearman's correlation analysis was used to examine correlation between the variables. For binary comparisons, One-Way ANOVA test was used for the numerical data that conformed to the normal distribution, and the Mann Whitney-U test was used for those who did not comply. As a four group comparison test, One-Way ANOVA was used for the data with normal distribution and the Kruskal-Wallis test was used for those who did not comply. Chi-square test was used to analyse discrete variables. A value of $P < 0.05$ was considered statistically significant.

Sample size calculation

Based on a 25% reduction in the use of O_2 with > 60% FiO_2 during OLV, it was necessary to take a total of 100 patients in this study. At a significance level of 95% the standard effect size was taken as 0.65 with a power of 90%. Therefore min 25 patients per group were enrolled.

3. Results

A total of 103 patients aged 18 to 79 years (54.53 ± 14.46), were included in the study (Table 1). Of these patients, 27 (26.2%) were female and 76 (73.8%) were male. None of the patients were excluded. The duration of OLV with >%60 FiO_2 was significantly lower in ORI study groups: 67.6±97.5 min, 97.32±99.7 min, 39.2±74.1 min and 22.4±49.4 min in Group 1,2,3 and 4 respectively (p=0.003). Mean FiO_2 values during OLV were

71.6±12.25%, 74.64±16.66%, 62.8±13.08% and 56.4±11.5% in Group 1,2,3 and 4 respectively (p=0.001).

The types of surgeries were VATS biopsy, VATS lobectomy and VATS Wedge Resection (p=0.085). There was no statistically significant difference between groups in terms of hemodynamic parameters (Table 2). In Group 3, both PaO_2 and SpO_2 were significantly lower than the others both before and during OLV (Table 3). Other blood gas parameters were similar.

There was no significant difference in terms of ORI parameters between low flow and high flow anesthesia groups. There was a strong, positive correlation between the duration of hospital stay and FiO_2 used above 80% during OLV (Table 4, p <.001). There was no significant relationship between the duration of Intensive Care Unit stay and OLV with above 80% FiO_2. No complication was recorded including thromboembolism, arrhythmia or pneumonia.

4. Discussion

In this study, the ORI monitor was associated with lower mean FiO_2 values during OLV. With the addition of ORI monitor, lower PaO_2 values were recorded. A strong significant correlation was found between the duration of OLV with above 80% FiO_2 and the duration of hospital stay.

The hypoxic pulmonary vasoconstriction during OLV is characteristically biphasic. It is activated within the first few seconds in its first phase and reaches its maximum within 15 minutes. The second phase begins 30-40 min later and makes a late peak at the second hour. The maximal hypoxic pulmonary vasoconstriction response during OLV reduces blood flow to the nondependent lung by 50% [6]. In this process, increasing the FiO_2 up

to 1.0% and alveolar recruitment maneuvers are among the initial treatment options. However, high FiO_2 is associated with hyperoxia-induced oxidative acute lung injury [8]. Characteristics of injury are increased inflammatory-cell counts, reabsorption atelectasis and rised pulmonary permeability, which may result in necrosis. The FiO_2 should be reduced as soon as possible. For this purpose, continuous monitoring is not possible when the analysis of blood gas parameters is intermittent. The values of the patient are recorded noninvasively with ORI measurements which is a unit-less scale. When the PaO_2 value exceeds 100 mmHg, it exceeds 0.1. In this way it is possible to protect the patient from the harmful effects of hyperoxia. ORI is a relative indicator of changes in PaO_2 in the hyperoxic range between 100 to 200 mmHg.

The use of ORI monitor is becoming increasingly common during OLV. It has been used for the determination of hypoxia however, studies on hyperoxia are extremely limited [9]. 1.0% FiO_2 is often used during OLV. In our study, mean FiO_2 during OLV was 62.8 ± 13.08% and 56.4 ± 11.5% in patients undergoing ORI monitor. The values were 71.6 ± 12.25% and 74.64 ± 16.66% in traditionally monitored patients and were significantly higher. This result indicates that the risk of hyperoxia will be lower in patients undergoing the ORI monitor.

Arterial blood gas analysis is essential for the management of patients. However, it is not a continuous monitoring method and besides takes a long time. We obtained real time data with the ORI monitor. Thus it was possible to detect changes in pulmonary function. As Campos and Sharma [10] mentioned, ORI cannot replace arterial blood gases analysis, however it is useful to assess oxygenation. In groups without ORI monitors, the FiO_2 was

significantly higher than 80%. Moreover, in our study, it was revealed that these patients had a longer hospital stay.

