Cardiology in the Young

cambridge.org/cty

Original Article

Cite this article: Cui B, Ou-Yang C, Xie S, Lin D, and Ma J (2021) Effects of different ventilation on cerebral oxygen saturation and cerebral blood flow before and after modified ultrafiltration in infants during ventricular septal defect repair. *Cardiology in the Young* **31**: 371–376. doi: 10.1017/S1047951120003984

Received: 23 April 2020
Revised: 3 October 2020
Accepted: 20 October 2020
First published online: 5 February 2021

Keywords:
Ventilation; end-expiratory tidal pressure of carbon dioxide; cerebral oxygen saturation; cerebral blood flow; modified ultrafiltration; ventricular septal defect; infant

Address for correspondence: Jun Ma MD, Anesthesia Center, Capital Medical University affiliated Beijing An Zhen Hospital, Beijing, China. Tel: +860 106 445 6779; Fax: +860 106 445 6779. E-mail: majuntongxun@sohu.com

*Boqun Cui and Chuan Ou-Yang contributed equally to this work.

CAMBRIDGE UNIVERSITY PRESS

Effects of different ventilation on cerebral oxygen saturation and cerebral blood flow before and after modified ultrafiltration in infants during ventricular septal defect repair

Boqun Cui[1,*], Chuan Ou-Yang[1,*], Siyuan Xie[1,2], Duomao Lin[1] and Jun Ma[1]

[1]Anesthesia Center, Capital Medical University affiliated Beijing An Zhen Hospital, Beijing, China and [2]Department of Anesthesiology, Capital Institute of Pediatrics affiliated Children's Hospital, Beijing, China

Abstract

Objective: To analyse the changes of different ventilation on regional cerebral oxygen saturation and cerebral blood flow in infants during ventricular septal defect repair. *Methods:* Ninety-two infants younger than 1 year were enrolled in the study. End-expiratory tidal pressure of carbon dioxide was maintained at 40–45 and 35–39 mmHg in relative low and high ventilation groups. Regional cerebral oxygen saturation and flow velocity of the middle cerebral artery were recorded after anaesthesia (T0), cut pericardium (T1), separation from cardiopulmonary bypass (T2), the end of modified ultrafiltration, (T3) and at the end of operation (T4). *Results:* The relative low ventilation group exhibited a significantly high regional cerebral oxygen saturation at each time point except for T2 (T0:77 ± 4, T1:76 ± 5, T3:76 ± 8, T4:76 ± 8, respectively, $p < 0.001$). Flow velocity of the middle cerebral artery in the relative low ventilation group was higher compared to the relative high ventilation group at each time point except for T2 (T0:53 ± 14, T1:54 ± 15, T3:53 ± 17, T4:52 ± 16, respectively, $p < 0.001$). Between the two groups, T2 showed the lowest middle cerebral artery flow velocity (relative low ventilation: 39 ± 15, relative high ventilation: 39 ± 11, $p < 0.001$). *Conclusion:* The infants' regional cerebral oxygen saturation and middle cerebral artery flow velocity performed better in the range of 40–45 mmHg end-expiratory tidal pressure of carbon dioxide during CHD surgery. Modified ultrafiltration increased cerebral oxygen saturation. It was important to regulate ventilation in order to balance cerebral oxygen in infants.

There has been a decrease in mortality rates during the perioperative period amongst infants with CHD. Therefore, more studies are evaluating neurodevelopmental outcomes after surgery.[1] Occurrence rates of patients undergoing congenital heart surgery have been reported at 2–25%.[2,3] Children exhibit less tolerance for alterations in cerebral hyperemia or ischaemia and are at a higher risk for sustaining secondary brain injuries. In addition, children under 4 years are more likely to develop neurological dysfunctions.[4] Low regional cerebral oxygen saturation levels have been shown to play a key role in the pathogenesis of neurological dysfunctions.[5] However, evaluation of cerebral haemodynamics and regional cerebral oxygen saturation is not routine clinical practices for infants during CHD surgery in developing countries.

Mechanical ventilation affects cerebral oxygen saturation and cerebral blood flow in infants. Hypercapnia and hypocapnia are associated with hypoventilation and/or hyperventilation. They have been associated with the imbalance between brain oxygen supply and demand.[6–8] Studies have highlighted the influence of modified ultrafiltration on cerebral oxygen saturation. The findings from these studies were, however, not conclusive.[9] Due to the incomplete development in brain circulation and poor cerebral autoregulation of infants, the effects of carbon dioxide on cerebral oxygen saturation have not been determined in these paediatric patients under the age of [1,10,11] especially with modified ultrafiltration.[9]

This study aims to evaluate the effects of different ventilation levels on regional cerebral oxygen saturation and cerebral blood flow before and after modified ultrafiltration, during surgery in infants with ventricular septal defects. The flow velocity of middle cerebral artery was measured by transcranial Doppler (TCD) sonography while regional cerebral oxygen saturation was measured by near-infrared spectroscopy.

