Cardiology in the Young

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Effects of relative low minute ventilation on cerebral haemodynamics in infants undergoing ventricular septal defect repair

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Abstract

Background: Ventilation-associated changes in blood carbon dioxide levels are associated with various physiological changes in infants undergoing surgery. Studies on the effects of mechanical ventilation on cerebral haemodynamics especially for infants with CHD are scarce. *Aim:* This study was done to compare the changes in regional cerebral oxygen saturation and cerebral blood flow velocity when the end-tidal carbon dioxide partial pressure changed during different minute ventilation settings in infants undergoing ventricular septal defect repair. *Methods:* A total of 67 patients less than 1 year old with ventricular septal defect were enrolled, and 65 patients (age: 6.7 ± 3.4 months, weight: 6.4 ± 1.5 kg) were studied. After anaesthesia induction and endotracheal intubation, the same mechanical ventilation mode (The fraction of inspired oxygen was 50%, and the inspiratory-to-expiratory ratio was 1:1.5.) was adopted. The end-tidal carbon dioxide partial pressure of 30 mmHg (T1), 35 mmHg (T2), 40 mmHg (T3), or 45 mmHg (T4) were obtained, respectively, by adjusting tidal volume and respiratory rate. Minute ventilation per kilogram was calculated by the formula: minute ventilation per kilogram = tidal volume * respiratory rate/kg. Regional cerebral oxygen saturation was monitored by real-time near-infrared spectroscopy. Cerebral blood flow velocity (systolic flow velocity, end-diastolic flow velocity, and mean flow velocity), pulsatility index, and resistance index were measured intermittently by transcranial Doppler. Systolic pressure, diastolic pressure, stroke volume index, and cardiac index were recorded using the pressure recording analytical method. *Results:* As the end-tidal carbon dioxide partial pressure increased from 30 to 45 mmHg, regional cerebral oxygen saturation increased significantly from 69 ± 5% to 79 ± 4% ($p < 0.001$). Cerebral blood flow velocity (systolic flow velocity, end-diastolic flow velocity, and mean flow velocity) increased linearly, while pulsatility index and resistance index decreased linearly from T1 (systolic flow velocity, 84 ± 19 cm/second; end-diastolic flow velocity, 14 ± 4 cm/second; mean flow velocity, 36 ± 10 cm/second; pulsatility index, 2.13 ± 0.59; resistance index, 0.84 ± 0.12) to T4 (systolic flow velocity, 113 ± 22 cm/second; end-diastolic flow velocity, 31 ± 6 cm/second; mean flow velocity, 58 ± 11 cm/second; pulsatility index, 1.44 ± 0.34; resistance index, 0.72 ± 0.07) ($p < 0.001$). There were significant differences in changes of systolic flow velocity, end-diastolic flow velocity, mean flow velocity, pulsatility index, and resistance index as the end-tidal carbon dioxide partial pressure increased from 30 to 45 mmHg between subgroups of infants ≤6 and infants >6 months, while the changes of regional cerebral oxygen saturation between subgroups were not statistically different. Regional cerebral oxygen saturation and cerebral blood flow velocity (systolic flow velocity, end-diastolic flow velocity, and mean flow velocity) were negatively correlated with minute ventilation per kilogram ($r = -0.538$, $r = -0.379$, $r = -0.504$, $r = -0.505$, $p < 0.001$). Pulsatility index and resistance index were positively related to minute ventilation per kilogram ($r = 0.464$, $r = 0.439$, $p < 0.001$). The diastolic pressure was significantly reduced from T1 (41 ± 7 mmHg) to T4 (37 ± 6 mmHg) ($p < 0.001$). There were no significant differences in systolic pressure, stroke volume index, and cardiac index with the change of end-tidal carbon dioxide partial pressure from T1 to T4 ($p = 0.063$, $p = 0.382$, $p = 0.165$, $p > 0.05$). *Conclusion:* A relative low minute ventilation strategy increases regional cerebral oxygen saturation and cerebral blood flow, which may improve cerebral oxygenation and brain perfusion in infants undergoing ventricular septal defect repair.

Despite significant improvement in outcomes, infants undergoing surgery for CHDs have a persistent and troublesome incidence of neurologic complications.[1] Inadequate perfusion and oxygenation of brain tissue are often accompanied with poor prognosis.[2] Therefore,

more attention should be paid to cerebral haemodynamics and brain protection during the paediatric cardiac surgery for sake of reducing late neurodevelopmental and behavioural complications. It is much more important especially for infants.

Near-infrared spectroscopy has been proposed as one technique to monitor regional cerebral tissue oxygen saturation continuously, which represents a potentially important development for the detection of cerebral ischemia.[3] Using the temporal bony window, transcranial Doppler is capable of providing non-invasive measurement of the middle cerebral blood flow velocity.[4] Transcranial Doppler may provide a real-time measure of cerebral perfusion during CHD surgery.[5] Combined application of near-infrared spectroscopy and transcranial Doppler might thus be a better approach to monitor cerebral haemodynamics in infants undergoing cardiac surgery.

