ORIGINAL ARTICLE

Effect of slow versus rapid rewarming on jugular bulb oxygen saturation in adult patients undergoing open heart surgery

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ABSTRACT

Background: A debate has appeared in the recent literature about the optimum rewarming strategy (slow vs. rapid) for the best brain function. This study was designed to compare the effect of slow versus rapid rewarming on jugular bulb oxygen saturation (SjO_2) in adult patients undergoing open heart surgery. **Materials and Methods:** A total of 80 patients undergoing valve and adult congenital heart surgery were randomly allocated equally to rapid rewarming group 0.5 (0.136)°C/min and slow rewarming group 0.219 (0.055)°C/min in jugular bulb sampling was taken before, during and after surgery. Surgery was done at cardiopulmonary bypass (CPB) temperature of 28-30°C and rewarming was performed at the end of the surgical procedure. **Results:** CPB time, rewarming period were significantly longer in the slow rewarming group. Significant difference was observed in the number of the desaturated patients ($SjO_2 \leq 50\%$) between the two groups; 14 (35%) in rapid rewarming versus 6 (15%) in the slow rewarming group; $P = 0.035$ by Fisher's exact test. **Conclusions:** Slow rewarming could reduce the incidence of SjO_2 desaturation during rewarming in adult patients undergoing open heart surgery.

Key words: *Cardiopulmonary bypass, jugular bulb oxygen saturation, rapid rewarming, slow rewarming*

INTRODUCTION

Despites advances in cardiopulmonary bypass (CPB) practice, brain injury after cardiac surgery with CPB remains a major concern. Although the etiology of brain injury is complex, it may be due to cerebral hypoperfusion, cerebral emboli, impaired cerebral oxygenation, systemic inflammatory response and brain hyperthermia during rewarming.[1-3]

Several studies have examined the impact of bypass temperature on post-operative cerebral outcome with a resultant increased awareness of the importance of CPB temperature management strategies.[2-5] This increased awareness has likely led to evolution of temperature management.

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However, a debate has appeared in the recent literature about the optimum rewarming strategy (slow vs. rapid) for the best brain function. During the rewarming from cold CPB, the brain can be exposed to periods of hyperthermia, impaired cerebral oxygenation that may lead to impaired brain function after CPB.[2,6-9]

Jugular bulb oxygen saturation (SjO_2) reflects the global balance between cerebral oxygen supply and demand. This balance has been shown to be impaired during rewarming from cold CPB 28°C.[6-10] Croughwell *et al.*[9] found that $SjO_2 \leq 50\%$ occurred in 23% of patients during the rewarming and in 16 patients out of 19 (84%) in Sapire's *et al.* study.[8] Such periods of jugular bulb desaturation during the rewarming were associated of impaired neurocognitive function.[6,7]

Slow rewarming has been associated with better neurocognitive function[10] and improvement in SjO_2[11] than rapid rewarming in patients' undergoing coronary artery bypass graft (CABG) surgery.

The aim of this study was to compare the effect of two rewarming strategies (slow vs. rapid) on SjO_2, in adult patients undergoing open heart surgery using CPB.

MATERIALS AND METHODS

After obtaining the local research ethical committee approval and written informed consent, 80 patients were randomly allocated by block randomization into two groups according to the rewarming technique used; rapid rewarming or conventional (n = 40) and slow rewarming (n = 40).

Adult patients undergoing open heart surgery (either rheumatic valve surgery or correction of adult congenital heart disease ventricular septal defect and atrial septal defect) were involved in this study. Patients with previous cardiac surgery, uncontrolled hypertension, pre-operative history of neurological impairment (symptomatic cerebrovascular disease with residual deficits) or psychiatric illness requiring treatment or insulin-dependent diabetes mellitus were excluded from the study.

All patients were pre-medicated with oral diazepam 10 mg 60-90 min before surgery. Anesthesia was induced by propofol (2-3 mg/kg), fentanyl (5-10 μg/kg) and pancuronium (0.1 mg/kg) was given to facilitate endotracheal intubation. Anesthesia was maintained with supplemental isoflurane (0.5-1.0%) in O_2/air, propofol (2-5 mg/kg/h), fentanyl (1-2 μg/kg/h) and incremental doses of pancuronium were given as required.

Continuous monitoring of mean arterial pressure (MAP), right atrial pressure, electrocardiogram, oxygen saturation and intermittent monitoring of blood gases, electrolytes and clotting analysis were done.

