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Original Article

Effect of Optimizing Regional Cerebral Oxygen Saturation during Infant Cardiac Surgery on the Incidence of Postoperative Delirium: A Retrospective Study

Jian-Feng Liu, Si-Jia Zhou, Xiu-Hua Chen, Hua Cao, and Qiang Chen

Purpose: To investigate the effect of optimizing regional cerebral oxygen saturation ($rScO_2$) on the incidence of postoperative delirium and surgical outcome in infants with congenital heart disease.

Methods: Sixty-one infants experienced desaturation in $rScO_2$ of 10% from baseline for more than 30 seconds during surgery between January 2020 and January 2022. Among them, 32 cases (Group A) received the corresponding treatment in the process of desaturation and 29 cases (Group B) were observed without receiving any treatment. General information, cerebral oxygen saturation, the incidence of postoperative delirium, and other relevant clinical data were collected.

Results: The duration and severity of intraoperative $rScO_2$ desaturation in Group A were significantly lower than those in Group B. The incidence of postoperative delirium in Group A was significantly lower than that in Group B. There was no significant difference in the positive screening score for delirium between the two groups. Binary logistic regression analysis showed that the aortic cross-clamp time, mechanical ventilation duration, and severity of intraoperative $rScO_2$ desaturation were significantly correlated with the occurrence of postoperative delirium.

Conclusion: Aggressive $rScO_2$ desaturation treatment is associated with a lower incidence of postoperative delirium and improved surgical outcomes.

Keywords: cardiac surgery, regional cerebral oxygen saturation, infant, delirium

Department of Cardiac Surgery, Fujian Children's Hospital (Fujian Branch of Shanghai Children's Medical Center), College of Clinical Medicine for Obstetrics and Gynecology and Pediatrics, Fujian Medical University, Fuzhou, China

Received: April 3, 2023; Accepted: June 6, 2023
Corresponding author: Qiang Chen. Department of Cardiac Surgery, Fujian Children's Hospital (Fujian Branch of Shanghai Children's Medical Center), College of Clinical Medicine for Obstetrics and Gynecology and Pediatrics, Fujian Medical University, Fuzhou, China
Email: chenqiang2228@163.com

Introduction

Delirium is defined as an altered mental state characterized by acute impairment of consciousness and cognition, and it is a fluctuating process.[1)] Postoperative delirium of congenital heart disease (CHD) is a subtype of delirium. As most infants with CHD need to receive early surgical treatment, the incidence of postoperative delirium in these infants is higher than that in other infants receiving different operations at the same age due to the combined influence of young surgical age, poor nutritional conditions, cardiopulmonary bypass, and other factors.[2)] Studies have shown that the incidence of delirium in the cardiac intensive care unit (CICU) is as

high as 49%.[3] The severity of delirium, mechanical ventilation, infection, medications, and age are all closely related to the occurrence of postoperative delirium.[4,5] Many previous studies of regional cerebral oxygen saturation ($rScO_2$) during cardiac surgery in adults showed that intraoperative cerebral desaturation was associated with postoperative delirium occurrence and prognosis.[6–9] A study by de Tournay-Jetté et al. found that cerebral desaturation was associated with the occurrence of postoperative delirium in elderly patients.[10] Further intervention studies by Uysal et al. on desaturation of $rScO_2$ during adult cardiac surgery showed that intervention for intraoperative desaturation of $rScO_2$ was associated with better cognitive outcomes.[11] An observational study of $rScO_2$ during pediatric heart surgery by Carra et al. demonstrated that the desaturation of $rScO_2$ was associated with poorer neurodevelopmental outcomes and length of hospital stay.[12] However, there are few studies examining the relationship between $rScO_2$ and the incidence and prognosis of postoperative delirium in infants with CHD. The aim of this study was to investigate whether treatment with $rScO_2$ desaturation during cardiac surgery is associated with an improvement in postoperative delirium and adverse events. The results of this study may help determine the effectiveness of the corresponding treatments for intraoperative desaturation of $rScO_2$ in infants with CHD.