Koishi et al. [11] showed in their 15 subjects that ORi and PaO_2 were highly correlated during OLV. However in 13 of the 15 cases, PaO_2 was >240 mmHg at the start of OLV. Applegate et al. [12] concluded that when SpO_2 is >98%, ORI can distinguish PaO_2 between 100 and 150 mm Hg. The main difference of our study was the prevention of patients from hyperoxemia with the ORI monitor. The harmful effects of oxygen was eliminated by titrating the oxygen. There was a strong, positive correlation between the duration of hospital stay and FiO_2 used above 80% during OLV. There was no significant relationship between the duration of Intensive Care Unit stay and OLV with above 80% FiO_2.

Exaggerated perioperative inflammatory response in patients undergoing lung resection surgery has been shown to potentially increase the risk of postoperative pulmonary complications [6]. Also, patients undergoing thoracic surgery are at risk of hypoxemia and hypercarbia due to their existing disease. Besides one lung ventilation may cause ventilation perfusion rate changes and devastating effects due to mechanical ventilation [13]. In the present study we revealed that low flow anesthesia can be safely used during one lung ventilation. Using the ORI monitor, we had no complications.

Limitations

In this study, malignant and benign patients were studied together. The fact that only patients with malignancy were not included in the study might have had an impact on the

length of stay in the hospital or ICU. This was the most important limitation of the study. Studying in larger sample size, might have increased the reliability of the study.

Conclusion

The adjustment of ORi with peripheral oxygen saturation and blood gas analysis demonstrated that hyperoxemia could be prevented during OLV in patients under low flow or high flow anesthesia. We concluded that ORI-guided thoracic anesthesia may reduce hospital stay and increase patient safety.

Acknowledgement

The authors state no conflict of interest

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Tables

Table 1: Patients' demographic and clinical characteristics

	Group1 (n=25)	Group2 (n=28)	Group3 (n=25)	Group4 (n=25)	p
Gender					
Female	2(8%)	8(28.6%)	9(36%)	8(32%)	0.110[c]
Male	23(92%)	20(71.4%)	16(64%)	17(68%)	
Age (years)	49.48±18.7	58.82±12.73	53.52±12.19	55.8±12.54	0.207[b]
BMI (kg/m^2)	25.37±4.81	27.18±4.54	28.18±5.49	27.18±4.04	0.317[b]
ASA					
ASA1	3(12%)	0(0%)	0(0%)	1(4%)	0.053[c]
ASA2	22(88%)	21(75%)	21(84%)	20(80%)	
ASA3	0(0%)	7(25%)	4(16%)	4(16%)	
Reoperation	1(4%)	1(3.6%)	0(0%)	0(0%)	0.586[c]
Complication	3(12%)	2(7.1%)	3(12%)	2(8%)	0.898[c]
Duration of surgery (min)	181.25±79.58	204.82±96.69	194.4±100.8	199.4±89.4	0.824[a]

Duration of anesthesia (min)	230±83	255.43±98.39	239.8±103.2	257.8±94.1	0.696[a]
Duration of hospital stay (days)	6.56±3.03	6.21±2.63	6.44±3.44	5.52±1.64	0.734[b]
Duration of OLV (min)	121.9±72.41	146.79±82.7	135.4±87.6	156.6±80.2	0.364[b]
OLV with >%60 FiO_2 (min)	67.6±97.5	97.32±99.7	39.2±74.1	22.4±49.4	0.003*[b]A
Mean FiO_2 during OLV (%)	71.6±12.25	74.64±16.66	62.8±13.08	56.4±11.5	0.001*[b]B
Perioperative colloid (mL)	350±399	448±491	280±265	402±441	0.750[b]
Perioperative cristalloid (mL)	1096±414	1285±656	1196±616	1288±447	0.524[b]

[c] Chi-square test: values are given as frequency (percentage)

[b] Kruskal Wallis H test: values are given as mean ± standard deviation

[a] One-Way Anova test: values are given as mean ± standard deviation

*p<0.05 Statistically significant

A= G2 vs G3, p=0.005; G2 vs G4, p=0.001

B= G1 vs G3, p=0.019; G1 vs G4, p=0.001; G2 vs G3, p=0.006; G2 vs G4, p=0.001; G3 vs G4, p=0.021