A non-pulsatile heart-lung machine was used (COBE) (Cardiovascular, Inc. ARVADA and Co., 80004-3599, USA) with a flow rate of 2.2-2.4 l/min/m^2 body surface area and a membrane oxygenator. The pump was primed with crystalloid, non-glucose containing solution (Ringers' solution). Hematocrit was maintained above 20%. Alpha-stat blood gas strategy was used; $PaCO_2$ was maintained between 35 and 45 mmHg and moderate hypothermia (28-30°C) was used. Cold crystalloid cardioplegia was used and the solution was administered in the aortic root. The cardioplegia solution was given at a dose of 10-20 ml/kg. Further half-doses were given every 20-30 min as required. Continuous infusion of fentanyl (1-2 μg/kg/h) and propofol (2-5 mg/kg/h) was given to maintain anesthesia during CPB. Furthermore, the MAP was kept between 50 and 70 mmHg by using either glyceryl trinitrate or incremental doses of phenylephrine, as appropriate.

All patients were cooled to a temperature of 28-30°C. Rewarming was performed at the end of the surgical procedure to a nasopharyngeal (NP) temperature of 37°C. Patients in the rapid rewarming group were conventionally warmed by keeping NP-CPB perfusate temperature gradients between 4°C and 6°C and in slow rewarming group, NP-CPB perfusate temperature gradients were maintained between 1°C and 2°C.[10]

The jugular bulb catheter (Hydrocath 16 G, 15-20 cm) was placed by retrograde cannulation of the right internal jugular vein and its position was checked radiologically.[12] Intermittent samples were taken before CPB, at stable hypothermia, start of rewarming, at 32°C, at 34°C and at 36°C during rewarming, at 20 min after CPB. Jugular bulb samples (1 ml) were taken at a rate of 0.5 ml/min to avoid extracranial contamination.[13]

All data were analyzed with SPSS version 13 for Windows (SPSS Inc., Chicago, IL). Data was presented as mean (standard deviation or range) unless otherwise stated. Comparison between both groups was done using the independent samples t-test. While within groups' analysis was done using Wilcoxon signed ranks test compared with baseline values. Fisher's exact test was used for analyzing the number of patients with jugular bulb desaturation between rapid and slow rewarming groups.

Furthermore, multivariate analysis was done using lowest SjO_2 during rewarming as dependent variable and age, rewarming time, CPB time and ischemic time as independent variables. $P < 0.05$ was considered significant.

RESULTS

Both groups were comparable in terms of age, sex, type of surgery, ejection fraction and number of patients with atrial fibrillation and those with the left atrial thrombus [Table 1].

CPB time and rewarming period were significantly longer in the slow rewarming group. The mean rate of rewarming was 0.5 (0.136)°C/min in rapid rewarming group, versus 0.219 (0.055)°C/min in slow rewarming group, $P = 0.001$ [Table 2].

The lowest NP temperature was 29.11 (0.75)°C and 29.24 (0.68)°C in rapid and slow rewarming groups respectively. Furthermore, no significant differences were observed in the mean temperatures values between both groups [Table 3].

Table 1: Comparison of patient characteristics between rapid rewarming and slow rewarming groups

Variables	Rapid rewarming	Slow rewarming
Age (years)	29.5 (8.77)	31 (11.3)
Gender (male/female)	24/16	21/19
Weight (kg)	56.6 (13)	56.9 (16)
Height (cm)	166 (8.2)	163 (8.52)
Type of the operation		
MVR	24	21
AVR	4	8
MVR and AVR	6	6
VSD	1	
ASD	3	4
ASD and VSD	1	
Congenital subaortic membrane	1	1
Patients' with atrial fibrillation	11	12
Patients' with left atrial thrombus	8	7
EF %	62.67 (6.44)	62.07 (9.67)

MVR: Mitral valve replacement; AVR: Aortic valve replacement; VSD: Ventricular septal defect; ASD: Atrial septal defect; EF: Ejection fraction

Table 2: Comparison of intraoperative and post-operative variables between rapid and slow rewarming groups

Variables	Rapid rewarming	Slow rewarming	*P*
Cross-clamping time (min)	87.05 (28.57)	94.87 (33.5)	0.294
CPB time (min)	112.83 (32.16)	131.03 (45.27)	0.034
Rewarming time (min)	15.65 (2.96)	35.1 (6.06)	0.001
Rewarming speed (°C/min)	0.5 (0.136)	0.219 (0.055)	0.001
ICU stay (days)	5.45 (1.55)	5.83 (4.3)	0.159

ICU: Intensive Care Unit; CPB: Cardiopulmonary bypass

No significant differences were observed in mean arterial blood pressure, hematocrit and arterial carbon dioxide tension between both groups at any of the studied periods [Table 3].

