Effect of different mechanical ventilation modes on cerebral blood flow during thoracoscopic surgery in neonates: A randomised controlled trial

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ABSTRACT

Background and Aims: Infants exposed to major surgery are at risk of injuries to the immature brain because of reduced arterial oxygen saturation. This study compared the effect of volume-controlled ventilation (VCV) versus pressure-controlled ventilation (PCV) on cerebral oxygenation in neonates subjected to repair of tracheoesophageal fistula (TEF) under video-assisted thoracoscopic surgery (VATS). Methods: This randomised controlled study included 30 full-term neonates scheduled for VATS for managing TEF under general anaesthesia. They were randomised to either VC group (n = 15), who received VCV, or PC group (n = 15), who received PCV. Cerebral oxygenation (rScO₂) was monitored throughout the surgery with documentation of episodes of cerebral desaturation. Peripheral oxygen saturation, partial pressure of carbon dioxide (PaCO₂), and end-tidal carbon dioxide were recorded at baseline, after induction of anaesthesia, and every 30 min till the end of the surgery. Results: rScO₂ was significantly higher in the PC group than the VC group at baseline and was significantly higher in the VC group after 15 min (P = 0.041). Later, it was comparable in both the groups up to 60 min after starting the surgery. Cerebral desaturation was significantly more common in the PC group (80%) compared to VC group (33.3%) (P = 0.010). PC group required higher fraction of inspired oxygen and positive end-expiratory pressure to prevent cerebral desaturation. PaCO₂ was significantly higher in the PC group than the VC group at 30 and 60 min (P = 0.005 and 0.029). Conclusion: VCV is safer than PCV for cerebral oxygenation during VATS in neonates.

Key words: Brain, intermittent positive-pressure ventilation, newborn, oximetry, pulmonary gas exchange, thoracic surgery, video-assisted tracheoesophageal fistula

INTRODUCTION

Cardiac and non-cardiac congenital anomalies usually necessitate surgical intervention during the first few months of life.^[1] Infants exposed to such major surgery are at risk of injuries to the immature brain.^[2] Thoracoscopy is now adopted by many centres worldwide for several procedures, including oesophageal surgery, diaphragmatic hernia repair, and lobectomies in newborns and infants.^[3] However, there is a debate concerning carbon dioxide (CO₂) insufflation during thoracoscopy. Elevated intrathoracic pressure leads to decreased venous return and cardiac output and subsequently reduced cerebral blood flow (CBF).^[4]

Therefore, monitoring CBF during neonatal surgery is recommended to preserve cerebral physiology. Intraoperative monitoring can help optimise cerebral oxygenation to protect the neonatal brain.^[4] Various invasive methods are available for assessing

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CBF. Among non-invasive methods, transcranial Doppler ultrasonography and cerebral oximetry with near-infrared spectroscopy (NIRS) are commonly employed.^[5] As the factors affecting oxygen metabolism are relatively stable over short time periods, NIRS can be used for monitoring intraoperative changes in CBF.^[6] NIRS measures the regional cerebral oxygen saturation (rScO₂).^[7]

Few studies have shown that different modes of mechanical ventilation have different effects on CBF in neonates.^[8] However, there is no study comparing volume-controlled ventilation (VCV) versus pressure-controlled ventilation (PCV) modes. This study tried to bridge this literature gap by comparing these two ventilation modes in neonates subjected to the repair of oesophageal atresia with tracheoesophageal fistula (TEF) using video-assisted thoracoscopic surgery (VATS) in terms of cerebral oxygen saturation, and changes of peripheral oxygen saturation (SpO₂), partial pressure of carbon dioxide (PaCO₂), end-tidal carbon dioxide (ETCO₂), and fraction of inspired oxygen (FIO₂).

METHODS

This randomised controlled study was conducted in 30 full-term neonates between August 2020 and August 2021 in a tertiary referral centre. Inclusion criteria were full-term (gestational age 37–42 weeks) neonate (age less than 1 month), with body weight of more than 2,500 g, scheduled for repair of TEF under VATS. The study was approved by the research committee and the institutional ethics committee (Approval no.: MS-271-2019). The study was registered on Clinical Trials.gov with study ID NCT04507295 and was conducted in accordance with the principles of the Declaration of Helsinki.