During the operation, mechanical ventilation is an important factor affecting cerebral haemodynamics in infants undergoing cardiac surgery. Changes in minute ventilation can change the end-tidal carbon dioxide partial pressure and arterial carbon dioxide partial pressure. Increased arterial carbon dioxide partial pressure result in cerebrovascular dilatation and cerebral blood flow velocity of middle cerebral artery increased significantly.[6] Hypoventilation-induced hypercapnia decreases cerebral vascular resistance, thus increasing cerebral blood flow, and hypoventilation may be a useful clinical cerebroprotective strategy in patients who are undergoing cardiac surgery.[7] However, severe hypoventilation can lead to hypoxemia or pulmonary atelectasis.[8]

Ventricular septal defect is the most common CHD in children, and most children with ventricular septal defect require repair surgery during the first year of life. Although the effects of mechanical ventilation on cerebral oxygen saturation and cerebral blood flow in adults have been studied, studies about effects of mechanical ventilation on cerebral haemodynamics in infants are scarce. So it is necessary for us to seek the optimal mechanical ventilation strategy for infants who undergo cardiac surgery.

Materials and methods

Study design and patients

This was a prospective observational study conducted at Capital Medical University affiliated Beijing Anzhen Hospital from July 2018 to December 2018, approved by the Institutional Ethics Committee. After written informed consent was obtained from parents or legal guardians of the patients, 67 patients less than 1 year old (American Society of Anesthesiologists status I or II, NYHA classification II) who were scheduled to undergo ventricular septal defect repair surgery were enrolled in the clinical trial. Patients were excluded if they had pneumonia, poor physical growth, severe pulmonary arterial hypertension (mean pulmonary artery pressure > 50 mmHg), severe ventricular dysfunction (left ventricular ejection fraction < 50%), or heart failure. Infants with asthma, neurologic disease, and abnormal hepatic or renal function insufficiency were also excluded from the study.

Anaesthesia and mechanical ventilation strategies

Endotracheal intubation general anaesthesia was administered by the same paediatric anaesthesiologist using an inhalation-intravenous anaesthesia technique. Induction of anaesthesia was conducted by 1.5–2.0 minimum alveolar concentration of sevoflurane, after peripheral vein catheter was inserted, and midazolam (0.2 mg/kg), sufentanil (1 μg/kg), and pipecuronium (0.2 mg/kg) were successively administered intravenously. Then the end-expiratory concentration of sevoflurane was adjusted to 0.3 minimum alveolar concentration. Followed by cuffed endotracheal tube was inserted successfully, synchronized intermittent mandatory ventilation – pressure control ventilation – volume guarantee mechanical ventilation mode (Ohmeda Avance CS2, Madison, WI, USA) was executed. The fraction of inspired oxygen was 50%, and the inspiratory-to-expiratory ratio was 1:1.5. By adjusting the tidal volume and respiratory rate, the end-tidal carbon dioxide partial pressure was, respectively, maintained at the level of 30 mmHg (T1), 35 mmHg (T2), 40 mmHg (T3), or 45 mmHg (T4). The end-tidal carbon dioxide partial pressure was continuously monitored by a CO_2 analyser (Capnomac Ultima, Datex, Tewksburg, Massachusetts, United States of America). The mechanical ventilation strategies were as follows: First, tidal volume was set to 10 ml/kg, and respiratory rate was adjusted until the end-tidal carbon dioxide partial pressure reached 30 mmHg, which was recorded as T1; then, respiratory rate was fixed at the T1 level and tidal volume was reduced to increase the end-tidal carbon dioxide partial pressure to 35 mmHg, which was recorded as T2. If the tidal volume was modulated at 6 ml/kg, the end-tidal carbon dioxide partial pressure still could not reach 35 mmHg and the respiratory rate was reduced to make the end-tidal carbon dioxide partial pressure reach T2. With a fixed tidal volume (6 ml/kg), the end-tidal carbon dioxide partial pressure was gradually increased to 40 mmHg (T3) and 45 mmHg (T4) by further reduction of respiratory rate. The different time points (T1, T2, T3, and T4) were recorded when respective end-tidal carbon dioxide partial pressure level had sustained a steady-state condition for 2 minutes.[9] Tidal volume and respiratory rate were recorded at different time points.

Regional cerebral oxygen saturation measurement by near-infrared spectroscopy

Right forehead regional cerebral oxygen saturation of all patients was continuously monitored with the near-infrared spectroscopy FORESIGHT cerebral oximeter (CAS Medical Systems, Branford, Connecticut, United States of America). Foresight oximeter uses five wavelengths (680, 730, 770, 805, and 870 nm) of light and multiple source detector separations to enhance accuracy and reduce extracranial distraction.[10] The medium sensor with an emitter–detector distance of 4.0 cm and a depth of light penetration of 2.0 cm was used as recommended by the manufacturer for children weighing 3 kg and above.[11] The emitting probe was placed on the right frontal side of each patient and fixed with a bandage. Real-time regional cerebral oxygen saturation readings were displayed on the screen continuously, and the values of regional cerebral oxygen saturation at T1, T2, T,3 and T4 were recorded, respectively.

