Normothermia versus Hypothermia during Cardiopulmonary Bypass in Cases of Repair of Atrioventricular Septal Defect

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Abstract

Background: Cardiopulmonary bypass (CPB) used for cardiac surgery is now uniformly carried out under normothermic conditions in adult patients; however, the temperature applied in pediatric CPB vary significantly, ranging from deep hypothermia to normothermia due to the lack of a consistent approach to CPB temperature in pediatric cardiac surgery, which is related to a lack of supportive evidence. Organs protection aim to decrease metabolic requirement and provide energy and oxygen, hypothermia has reached these goals by arresting and cooling the heart, delivering oxygen, and modifying reperfusion. Recently, a large number of studies investigated effect of hypothermia to decrease the negative impact of hypothermia. It has been suggested that the degree of hypothermia affects the inflammatory responses triggered by CPB. However, the use of normothermia during CPB had been introduced and resulted in acceptable results. We hypothesized that the use of normothermia during corrective surgery of AV septal defects improves the outcome of the CPB. Objective: The study aimed to compare the outcome of normothermic technique and mild hypothermic technique during (CPB) in pediatric cardiac patients undergoing repair of atrioventricular (AV) septal defect and their effect on tissue perfusion, serum lactate level, duration of patient intubation, and postoperative hospital stay. Patients and Methods: Forty patients presented for repair of AV defect aged from 1 month to 36 months were divided randomly into two equal groups (20 patients in each): Group I (Normothermic group) of body temperature more than 35°C up to 37°C and Group II (mild Hypothermic group) body temperature between (32°C–35°C). Basal data include complete blood count, electrolytes, arterial blood gases (ABGs), coagulation profile, and liver function tests were collected. Hemodynamic variables, ABG, serum lactate, and activated clotting time (ACT) measured in different time intervals related to CPB. With the termination of CPB, aortic cross-clamping time (minutes), CPB time (minutes), spontaneous regaining of the heart function, need for inotropic administration, and/or vasopressor requirements to wean the heart from CPB were reported in all patients. Results: This study showed statistically significant lower PH and HCO3 levels and significantly higher serum lactate levels in Group I after weaning of CPB. Furthermore, ACT level was statistically significantly higher in Group II than Group I after weaning of CPB. During postoperative period, hypothermic group showed significantly higher liver enzymes than the normothermic group. The duration of inotropes administration and duration of intubation were significantly longer in Group II than Group I. Conclusion: Normothermia during CPB showed better global tissue perfusion than hypothermia in elective surgeries for repair of AV defects in the form of less degree of lactic acidosis, less effect on coagulation system, shorter duration of inotropic support, shorter intubation period, and shorter stay in the intensive care unit.

Keywords: Atrioventricular canal repair, cardiopulmonary bypass, hypothermia, normothermia, tissue perfusion

INTRODUCTION

Congenital heart defects usually presented with physiological disturbances, so it has anesthetic challenges, especially for cardiac surgeries. Atrioventricular (AV) septal defect results from the failure of separation of atria from the ventricles into separate chambers, resulting in a large connection between the atria and ventricles.11 Surgical repair of AV septal defect dates back to the early years of cardiac surgery, its results have steadily improved.12 Although this improvement of the results, there still is a certain proportion of morbidity and mortality occurs with cardiopulmonary bypass (CPB). Maintain adequate tissue perfusion during CPB avoids end-organ damage which
causes the majority of postoperative adverse effects. CPB is needed for the repair with its known side effects on the brain, more hospital, and intensive care stay with increased risk for neurological insults. Hypothermia is used to protect the brain in case of failure of oxygen delivery whatever the cause. Furthermore, hypothermic bypass helps complete cold myocardial protection by maintaining a low metabolic state. However, the goals of using normothermic CPB are the increase of safety against possible side effects on CPB. The variable effects on tissue perfusion are presented as low cardiac output syndrome needing for inotropic drugs, decreased pulmonary function needing respiratory support, metabolic abnormalities with acidosis, coagulation defects, and neurologic side effects as seizures, and neurological abnormalities. CPB temperature and its effect on the function of vital organs are the subjects of researches carried out on adult patients, and the results cannot necessarily be applied to pediatric patients; however, some studies recommended the use of normothermia in pediatric cardiac surgery, other studies favored hypothermia.