The neonates were randomised into two groups. Group VC (n = 15) was ventilated with VCV, whereas the PC group (n = 15) was ventilated with PCV. Randomisation was done based on computer-generated numbers using an online randomisation programme (research randomiser) by selecting two sets with a range of numbers between 1 and 30. The preoperative assessment was done on the day before surgery, including history-taking from parents, complete examination, routine laboratory investigations, and radiological investigations.

The patients were put in the prone position with no head elevation and in neutral neck position. They were monitored throughout the surgical procedure using pulse oximetry, invasive blood pressure monitor, capnogram, and electrocardiography. The $\mathrm{rScO}_{_2}$ was measured continuously by the NIRS monitor (INVOS 5100-P Cerebral Oximeter; Covidien, Mansfield, Massachusetts, the USA). The rScO, reflects the venous (70-80%), capillary, and arterial oxygen saturation. It is a reliable method to detect significant changes in cerebral oxygenation.^[7] The rScO₂ is calculated using the oxygenated haemoglobin and the total haemoglobin. Two transducers (OxyAlert TM neonatal sensor®) for cerebral oximetry were applied to the patient on both sides of the forehead. The monitor displayed the cerebral oxygen saturation from the right and the left side of the brain digitally as a graph. Other variables influencing cerebral oxygenation, including ETCO₂, SpO₂, and the FiO₂ were monitored.

General anaesthesia was induced using intravenous (IV) fentanyl 1–2 μ g/kg and propofol 2–3 mg/kg. Tracheal intubation (uncuffed endotracheal tube, German Medical Solutions Company, Code TT35, Egypt) was facilitated using IV atracurium 0.5 mg/kg. Ventilation was mechanically controlled using the standard pressure-controlled mode to maintain ETCO₂ between 30 and 35 mmHg. Anaesthesia was maintained using 1.6% isoflurane adjusted according to haemodynamic changes with top-up doses of atracurium as required (MaquetFlow-IC20, Sweden). After starting CO₂ insufflation using a flow of 0.5–1.0 l/min and pressure at 4–6 mmHg, the ventilation of patients was managed according to group allocation.

Patients in the VC group were ventilated during gas insufflation using volume-controlled mode with the following parameters: FiO_2 of 60%, tidal volume (TV) of 6–8 ml/kg, inspiratory to expiratory ratio (I:E) of 1:2, and inspiratory pause of 10% duration, using a minimal positive end-expiratory pressure (PEEP) of at least 2 cm H₂O. The respiratory rate was then modified to maintain ETCO₂ between 30 and 35 mm Hg.

Patients in the PC group were ventilated using pressure-controlled mode with the following parameters: FiO₂ of 60%, inspiratory pressure adjusted to acquire a TV of 6–8 ml/kg (according to the weight of the patient), respiratory rate of 30 breaths/min, and I:E ratio of 1:2 using a minimal PEEP of at least 2 cm H_2O . Then, the insufflation pressure was added to the driving pressure. The inspiratory pressure and respiratory rate were modified to maintain the ETCO₂

between 30 and 35 mmHg. Cerebral oxygenation was monitored throughout the surgery with documentation of episodes of cerebral desaturation (defined as a decrease in the $rSCO_2$ by 20% from the baseline reading). Once cerebral desaturation occurred, the following actions were done: stepwise increase of FiO₂ up to 100%, PEEP up to 5 cm H₂O and inspiratory pause to 15%, and decreasing the insufflation pressure.

Demographic data and serial $rScO_2$ recordings were collected every 15 min till the end of surgery. SpO₂, PaCO₂, and ETCO₂ were recorded at baseline, after the induction of anaesthesia, and every 30 min till the end of surgery.

The primary outcome measure was the cerebral oxygen saturation during surgery. The secondary outcomes were intraoperative changes of SpO_2 , PaCO_2 , ETCO_2 , FIO_2 , and PEEP.

The sample size was calculated using G-power software. The mean \pm standard deviation of rScO₂ in neonates undergoing thoracoscopic surgery was derived from a previous study^[4] and was 73 \pm 7%. We assumed that different ventilation modes might cause a change of 10% in rScO₂. Considering a power of 80% and an alpha error of 0.05, the total sample size was calculated to be 30 patients (15 in each group).

