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Outcome of inflammatory response after normothermia during cardiopulmonary bypass surgery in infants with isolated ventricular septal defect

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Purpose: A recent study analyzing several cytokines reported that long cardiopulmonary bypass (CPB) time and long aortic cross clamp (ACC) time were accompanied by enhanced postoperative inflammation, which contrasted with the modest influence of the degree of hypothermia. In this present study, we aimed to examine the effect of CPB temperature on the clinical outcome in infants undergoing repair of isolated ventricular septal defect (VSD).
Methods: Of the 212 infants with isolated VSD who underwent open heart surgery (OHS) between January 2001 and December 2010, 43 infants were enrolled. They were classified into 2 groups: group 1, infants undergoing hypothermic CPB (26°C–28°C; n=19) and group 2, infants undergoing near-normothermic CPB (34°C–36°C; n=24).
Results: The age at the time of the OHS, and number of infants aged<3 months showed no significant differences between the groups. The CPB time and ACC time in group 1 were longer than those in group 2 (88 minutes vs. 59 minutes, *P*=0.002, and 54 minutes vs. 37 minutes, *P*=0.006 respectively). The duration of postoperative mechanical ventilation was 1.6 days in group 1 and 1.8 days in group 2. None of the infants showed postoperative neurological and developmental abnormalities. Moreover, no postoperative differences in the white blood cell count and C-reactive protein levels were noted between two groups.
Conclusion: This study revealed that hypothermic and near-normothermic CPB were associated with similar clinical outcomes and inflammatory reactions in neonates and infants treated for simple congenital heart disease.

Key words: Cardiopulmonary bypass, Ventricular heart septal defect, Hypothermia

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Introduction

Cardiac operations involving cardiopulmonary bypass (CPB) can induce a systemic inflammatory response involving activated neutrophils, a disturbed balance between proinflammatory and anti-inflammatory cytokines, with interactions among many other mediators such as arachidonic acid derivatives, products from oxidative stress, nitric oxide, endothelin-1 and platelet activating factor[1].

In many centers performing pediatric open heart surgery (OHS), the use of hypothermia is common. The main aim of cooling the body is to protect major organs from ischemic injury by reducing the oxygen consumption and whole body inflammatory response to CPB[2,3].

A recent study analyzing several cytokine demonstrated that long CPB time and long aortic cross clamp (ACC) time were accompanied by enhanced postoperative inflammation in contrast to the modest influence of the degree of hypothermia[4].

This study evaluated through laboratory findings whether hypothermia during OHS is related to inflammation in infants undergoing OHS.

Materials and methods

1. Patient selection

Between January 2001 and December 2010, 621 infants underwent OHS in Kyungpook National University Medical Center. Among them, 212 patients were VSD patients. The lowest bypass temperature of hypothermia (26°C–29°C) and near-normothermia (34°C–36°C) were selected[3] (Fig. 1). Sixty-five infants were in two temperature groups. Twenty-two patients with insufficient laboratory data and records were excluded. Forty-three infants were enrolled and they were classified into 2 groups: group 1, infants undergoing hypothermic CPB (26°C–29°C) and group 2, infants undergoing near-normothermic CPB (34°C–36°C).

As a laboratory parameter for inflammatory reaction, white blood cell (WBC) count and C-reactive protein (CRP) of preoperative and postoperative day 1, 2, and 4 were serially reviewed[3,4].

2. Statistical analysis

Values are expressed as the mean±standard deviation. Univariate comparisons of continuous variables were conducted using the unpaired Student *t* test. Univariate analyses of the differences in proportion between the two groups were accomplished using the chi-square analysis. Differences with a *P* value of <0.05 were considered to be statistically significant. To examine changes over time after surgery, mixed model analysis were employed using PASW statistics 18.0 (SPSS Inc., Chicago, IL, USA).

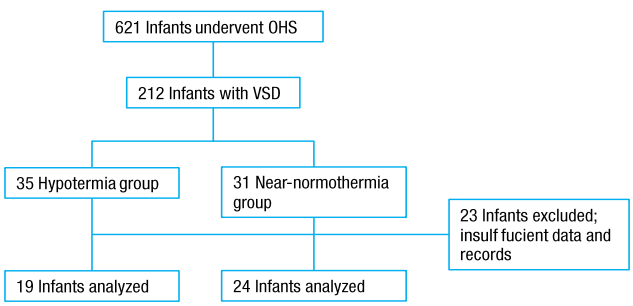

Fig. 1. Flow diagram for the classification of infants. OHS, open heart surgery; VSD, ventricular septal defect.

Table 1. Patient characteristics

Characteristic	Group 1	Group 2	*P* value
Sex			
Male/female	11/8	15/9	0.022
Age (mo)	3.3±2.12	4.1±2.9	0.201
Weight (kg)	4.8±0.83	5.6±2.1	0.004

Values are presented as mean±standard deviation.
Group 1, hypothermia; group 2, near normothermia.

Results

Among of them, 19 infants were group 1 and 24 were group 2. Age on OHS, and number of patients below 3 months old showed no significant differences between groups 1 and 2 (Table 1). Patients' body weight was significant different between groups 1 and 2 (*P*=0.004). In group 1, 4 infants were Down syndrome and 8 infants had admission for respiratory infection before OHS. There were no patients with pneumonia or sepsis at the time of surgery. In group 2, number of infants with Down syndrome and pre-OHS admission were 2 and 3, respectively. The duration of postoperative mechanical ventilation was 1.6 days in group1 and 1.8 days in group 2.