High SjO_2 levels occurred during cooling and desaturation appeared during rewarming in both groups [Figures 1 and 2]. Although, there was no significant difference in mean SjO_2 at any time of the studied periods [Figure 1]. Significant difference was observed in the number of the desaturated patients ($SjO_2 \leq 50\%$) between the two groups; 14 (35%) in rapid rewarming versus 6 (15%) in the slow rewarming; $P = 0.035$ by Fisher's exact test.

All patients had uneventful post-operative course except one patient in the rapid rewarming group was comatosed and died 5 days after surgery. He had multiple cerebral infarctions and his lowest SjO_2 value during rewarming was 37%. This patient underwent mitral valve replacement for mitral stenosis and had atrial fibrillation.

There was no significant relationship between lowest SjO_2 during rewarming as dependent variable and age, rewarming time, CPB time and ischemic time as independent variables [Table 4].

DISCUSSION

Reduction of SjO_2 occurred during rewarming from cold CPB in patients' undergoing CABG.[6-9] In addition, it has been reported that such patients who experience SjO_2 desaturation during rewarming have an increased risk of post-operative cognitive deficits.[6,7] Therefore, new rewarming strategies should be thought, examined and used.

Table 3: Comparison of MAP, $PaCO_2$, hematocrit and NP before, during and after CPB between slow rewarming and in rapid rewarming groups

Rewarming strategy	After induction	Stable hypothermia	Start of rewarming	At 32°C	At 34°C	At 36°C	20 min after CPB
MAP (mmHg)							
Slow	90.62 (13.95)	63.37* (9.91)	57.62* (7.61)	63.92*(11.25)	58.77* (10.58)	62.52* (13.57)	76.82* (10.24)
Rapid	86.42 (11.69)	61.15* (11.72)	57.20* (9.65)	63.02* (8.74)	62.50* (9.14)	67.47* (12.43)	79.07* (8.99)
$PaCO_2$ (mmHg)							
Slow	30.42 (5.67)	36.42* (5.45)	36.78* (5.66)	36.39* (5.25)	37.09* (5.93)	37.38* (6.30)	34.10* (4.68)
Rapid	32.53 (7.23)	36.98* (7.26)	37.61* (6.75)	36.97* (5.99)	37.79* (6.24)	36.13* (7.64)	35.01* (6.46)
Hematocrite (%)							
Slow	38.67 (3.9)	25.29* (4.08)	24.93* (4.08)	26.43* (6.09)	25.35* (5.4)	23.94* (4.98)	27.18* (5.22)
Rapid	38.55 (5.19)	25.50* (5.34)	24.96* (4.38)	26.13* (5.4)	24.72* (5.22)	24.06* (5.1)	26.64* (4.74)
NP temperature (°C)							
Slow	36.06 (0.67)	33.32* (0.95)	29.11* (0.75)	32.01* (0.12)	34.11* (0.10)	36.67* (0.38)	35.49* (0.70)
Rapid	35.89 (0.53)	33.28* (0.94)	29.24* (0.69)	32.12* (0.11)	34.20* (0.12)	36.62* (0.41)	35.30* (0.68)

*$P<0.05$ (significant within each group using Wilcoxon Signed Ranks test) compared with baseline values. MAP: Mean arterial pressure; $PaCO_2$: Arterial carbon dioxide tension; NP: Nasopharyngeal temperature; CPB: Cardiopulmonary bypass

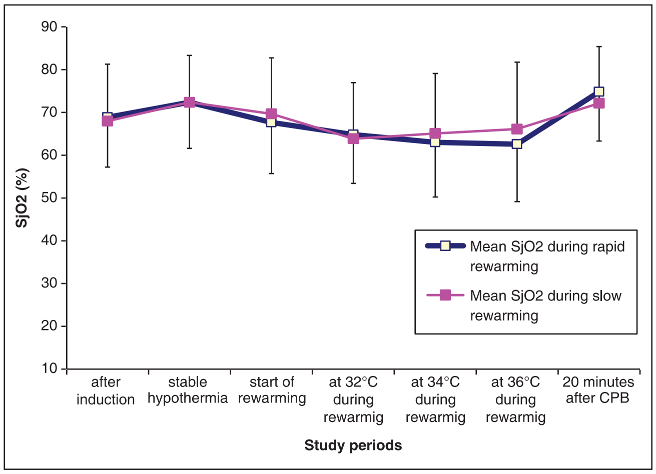

Figure 1: Comparison of jugular bulb oxygen saturation between rapid and slow rewarming before, during and after cardiopulmonary bypass