Group 1: Low-flow anesthesia and oxygen titration without ORI monitoring

Group 2: Normal-flow anesthesia and oxygen titration without ORI monitoring

Group 3: Low-flow anesthesia and oxygen titration with ORI monitoring

Group 4: Normal-flow anesthesia and oxygen titration with ORI monitoring

Table 2: Hemodynamic parameters, SpO_2, $etCO_2$ and temperature variables of patients before and during OLV

Before OLV	**Group1**	**Group2**	**Group3**	**Group4**	
	(n=25)	(n=28)	(n=25)	(n=25)	**p**

MAP (mmHg)	73.87±13.67	79.82±10.36	83.08±16.4	82.64±20.24	0.176[b]
Heart Rate (beat/min)	68.72±12.71	74.57±14.95	73.4±13.37	87.4±99.73	0.265[b]
SpO_2 (%)	99.08±1.85	99.46±0.69	98.16±1.72	98.6±1.41	0.006*[b]A_1
$etCO_2$ (mmHg)	34.68±3.57	34.54±3.99	33.58±3.68	34.25±3.45	0.763[b]
Temperature (°C)	35.64±1.0	35.78±0.68	35.80±0.60	35.79±0.72	0.960[b]
15 min after OLV	**Group1**	**Group2**	**Group3**	**Group4**	
	(n=25)	(n=28)	(n=25)	(n=25)	**p**
MAP (mmHg)	73.08±11.85	75.96±8.58	77.56±11.19	74.84±8.61	0.636[a]
Heart Rate (beat/min)	72.44±11.72	74.14±12.25	74.56±15.98	68.64±10.64	0.346[a]
SpO_2 (%)	97.72±5.37	97.46±1.77	94.84±11.8	96.48±2.2	0.001*[b]A_2
$etCO_2$ (mmHg)	33.68±4.05	34.03±3.74	38.21±12.63	34.64±3.56	0.146[b]
Temperature (°C)	35.39±1	35.44±0.27	35.63±0.76	35.35±0.79	0.719[b]

45 min after OLV	Group1 (n=25)	Group2 (n=28)	Group3 (n=25)	Group4 (n=25)	P
MAP (mmHg)	73.54±9.04	79.39±9.52	74.19±12.15	77.63±7.35	0.071[b]
Heart Rate (beat/min)	69.63±12.15	74±11.43	70±11.04	65.83±7.94	0.065[a]
SpO_2 (%)	98.21±1.67	97.36±1.95	95.73±2.41	97.46±2.23	0.004*[b]
$etCO_2$ (mmHg)	33.21±4.76	33.36±3.55	33.68±3.18	33.92±3.64	0.902[b]
Temperature (°C)	35.3±0.99	35.23±0.67	35.27±0.60	35.2±0.77	0.968[a]
At the end of OLV	**Group1** (n=25)	**Group2** (n=28)	**Group3** (n=25)	**Group4** (n=25)	**p**
MAP (mmHg)	73.77±12.9	79.71±10.06	81.27±9.06	80.25±8.08	0.135[b]
Heart rate (beat/min)	70.78±12.26	75.61±11.91	73.55±13.45	67.33±6.85	0.063[a]
SpO_2 (%)	98.57±2.13	98.86±1.65	97.77±2.16	98.54±1.22	0.125[b]
$etCO_2$ (mmHg)	33.43±5.18	34.57±9.89	33.23±3.25	34.71±3.76	0.457[b]

Temperature (°C)	35.41±1.0	35.37±0.77	35.15±0.65	35.06±0.75	0.390[a]