Cerebral blood flow velocity measurements by transcranial Doppler

A 2-MHz, pulsed-wave transcranial Doppler sonographic probe (DWL Elektronische Systeme GmbH, Sipplingen, Germany) was placed over the right temporal window approximately 1 cm in front of the external auditory meatus and 1–2 cm above the zygomatic arch, which is the proximal segment of the middle

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Table 1. Characteristics of patients with ventricular septal defect (n = 65)

Variable	
Age (months)	6.7 ± 3.4
Sex, M/F	38/27
Height (cm)	65.3 ± 5.9
Weight (kg)	6.4 ± 1.5
Body surface area (m^2)	0.33 ± 0.05
VSD type: Perimembranous/subarterial	57/8
VSD size (mm)	9.2 ± 2.8

VSD = ventricular septal defect.
Data are shown as mean ± SD or number.

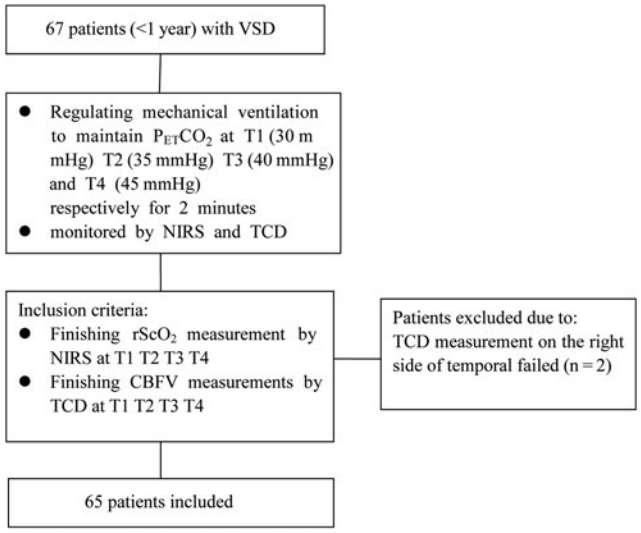

Figure 1. Study flowchart. VSD = ventricular septal defect; $P_{ET}CO_2$ = end-tidal carbon dioxide partial pressure; NIRS = near-infrared spectroscopy; TCD = transcranial Doppler; $rScO_2$ = regional cerebral oxygen saturation; CBFV = cerebral blood flow velocity.

cerebral artery. Static intermittent measurement of cerebral blood flow velocity was performed as the time-averaged mean velocity from consecutive Doppler tracings.[12] The systolic flow velocity, end-diastolic flow velocity, mean flow velocity, pulsatility index, and resistance index were measured and recorded at the T1, T2, T3, and T4 time points.

Systemic haemodynamic monitoring by pressure recording analytical method

A radial arterial catheter was inserted in all patients and connected to a systemic haemodynamic monitor (MostCare, Vygon, Vytech, Padova, Italy) which used a pressure recording analytical method to provide continuous beat-to-beat monitoring of stroke volume with assessment of left ventricular function.[13] Systolic pressure, diastolic pressure, stroke volume index, and cardiac index were recorded, respectively, at T1, T2, T3, and T4.

Statistical analysis

Data were analysed with IBM SPSS 20.0 statistical software (SPSS, Chicago, Illinois, United States of America). Quantitative variables were described as mean and standard deviation (mean ± SD). One-way repeated measures analysis of variance test was used to compare the values from T1 to T4. For subgroup analysis, two-way repeated measures analysis of variance was used to compare cerebral haemodynamic changes by end-tidal carbon dioxide partial pressure and age. Pearson's correlation test was used to analyse the relationships between regional cerebral oxygen saturation, cerebral blood flow velocity, and minute ventilation per kilogram. A two-tailed p level less than 0.05 ($p < 0.05$) was considered statistically significant.

Results

Subjects

Sixty-seven infants with ventricular septal defect were enrolled, and two patients were excluded when transcranial Doppler measurement on the right side of the temporal window failed. Finally, 65 patients were analysed in the study (Fig 1). Demographic data, including age, sex, height, weight, body surface area, ventricular septal defect type, and size, were obtained. Patient characteristics are presented in Table 1.