This study was designed to compare normothermic technique and mild hypothermic technique during CPB as regards its effect on tissue perfusion, serum lactate level, duration of patient intubation, and postoperative hospital stay in pediatric cardiac patients undergoing repair of AV septal defect.

**Patients and Methods**

After approval of the Institutional Review Board of Mansoura Faculty of Medicine, Mansoura University, this prospective, randomized, comparative study was conducted in Mansoura University Children Hospital in the period between October 2017, and February 2019. Informed written consent from all patients’ guardians was taken. Forty patients aged 1–36 months of either gender, with physical status III–IV, according to the American Society of Anesthesiologists who were scheduled for elective corrective surgery of AV septal defect were enrolled in this study.

**Exclusion criteria**

Pulmonary artery pressure more than 50 mmHg, severe heart failure, renal, pulmonary, liver, endocrine disease, re-do surgery.

**Sample size**

G power analysis program (Universtitat Dusseldorf, Germany) was used to estimate the difference in serum lactate levels between the normothermic and hypothermic groups with an effective size of 0.8 and power of 80% and an alpha error of 0.05. It produced a sample size of 40 patients 20 patients in each group.

Patients were randomly allocated into two equal groups (20 patients in each) according to temperature:

- **Group I** (normothermic group): body temperature more than 35°C–37°C
- **Group II** (hypothermic group): body temperature between (32°C and 35°C).

**Preoperative**

All patients were subjected to preoperative clinical examination. Laboratory investigations include complete blood count, arterial blood gas (ABG), coagulation profile, liver, and renal function tests. On arrival to the preoperative area, all patients were premedicated with intramuscular injection of ketamine 5 mg.kg⁻¹ and atropine 0.02 mg.kg⁻¹ 30 min before the operation.

**Intraoperative**

Before surgery, standard monitoring (ECG, NIBP, and SpO2) was connected to the patients. Oxygen 2 L.min⁻¹ was introduced through face mask. Inhalational induction with sevoflurane, then insertion of peripheral cannula (24 G) then intravenous fentanyl 5 µg.kg⁻¹, and rocuronium 0.6 µg.kg⁻¹ with propofol 1 µg.kg⁻¹ when needed to deepen anesthesia. After insertion and securing of endotracheal tube, ventilation was maintained by positive pressure ventilation at a rate of 20–25 breathes/min with 30% O₂ using Datex Ohmeda S/5 (manufacturer, location (Datex-Ohmeda Division, Instrumentarium Corp., Helsinki, Finland) and the end-tidal CO₂ was monitored by side-stream capnograph and maintained 30–35 mmHg. Anesthesia was maintained with total intravenous anesthesia composed of propofol infusion at a rate of 100–150 µg.kg⁻¹.min⁻¹ and fentanyl 0.05 µg.kg⁻¹.min⁻¹, to maintain blood pressure within 75%–85% of its basal value and with infusion requirements for rocuronium 10 µg.kg⁻¹.min⁻¹ to maintain muscle relaxation. A radial artery catheter (22 G) was inserted after doing modified Allen’s test to monitor the invasive arterial blood pressure and blood gas sampling during the entire procedure. A central venous catheter (CVP) was inserted under the complete aseptic condition for central os pressure monitoring and infusion of vasoactive medications, a urinary catheter was placed to monitor urine output, and the nasopharyngeal temperature was continuously monitored through a nasopharyngeal probe.

**Before cardiopulmonary bypass**

The surgeon approached the heart through a standard median sternotomy in all patients. Surgical manipulations might lead to tachycardia and hypertension which needed adjustment of anesthetic depth. During sternal splitting, the lungs were deflated to avoid lung injury. The ascending aorta is first cannulated, then cannulation of great veins for CPB. Tranexamic acid was used before anticoagulation to reduce the possible incidence of thrombotic complications. Heparin is used to produce anticoagulation 300–400 units.kg⁻¹ through CVP with aortic purse string sutures. Activated clotting time (ACT) was measured before heparin to get baseline value then 3–5 min after heparin. ACT should be >400–500 s and if <400 s, additional heparin 100 units.kg⁻¹ was given.