Statistical analysis was done using Statistical Package for Social Sciences[©] statistics version 23 (International Business Machines[©] Corp., Armonk, New York, the USA). Chi-square test (Fisher's exact test) was used to examine the relation between qualitative variables. For quantitative data, comparison between the two groups was made using Mann–Whitney test. Comparison of repeated measures was made using Friedman test, followed by Wilcoxon signed-ranks test. A *P* value <0.05 was considered significant.

RESULTS

Thirty-six patients were evaluated for eligibility. Four patients did not fulfil the inclusion criteria, and two parents refused to participate. Thirty neonates were enroled in the study [Figure 1]. Demographic data and diagnosis were comparable between both the groups [Table 1]. All patients were extubated on table and transferred to the neonatal intensive care unit.

Cerebral saturation on the right and left sides of the brain was significantly higher in the PC



Figure 1: Consolidated Standards of Reporting Trials (CONSORT) flow diagram

Table 1: Demographic data and operative details of the two studied groups			
	VC Group (n=15)	PC Group (n=15)	Ρ
Age (days)	10 (2-15)	8 (3-20)	0.870
Gender (male/female)	6/9	7/8	0.713
Weight (g)	2810±185	2843±203	0.642
Duration of surgery (min)	85±17	87±16	0.780
Surgical Procedure			
Ligation of fistula + primary repair	12	11	1.000
Ligation of fistula + diversion	3	4	

VC=volume-controlled ventilation group, PC=pressure-controlled ventilation group. Data are expressed as median (range) or mean±standard deviation

group than the VC group at baseline (P = 0.008)and 0.050, respectively). Cerebral saturation on the left side was significantly higher in the VC group after 15 min (P = 0.041). Otherwise, the cerebral saturation was comparable in both groups up to 60 min after starting the surgery. Cerebral desaturation was significantly more common in the PC group [Table 2]. Few patients needed an extended operative time beyond 60 min. Therefore, statistical comparisons were limited to 60 min. Ten patients (66.7%) in the VC group required a maximum FiO, of 60% to prevent cerebral desaturation, whereas 12 patients (80%) of the PC group needed FiO, of 80% or 100% (P = 0.035) [Table 3]. PEEP was higher in the PC group $(4.4 \pm 1.2 \text{ cm H}_{2}\text{O})$ compared to the VC group (2.8 \pm 1.4 cm H₂O) between 30 and 60 min (P = 0.011) [Table 4].

 $PaCO_2$ increased significantly in the two groups at 30 and 60 min compared to baseline readings (P < 0.001 for all comparisons). $PaCO_2$ was significantly higher

0 505

0.010

Table 2: Perioperative cerebral saturation on the right andleft sides of the brain in the two studied groups			
	VC Group (<i>n</i> =15)	PC Group (<i>n</i> =15)	Р
Cerebral saturation (right)			
Baseline	73.3±5.5	80.1±7.1	0.008

77 /+13 2

72 8+15 3

Alter 13 min	11.4113.2	72.0115.5	0.555
After 30 min	73.1±12.3	73.1±13.8	1.000
After 45 min	81.7±6.8	82.9±5.8	0.595
After 60 min	82.4±8.7	83.2±6.3	0.775
Cerebral saturation (left)			
Baseline	74.9±4.8	79.0±5.3	0.050
After 15 min	80.4±14.1	72.2±13.2	0.041
After 30 min	77.5±12.8	73.0±14.9	0.412
After 45 min	85.5±5.8	84.4±7.3	0.713
After 60 min	84.3±6.4	83.9±6.3	0.744

After 15 min

5 (33.3%) 12 (80.0%) Cerebral desaturation VC=volume-controlled ventilation group, PC=pressure-controlled ventilation group. Data are expressed as mean±standard deviation in percentage

Table 3: The maximum FiO ₂ used to maintain cerebral saturation in the two studied groups			
FiO ₂ (%)	VC Group (<i>n</i> =15)	PC Group (<i>n</i> =15)	Р
60	10 (66.7%)	3 (20.0%)	0.035
80	2 (13.3%)	4 (26.7%)	
100	3 (20.0%)	8 (53.3%)	