Regional cerebral oxygen saturation and cerebral blood flow velocity values

The end-tidal carbon dioxide partial pressure ranged from 30 to 45 mmHg (1 mmHg = 0.133 kPa). Minute ventilation per kilogram was calculated according to the formula: minute ventilation per kilogram = tidal volume * respiratory rate/kg. Minute ventilation per kilogram was regulated between 240 ± 48 and 107 ± 25 ml/minute/kg (Table 2). As the end-tidal carbon dioxide partial pressure increased from 30 to 45 mmHg, regional cerebral oxygen saturation increased significantly from 69 ± 5% to 79 ± 4% ($p < 0.001$) (Table 2 and Fig 2). Cerebral blood flow velocity increased linearly, while pulsatility index and resistance index decreased linearly from T1 (systolic flow velocity, 84 ± 19 cm/second; end-diastolic flow velocity, 14 ± 4 cm/second; mean flow velocity, 36 ± 10 cm/second; pulsatility index, 2.13 ± 0.59; resistance index, 0.84 ± 0.12) to T4 (systolic flow velocity, 113 ± 22 cm/second; end-diastolic flow velocity, 31 ± 6 cm/second; mean flow velocity, 58 ± 11 cm/second; pulsatility index, 1.44 ± 0.34; resistance index, 0.72 ± 0.07) ($p < 0.001$) (Table 2 and Fig 3). There were significant differences in changes of systolic flow velocity, end-diastolic flow velocity, mean flow velocity, pulsatility index, and resistance index as the end-tidal carbon dioxide partial pressure increased from 30 to 45 mmHg between subgroups of infants ≤6 and >6 months, while the changes of regional cerebral oxygen saturation between subgroups were not statistically different (Table 3). There was significantly negative correlation between regional cerebral oxygen saturation and minute ventilation per kilogram ($r = -0.538$, $p < 0.001$) (Fig 4). Systolic flow velocity, end-diastolic flow velocity, and mean flow velocity were negatively correlated with minute ventilation per kilogram ($r = -0.379$, $r = -0.504$, $r = -0.505$, $p < 0.001$), while pulsatility index and resistance index were positively related to minute ventilation per kilogram ($r = 0.464$, $r = 0.439$, $p < 0.001$) (Fig 4).

Pressure recording analytical method haemodynamic parameters

There were no significant differences in systolic pressure, stroke volume index, and cardiac index with the change of end-tidal

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Table 2. $rScO_2$, cerebral blood flow velocity, and haemodynamic parameters ($\bar{x} \pm s$)

Variable	T1	T2	T3	T4	p value
End-tidal carbon dioxide partial pressure (mmHg)	30	35	40	45	
Minute ventilation per kilogram (ml/minute/kg)	240 ± 48	168 ± 33	128 ± 29	107 ± 25	<0.001
$rScO_2$ (%)	69 ± 5	72 ± 5	76 ± 5	79 ± 4	<0.001
V_s (cm/second)	84 ± 19	91 ± 20	103 ± 19	113 ± 22	<0.001
V_d (cm/second)	14 ± 4	20 ± 5	26 ± 5	31 ± 6	<0.001
V_m (cm/second)	36 ± 10	42 ± 11	50 ± 10	58 ± 11	<0.001
Pulsatility index	2.13 ± 0.59	1.79 ± 0.43	1.55 ± 0.44	1.44 ± 0.34	<0.001
Resistance index	0.84 ± 0.12	0.78 ± 0.11	0.74 ± 0.09	0.72 ± 0.07	<0.001
P_{sys} (mmHg)	83 ± 12	83 ± 11	82 ± 11	82 ± 13	0.063
P_{dia} (mmHg)	41 ± 7	39 ± 6	38 ± 6	37 ± 6	<0.001
Stroke volume index (ml/m^2)	25 ± 5	26 ± 6	26 ± 6	26 ± 5	0.382
Cardiac index (L/minute/m^2)	2.84 ± 0.48	2.83 ± 0.47	2.78 ± 0.49	2.78 ± 0.45	0.165

P_{dia} = diastolic blood pressure; P_{sys} = systolic blood pressure; $rScO_2$ = regional cerebral oxygen saturation; V_s = systolic flow velocity; V_d = end-diastolic flow velocity; V_m = mean flow velocity.