Materials and methods

Study design and patients

This was an interventional study performed at Capital Medical University affiliated Beijing An Zhen Hospital. This study was carried out from July, 2017 to April, 2018. Ethical approval was obtained from the Institutional Review Board (IRB 2017030X). Verbal and written informed

consents were obtained from the infants' parents or guardians before surgery. Infants undergoing cardiopulmonary bypass for the complete repair of ventricular septal defects were enrolled. Exclusion criteria included emergent or urgent procedure, and pre-existing congenital abnormality of any other organs, especially neurological disorders. The study process was show in Figure 1.

Anaesthesia and mechanical ventilation strategies

After placement of the routine monitors (electrocardiogram, blood pressure, and pulse oximetry), a standardised anaesthetic technique was used. Anaesthesia was performed with sevoflurane 1.0–1.5 minimum alveolar concentration (MAC), and a peripheral intravenous line was inserted. Then, sufentanil 0.5 $\mu g \cdot kg^{-1}$, and pipecuronium 0.1 mg kg^{-1} were inducted. Followed by cuffed endotracheal tube was inserted successfully, volume-controlled ventilation was implemented. By adjusting the tidal volume (6–10 $ml \cdot kg^{-1}$) and respiratory frequency, the end-expiratory tidal pressure of carbon dioxide was maintained at 35–39 mmHg (relative high ventilation group) or 40–45 mmHg (relative low ventilation group) before and after cardiopulmonary bypass, respectively. The fraction of inspired oxygen was set at 50%, the inspiratory to expiratory ratio was set at 1:1.5 in both groups. The end-expiratory tidal pressure of carbon dioxide was continuously monitored by a CO_2 analyzer (Capnomac Ultima, Datex, Tewksburg, Massachusetts, United States of America). Before cardiopulmonary bypass was initiated, all the infants received the same anaesthetic maintained with sevoflurane 0.5–1.0 MAC, sufentanil (2–4 $\mu g\ kg^{-1} \cdot h^{-1}$), and pipecuronium (0.08–0.16 $mg \cdot kg^{-1} \cdot h^{-1}$). Depending on the age, weight, and haematocrit of the infants, the cardiopulmonary bypass procedures were performed with standard techniques. Priming volume was approximately 250 ml and contained crystalloid, albumin, and preserved red blood cells. The amount of preserved red blood cells in the priming was calculated to achieve a haematocrit >28% during cardiopulmonary bypass. The prime was always completed with 0.5 $g \cdot kg^{-1}$ body weight mannitol 200 $g \cdot L^{-1}$ and 0.5 $g \cdot kg^{-1}$ body weight human albumin 200 $g \cdot L^{-1}$. Perfusion flow was maintained between 100 and 120 $ml \cdot kg^{-1} \cdot min^{-1}$ while haematocrit was maintained between 28 and 30%. After cardiopulmonary bypass, modified ultrafiltration was used in all infants. A blood cell saver device was used for blood protection during operation.

Haemodynamic monitoring

All infants were instrumented with radial arterial and internal jugular venous catheters to allow routine arterial pressure monitoring and advanced haemodynamic monitoring by pressure recording analytical method (MostCare, Vygon, Vytech, Padova, Italy). Fluctuations of the heart rate, cardiac index, and mean artery pressure, within 20% of the base value, were maintained by using fluid boluses or vasodilatory/inotropic (dopamine 2–5 $\mu g \cdot kg^{-1} \cdot min^{-1}$).

Blood samples for arterial blood gas analysis were obtained at three time points and are as follows: after induction of anaesthesia (T0), during separation from cardiopulmonary bypass (T2), and at the end of modified ultrafiltration (T3). Arterial carbon dioxide pressures and haematocrit were also measured as well at these time points. Arterial blood sample collection at the three time points was chosen because of the low blood volume in infants.

Cerebral oxygen saturation and cerebral blood flow monitoring

A near-infrared spectroscopy sensor was placed centrally on the forehead at 1 cm above the eyebrow. It was used to monitor the regional cerebral tissue oxygen saturation (neonatal or infant sensors; INVOS 5100 C, Somanetics, Troy, MI, USA) of each frontal cortex. A 2-MHz pulsed-wave transcranial Doppler sonographic probe (DWL Elektronische Systeme, Sipplingen, Germany), which was placed in the proximal segment of the middle cerebral artery, and is used to measure the middle cerebral artery blood flow velocity.