FiO₂=Fraction of inspired oxygen, VC=volume-controlled ventilation group, PC=pressure-controlled ventilation group. Data are expressed as number (%), n - number

Table 4: Intraoperative vital parameters in the two studied groups			
	VC Group (<i>n</i> =15)	PC Group (<i>n</i> =15)	Р
SpO ₂ (%)			
Baseline	93.7±1.6	94.1±1.9	0.624
After 15 min	93.1±4.2	90.5±6.6	0.345
After 30 min	92.0±4.3	90.8±5.8	0.902
After 45 min	94.3±2.0	94.5±2.8	0.539
After 60 min	94.4±2.9	94.4±2.3	0.775
PaCO ₂ (mmHg)			
Baseline	39.1±5.6	34.9±3.2	0.033
After 30 min	70.7±9.6	79.5±8.1	0.005
After 60 min	66.3±7.8	73.5±9.2	0.029
FiO ₂ (%)			
After 15 min	65.3±11.9	74.7±17.7	0.187
After 30-60 min	70.7±16.7	86.7±16.3	0.023
PEEP (cm of H ₂ O)			
After 15 min	2.6±1.2	3.2±1.5	0.367
After 30-60 min	2.8±1.4	4.4±1.2	0.011

FiO₂=fraction of inspired oxygen, SpO₂=peripheral oxygen saturation, PaCO₂=partial pressure of carbon dioxide, PEEP=positive end-expiratory pressure, VC=volume-controlled ventilation group, PC=pressure-controlled ventilation group. Data are expressed as mean±standard deviation

in the PC group compared to the VC group at 30 and 60 min (P = 0.005 and 0.029). SpO₂ was comparable in the two groups [Table 4]. There were no significant differences between the two groups in intraoperative heart rate and mean arterial pressure [Table 5].

DISCUSSION

This study demonstrated that VCV appears safer than PCV regarding cerebral oxygenation during VATS in neonates. PCV was associated with more frequent episodes of cerebral desaturation compared to VCV. Cerebral saturation was significantly higher in the VC group after 15 min. Then, it became comparable in the two groups up to 60 min. The PCV group needed higher FiO₂ to maintain cerebral oxygenation. PaCO₂ was significantly higher in the PC group compared to the VC group at 30 and 60 min. The improvement in cerebral saturation may have been due to better pulmonary oxygenation. However, further studies are needed to document this finding as we did not measure the partial pressure of arterial oxygen during the episodes.

Neonates are likely to develop atelectasis and hypoxaemia because of low body weight, small tidal volumes, low functional residual capacity, and high closing volumes. Besides, many neonates with TEF may have variable degrees of pulmonary dysplasia.^[9] In addition, CO₂ insufflation contributes to more hypoxaemia and hypercapnia.^[10] VATS has been widely used for various procedures in neonates.^[11] Compared to open surgery, VATS has some advantages, including shorter postoperative ventilation and hospital stay and shorter time to remove the chest drain. However, anaesthetic management of these procedures is still challenging because of many reasons.

One of the most frequent disadvantages is a longer operative time.^[12] Longer operations put the brain at the possible risk of prolonged duration of hypoxaemia. Besides, increased intrathoracic pressure because of the CO₂ insufflation can decrease venous return and cardiac output with consequent systemic hypotension.^[13] In neonates, cerebral autoregulation is still immature and becomes unstable during surgery.^[14] Therefore, securing adequate oxygen flow to the brain is crucial during anaesthesia.