[b] Kruskal Wallis H test: values are given as mean ± standard deviation

[a] One-Way Anova test: values are given as mean ± standard deviation

A_1= G1 vs G3, p=0.012; G2 vs G3, p=0.003; G2 vs G4, p=0.021

A_2= G1 vs G3, p=0.001; G2 vs G3, p=0.001; G3 vs G4, p=0.013

Group 1: Low-flow anesthesia and oxygen titration without ORI monitoring

Group 2: Normal-flow anesthesia and oxygen titration without ORI monitoring

Group 3: Low-flow anesthesia and oxygen titration with ORI monitoring

Group 4: Normal-flow anesthesia and oxygen titration with ORI monitoring

*p<0.05 Statistically significant between groups

Table 3: The comparison of blood gas parameters

Before OLV	**Group1**	**Group2**	**Group3**	**Group4**	**p**

	(n=25)	(n=28)	(n=25)	(n=25)	
Ph	7.42±0.4	7.41±0.5	7.41±0.05	7.39±0.04	0.557[b]
CO_2 (mmHg)	39.8±4.9	39.3±4.2	40.3±4.8	39.67±5.09	0.821[b]
PaO_2 (mmHg)	236±79	190±52	166±75	175.5±47.8	0.001*[b]A_1
SpO_2 (%)	99.5±0.7	99.6±0.6	98.6±1.2	99.01±0.9	0.001*[b]B_1
Base Excess	1.64±2.31	0.53±2.4	0.82±2.5	0.16±2.7	0.199[a]
Lactate	1.12±0.4	1.24±0.6	1.24±0.4	1.4±0.6	0.596[b]
15 min after OLV	**Group1**	**Group2**	**Group3**	**Group4**	
	(n=25)	**(n=28)**	**(n=25)**	**(n=25)**	**p**
Ph	7.4±0.04	7.18±1.1	7.4±0.04	7.39±0.05	0.476[b]
CO_2 (mmHg)	39.75±4.89	40.89±4.9	42.8±5.6	40.32±4.2	0.282[b]
PaO_2 (mmHg)	135.6±72.1	116.5±53.3	93.0±36.7	97.1±24.5	0.071[b]
SpO_2 (%)	97.6±1.9	97.5±2.3	95.2±3.2	96.5±2.6	0.006*[b]A_2
Base Excess	1.05±2.3	0.5±2.6	1.2±2.4	0.6±3.1	0.743[a]
Lactate	1.06±0.3	1.24±0.5	1.26±0.4	1.2±0.5	0.379[b]
45 min after OLV	**Group1**	**Group2**	**Group3**	**Group4**	**p**

	(n=25)	(n=28)	(n=25)	(n=25)	
Ph	7.41±0.03	7.4±0.04	7.39±0.04	7.39±0.05	0.787[b]
CO_2 (mmHg)	40.74±3.6	41.24±9.93	41.66±4.71	41.08±9.75	0.221[b]
PaO_2 (mmHg)	142.7±81.3	116.9±53.2	94.4±39.3	118.2±46.1	0.014*[b]A_3
SpO_2 (%)	97.8±2.4	97.6±1.8	95.8±2.3	96.9±2.1	0.004*[b]B_2
Base Excess	0.81±2.63	0.56±2.86	0.97±3.13	0.17±2.9	0.368[b]
Lactate	1.13±0.38	1.21±0.62	1.36±0.4	1.31±0.6	0.159[b]
At the end of OLV	**Group1**	**Group2**	**Group3**	**Group4**	**p**
	(n=25)	**(n=28)**	**(n=25)**	**(n=25)**	
Ph	7.4±0.04	7.4±0.06	7.4±0.03	7.38±0.06	0.597[b]
CO_2 (mmHg)	40.25±4.2	38.4±4.69	39.9±5.1	41.73±10.1	0.406[b]
PaO_2 (mmHg)	164.5±67.6	163.2±63.8	120.1±47.6	152.87±68.7	0.045*[b]A_4
SpO_2 (%)	98.4±1.7	98.4±1.7	94.6±12.9	98.18±1.46	0.059[b]
Base Excess	0.75±2.1	0.21±2.6	0.15±2.6	0.5±3.45	0.436[a]
Lactate	1.27±0.35	1.67±0.81	1.52±0.8	1.53±0.6	0.423[b]

A_1= G1-G2, p=0.023 vs G1-G3, p=0.001 vs G1-G4, p=0.003 vs G2-G3, p=0.030

A_2= G1-G3, p=0.002 vs G2-G3, p=0.004

A_3= G1-G3, p=0.005 vs G2-G3, p=0.027 vs G3-G4, p=0.009

A_4= G1-G3, p=0.019 vs G2-G3, p=0.014

B_1= G1-G3, p=0.001 vs G1-G4, p=0.028 vs G2-G3, p=0.001 vs G2-G4, p=0.018

B_2= G1-G3, p=0.002 vs G1-G4, p=0.029 vs G2-G3, p=0.005

*p<0.05 Statistically significant between groups

Group 1: Low-flow anesthesia and oxygen titration without ORI monitoring

Group 2: Normal-flow anesthesia and oxygen titration without ORI monitoring

Group 3: Low-flow anesthesia and oxygen titration with ORI monitoring

Group 4: Normal-flow anesthesia and oxygen titration with ORI monitoring

Table 4: Multivariate analysis of outcomes

Correlations

	OLV %80 O_2	ICU stay	Hospital stay

OLV 80% O_2	Pearson Correlation	1	.069	.315
	Sig. (2-tailed)		.488	.001

Correlation is significant at the 0.01 level (2-tailed).**

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