Materials and Methods

This study was a retrospective cohort study. This study was approved by the institutional review board of our hospital, and patients' privacy fully protected during the study. The clinical data on infants who underwent cardiac surgery were collected from the medical record system at a provincial children's hospital in Fujian Province between January 2020 and January 2022. The hospital is a regional children's cardiac medical center that performs more than 300 congenital cardiac surgeries per year. Inclusion criteria were as follows: 1) patients who underwent surgical treatment for CHD, 2) patients aged less than 1 year old, and 3) $rScO_2$ desaturation of 10% from baseline for more than 30 seconds during surgery. Exclusion criteria were as follows: 1) patients with severe hepatic and renal insufficiency before the operation, 2) preoperative delirium or epilepsy and other neuropsychiatric diseases, 3) patients who underwent emergency surgery, and 4) patients with incomplete clinical data.

Sixty-one infants who experienced a desaturation in $rScO_2$ of 10% from baseline for more than 30 seconds during surgery were included in this study. Patients were divided into two groups based on whether they received the corresponding treatments: 32 patients (Group A) were treated during the process of desaturation and 29 patients (Group B) did not receive treatment.

Sample size calculation

The sample size was analyzed by PASS 11.0.[13] Based on previous research and clinical experience, we set an odds ratio of 2.5, $\alpha = 0.05$, and a power of 0.80. The case ratio between the two groups was 1:1. For that purpose, the sample needed was 52. The sample size was increased to 61 to account for the loss to follow-up.

Treatment of $rScO_2$ desaturation

The same team performed all operations in this study. This team consisted of 3 cardiac surgeons, 3 anesthesiologists, and 2 cardiopulmonary bypass physicians. As the treatment philosophy of one anesthesiologist was to actively intervene in the early stage of $rScO_2$ desaturation, his strategy was to take corresponding measures when $rScO_2$ desaturation by 10% from baseline for more than 30 seconds occurred.[14] The treatment philosophy of the other two anesthesiologists was more conservative given the same situation. Thus, infants with and without exposure to "treatment of $rScO_2$ desaturation" could be found when medical records were retrieved. All anesthesiologists and cardiopulmonary bypass physicians followed the same philosophy and procedures for the rest of the operation. INVOS™ 5100C was used to monitor $rScO_2$. Bilateral near-infrared probes were placed on the patient's forehead, and bilateral baseline $rScO_2$ readings were recorded before the induction of anesthesia.

When the left or right $rScO_2$ of the patient in Group A was desaturated by 10% from baseline for more than 30 seconds, anesthesiologists and cardiopulmonary bypass physicians took the corresponding treatments to maintain the $rScO_2$ at normal baseline, based on the $rScO_2$ intervention algorithm proposed by Denault et al.[15] The corresponding treatments included increasing mean arterial pressure, increasing the oxygen concentration, normalizing partial pressure of carbon dioxide ($PaCO_2$), optimizing hemoglobin, and increasing cardiac output or pump flow rate. During surgery, information about each treatment was recorded in detail. In Group B, $rScO_2$ was only recorded during surgery without any further treatment. After surgery, all patients were transferred to the CICU

for further treatment. During the CICU stay, treatment decisions were made by CICU physicians. All patients received the same extubation indications, sedation, and analgesia.

During the CICU stay, bedside nurses performed delirium assessment twice daily, at the end of each 12-hour shift, and sedation was assessed using the Richmond Agitation-Sedation Scale before the assessment.[16] Delirium assessment was not performed if the patient was unable to respond to stimuli. Delirium assessment was performed using the Cornell Assessment of Pediatric Delirium (CAPD), a reliable and simple bedside tool for children of all ages (Cronbach's alpha coefficient = 0.92).[17] The scale comprised eight questions, including questions about patients' consciousness, cognition, psychomotor activity, and emotion, with scores ranging from 0 to 4 for each question and total scores ranging from 0 to 32. The developmental anchor point reference chart was used to evaluate the infants' delirium score.[18] An overall score ≥9 was considered a diagnosis of delirium.

Data collection

Preoperative $rScO_2$ baseline and $rScO_2$ desaturation of 10% from baseline for more than 30 seconds were collected through the electronic medical record system. The area under the curve of the desaturation of more than 10% was calculated ($rScO_2$ area under the curve [AUC] = integration of decreased by more than 10% of baseline over time, min%) to indicate the severity of cerebral oxygen saturation. Data were collected for postoperative delirium assessment in both groups. General clinical data such as age, gender, weight, surgical duration, anesthesia duration, cardiopulmonary bypass time, and aortic cross-clamp time were collected. Short-term prognosis data such as the length of CICU stay, mechanical ventilation duration, incidence of postoperative pneumonia, and incidence of feeding intolerance of the two groups were collected.