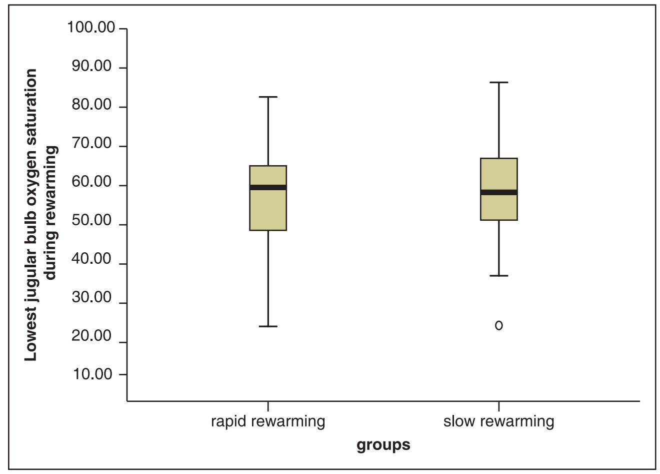

Figure 2: Box plot of lowest jugular bulb saturation (%) during rewarming (median and interquartile range)

Table 4: Multivariate analysis using lowest jugular bulb oxygen saturation as dependent variable and age, rewarming time, CPB time and ischemic time as independent variables

Dependent variable is the lowest jugular bulb oxygen saturation during rewarming						
Independent variables	Slow rewarming (*n*=40)		Rapid rewarming (*n*=40)		Both groups (*n*=80)	
	β	*P*	*β*	*P*	*β*	*P*
Age	0.015	0.929	0.027	0.880	0.015	0.929
Rewarming time	0.080	0.637	0.026	0.877	0.080	0.637
CPB time	0.903	0.203	0.042	0.889	0.903	0.203
Ischemic time	−1.052	0.139	−0.027	0.404	−1.052	0.139

CPB: Cardiopulmonary bypass

In this study, we have examined the effect of slow versus rapid rewarming on SjO_2 in adult patients undergoing open heart surgery. Although there were no significant differences in mean SjO_2 between groups, but 14 patients were desaturated ($SjO_2 \leq 50\%$) in rapid rewarming group versus six in slow rewarming group ($P = 0.035$).

These periods of desaturation during rapid rewarming could be explained by an imbalance between cerebral oxygen supply and demand.[8,9] Animal[14] and human[15] studies revealed that SjO_2 desaturation during rapid rewarming occurred due to an increase in cerebral metabolic rate that is temporarily unmatched by an increase in cerebral blood flow.

There have been controversial reports regarding the effect of rewarming rate on SjO_2 in patients who had CABG.[8,16-21]

Kadoi *et al.*[16] in a small randomized study found no significant differences between slow or rapid rewarming in terms of the SjO_2 value or neurocognitive outcome either between diabetic or non-diabetic patients (15 patients in each group). Other authors have found that SjO_2 desaturation during rewarming was not a function of rewarming rate, but was related to increase in jugular bulb temperature.[17,18]

Furthermore, Newman *et al.*[19] in a prospective study reported that rewarming rate had no independent effect on post-operative cognitive decline in non-diabetic patients.

This discrepancy between the previous reports[17-19] and our study can be attributed to different age groups, different types of surgery, different anesthetic techniques or to the non-randomized nature of most of the studies that examined the effect of rewarming rate.

On the other hand, retrospective examination of the effect of rewarming rate on SjO_2 revealed that patients who warmed rapidly had a greater reduction in SjO_2 than who warmed slowly.[8,20,21] Also, rapid rewarming, low hematocrit and mean arterial blood pressure less than 60 mmHg appeared as contributing factors to SjO_2 desaturation during rewarming.[8] In our study, hematocrit and mean arterial blood pressure were comparable during the studied periods between the two groups.

Furthermore, two randomized studies addressed the effects of slow rewarming on improving jugular bulb saturation[11] and on getting better neurocognitive outcome than rapid rewarming.[10] The previous reports[8,11,20,21] are in agreement with our study.

One patient in the rapid rewarming group had multiple cerebral infarctions and his lowest SjO_2 during rewarming was 37%. This gives us an idea about the importance of monitoring cerebral oxygenation in detecting patients at risk of brain injury during cardiac surgery. This issue has been addressed by using non-invasive regional cerebral oxygenation monitor (near infrared spectroscopy) in Slater's *et al*.[22] and Mohands' *et al*.[23] studies.

Examining SjO_2 during slow and rapid rewarming without any neurological outcome and using patients' with different cardiac lesions (valve lesions and congenital heart defects) are considered limitations of this study.

CONCLUSION

SjO_2 appeared to be more preserved with slow rewarming in adult patients undergoing open heart surgery.

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