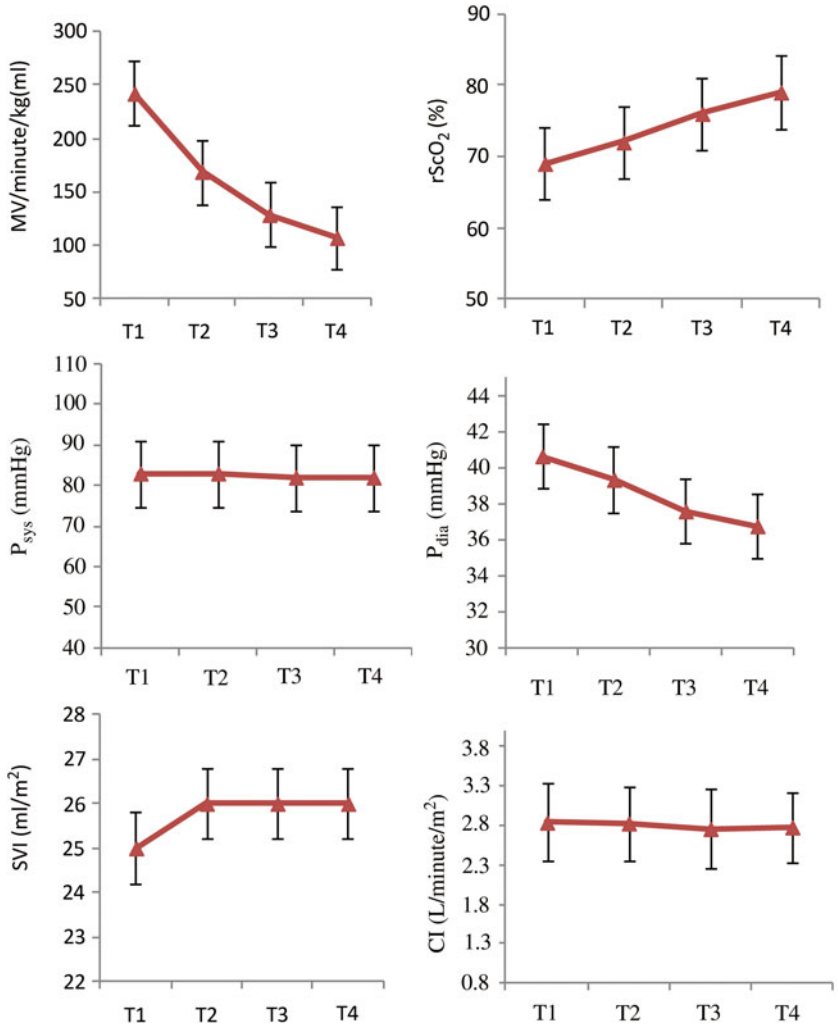

Figure 2. Line graphs showing MV decreased from 240 ± 48 to 107 ± 25 ml/minute/kg with $P_{ET}CO_2$ rising from T1 to T4 (T1: $P_{ET}CO_2$ 30 mmHg; T2: $P_{ET}CO_2$ 35 mmHg; T3: $P_{ET}CO_2$ 40 mmHg; T4: $P_{ET}CO_2$ 45 mmHg). $rScO_2$ increased linearly ($p < 0.001$), P_{dia} decreased linearly ($p < 0.001$) from T1 to T4. No significant differences in P_{sys}, SVI, and CI with the change of $P_{ET}CO_2$ from T1 to T4 ($p = 0.063$, $p = 0.382$, $p = 0.165$, $p > 0.05$). CI = cardiac index; MV = minute ventilation per kilogram; $P_{ET}CO_2$ = end-tidal carbon dioxide partial pressure; SVI = stroke volume index.

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Table 3. Subgroup analysis of cerebral haemodynamic parameters ($\bar{x} \pm s$)

Subgroup	Time	$rScO_2$ (%)	V_s (cm/second)	V_d (cm/second)	V_m (cm/second)	Pulsatility index	Resistance index
Infants ≤6 months (n = 35)	T1	69 ± 5	84 ± 18	8 ± 4	33 ± 9	2.4 ± 0.8	0.9 ± 0.1
	T2	72 ± 6	89 ± 17	14 ± 8	38 ± 9	2.0 ± 0.6	0.8 ± 0.1
	T3	75 ± 5	99 ± 17	23 ± 8	46 ± 8	1.7 ± 0.5	0.8 ± 0.1
	T4	78 ± 5	109 ± 18	27 ± 7	52 ± 9	1.5 ± 0.4	0.7 ± 0.1
Infants >6 months (n = 30)	T1	70 ± 5	85 ± 19	20 ± 9	39 ± 11	1.8 ± 0.7	0.8 ± 0.1
	T2	73 ± 5	93 ± 23	26 ± 10	47 ± 14	1.5 ± 0.6	0.7 ± 0.1
	T3	77 ± 5	108 ± 21	32 ± 11	56 ± 13	1.4 ± 0.3	0.7 ± 0.1
	T4	80 ± 4	118 ± 26	35 ± 11	64 ± 17	1.3 ± 0.2	0.7 ± 0.1
p value	0.371	0.026	<0.001	0.001	0.001	<0.001	

$rScO_2$ = regional cerebral oxygen saturation; V_d = end-diastolic flow velocity; V_m = mean flow velocity; V_s = systolic flow velocity.