Statistical analysis

Quantitative variables were expressed as mean and standard deviation, while qualitative variables were expressed as frequency and percentage values (%). This study used skewness and kurtosis coefficients to analyze whether variables were normally distributed. If all measurement data conformed to a normal distribution through a normal test, an independent-sample T test was used. If not, a nonparametric test (Mann–Whitney U test) was used for comparative analysis. The $\alpha\chi^2$ or Fisher's test was used for categorical variables between the two groups. The binary logistic regression analysis model was used to measure the independent association between delirium development and each relevant demographic and clinical factor. The data were analyzed using the software IBM SPSS Statistics, version 22. A significance level of $p < 0.05$ was used for the statistical tests.

Table 1 The measures and results taken for the patient in Group A was desaturated by 10% from baseline for more than 30 seconds

	n (%)
Measures	
Increase mean arterial pressure	19 (46.3)
Increase the oxygen concentration	13 (31.7)
Normalize $PaCO_2$	6 (14.6)
Optimize hemoglobin	1 (2.4)
Increase cardiac output or pump flow rate	2 (4.9)
Effect of measures	
$rScO_2$ restored	25 (78.1)

$PaCO_2$: partial pressure of carbon dioxide; $rScO_2$: regional cerebral oxygen saturation

Results

A total of 61 eligible infants with CHD were included in this study, including 32 in Group A and 29 in Group B. The use of treatments for $rScO_2$ desaturation of 10% in group A is shown in **Table 1**. Among them, "Increase mean arterial pressure" was used 19 times, "Increase the oxygen concentration" was used 13 times, "Normalize $PaCO_2$" was used 6 times, "Optimize hemoglobin" was used 1 time, and "Increase cardiac output or pump flow rate" was used 2 times. The effective rate after treatments was 78.1%. There were no significant differences in general data such as age, weight, and gender between the two groups ($P > 0.05$) (**Table 2**).

Table 3 shows that there was no significant difference between the two groups in terms of surgical duration, anesthesia duration, cardiopulmonary bypass time, aortic cross-clamp time, and other general information ($P > 0.05$). There was no statistically significant difference in baseline rScO2 levels between the two groups before surgery. The duration and severity of intraoperative rScO2 desaturation in Group A were significantly lower than those in Group B (4.5 ± 2.2 min vs. 6.8 ± 3.2 min, $P = 0.001$; 9.4 ± 3.7 min% vs. 11.9 ± 4.8 min%, $P = 0.024$).

Table 4 shows that there was no significant difference in the incidence of postoperative pneumonia, the incidence of feeding intolerance, or other short-term complications between the two groups ($P > 0.05$). There was no significant difference in the cumulative dose of intraoperative

Table 2 Demographics and baseline characteristics

	Group A (n = 32)	Group B (n = 29)	P value
Age, m	3.5 ± 1.5	3.3 ± 1.6	0.652
Gender (male), n (%)	19 (59.4)	15 (51.7)	0.611
Gestational age, wk	37.3 ± 1.7	37.9 ± 1.6	0.181
Weight, kg	4.6 ± 0.8	5.0 ± 1.9	0.308
Diagnosis			0.919
Ventricular septal defect	19	18	
Tetralogy of Fallot	1	1	
Coarctation of the aorta	9	8	
Total anomalous pulmonary venous connection	2	2	
Transposition of great arteries	1	0	
Preoperative mechanical ventilation, n (%)	12 (37.5)	9 (31.0)	0.788

Table 3 Comparison of clinical data between the two groups

	Group A (n = 32)	Group B (n = 29)	P value
Surgical duration, h	3.8 ± 0.7	3.9 ± 0.6	0.902
Anesthesia duration, h	4.4 ± 0.6	4.3 ± 0.6	0.926
Cardiopulmonary bypass time, min	97.9 ± 12.9	99.0 ± 13.8	0.713
Aortic cross-clamp time, min	62.0 ± 12.4	61.8 ± 13.3	0.950
Cerebral data in the operating room			
Baseline $rScO_2$, left	67.8 ± 4.9	69.0 ± 4.9	0.336
Baseline $rScO_2$, right	69.0 ± 4.0	68.5 ± 4.1	0.665
Duration of patients with cerebral desaturation*, min	4.5 ± 2.2	6.8 ± 3.2	0.001
$rScO_2$ AUC†, min%	9.4 ± 3.7	11.9 ± 4.8	0.024