Data collection

We studied patients during the period between endotracheal intubation and the end of surgery. Two repeated measurements of middle cerebral artery flow velocity, resistance index, and pulsation index were made at 1-minute intervals after induction of anaesthesia (T0), on opening the pericardium (T1), separation from cardiopulmonary bypass (T2), the end of modified ultrafiltration (T3), and at the end of operation (T4). Regional cerebral oxygen saturation, mean artery pressure, heart rate, cardiac index data, haematocrit, and temperature were continuously recorded. Surgical information that was recorded was the time of cardiopulmonary bypass and detailed operational procedure. The use of inotropes was also recorded.

Statistical analysis

Statistical analysis was performed using SPSS 22.0 (IBM Corp, Armonk, New York, United States of America). Measurement data were reported as mean ± standard deviation. Statistical differences in regional cerebral oxygen saturation, middle cerebral artery flow velocity, resistance index, pulsation index, mean artery pressure, heart rate, and cardiac index amongst the different time points in each group were determined by repeated-measures analysis of variance. The Student's t-test was performed to analyse statistical differences between the two groups. The proportions of the binary variables were compared using the χ^2 test. A p-value of <0.05 was considered to be significant.

Results

Patients

A total of 92 infants with ventricular septal defects were enrolled in this study. In accordance with an end-expiratory tidal pressure of carbon dioxide, 46 patients were enrolled in the relative high ventilation group while 46 patients were enrolled in the relative low ventilation group. There were no complications observed during transcranial Doppler measurements and regional cerebral oxygen saturation monitoring.

There were no significant statistical differences in gender, mean age, weight of infants, inotropic use, blood products use, cardiopulmonary bypass time, and time of operation between the two groups (summered in Table 1). There were also no significant statistical differences in all kinds of blood products during CPB.

Regional cerebral oxygen saturation and cerebral blood flow values

Cerebral haemodynamic parameters of the two groups at each time point during the operation were presented in Table 2. The relative

https://doi.org/10.1017/S1047951120003984 Published online by Cambridge University Press

Table 1. Demographics and perioperative clinical data

Variable	LG	HG	P-value
Number	46	46	–
Age (months)	6 ± 2	6 ± 3	0.838
Gender = boy (%)	46	43	0.426
Weight (kg)	6.7 ± 1.2	6.4 ± 1.4	0.517
CPB time (min)	49 ± 12	50 ± 13	0.901
Operation time (min)	108 ± 21	110 ± 23	0.317
Dopamine (%)	11	15	0.951

Data are in mean ± SD for continuous variables and in percentage (%) for binary variables
CPB = cardiao pulmonary bypass; HG = relative high ventilation group; LG = relative low ventilation group.

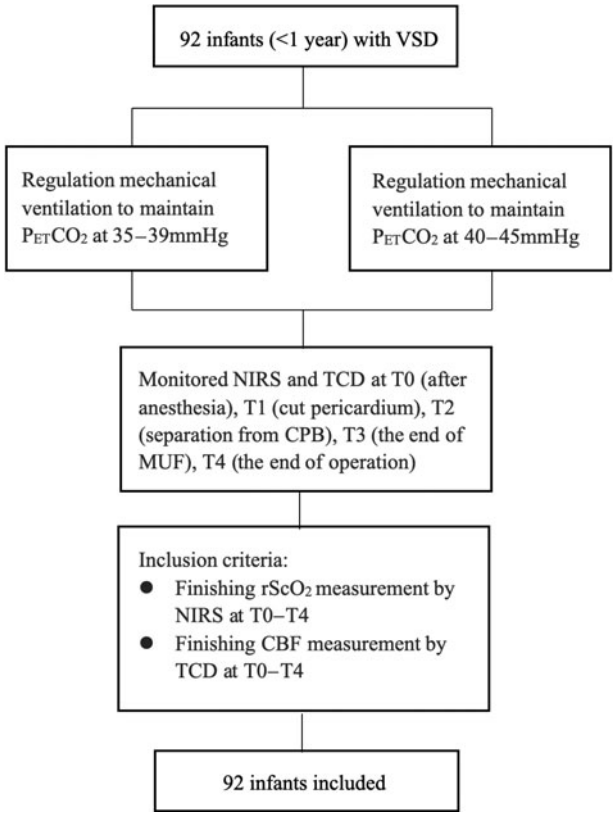

Figure 1. Study flowchart. CBF = cerebral blood flow; CPB = cardiopulmonary bypass; MUF = modified ultrafiltration; NIRS = near-infrared spectroscopy; $PETCO_2$ = end-expiratory tidal pressure of carbon dioxide; $rScO_2$ = regional cerebral oxygen saturation; TCD = transcranial Doppler; VSD = ventricular septal defect.