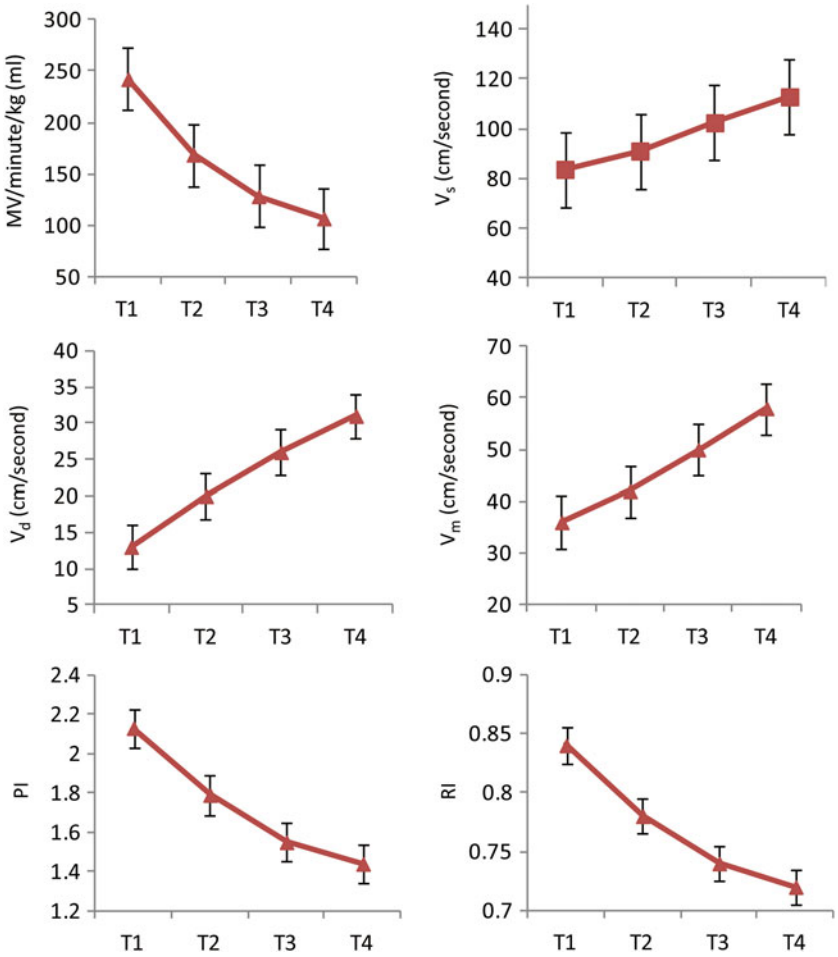

Figure 3. Line graphs showing V_s, V_d, V_m increased linearly ($p < 0.001$), while pulsatility index and resistance index decreased linearly ($p < 0.001$) as $P_{ET}CO_2$ rising from T1 to T4 (T1: $P_{ET}CO_2$ 30 mmHg; T2: $P_{ET}CO_2$ 35 mmHg; T3: $P_{ET}CO_2$ 40 mmHg; T4: $P_{ET}CO_2$ 45 mmHg). $P_{ET}CO_2$ = end-tidal carbon dioxide partial pressure.

carbon dioxide partial pressure from T1 to T4 ($p = 0.063$, $p = 0.382$, $p = 0.165$, $p > 0.05$) (Table 2 and Fig 2). As the end-tidal carbon dioxide partial pressure increased from 30 to 45 mmHg, diastolic pressure showed a significant decrease from 41 ± 7 to 37 ± 6 mmHg ($p < 0.001$) (Table 2 and Fig 2).

Discussion

Infants who undergo ventricular septal defect repair surgery are at risk of cerebral haemodynamic instability due to the effects of the surgery, general anaesthesia, and cardiopulmonary bypass. CO_2 is a potent vasodilator; increased arterial carbon dioxide partial

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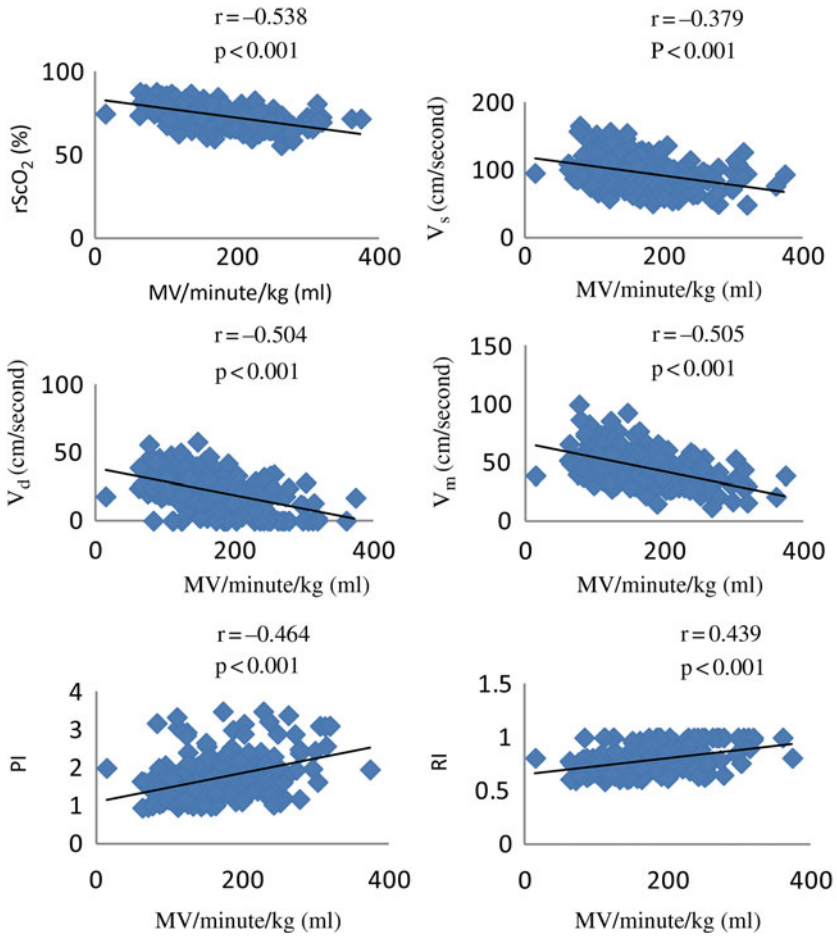