*$rScO_2$ decreased by more than 10% at baseline. †$rScO_2$ AUC was quantified as the "area under the threshold" (integration of decreased by more than 10% of baseline over time, min%). The rScO2 AUC data in this study were directly derived from INVOS 5100C, which was automatically computed by INVOS 5100C based on a set threshold. $rScO_2$: regional cerebral oxygen saturation; AUC: area under the curve

Table 4 Comparison of postoperative clinical results between the two groups

	Group A (n = 32)	Group B (n = 29)	P value
Total intraoperative and postoperative sedative and analgesic drugs, mg/kg			
Midazolam	9.9 ± 2.2	10.9 ± 2.5	0.102
Sufentanil	0.014 ± 0.0015	0.013 ± 0.0015	0.926
Rocuronium	2.7 ± 0.4	2.6 ± 0.3	0.823
Number of patients with delirium	8 (25.0)	16 (55.2)	0.020
Diagnosis time for delirium (postoperative), days	5.3 ± 1.4	6.2 ± 1.5	0.028
Positive screening score for delirium	14.9 ± 4.1	16.1 ± 4.4	0.510
Postoperative pneumonia, n (%)	19 (59.4)	20 (69.0)	0.594
Feeding intolerance, n (%)	9 (28.1)	12 (41.4)	0.296
Duration of mechanical ventilation, days	4.2 ± 1.3	5.0 ± 1.6	0.023
Length of CICU stay, days	8.2 ± 1.4	9.1 ± 1.7	0.046

CICU: cardiac intensive care unit

Table 5 Binary logistic regression analysis of the different predictors of delirium

Predictors	OR (95% CI)	P value
Gender	0.61 (0.13, 2.92)	0.531
Age	0.72 (0.43, 1.22)	0.221
Aortic cross-clamp time	1.09 (1.02, 1.17)	0.007
Duration of mechanical ventilation	2.64 (1.24, 5.63)	0.012
$rScO_2$ AUC	1.24 (1.06, 1.51)	0.008

OR: odds ratio; CI: confidence interval; $rScO_2$: regional cerebral oxygen saturation; AUC: area under the curve

and postoperative sedation, analgesia, and muscle relaxants between the two groups (P >0.05). The incidence of postoperative delirium in Group A was significantly lower than that in Group B (25.0% vs. 55.2%, P = 0.020). There was no significant difference in the positive screening score for delirium between the two groups. In addition, the mechanical ventilation duration and the length of CICU stay in Group A were significantly shorter than those in Group B (4.2 ± 1.3 days vs. 5.0 ± 1.6 days, P = 0.023; 8.2 ± 1.4 days vs. 9.1 ± 1.7 days, P = 0.046). In **Table 5**, age, gender, aortic cross-clamp time, mechanical ventilation duration, and $rScO_2$ AUC are included in binary logistic regression analysis, and it is found that aortic cross-clamp time, mechanical ventilation duration, and $rScO_2$ AUC are significantly correlated with the occurrence of postoperative delirium in infants who underwent congenital cardiac surgery.