low ventilation group exhibited a significantly higher regional cerebral oxygen saturation at each time point, except at the T2 time point (77 ± 4, 76 ± 5, 76 ± 8, 76 ± 8, $p < 0.001$, respectively). The regional cerebral oxygen saturation for all infants was the lowest at T2. In addition, the middle cerebral artery flow velocity value was high in the relative low ventilation group compared to the relative high ventilation group at each time point, except for T2 (53 ± 14, 54 ± 15, 53 ± 17, 52 ± 16, $p < 0.001$, respectively). The T2 time point exhibited the lowest regional cerebral oxygen saturation and middle cerebral artery flow velocity between the two groups ($p < 0.001$). On the contrary, pulsation index and resistance index showed the opposite trend.

Haemodynamic variables

The haematocrit was significantly elevated from 28.5 ± 4.3 at T2 to 35.7 ± 5.4 at T3 ($p < 0.001$) in the relative low ventilation group, and was elevated from 27.9 ± 5.1 at T2 to 36.0 ± 5.7 at T3 ($p < 0.001$) in the relative high ventilation group. In addition, the mean artery pressure significantly increased from 50 ± 11 at T2 to 62 ± 11 at T3 ($p = 0.003$) in the relative low ventilation group, and increased from 51 ± 11 at T2 to 61 ± 9 at T3 ($p = 0.019$) in the relative high ventilation group. Other haemodynamic data (heart rate and cardiac index) did not show any significant differences between the two groups at each time point. There was no significant difference in temperature between the two groups.

Respiratory parameters

Compared to the relative high ventilation group, the relative low ventilation group showed a lower respiratory frequency, tidal volume, and peak airway pressure and a higher end-expiratory tidal pressure of carbon dioxide ($p < 0.001$). These results are shown in Table 3.

Discussions

Few studies have documented the impact of carbon dioxide at a range of 35–45 mmHg and modified ultrafiltration on regional cerebral haemodynamics in infants. In this study, the regional cerebral oxygen saturation and middle cerebral artery flow velocity were impacted by modified ultrafiltration, significantly low upon separation from cardiopulmonary bypass when compared to other time points, and significantly high in the 40–45 mmHg end-expiratory tidal pressure of carbon dioxide range than in the 35–39 mmHg range.

Oxygen supply to the brain relies on tight regulation of cerebral blood flow.[10,11] Therefore, a decrease in regional cerebral oxygen saturation could signal a decrease in cerebral blood flow and/or inadequate oxygen supply[5] and vice versa. Adjustment of the mean artery pressure and end-expiratory tidal pressure of carbon dioxide increases cerebral blood flow and improves the balance between oxygen supply and demand in the brain during paediatric cardiac surgery. However, changes in mean artery pressure could exhibit a negative impact on infants with concomitant CHD.[12] Due to these outcomes, it's important to determine the influence of different end-expiratory tidal pressures of carbon dioxide on regional cerebral oxygen saturation and cerebral blood flow in those infants.

Existing scientific evidence suggests that carbon dioxide is a powerful modulator of cerebral vasomotor tone, which can dilate the cerebral arteriole, facilitate oxygen transport and cerebral perfusion.[8] However, these studies seldom researched the effect of normocapnia, which was mostly adopted for cardiac surgery patients, and mostly investigated the active role of carbon dioxide in adults or children but not infants. In this study, we found that the middle cerebral artery flow velocity and regional cerebral oxygen saturation in the 40–45 mmHg end-expiratory tidal pressure of carbon dioxide range were improved. Studies have established a 30% increase in cerebral blood flow for every 7.5 mmHg increase in the end-expiratory tidal pressure of carbon dioxide in healthy volunteers.[10] In this study, we observed a 24% increase in cerebral blood flow for infants younger than 1 year, a finding that is not in

https://doi.org/10.1017/S1047951120003984 Published online by Cambridge University Press

Table 2. $rScO_2$, VMCA, and haemodynamic parameters ($\overline{X} \pm s$)