**Cardiopulmonary bypass period**

Initiation of the CPB was done after proper cannulation with acceptable ACT. Removal of clamps across the venous cannula was done then arterial cannula. The main CPB pump was started and the pump flow was gradually increased which should be >70% of COP to maintain tissue perfusion.
A membrane oxygenator and a roller, nonpulsatile pump flow with average rate around 1.6–2.4 L.min⁻¹. A α-stat carbon dioxide management strategy was employed. The pump flow was adjusted according to the temperature changes and the hemodilution. Mean blood pressure (MAP) was maintained around 40 mmHg. If MAP decreased <30 mmHg vasopressor (noradrenaline 0.5 mg incremented up to 50 mmHg. If MAP increased >80 mmHg depth of anesthesia was increased and vasodilators in severe cases (nitroprusside).

All patients received cold crystalloid cardioplegia (Custodiol; Köhler Chemie, Alsbach-Haenlien, Germany) 50 mL.kg⁻¹ as a single bolus dose in anterograde 6 manner in the aortic root. Serial ACT was measured immediately after the bypass and every 20–30 min; therefore, extra heparin is needed if it is <480 s. After receiving of cardioplegia, the body temperature of the patient either maintained in the normothermic range between (35°C and 37°C) or low-to-mild hypothermia between (32°C and 35°C) by a heat exchanger unit (Heater-cooler System) depending on the temperature of the water flowing through the exchanger (4°C–42°C) as heat transfer occurred by conduction.

Patients were randomly allocated into two groups using computer-generated randomization program:
- Group I (n = 20) (Normothermia): The body temperature was maintained between (35°C and 37°C) during CPB
- Group II (n = 20) (hypeothermia): mild systemic hypothermia (32°C–35°C) will be used during CPB.

**Termination of cardiopulmonary bypass**
- Head down positioning and lung inflation: To ensure evacuation of any air emboli
- Rewarming: Gradual rewarming (nearly it was completed in 1/3 CPB time) and complete rewarming (nasopharyngeal temperature should reach 37)
- Removal of aortic cross clamp:
- Regaining of the lung ventilation with 100% O₂:
- Monitoring:

Ventricular filling and contractility were estimated visually. Laboratory values should be within acceptable limits, and any abnormality was managed like acidosis (pH <7.2) or hyperkalemia (>5.5 mEq.L⁻¹). A stable heart rhythm (sinus) and adequate heart rate were a mandatory finding to wean from CPB. Pacing and inotropic agents were needed in cases of slow heart rate, internal cardioversion (DC shock with 5–10 Watt-seconds [joules]) was needed if supraventricular tachycardia occurred with prior 1–2 mg.kg⁻¹ lidocaine.

Weaning: Pump flow was gradually decreased as MAP increased. When MAP is around 80 mmHg the pump flow was stopped.

After weaning patient either with:
- Normal ventricular function (assessed by direct vision): patient was separated immediately from CPB
- Hypovolemic (assessed by low CVP, low MAP): patient was separated after volume replacement
- Pump failure (sluggish poor contracted distended heart, with normal or high CVP): Inotropic support was needed, epinephrine (50–200 ng.kg⁻¹.m⁻¹) ± Milrinone (0.5–0.7 µg.kg⁻¹.m⁻¹) which is inodilator decreasing the afterload and synergetic inotropic effect with epinephrine
- Hyperdynamic circulation: (good contracting heart with low CVP, low MAP): patient needed blood transfusion (increasing Ht) ± vasoconstrictor (norepinephrine 50–200 ng.kg⁻¹.m⁻¹).

**Postcardiopulmonary bypass period**
Reversal of anticoagulant drugs with protamine sulfate. Venous cannula removed, blood remained in reservoir was transfused through aortic cannula before it was removed. Blood, fresh frozen plasma, and platelet transfusion were usually needed according to post-CPB ACT and Ht, especially in cases of persistent bleeding and oozing. Rewarming was continued as heat redistribution might occur resulting in rebound hypothermia. Anesthesia was maintained by TIVA, and any hemodynamic abnormality was managed, for example, hypertension (anesthesia was deepened) ventricular arrhythmia (lidocaine).

**Postoperative**
Patients were maintained on mechanical ventilation, and extubation was only done when fulfilling criteria of extubation: awake and alert patient with stable hemodynamic parameters with shutoff inotropic support or vasopressors, acceptable blood gases, and acceptable respiratory mechanics.