Discussion

The purpose of this study was to investigate the effects of the treatments on intraoperative $rScO_2$ desaturation on postoperative delirium in infants undergoing surgery for CHD. The incidence of postoperative delirium in all infantile patients in this study was 39.3%, similar to previous findings on the incidence of pediatric delirium after cardiac surgery.[19–21] Our study also found that the incidence of postoperative delirium in infantile patients in Group A was significantly lower than that in Group B. Previous studies have shown that infantile patients with intraoperative $rScO_2$ desaturation had a higher risk of postoperative delirium, similar to the results of some studies in adults.[22,23] These results were also supported by an observational study conducted by Flechet et al., which showed that a desaturation in $rScO_2$ in children was associated with an increase in the length of hospital stay and mechanical ventilation duration after surgery.[23] The important factor in this study was initiating treatment when the $rScO_2$ desaturation was 10% from baseline for more than 30 seconds during surgery.[14] The choice of this cutoff for treatment was controversial, as one of the anesthesiologists in our center chose to treat at this cutoff, while others did not. The purpose of this retrospective study was to explore whether it was beneficial for these infants to receive treatment during early $rScO_2$ desaturation to provide some basic reference and support for future treatment studies on the decrease in cerebral oxygen saturation. The results of this study also indicated that the treatments for intraoperative changes in cerebral oxygen saturation summarized by Denault et al. were successful and could effectively optimize perioperative cerebral oxygen saturation.[15] However, although the critical point of $rScO_2$ desaturation of 10% from baseline for more than 30 seconds could detect changes in $rScO_2$ quite early and improve the sensitivity of discrimination, it could also reduce the specificity of the detection of changes in cerebral oxygen saturation to a certain extent. Therefore, more research is needed to define the regulation zero boundary point.

In this study, the delirium of the infants was assessed by the CAPD scale. Considering that the bedside nurses were familiar with the mental state of the infants during continuous care, delirium assessments of the infants were performed daily by the bedside nurse. All bedside nurses involved in delirium assessments had undergone systematic training. After the infants entered the CICU post surgery, the bedside nurses conducted delirium assessments every 12 hours (08:00 and 20:00) to record the occurrence of postoperative delirium. When the delirium assessment was positive, the CICU physicians would take appropriate medical measures according to the patients' condition. Based on the situation, they would also provide appropriate treatments for the underlying cause. For example, the infants were moved from a noisy to a quieter environment.[24,25] An observational study conducted by Alvarez et al. found that the onset of

delirium was closely related to the length of hospital stay after cardiac surgery and that the longer the duration of delirium, the worse the prognosis.[26] Similar results were found in this study. Kunst et al. conducted a study on the treatment of desaturation in $rScO_2$ during cardiac surgery in elderly individuals, demonstrating that the treatments for intraoperative desaturation in $rScO_2$ were effective and significantly reduced the incidence of delirium after cardiac surgery.[27] The results of this study also indicate that aggressive $rScO_2$ desaturation treatment can have positive effects in infants who underwent cardiac surgery. The present retrospective study could provide a basis and reference values for future research on the treatments for $rScO_2$ desaturation during congenital cardiac surgery.

Limitations

Although many factors were considered in this study, there were still some deficiencies. First, this study was a retrospective study, and limited data could be collected and used. The objective of this study was to investigate whether exposure to treatment of $rScO_2$ desaturation could reduce the incidence of postoperative delirium. Although we controlled for some interfering factors, confounding factors existing in the actual study were very complex. Second, the occurrence of delirium in this study was assessed by CICU bedside nurses using the CAPD scale. There were some subjective differences in this process, which might affect the accuracy of the assessment of the occurrence of delirium. The small sample size of this study might further amplify the influence of this bias. The accuracy of the results might be affected by the limited degree of control for sedative withdrawal syndrome as an interfering factor in this study. Prospective randomized controlled studies with larger sample sizes and more rigorous experimental designs are needed in the future to more accurately evaluate the influence of intraoperative optimized rScO2 on postoperative delirium. Finally, this study was conducted in a single medical institution in China, so our results might not be generalizable to other medical institutions. Future multi-institutional studies are therefore needed to further confirm the effectiveness of this approach.

Conclusion

The results of our study show a correlation of aggressive $rScO_2$ desaturation treatment with a lower incidence of postoperative delirium. Aggressive $rScO_2$ desaturation treatment may be associated with improved surgical outcomes. This study may establish justification for a further prospective study.

Author Contributions

Jian-Feng Liu and Qiang Chen designed the study, performed the statistical analysis, participated in the operation, and drafted the manuscript. Si-Jia Zhou, Xiu-Hua Chen, and Hua Cao collected the clinical data. All authors read and approved the final manuscript.

Data Sharing and Data Accessibility

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Ethical Approval and Consent to Participate

This study was approved by the ethics committee of Fujian Children's Hospital and followed the guidelines outlined in the Declaration of Helsinki. Written informed consent was obtained from all the patient's parents.

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Disclosure Statement

All authors declare that they have no competing interests.

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