Priming volume showed no differences between two groups. The CPB time and ACC time in group 1 were longer than those in group 2 (*P*=0.002 and *P*=0.006) (Table 2). In both groups, postoperative WBC and CRP increased after the surgery and decreased gradually. But there was no difference between two groups. (Figs. 2 and 3; *P* value of WBC difference 0.27, and *P* value of CRP difference 0.29)

There were no infants with postoperative seizure, prolonged low Glasgow Coma Scale score and developmental abnormalities.

Discussion

VSD is the most commonly recognized congenital heart defect and one of the most common defects requiring surgical closure[4]. Surgical closure of isolated VSD is known to be safe and effective[4,5]. CPB has been widely utilized in the surgical correction of VSD for decades[6].

CPB activates blood cells, such as endothelial cells, neutrophils,

Table 2. Cardiopulmonary bypass time, aortic cross clamp time and duration of mechanical ventilation for the groups

	Group 1	Group 2	*P* value
Cardio pulmonary bypass time (min)	88±25	59±12	0.002
Aortic cross clamp time (min)	54±16	37±9	0.006
Postoperative mechanical ventilation (day)	1.6±0.7	1.8±0.6	0.331

Values are presented as mean±standard deviation.
Group 1, hypothermia; group 2, near normothermia.

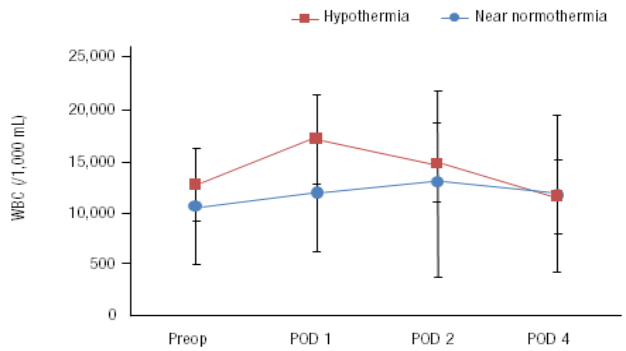

Fig. 2. Preoperative and postoperative (day 1, 2, and 4) white blood cell (WBC) count of both groups. The differences between the 2 groups were not statistically significant (*P*=0.27). POD, postoperative day.

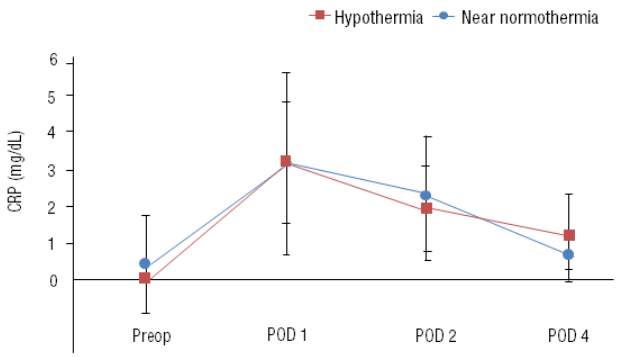

Fig. 3. Preoperative and postoperative (day 1,2, and 4) C-reactive protein (CRP) level of both groups. The differences between the 2 groups were not statistically significant (*P*=0.29).

platelets and stimulates the cytokines such as tumor necrosis factor-a, interleukin (IL) 1, IL-6, and IL-8[7,8]. These series of responses induce inflammatory reaction and these factors induce complications like bleeding, thromboembolism, and organ dysfunction[9,10].

Various treatment strategies have been tested to reduce the systemic inflammation induced by CPB. Medical treatment includes corticosteroids. In the several adult studies, hypothermia during the surgery is known to protect major organs from ischemic injury by reducing the oxygen consumption, the complement activation, and whole body inflammatory response to CPB[11-13].

The recent studies have shown that hypothermia does not offer significant advantages over near-normothermia during pediatric CPB. Stocker et al.[3] studied the influence of CPB temperature of pediatric patients. Mild hypothermia group showed similar clinical outcomes and inflammatory markers with hypothermia group. Eggum et al.[4] evaluated the inflammatory response in children with mild or moderate hypothermia. Clinical postoperative outcomes were similar in two groups.

Long CPB time tends to increase plasma cytokine levels. Long ACC time also increases cytokine levels and inflammatory responses[4]. In our study, hypothermia group had longer CPB and ACC times. Even though hypothermia decreased inflammatory reaction, longer CPB and ACC time may resulted in similar clinical and laboratory outcomes in both groups. Overall in our study, neonates and infants requiring correction of simple VSD, hypothermic and near-normothermic CPB could have similar clinical outcome. And there was no laboratory differences suggesting inflammatory reaction between two groups.

This study has limitations. This study was designed under the retrospective chart review and could only include WBC count and CRP as inflammatory markers. Cytokines could not be included. And patients with diverse age, different type of congenital heart disease needs to be investigated.

Inflammation and organ damage is a concern after the OHS. In this study, near-normothermic CPB showed similar clinical outcome and inflammatory response compared to hypothermic patients. Near-normothermic bypass should be concerned in pediatric OHS.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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