Neunhoeffer et al.^[15] noted a significant linear correlation between intrathoracic CO, insufflation pressure and rScO2. Cerebral desaturation periods were more frequent during thoracoscopy than abdominal surgery. In a prospective case series of five infants subjected to 16 thoracoscopic procedures, cerebral oxygenation remained almost stable. Because of the haemodynamic changes, transient cerebral

Table 5: Intraoperative heart rate and mean arterial pressure in the two studied groups			
	VC Group (<i>n</i> =15)	PC Group (<i>n</i> =15)	Р
Heart rate (beats per minute)			
Baseline	140±7	141±7	0.850
After 15 min	128±6	129±6	0.901
After 30 min	126±5	127±5	0.821
After 45 min	123±4	123±4	0.932
After 60 min	121±4	122±4	0.806
Mean arterial pressure (mmHg)			
Baseline	60±6	62±5	0.312
After 15 min	52±3	54±4	0.065
After 30 min	53±3	54±4	0.155
After 45 min	53±3	54±4	0.297
After 60 min	54±4	56±3	0.269

group. Data are expressed as mean±standard deviation

desaturation was observed in two patients.^[16] In another observational study, cerebral oxygenation remained stable intraoperatively. Intrathoracic CO_2 insufflation was associated with a transient drop of $rSCO_2$ but the values remained within normal limits.^[4] A retrospective study investigated the effect of thoracoscopic surgery in 34 neonates. The neonates developed intraoperative acidosis and hypercapnia that was more severe compared to another group subjected to open surgery.^[17]

The optimal CO_2 insufflation pressure during thoracoscopy is a matter of debate. Some studies used a pressure between 5 and 10 mmHg.^[18,19] CO₂ insufflation was done with 5 or 10 mmHg pressure during 1-h thoracoscopy in 10 piglets in an experimental study. The 10-mmHg insufflation pressure was associated with more severe haemodynamic instability. The authors found that a pressure of 5 mmHg produced no adverse effects on cerebral oxygenation.^[13] Another study found that an inflation pressure of more than 4 mmHg was associated with a transient decrease in rScO2 by 12.7%.^[15]

In the present study, we were concerned with the appropriate ventilation strategy that can maintain adequate cerebral oxygenation in neonates subjected to VATS. Almost all previous studies have investigated the effect of ventilation mode on lung physiology and guarding against lung injury. In fact, the optimal modalities to minimise intraoperative derangements in blood gases during thoracoscopic surgery are not yet established. Some studies have found volume-targeted ventilation to be the mode of choice in neonates while measuring a small volume of delivered gases using advanced technology.^[20] Others used PCV, maintaining the peak airway pressure at 15–25 cm H_2O , with a FiO₂ of 60–80%, and I: E ratio of 1:1–1.5.^[9] PCV was shown to offer more effective ventilation at lower airway pressures with more lung protection than VCV.^[21] However, most previous studies investigated neonates, especially preterm, under mechanical ventilation because of the lung diseases. Only few studies are available on neonates subjected to thoracoscopic surgery.

Regarding cerebral oxygenation, we found that VCV was superior to PCV in the prevention of intraoperative episodes of cerebral desaturation. We believe that this advantage might be attributed to maintaining a regular minute volume throughout the surgery. However, the PCV technique used in this study was a 'volume-targeted' PCV, adjusted to the required TV of 6–8 ml/kg. This explains the comparable cerebral oxygenation levels at most of the time points during surgery. Continuous adjustment of pressure to achieve the targeted volume can guarantee a decrease in the episodes or severity of desaturation or shortening of the periods to a minimal or negligible time.

In a retrospective study, volume-guaranteed PCV (PCV-VG) was compared with VCV in infants subjected to VATS with one-lung ventilation (OLV). PCV-VG was associated with a lower incidence of hypoxaemia and better oxygenation.^[22] A meta-analysis reported significantly lower peak inspiratory pressures in PCV-VG than in VCV in adults undergoing OLV.^[23] Older studies showed better arterial oxygenation with PCV than VCV during OLV.^[24]

This study had some limitations. The first is the small number of cases; however, the prospective nature of the study may compensate for this defect. In addition, the data about changes in SpO_2 were not presented. Another limitation is the indirect measurement of CBF; however, measuring cerebral oxygen saturation using NIRS is a significant indicator of the safety of the anaesthetic technique.

CONCLUSION

VCV is a safer ventilation modality in neonates subjected to VATS under general anaesthesia compared to PCV. Cerebral desaturation is a more common incident in cases ventilated with PCV compared to VCV. Prevention of cerebral desaturation can be effectively accomplished with increasing FiO,; however, PCV needs higher FiO_2 and PEEP to maintain cerebral oxygenation.

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Conflicts of interest

There are no conflicts of interest.

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