Variable	Group	T0	T1	T2	T3	T4	P-value
$rScO_2$ (%)	LG	77 ± 4*,**	76 ± 5*,**	65 ± 7	76 ± 8*,**	76 ± 8*,**	<0.001
	HG	71 ± 6**	71 ± 6**	64 ± 9	72 ± 9**	71 ± 9**	<0.001
V_{MCA} (cm/s)	LG	53 ± 14*,**	54 ± 15*,**	39 ± 15	53 ± 17*,**	52 ± 16*,**	<0.001
	HG	45 ± 13**	47 ± 12**	39 ± 11	45 ± 13**	42 ± 11**	<0.001
PI	LG	1.6 ± 0.4**	1.5 ± 0.5*,**	2.8 ± 0.8	1.7 ± 0.8*,**	1.8 ± 0.7**	<0.001
	HG	1.9 ± 0.5**	1.8 ± 0.6**	2.9 ± 0.9	2.1 ± 0.9**	2.0 ± 0.0.9**	<0.001
RI	LG	0.76 ± 0.08*,**	0.76 ± 0.12**	0.95 ± 0.09	0.77 ± 0.12*,**	0.75 ± 0.11*,**	<0.001
	HG	0.81 ± 0.10**	0.80 ± 0.11**	0.93 ± 0.07	0.82 ± 0.14**	0.85 ± 0.12**	<0.001
MAP (mmHg)	LG	55 ± 9	58 ± 8	50 ± 11	62 ± 12	61 ± 9	0.003
	HG	56 ± 9	57 ± 9	51 ± 11	61 ± 9	60 ± 9	0.019
HR (bpm)	LG	109 ± 10	106 ± 10	121 ± 15	117 ± 12	111 ± 11	0.061
	HG	107 ± 9	110 ± 10	119 ± 15	115 ± 11	110 ± 10	0.073
CI (L/min/m^2)	LG	2.7 ± 0.4	2.7 ± 0.5	2.7 ± 0.4	2.8 ± 0.4	2.8 ± 0.5	0.165
	HG	2.7 ± 0.4	2.8 ± 0.4	2.9 ± 0.5	2.7 ± 0.5	2.7 ± 0.5	0.127
T (°C)	LG	36.6 ± 6.3	36.3 ± 7.5	36.7 ± 7.4	36.4 ± 6.9	36.6 ± 7.9	0.517
	HG	36.8 ± 6.1	36.2 ± 8.0	36.6 ± 6.7	36.2 ± 7.1	36.5 ± 7.7	0.632
Hct (%)	LG	36.8 ± 6.3**	–	28.5 ± 4.3	35.7 ± 5.4**	–	<0.001
	HG	37.1 ± 5.9**	–	27.9 ± 5.1	36.0 ± 5.7**	–	<0.001

CI = cardiac index; Hct = haematocrit; HR = heart rate; MAP = mean artery pressure; PI = pulsation index; RI = resistance index; $rScO_2$ = regional cerebral oxygen saturation; T = temperature; V_{MCA} = flow velocity of the middle cerebral artery
*$p < 0.05$ when LG compared to HG
**$p < 0.05$ compared with T2

Table 3. Respiratory parameters of two groups during anaesthesia ($\overline{X} \pm s$)

Variable	Group	T0	T1	T2	T3	T4
TV/weight(ml/kg)	LG	6 ± 1	6 ± 1	7 ± 1	6 ± 1	6 ± 1
	HG	9 ± 1	9 ± 1	9 ± 1	9 ± 1	9 ± 2
Respiratory frequency (times/min)	LG	16 ± 3*	17 ± 3*	18 ± 4*	19 ± 4*	20 ± 4*
	HG	22 ± 4	23 ± 3	24 ± 3	23 ± 3	24 ± 3
P_{Peak} (mmHg)	LG	15 ± 2*	16 ± 2*	17 ± 3*	17 ± 3*	16 ± 3*
	HG	19 ± 3	20 ± 4	22 ± 3	21 ± 4	20 ± 4
$P_{ET}CO_2$ (mmHg)	LG	43 ± 3*	44 ± 3*	42 ± 3*	43 ± 4*	44 ± 4*
	HG	36 ± 2	36 ± 2	36 ± 2	37 ± 2	36 ± 2
$PaCO_2$(mmHg)	LG	43 ± 4*	–	42 ± 8*	44 ± 7*	–
	HG	37 ± 6	–	36 ± 7	38 ± 8	–

$P_{ET}CO_2$ = end-expiratory tidal pressure of carbon dioxide; P_{Peak} = peak airway pressure; TV = tidal volume
*$p < 0.05$ when LG compared to HG

concordance with that found by. Thus, our results imply that small changes in end-expiratory tidal pressure of carbon dioxide might have a clinically significant impact on cerebral haemodynamics during CHD surgery in infants younger than 1 year.