Figure 4. Scatter plots showing the negative correlation of $rScO_2$, V_s, V_d, and V_m with MV ($r = -0.538$, $r = -0.379$, $r = -0.504$, $r = -0.505$, $p < 0.001$), while positive correlation of pulsatility index and resistance index with MV ($r = 0.464$, $r = 0.439$, $p < 0.001$). MV = minute ventilation per kilogram.

pressure results in the vasodilation of cerebral vessels with subsequent increase in cerebral blood flow, while decreased arterial carbon dioxide partial pressure has the opposite effects.[14] Each 1-mmHg increase in arterial carbon dioxide partial pressure increases cerebral blood flow by 1–2 ml/100 g/minute.[15] Paediatric anaesthesiologists tend to take the hyperventilation strategy in order to decrease pulmonary arterial pressure in patients with ventricular septal defect. However, hyperventilation causes cerebral vasoconstriction and reduces brain perfusion, which may result in neural dysfunction. It is critical to seek the optimal mechanical ventilation strategy and minimise the risk of both brain damage and pulmonary hypertension. Our study aims to identify the best ventilatory strategy for both the heart and brain. It had been shown that the end-tidal carbon dioxide partial pressure closely approximated arterial carbon dioxide partial pressure in children with acyanotic CHD.[16] Therefore, in this study, we did not measure arterial carbon dioxide partial pressure at different time points considering that the end-tidal carbon dioxide partial pressure was easily obtainable and similar to arterial carbon dioxide partial pressure in infants with ventricular septal defect. The end-tidal carbon dioxide partial pressure was, respectively, maintained at the level of 30 mmHg (T1), 35 mmHg (T2), 40 mmHg (T3), and 45 mmHg (T4) by adjusting the tidal volume and respiratory rate in the post-induction but pre-surgical phase. This procedure was conducted before surgical incision in order to avoid the impact of surgical stimulation on cerebral haemodynamics.

Transcranial Doppler was used to monitor cerebral blood flow velocity of middle cerebral artery with change of the end-tidal carbon dioxide partial pressure during different minute ventilation in the study. As an ultrasound technique, transcranial Doppler is capable of providing non-invasive measurements of systolic flow velocity, end-diastolic flow velocity, mean blood flow velocity in the middle cerebral artery, as well as the pulsatility index and resistance index which are markers for cerebrovascular resistance.[4] Although the monitoring method may provide only semi-quantitative information on cerebral blood flow, transcranial Doppler can help to optimise brain perfusion during the paediatric cardiac surgery.[17] Some studies about transcranial Doppler detect alterations in cerebral perfusion have shown close relationships between worse neurodevelopmental outcomes and cerebral hypoperfusion which may lead to cerebral ischemia and ultimately neurologic injury following paediatric congenital heart surgery.[5,18] This study indicated that as the end-tidal carbon dioxide partial pressure increased from 30 to 45 mmHg, cerebral blood flow velocity (systolic flow velocity, end-diastolic flow velocity, and mean flow velocity) increased significantly, while pulsatility index and resistance index showed significant reductions; systolic flow velocity, end-diastolic flow velocity, and mean flow velocity were significantly negatively correlated with minute ventilation

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per kilogram, while pulsatility index and resistance index were positively related to minute ventilation per kilogram. It might be the results of cerebral vasodilation of increased arterial carbon dioxide partial pressure. The cerebral blood circulation is anatomically divided into five groups.[19] The first group consists of large arteries, which include the middle cerebral artery and the Circle of Willis. The second group includes distal arterial branches and arterioles that primarily regulate blood flow. The third group consists of end arterioles, capillaries, and post-capillary venules, which mainly perform gas exchange. The fourth and fifth groups include venules and large collecting veins, respectively. Transcranial Doppler views blood flow velocity of the middle cerebral arteries which are larger vessels. Our results indicate that CO_2 plays an important role in improving cerebral blood flow as it acts on larger cerebral artery, and the cerebral blood flow velocity is sensitive to changes in the end-tidal carbon dioxide partial pressure in infants. However, using infants age for subgroup analysis, we found that as the end-tidal carbon dioxide partial pressure increased, cerebral blood flow velocity increased less in infants ≤6 months than in infants >6 months. A likely explanation is that the cerebrovascular pressure autoregulation in younger infants is less developed than that in older infants.