**Collected data**
1. ABGs which included pH, HCO₃⁻
2. Serum lactate level which was measured by samples from the arterial catheter in the radial artery
3. Hemodynamic variables (ABP, heart rate) as arterial catheter in the radial artery was connected to a pressure transducer monitoring ABP moment to moment on the monitor, also ECG and pulse oximetry monitor HR continuously
4. ACT was measured by arterial blood samples from radial artery catheter and rolled well in ACT tube.
5. Liver function test (serum glutamic pyruvic transaminase [SGPT], serum glutamic oxaloacetic transaminase [SGOT]).

These data were recorded in the following time intervals:
- (1) Basal, (2) after 10 min from induction of the anesthesia, (3) 30 min from induction of the CPB (time of induced hypothermia), (4) 10 min after rewarming, (5) 1 h after weaning from the CPB, and (6) after 8 h in the cardiac care unit (CCU).

In the following time intervals: Basal, 10 min. After induction of the CPB, 30 min from induction of the CPB, 10 min after weaning from the CPB, 30 min after weaning from the CPB, 1 h after weaning from the CPB, and after 8 h in the CUC and After 24 h in CUC

6. Aortic cross clamping time (ACCT) and CPB time (CPBT) were recorded in minute
7. The use of inotropes was recorded whether the need to use a single inotropic drug (Adrenaline) or two inotropic drug (adrenaline and milrinone lactate). Furthermore, the duration of inotropic administration which defined
as time between weaning from CPB not from the start of inotropic administration and termination of inotropic administration.

The need to use a vasopressor in addition to the inotropes was recorded either used or not and if used we recorded the duration of vasopressor. The administration which defined as the time between the start of vasopressor administration and termination of vasopressor administration.

8. In CCU, intubation duration was recorded to each patient and it was defined as the duration between intensive care unit (ICU) admission and extubation. Furthermore, ICU stay and hospital stay will be also recorded.

9. The incidence of re-exploration of the patient due to postoperative bleeding was recorded for each patient.

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences program version 22 (IBM corporation, NY, USA). A descriptive statistical analysis was performed. Continuous data were presented as average ± standard deviation and compared by two-tailed Student’s t-test for unpaired data Categorical data were expressed as proportions and compared by Pearson’s Chi-square test. P < 0.05 was considered statistically significant.

Results

Patients in both groups showed no significant differences as regards patient demographic data (age, sex and body surface area) also data of CPB as aortic cross-clamp time (ACCT) and CPB time (CPBT) showed no statistically significant differences between the two studied groups [Table 1].

Mean arterial blood pressure showed no statistically significant differences between the studied groups in all time intervals [Table 2].

Furthermore, patients’ heart rate showed no statistically significant difference between the two groups in all time intervals [Table 3].

The PH value after 1 h from weaning from CPB showed statistically significant lower values in Group II when compared to Group I with P = 0.022; however, there was no statistically significant difference in the other time intervals [Table 4].

Bicarbonate levels were significantly lower in Group II when compared to Group I 10 min and 1 h after weaning from CPB and after 8 h. in CCU with P = 0.01, P = 0.02, respectively [Table 5].

Serum lactate level was statistically significantly higher in Group II when compared to Group I after 1 h of weaning from CPB and after 8 h. in CCU with P = 0.005, 0.04, respectively [Table 6].

ACT was statistically significantly higher in Group II when compared to Group I 60 min. after weaning from CPB P = 0.009 [Table 7].

SGOT, SGPT levels were statistically significantly higher in Group II when compared to Group I when measured after

| Table 1: Patients demographic data (age, gender, body surface area) and cardiopulmonary bypass data (aortic cross clamping time aortic cross-clamping time minutes in and cardio pulmonary bypass time cardiopulmonary bypass time in minutes) |
|-------------------------------------------------|-----------------|-----------------|-------------|
| Group I (n=20) | Group II (n=20) | P |
| Age (months) | 13.5±17.9 | 15.5±18.3 | 0.86 |
| Gender, n (%) | | | |
| Male | 13 (65) | 12 (60) | 1.000 |
| Female | 7 (35) | 8 (40) | |
| BSA (m²) | 0.55±0.12 | 0.63±0.35 | 0.32 |
| ACCT | 72.45±11.97 | 76.85±10.07 | 0.12 |
| CPBT | 96.40±14.36 | 103.25±13.92 | 0.16 |