The early post-bypass phases do not supply adequate cerebral oxygenation because the blood pressure is unstable at a time before the brain is fully protected by hypothermia. Studies have shown that cardiopulmonary bypass is prone to brain damage and continuous regional cerebral oxygen saturation. Transcranial Doppler monitor inhibits these neurological complications.[13] In this study, regional cerebral oxygen saturation and middle cerebral artery flow velocity decreased while pulsation index and resistance index increased when after separation from cardiopulmonary bypass. Some studies demonstrated that a gradual decrease in regional cerebral oxygen saturation did have close influences on coronary reperfusion and rewarming.[14] During rewarming, cerebral metabolism and oxygen consumption would increase beyond the increase in cerebral blood flow. With transcranial Doppler, it has been shown that after rewarming, the cerebral blood flow velocity increases 65% while the regional cerebral oxygen

https://doi.org/10.1017/S1047951120003984 Published online by Cambridge University Press

saturation decreases by 25%.[15] Pulsation index is an important index for measuring cerebrovascular elasticity. Intracranial hypertension or focal oedema increases pulsation index. Resistance index indicates the blood flow resistance, and is high when there is a buildup of acidic metabolites, ischaemia hypoxic stage, etc. We demonstrated that ischaemia–reperfusion injury, hypothermia, inflammation, and hemodilution that were caused by cardiopulmonary bypass increased cerebrovascular resistance, decreased elasticity of cerebral vessels, reduced carbon dioxide reactivity, impaired cerebrovascular autoregulation, and decreased cerebral blood flow. These effects triggered an imbalance in cerebral perfusion and cerebral oxygen supply and demand.[13,16] Cerebral blood flow and cerebral oxygen saturation were highly dependent on the end-expiratory tidal pressure of carbon dioxide. These factors did not vary after cardiopulmonary bypass. It might be caused by the impaired carbon dioxide activity and poor cerebral autoregulation.

After CPB, modified ultrafiltration was used to reduce hemodilution and its potential adverse effects.[9] The concept of modified ultrafiltration was first proposed by Naik et al[17] and is now routinely used in cardiac surgery for infants. In this study, there was an increase in cerebral blood flow, cerebral oxygen saturation, mean artery pressure, and haematocrit after modified ultrafiltration. A short duration ultrafiltration circuit leads to a severe left-to-right shunt (steal blood phenomenon), no matter the modified ultrafiltration flow rate.[18] An increase in cardiac function could supplement for this "steal" and causes a lower oxygen extraction ratio.[9,19,20] Moreover, the increased cerebral oxygen saturation might be associated with an increased mean artery pressure. Autoregulatory studies in neonates have reported a linear relationship between regional cerebral oxygen saturation and mean artery pressure.[10,21] Some studies have, however, documented that no correlation exists between regional cerebral oxygen saturation and mean artery pressure in humans.[22] There is no conclusive evidence on the correlations between mean artery pressure and regional cerebral oxygen saturation. Recent studies determining the coherence between continuous bedside near-infrared spectroscopy and arterial pressure have suggested that cerebral autoregulation can transiently be impaired in critically ill infants.[11,23] The frequency of impaired cerebral autoregulation is associated with low regional cerebral oxygen saturation and systemic hypotension.[23,24] Furthermore, increased cerebral oxygen saturation could be attributed to increased haematocrit[9] that promotes arterial oxygen content and lowers the oxygen extraction ratio. In this study, modified ultrafiltration gradually decreased the resistance index and pulsation index. This could be attributed to the fact that increased haematocrit, reduced inflammatory mediators and relieved cell oedema, reduce cerebrovascular resistance, increase elasticity of cerebral vessel, improve carbon dioxide reactivity, recover cerebrovascular autoregulation,[25] and therefore, improve cerebral perfusion and cerebral oxygen metabolism. These factors elevate the regional cerebral oxygen saturation and middle cerebral artery flow velocity. However, these conclusions need to be verified by more studies.

For infants with ventricular septal defects, the lower the obstructive pulmonary hypertension, the better the recovery of cardiopulmonary vascular function after surgery. However, studies have suggested that these children exhibit difficulties in cerebral oxygenation maintenance during surgery, and therefore, the incidences of long-term cognitive decline may be higher.[26] Hyperventilation reduces pulmonary vascular resistance and increases cerebrovascular resistance. These outcomes decrease cerebral blood flow.[6,7,27] It has been demonstrated that hyperventilation might result in the poor cerebral autoregulation and low cerebral oxygen saturation.[28] Maintaining an end-expiratory tidal pressure of carbon dioxide at 40–45 mmHg improved cerebral perfusion and cerebral oxygen saturation, avoided pulmonary vascular bed over-exploitation, and limited the left-to-right shunt. We recommend that in infants younger than 1 year who undergo VSD repair, attention must be paid to adequate cerebral blood flow and balance of cerebral oxygen supply and demand to avoid hyperventilation.