Besides transcranial Doppler, we combined near-infrared spectroscopy to measure regional cerebral oxygen saturation for continuous monitoring cerebral oxygenation and brain perfusion in this study. Near-infrared spectroscopy is an effective non-invasive tool for monitoring regional cerebral oxygen saturation, the ratio of oxyhaemoglobin to total haemoglobin in all cerebrovascular compartments of arteries, arterioles, capillaries, venules, and veins.[20] Cerebral near-infrared spectroscopy has been successfully utilised as a bedside monitor to timely detect cerebral hypoxic-ischemia in infants with congenital cardiac disease.[3] The near-infrared spectroscopy method of assessment of cerebral oxygen metabolism promises new insights into perioperative cerebral perfusion in infants with CHDs.[21,22] Previous studies have reported that regional cerebral oxygen saturation is mostly influenced by cerebral venous oxygen saturation in which cerebral arterial to venous volume ratio (A:V ratio) is 1:3 (25%:75%) in humans under normal physiological conditions.[19,23] Lee et al[24] reported an increase in the arterial volume fraction from 25 to 40% in response to hypercapnia. This study showed that regional cerebral oxygen saturation increased significantly with the end-tidal carbon dioxide partial pressure rising from 30 to 45 mmHg. Although we did not measure the changes in the cerebral arterial to venous volume ratio, our results also reveal the arterial contribution to regional cerebral oxygen saturation because middle cerebral arterial vasodilation occurred significantly at low minute ventilation according to the measurements of transcranial Doppler monitoring. The relative low minute ventilation not only decreases cerebrovascular resistance, thus causing an increase in cerebral blood flow velocity, but also expands the cerebral vascular bed, at least in the arterial side, thus causing an increase in cerebral blood flow and regional cerebral oxygen saturation, which can help explain why cerebral blood flow velocities increase as the end-tidal carbon dioxide partial pressure increased was smaller in infants ≤6 months than in infants >6 months, while the changes of regional cerebral oxygen saturation between subgroups were not statistically different. Regional cerebral oxygen saturation increase is the consequence of a positive balance between oxygen supply and oxygen consumption. Because oxygen delivery is the product of cerebral blood flow and arterial oxygen content, changes in regional cerebral oxygen saturation reflect changes in cerebral blood flow when haemoglobin concentration, arterial oxygen tension, and cerebral oxygen metabolism are constant. The regional cerebral oxygen saturation values measured with near-infrared spectroscopy probably more accurately reflect cerebral blood flow and oxygen supply in younger infants.

Pressure recording analytical method (Vytech, Padova, Italy) is a direct systemic haemodynamic monitoring technique based on mathematical analysis of the arterial waveform, such a system would estimate systemic cardiac index by adding the stroke volume index of each beat during a 1-minute period.[13] Pressure recording analytical method is currently considered more reliable in children.[25] In our study, there were no significant changes in systolic pressure, stroke volume index, and cardiac index at different time points, which demonstrated that relative low minute ventilation did not influence the cardiac function. It was likely that these patients without significant pulmonary arterial hypertension or heart failure had relatively preserved global haemodynamics, and the findings might be different in patients with more severe circulatory limitations. However, the diastolic pressure significantly reduced from T1 to T4, which might be the result of peripheral vascular resistance decreased with increasing of the end-tidal carbon dioxide partial pressure. According to the ohm's law, we can decode circulatory changes: a reduction in cerebrovascular resistance with increase in cerebral blood flow will result in peripheral blood flow reduction and lower diastolic pressure.

There were several limitations in our study. The main limitation of this study was that we utilised a short-term observational design in which we observed the effects of different minute ventilation on cerebral haemodynamics in a relatively short time. Second, the near-infrared spectroscopy and transcranial Doppler monitoring methods used in this study had their own limitations with regard to cerebral haemodynamics. Although regional cerebral oxygen saturation was considered to be a good estimate of frontal lobe oxygenation, regional cerebral oxygen saturation only evaluates a superficial part of the brain and does not measure global cerebral oxygenation. Potential transcranial Doppler measurement errors may include the Doppler display, colour resolution display, measures of depth range, and measures of standard test parameters. In addition, this study failed to conduct other comprehensive clinical laboratory index and neurophysiological function tests of the brain. Therefore, our study could not provide information about the relationship between different minute ventilation and neurological outcome. Although the current study does not provide direct link between different minute ventilation and neurological outcome, we are planning a randomised trial to compare higher end-tidal carbon dioxide and normal end-tidal carbon dioxide in terms of long-term neurological outcomes in paediatric cardiac surgery.

Conclusion

A relative low minute ventilation strategy increases regional cerebral oxygen saturation and cerebral blood flow, which may improve cerebral oxygenation and brain perfusion in infants undergoing ventricular septal defect repair. It is critical to regulate and control ventilation precisely for infants undergoing cardiac surgery.

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