Data are expressed as number, percentages, mean±SD. Group I=Normothermic CPB, Group II=Mild hypothermic CPB. BSA=Body Surface Area, ACCT=Aortic cross clamping time, CPBT=Cardiopulmonary bypass time, n=Number of patients. SD=Standard deviation, CPB=Cardiopulmonary bypass

| Table 2: Mean arterial blood pressure (mmHg) of the studied groups (n=20) |
|-------------------------------------------------|-----------------|-------------|
| Time interval | Group I | Group II | P |
| Basal | 62.85±7.55 | 64.9±6.71 | 0.37 |
| 10 min on pump | 41.5±2.92 | 40.05±3.73 | 0.18 |
| 30 min on pump | 44.1±2.67 | 43.15±1.84 | 0.19 |
| 10 min off pump | 52.6±5.51 | 50.9±5.37 | 0.5 |
| 30 min off pump | 62.8±6.02 | 59.8±5.6 | 0.11 |
| 60 min off pump | 64.3±3.46 | 64.00±3.29 | 0.21 |
| 8 h in ICU | 66±4.25 | 63.95±3.75 | 0.12 |
| 24 h in ICU | 66.85±4.22 | 65.1±4.26 | 0.2 |

Data are expressed as mean±SD. Group I=Normothermic CPB, Group II=Mild hypothermic CPB, n=Number of patients, SD=Standard deviation, ICU=Intensive care unit, CPB=Cardiopulmonary bypass

| Table 3: Heart rate (beat/min) of the studied groups (n=20) |
|-------------------------------------------------|-----------------|-------------|
| Time interval | Group I | Group II | P |
| Basal | 109.9±10.12 | 113.5±7.82 | 0.216 |
| 10 min on pump | 0 | 0 | 0 |
| 30 min on pump | 0 | 0 | 0 |
| 10 min off pump | 66±17 | 57±12 | 0.07 |
| 30 min of pump | 88.80±15.19 | 90±19.56 | 0.8 |
| 60 min of pump | 101.50±10.63 | 96.10±8.92 | 0.09 |
| 8 h in ICU | 105±11 | 99±14 | 0.12 |
| 24 h in ICU | 108±10.29 | 102.15±10.17 | 0.079 |

Data are expressed as mean±SD. Group I=normothermic CPB, Group II=Mild hypothermic CPB, n=Number of patients, SD=Standard deviation, ICU=Intensive care unit, CPB=Cardiopulmonary bypass

8 h. in the ICU P = 0.02 and 0.008 for SGPT and SGOT, respectively. Uuu/[Table 8].

Duration of inotropic administration was significant longer in Group II when compared to Group I (P = 0.002), but the duration of vasopressor administration showed no significant differences between the two groups [Table 9].
The intubation duration in hours was statistically significant longer in Group II in relation to Group I (P = 0.012). However, the duration of ICU stay and hospital stay in days showed no statistically significant difference between the two groups. The incidence of re-exploration of the patient due to postoperative bleeding showed no statistically significant differences between two studied groups [Table 10].

**Table 4: pH values of the studied groups (n=20)**

| Time interval | Group I | Group II | P  |
|---------------|---------|----------|----|
| Basal         | 7.24±0.12 | 7.21±0.06 | 0.27 |
| 10 min on pump| 7.34±0.076 | 7.34±0.02 | 0.913 |
| 30 min on pump| 7.35±0.04 | 7.36±0.01 | 0.86 |
| 10 min off pump| 7.35±0.04 | 7.35±0.02 | 0.73 |
| 30 min of pump| 7.31±0.09 | 7.29±0.1 | 0.604 |
| 60 min off pump| 7.33±0.023 | 7.28±0.10* | 0.022 |
| 8 h in ICU    | 7.35±0.04 | 7.34±0.05 | 0.245 |
| 24 h in ICU   | 7.36±0.02 | 7.35±0.03 | 0.089 |

Data are expressed as mean±SD. *Statistically significant difference when compared Group II to Group I. P<0.05 is statistically significance. pH=Potential of Hydrogen, Group I=Normothermic CPB, Group II=Mild hypothermic CPB, n=Number of patients, SD=Standard deviation, ICU=Intensive care unit, CPB=Cardiopulmonary bypass