There are several limitations in our study. Although, middle cerebral artery flow velocity by transcranial Doppler ultrasonography, rather than cerebral blood flow, most researches validated that the middle cerebral artery flow velocity is a reliability index of cerebral blood flow (measured using intravenous Xenon-133).[29,30] End-expiratory tidal pressure of carbon dioxide is significantly correlated with arterial carbon dioxide pressure amongst infants, however, in this study, no arterial carbon dioxide pressure data were obtained.[31] Besides technical factors, several physiological factors have been found to have an influence on regional cerebral oxygen saturation and middle cerebral artery flow velocity. These physiological factors include cardiac output and body temperature. All measurements were done before surgery to eliminate the impact of surgical stimulation on cerebral haemodynamics changes. Body temperature remained unchanged throughout the study. In addition, it is important to evaluate the impact of near-infrared spectroscopy and transcranial Doppler monitoring on the incidence of perioperative complications in infants. It is also important to determine how near-infrared spectroscopy and transcranial Doppler provides continuous regional cerebral oxygen saturation. Outcomes from these studies may be a suitable target for cerebral directed therapy.

Conclusion

Modified ultrafiltration improved cerebral oxygen haemodynamics. The regional cerebral oxygen saturation and middle cerebral artery flow velocity performed better when the end-expiratory tidal pressure of carbon dioxide was 40–45 mmHg during relative low ventilation in infants. It is important to regulate ventilation to precisely achieve cerebral oxygen balance in infants undergoing ventricular septal defect surgery.

Acknowledgements. We thank Dongni Zhang and Nan Wang for their assistance in data collection.

Financial support. The work was supported by grants from the National Natural Science Foundation of China (No. 81471902 and No. 81871592), Beijing Municipal Administration of Hospitals Clinical Medicine Development of Special Funding Support (ZYLX 201810), and Beijing Hospitals Authority Youth Program (QML20180602).

Conflict of interests. The authors declare no conflict of interest.

Ethical standards. Ethics approval for this trial was obtained from the Institutional Ethics Committee of Capital Medical University affiliated Beijing Anzhen Hospital (IRB: 2017030X).

References

1. Picciolini O, Squarza C, Fontana C, et al. Neurodevelopmental outcome of extremely low birth weight infants at 24 months corrected age: a comparison between Griffiths and Bayley Scales. BMC Pediatr 2015; 15: 139.
2. Furnish C, Mueller SW, Kiser TH, Dufficy L, Sullivan B, Beyer JT. Hydroxocobalamin versus methylene blue for vasoplegic syndrome in

https://doi.org/10.1017/S1047951120003984 Published online by Cambridge University Press