**Table 5: Bicarbonate level (HCO₃⁻) (mmol/L) of the studied groups**

| Time interval | Group I (n=20) | Group II (n=20) | P  |
|---------------|---------------|----------------|----|
| Basal         | 19.76±2.62   | 18.63±1.95    | 0.13 |
| 10 min on pump| 19.91±2.19   | 19.25±1.31    | 0.25 |
| 30 min on pump| 20.06±1.81   | 19.37±1.44    | 0.19 |
| 10 min off pump| 20.47±2.23  | 18.80±1.92*   | 0.01 |
| 30 min off pump| 18.28±1.10  | 17.87±1.74    | 0.37 |
| 60 min off pump| 20.25±2.26  | 18.71±1.72*   | 0.02 |
| 8 h in ICU    | 21.06±2.16   | 19.85±1.63    | 0.06 |
| 24 h in ICU   | 20.30±1.64   | 19.54±1.11    | 0.095 |

Data are expressed as mean±SD. P<0.05 is statistically significance. *Statistically significant difference when compared Group II to Group I. n=Number of patients, Group I=Normothermic CPB, Group II=Mild hypothermic CPB, ICU=Intensive care unit, SD=Standard deviation, CPB=Cardiopulmonary bypass

**Table 6: Serum lactate level (mmol/L) of the studied groups**

| Time interval | Group I (n=20) | Group II (n=20) | P  |
|---------------|---------------|----------------|----|
| Basal         | 1.9±0.48      | 1.61±0.64      | 0.117 |
| 10 min on pump| 2.46±0.5     | 2.1±0.50       | 0.095 |
| 30 min on pump| 3.01±0.59    | 3.08±0.60      | 0.695 |
| 10 min off pump| 3.80±0.62   | 3.7±0.73       | 0.645 |
| 30 min of pump| 4.03±0.54    | 4.39±0.76      | 0.114 |
| 60 min off pump| 4.13±0.75   | 4.94±0.92*     | 0.005 |
| 8 h in ICU    | 3.88±0.62    | 4.31±0.70*     | 0.049 |
| 24 h in ICU   | 3.57±0.62    | 4.94±0.74      | 0.120 |

Data are expressed as mean±SD. P<0.05 is statistically significance. *Statistically significant difference when compared Group II to Group I. n=Number of patients, Group I=Normothermic CPB, Group II=Mild hypothermic CPB, n=Number of patients, CPB=Cardiopulmonary bypass, ICU=Intensive care unit

**Discussion**

This randomized study compared the normothermic and hypothermic CPB in cases of repair of AV septal defect. The results showed that mild hypothermic CPB leads to metabolic changes in form of metabolic acidosis and increase in serum lactate levels. The study reported increase in ACT levels in hypothermic patients after weaning from CPB. The use of inotropic support is needed to longer periods in hypothermic group of patients and also the need for mechanical ventilation is needed for longer periods than in normothermic patients. Prior to the end of CPB, the affected patient needed to be rewarmed when hypothermia was employed. The drop in temperature usually causes expanded oxygen utilization, cardiovascular beat unsettling influences, and expanded peripheral vascular resistance.\(^9\)

In this study protocol, we clearly defined the target nasopharyngeal temperature during CPB to be either above 35°C–37°C or 32°C–35°C. We found that the pH value after 1 h from weaning from CPB was statistically significant lower in hypothermic patients when compared to normothermic patients. In the same time, serum bicarbonate levels was statistically significant lower in hypothermic group when compared to normothermic group, and serum lactate level was statistically significant higher in hypothermic group when compared to normothermic group.

Under normal conditions, there is a balance between excess lactate production and removal. This balance is disturbed when a decrease in temperature exists since the speed of all enzymatic reactions is affected by temperature. Hence, during cooling, a metabolic acidosis is observed which is proportional to the degree of cooling. As cooling progresses, there is an accumulation of excess lactate.\(^9\)

In the current study, the PH and serum bicarbonate were lower in hypothermic than normothermic patients and serum lactate was higher in hypothermic group. These differences became significant after 1 h from weaning from CPB and that may be due to rebound hypothermia after rewarming and effect of hypothermia on metabolic balance appeared again. When any metabolic imbalance occurs while patient on CPB is corrected rapidly. The cause of lactate level increase might be due to decreased tissue perfusion and oxygen supplementation, decreased oxygen extraction, and decreased lactate clearance by liver.\(^10\)

Lactic acidosis is metabolic acidosis occurs as a result of the insufficient lactic acid clearance. Lactate resulting in a pH of ≤7.25 with plasma lactate ≥5 mmol.L⁻¹. Hyperlactatemia means increased plasma lactate >2 mmol.L⁻¹. It is caused by the tissue hypoperfusion and/or hypoxia. Lactate is an end result of anaerobic metabolism and is normally cleared from the body by hepatic clearance, renal system and skeletal muscle.\(^10\)
Furthermore, in the period of hypothermic CPB local metabolic needs might be exaggerated due to nonhomogeneous cooling and rewarming and due to hypoperfusion in the time of CPB. The inflammatory reactions, cytokines release and the release of endogenous stress by-products that occur in the time of hypothermic CPB will increase local metabolic requirements. Eggum et al. studied the impact of temperature on inflammatory reactions in the time of pediatric open heart surgeries; they found that serum lactate levels was increased in correlation to degree of hypothermia and also increased with time from cooling to rewarming up to 2 h postoperative, these results come in correlation with our study as rebound hypothermia may be the cause of increased serum lactate and acidosis after rewarming.\[^{[11]}\]

In contrast to our study Xiong et al., published meta-analysis of advantages and disadvantages of normothermia and hypothermia in the time of CPB in pediatric open heart surgery and they found that no differences between normothermia and mild hypothermia concerning serum lactate level this contrast in the results may be due to that meta-analysis studied all type of pediatric open heart surgeries unlike our study which specify cases of repair of AV septal defects.\[^{[12]}\]

Parallel to the results of this study, Sabzi and Faraji studied the impact of hypothermia on liver enzymes which was investigated in three following days, they found that reducing the temperature has significant impact on liver enzymes in the postoperative period. These results are in correlation with our study results, as we found that liver enzymes were significantly increased in hypothermic group after 8 h in ICU when compared to normothermic group.\[^{[13]}\] Furthermore, Laupacis and Fergusson found that liver sinusoidal endothelial cells are more liable to hypoxia or hypothermia than liver cells, and proved that hepatosplanchnic oxygen utilization was aggravated in periods of normothermia.\[^{[14]}\]

The study found that ACT value was significantly higher in hypothermic group than normothermic group after 1 h from weaning from the CPB, this is in agreement with the results of Machin and Devine who studied the effect of temperature during CPB on ACT measurement, they listed that hypothermia resulted in increase in ACT level while the patient was cooled and increased also after rewarming.\[^{[15]}\] This may be attributed to that the hypothermia induces reversible platelet membrane dysfunction, partially inhibits platelet aggregation, and reduces platelet count and function rate also disordered fibrinolytic cascade activity has been observed in patients undergoing hypothermic CPB, thus reducing the blood clotting process, anticoagulation substances also may be released during hypothermia, which specifically inhibits factor Xa.\[^{[16]}\]

The study concluded that hypothermic group of patients needed significantly longer durations of inotropic drug administration than normothermic group this is in parallel with, Ali Aydemir et al. who randomly classified 40 infants into two groups according to perfusion temperature (32°C and 24°C) before an arterial switch surgery, they reported more benefits in the group of the higher temperature of 32°C, as this group showed shorter durations of inotropic drug administration.\[^{[17]}\]

In contrast to the current study, Stocker et al. studied 54 neonates randomly assigned to perfusion temperatures of 34 or 24°C. They did not find any impacts of perfusion technique on outcomes, this may be due to the comparison of different grades of temperature from that of our study.\[^{[18]}\]

Multiple studies have proved a longer period of mechanical ventilation posthypothermic CPB in parallel to our results which demonstrated a significant increase in intubation period in hypothermic group of patients.\[^{[19]}\]\[^{[20]}\]

This study has a number of limitations, however tight inclusion criteria and good data extraction, the limitations of the study were that we studied the effect of hypothermia on global tissue perfusion but did not study the direct effect on cerebral or cardiac perfusion because of defective investigation tools like Transcranial Doppler so, the effect on tissue perfusion might

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**Table 7: Activated clotting time activated clotting time (s) of the studied groups**

| Time interval | Group I (n = 20) | Group II (n = 20) | P |
|---------------|-----------------|-----------------|---|
| Basal         | 101.50±6.07     | 102.4±5.8       | 0.63 |
| 10 min on pump| 405.30±56.6     | 380.9±46.4      | 0.14 |
| 30 min on pump| 465.15±43.24    | 443.15±37.41    | 0.08 |
| 10 min off pump| 111.35±8.27    | 111.05±0.06     | 0.89 |
| 30 min off pump| 107.15±6.14    | 110.10±3.64     | 0.07 |
| 60 min off pump| 105.60±3.64    | 109.5±5.12     * | 0.009 |
| 8 h in ICU    | 105.7±5.65      | 107.35±5.13     | 0.34 |
| 24 h in ICU   | 104.35±5.1      | 105.8±5.32      | 0.38 |

*Statistically significant difference when compared Group II to Group I.