cardiothoracic surgery: a retrospective cohort. J Cardiothorac Vasc Anesth 2020; 34: 1763–1770.
3. Andropoulos DB, Stayer SA, Diaz LK, Ramamoorthy C. Neurological monitoring for congenital heart surgery. Anesth Analg 2004; 99: 1365–1375.
4. Hayashida M, Kin N, Tomioka T, et al. Cerebral ischaemia during cardiac surgery in children detected by combined monitoring of BIS and near-infrared spectroscopy. Br J Anaesth 2004; 92: 662–669.
5. Schober A, Feiner JR, Bickler PE, Rollins MD. Effects of changes in arterial carbon dioxide and oxygen partial pressures on cerebral oximeter performance. Anesthesiology 2018; 128: 97–108.
6. Ricci Z, Garisto C, Favia I, et al. Cerebral NIRS as a marker of superior vena cava oxygen saturation in neonates with congenital heart disease. Paediatr Anaesth 2010; 20: 1040–1045.
7. Li J, Zhang G, Holtby H, et al. Carbon dioxide–a complex gas in a complex circulation: its effects on systemic hemodynamics and oxygen transport, cerebral, and splanchnic circulation in neonates after the Norwood procedure. J Thorac Cardiovasc Surg 2008; 136: 1207–1214.
8. Zhang W, Xie S, Han D, Huang J, Ou-Yang C, Lu J. Effects of relative low minute ventilation on cerebral haemodynamics in infants undergoing ventricular septal defect repair. Cardiol Young 2020: 1–8.
9. Medlin WM, Sistino JJ. Cerebral oxygen saturation changes during modified ultrafiltration. Perfusion 2006; 21: 325–328.
10. Vutskits L. Cerebral blood flow in the neonate. Paediatr Anaesth 2014; 24: 22–29.
11. Rhondali O, Mahr A, Simonin-Lansiaux S, et al. Impact of sevoflurane anesthesia on cerebral blood flow in children younger than 2 years. Paediatr Anaesth 2013; 23: 946–951.
12. Grüne F, Kazmaier S, Stolker RJ, Visser GH, Weyland A. Carbon dioxide induced changes in cerebral blood flow and flow velocity: role of cerebrovascular resistance and effective cerebral perfusion pressure. J Cereb Blood Flow Metab 2015; 35: 1470–1477.
13. Abu-Sultaneh S, Hehir DA, Murkowski K, et al. Changes in cerebral oxygen saturation correlate with S100B in infants undergoing cardiac surgery with cardiopulmonary bypass. Pediatr Crit Care Med 2014; 15: 219–228.
14. Polito A, Ricci Z, Di Chiara L, et al. Cerebral blood flow during cardiopulmonary bypass in pediatric cardiac surgery: the role of transcranial Doppler–a systematic review of the literature. Cardiovasc Ultrasound 2006; 4: 47.
15. Kotlinska-Hasiec E, Czajkowski M, Rzecki Z, et al. Disturbance in venous outflow from the cerebral circulation intensifies the release of blood-brain barrier injury biomarkers in patients undergoing cardiac surgery. J Cardiothorac Vasc Anesth 2014; 28: 328–335.
16. Fogel MA, Li C, Elci OU, et al. Neurological injury and cerebral blood flow in single ventricles throughout staged surgical reconstruction. Circulation 2017; 135: 671–682.
17. Naik, SK, Knight A, Elliott M. A prospective randomized study of a modified technique of ultrafiltration during pediatric open-heart surgery. Circulation 1991; 84: III422–31.
18. Rodriguez RA, Ruel M, Broecker L, Cornel G. High flow rates during modified ultrafiltration decrease cerebral blood flow velocity and venous oxygen saturation in infants. Ann Thorac Surg 2005; 80: 22–28.
19. Aeba R, Katogi T, Omoto T, Kashima I, Kawada S. Modified ultrafiltration improves carbon dioxide removal after cardiopulmonary bypass in infants. Artif Organs 2000; 24: 300–304.
20. Kotani Y, Honjo O, Osaki S, et al. Effect of modified ultrafiltration on postoperative course in neonates with complete transposition of the great arteries undergoing arterial switch operation. Circ J 2008; 72: 1476–1480.
21. Wyatt J, Meek J. Commentary on cerebral intravascular oxygenation correlates with mean arterial pressure in critically ill premature infants. Pediatrics 2000; 106: 828.
22. Lucas SJE, Tzeng YC, Galvin SD, Thomas KN, Ogoh S, Ainslie PN. Influence of changes in blood pressure on cerebral perfusion and oxygenation. Hypertension 2010; 55: 698–705.
23. Wong FY, Leung TS, Austin T, et al. Impaired auto-regulation in preterm infants identified by using spatially resolved spectroscopy. Pediatrics 2008; 121: e604–e611.
24. Tsuji M, Saul JP, du Plessis A, et al. Cerebral intravascular oxygenation correlates with mean arterial pressure in critically ill premature infants. Pediatrics 2000; 106: 625–632.
25. Shen J, Wang W, Zhang W, Jiang L, Yang YY. A high-efficiency MUF method benefits post-operative hemodynamic stability and oxygen delivery in neonates with transposition of great arteries. J Card Surg 2019; 34: 468–473.
26. Robertson DR, Justo RN, Burke CJ, Pohlner PG, Graham PL, Colditz PB. Perioperative predictors of developmental outcome following cardiac surgery in infancy. Cardiol Young 2004; 14: 389–395.
27. Dodds C. Carbon dioxide and the cerebral circulation. Br J Anaesth 1999; 82: 813.
28. Redlin M, Koster A, Huebler M, et al. Regional differences in tissue oxygenation during cardiopulmonary bypass for correction of congenital heart disease in neonates and small infants: relevance of near-infrared spectroscopy. J Thorac Cardiovasc Surg 2008; 136: 962–967.
29. Giller CA, Bowman G, Dyer H, Mootz L, Krippner W. Cerebral arterial diameters during changes in blood pressure and carbon dioxide during craniotomy. Neurosurgery 1993; 32: 737–741; discussion 741–742.
30. Valdueza JM, Balzer JO, Villringer A, Vogl TJ, Kutter R, Einhäupl KM. Changes in blood flow velocity and diameter of the middle cerebral artery during hyperventilation: assessment with MR and transcranial Doppler sonography. AJNR Am J Neuroradiol 1997; 18: 1929–1934.
31. Karsli C, Luginbuehl I, Farrar M, Bissonnette B. Cerebrovascular carbon dioxide reactivity in children anaesthetized with propofol. Paediatr Anaesth 2003; 13: 26–31.

https://doi.org/10.1017/S1047951120003984 Published online by Cambridge University Press