Data are expressed as mean±SD. P<0.05 is statistically significance. Group I=Normothermic CPB, Group II=Mild hypothermic CPB, n=number of patients, ACT=Activated clotting time, CPB=Cardiopulmonary bypass, ICU=Intensive care unit, SD=Standard deviation

**Table 8: Liver enzymes of the studied groups**

| Time interval | SGOT (IU/L) | P | SGPT (IU/L) | P |
|---------------|-------------|---|-------------|---|
| Group I (n = 20) | Group II (n = 20) |       | Group I (n = 20) | Group II (n = 20) |       |
| Basal         | 64.7±38.03  | 51.05±29.83 | 0.214 | 27.70±8.27 | 29.85±9.69 | 0.455 |
| 1 h off pump  | 74.90±45.79 | 64.32±39.4 | 0.393 | 34.33±10.85 | 41.20±15.76 | 0.118 |
| 8 h in ICU    | 65.10±36.96 | 91.25±34.67* | 0.027 | 33.55±9.66 | 47.9±20.87* | 0.008 |

Data are expressed as mean±SD. P<0.05 is statistically significance. *Statistically significant difference when comparing Group II to Group I.

SGOT=Serum glutamic oxaloacetic transaminase, SGPT=Serum glutamic pyruvic transaminase, Group I=Normothermic CPB, Group II=Mild hypothermic CPB, n: Number of patients, CPB=Cardiopulmonary bypass, ICU=Intensive care unit, SD=Standard deviation
Table 9: Duration of inotropes and vaspressors administration (h)

| Durations | Group I (n=20) | Group II (n=20) | P |
|-----------|----------------|----------------|---|
| Intropic administration | 30.65±28.2 | 61.25±31.27* | 0.002 |
| Vasopressor administration | 3.80±11.80 | 11.70±16.94 | 0.095 |

Data are expressed as mean±SD. *Statistically significant difference when compared Group II to Group I. P≤0.05 is statistically significant. Group I=normothermic CPB, Group II=Mild hypothermic CPB, n=Number of patients, CPB=Cardiopulmonary bypass, SD=Standard deviation

Table 10: Cardiac care unit data, intubation duration (hours), duration of hospital stay (days), and occurrence of re-exploration

| Durations | Group I (n=20) | Group II (n=20) | P |
|-----------|----------------|----------------|---|
| Intubation duration | 17±19.36 | 44.05±41.54* | 0.012 |
| ICU stay | 3.55±1.14 | 4.15±1.26 | 0.125 |
| Hospital stay | 6.90±1.80 | 7.80±1.47 | 0.092 |
| Re-exploration | 1 (5) | 4 (20) | 0.342 |

Data are expressed as mean±SD. *Statistically significant difference when comparing Group II to Group I. Re-exploration data are presented as number of patients and percentage. P≤0.05 is statistically significant. Group I=Normothermic CPB, Group II=Mild hypothermic CPB, n=Number of patients, CPB=Cardiopulmonary bypass, SD=Standard deviation, ICU=Intensive care unit

With the combination of lesser degree of lactic acidosis, shorter duration of inotropic support, and lesser effect on coagulation system, shorter duration of intubation, and shorter ICU stay, to be a multifactorial not only due to temperature changes, another limitation that all of our patients were treated with tranexamic acid which could affect the inflammatory process of hypothermia, as it has previously been proven to increase postoperative inflammatory process.[21]

**Conclusion**

This study concluded that in elective pediatric cardiac surgeries for repair of AV septal defect, normothermic CPB is accompanied with a better global tissue perfusion than hypothermic CPB in the form of lesser degree of lactic acidosis, shorter duration of inotropic support, and lesser effect on coagulation system, shorter duration of intubation, and shorter ICU stay.

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**Conflicts of interest**

There are no conflicts of interest.

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