Atrial Septal Defect Surgery With Normothermic Cardiopulmonary Bypass and Normothermic Blood Cardioplegia in the Pediatric Age Group

Pediatrik Yaş Grubunda Normotermik Kardiyopulmoner By-Pass ve Normotermik Kan Kardiyoplejisi İle Atriyal Septal Defekt Cerrahisi

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ABSTRACT

Objective: The aim of this study is to present the outcomes of atrial septal defect (ASD) closure operations performed using normothermic cardiopulmonary bypass and normothermic blood cardioplegia in patients in the pediatric age group.

Material and Methods: Between 2014 and 2017, 62 pediatric patients (37 females, 25 males, mean age 7.6±4.6 years-body weight 27.09±18.4 kg) received normothermic cardiopulmonary bypass and normothermic blood cardioplegia during an ASD closure operation. A mini-skin incision and median 3/4 upper partial sternotomy were used. During cardiopulmonary bypass, nasopharyngeal temperature was maintained at 35-37°C and normothermic blood cardioplegia was administered at 10 ml/kg.

Results: The ASD was "low venosum" type in 8 patients and "secundum" type in 54 patients. The average Qp/Qs value was 2.57±1.2 and mean pulmonary artery pressure values were systolic 31.88±6.6 mmHg, diastolic 11.0±2.6 mmHg, general mean 18.54±3.8 mmHg. Primary closure was used in 51 patients and a fresh pericardial patch was used in 11 patients. Mean cardiopulmonary bypass time was 26.04±10.8 min and aortic clamp time was 15.38±8.2 min. Twenty-eight patients were extubated on the operation table and the mean extubation time of 34 patients who were extubated in the pediatric intensive care unit was 3.02±2.9 hours. The mean drainage volume of the patients was 58.95±44.3 ml, and none of the patients needed transfusion of blood products in the postoperative period. Mean duration of intensive care stay was found to be 1.3±0.4 days. The mean duration of hospital stay was 4.3±1 days.

Conclusion: The results suggest that normothermic cardiopulmonary bypass and normothermic blood cardioplegia may be used safely in ASD closure operations performed in the pediatric age group.

Key Words: Atrial Septal Defect, Blood Cardioplegia, Normothermia, Pediatric, Cardiac Surgery

ÖZ

Amaç: Bu çalışmanın amacı, pediatrik yaş grubundaki hastalarda, normotermik kardiyopulmoner bypass ve normotermik kan kardiyoplejisi kullanılarak yapılan atriyal septal defekt (ASD) kapatılması operasyonlarının sonuçlarını sunmaktır.

Gereç ve Yöntemler: 2014-2017 yılları arasında 62 pediatrik hastaya (37 kadın ve 25 erkek, ortalama yaş 7,6±4,6 yıl, ortalama vücut ağırlığı 27,09±18,4 kg) normotermik kardiyopulmoner bypass ve normotermik kan kardiyoplejisi kullanılarak ASD kapatılması operasyonu yapıldı. Hastalarda mini cilt insizyonu ve median 3/4 üst parsiyel sternotomi kullanıldı. Kardiyopulmoner bypass esnasında nazofarengeal ısı 35-37 °C arasında tutuldu ve normotermik kan kardiyoplejisi 10 ml/kg olarak uygulandı.

Bulgular: Saptanan ASD tipleri; 8 "low venosum" tip, 54 "sekundum" tip olup, ortalama Qp/Qs değerleri; 2,57±1,2, ortalama pulmoner arter basıncı değerleri; sistolik, 31,88±6,6 mmHg, diyastolik, 11,0±2,6 mmHg ve ortalama, 18,54±3,8 mmHg'dir. 51 hastada primer, 11 hastada taze perikard yama ile kapatma yöntemi kullanılmış olup, ortalama kardiyopulmoner bypass süresi 26,04±10,8 dk ve aortik klemp süresi 15,38±8,2 dk olarak saptanmıştır. Yirmisekiz hasta operasyon masasında ekstübe edilmiş olup, pediatrik yoğun bakım ünitesinde ekstübe edilen 34 hastanın ortalama ekstübasyon süresi 3,02±2,9 saattir. Hastaların ortalama drenaj miktarı 58,95±44,3 ml olarak tespit edilmiş olup, postoperatif dönemde kan ürünü verilme ihtiyacı olan hasta olmamıştır. Ortalama yoğun bakım kalış süreleri 1,3±0,4 gün olarak bulunmuştur. Ortalama hastanede kalış süresi 4,3±1 gün olarak saptanmıştır.

Sonuç: Elde edilen sonuçlar normotermik kardiyopulmoner bypass ve normotermik kan kardiyoplejisinin, pediatrik yaş grubundaki hastalarda uygulanan ASD kapatılması operasyonlarında güvenle kullanılabileceğini düşündürmektedir.

Anahtar Sözcükler: Atrial Septal Defekt, Kan Kardiyoplejisi, Normotermik, Pediatrik, Kalp Cerrahisi

INTRODUCTION

Atrial septal defect (ASD) is a common congenital heart disease and surgical and percutaneous methods are available whenever treatment is required. There are clinical and biochemical side effects of systemic hypothermia application aiming protection against the end organ damage that may occur during cardiopulmonary bypass (CPBP) in cases corrected by open heart surgery (1, 2). Normothermic CPBP applications are therefore gradually increasing. Blood cardioplegia, which can be hypothermic, tepid or normothermic, is the preferred method because it can carry oxygen to the tissues during cardiac arrest and can meet the metabolic needs of myocardial tissue. Decreasing the metabolic needs by reducing myocardial heat during cardiac arrest is an advantage of hypothermic cardioplegic solutions, but the negative effects of hypothermia on cell metabolism and coronary artery endothelium are also known (1). The metabolic activity decrease provided by hypothermia cannot be achieved with tepid or normothermic cardioplegia, and repetitive cardioplegia applications are used to alleviate this adverse event (1, 3-6). The use of normothermic CPBP and normothermic blood cardioplegia is the method of choice for ASD closure operations requiring short term CPBP and aortic clamping. The aim of this study was to investigate the clinical results of the use of normothermic CPBP and normothermic blood cardioplegia in ASD closure operations.

MATERIALS and METHODS

A total of 62 patients who had no additional cardiac or systemic pathology and were not eligible for percutaneous closure were included in the study. Their intervention decisions were made by the Pediatric Cardiology and Cardiovascular Surgery Council and the patients underwent correction with open heart surgery due to ASD between 2014 and 2017. Patients were sent home after preoperative examination had been completed at the Cardiovascular Surgery Clinic and they were accepted to the operating room in the morning of the operation day. After the operation, they were taken to the Pediatric Intensive Care Unit; after the intensive care requirement of the patients was over, they were taken to the Pediatric Cardiology Clinic for postoperative care.

In the patients, 3/4 upper median partial sternotomies were performed and CPBP was used by applying aortic and bicaval cannulation. All operations were performed by the same surgical team using normothermic CPBP and normothermic blood cardioplegia. During CPBP, the nasopharyngeal temperature was maintained between 35-37°C. The blood cardioplegia contained normotermic blood collected from the arterial outlet of the oxygenator and additional 30 mEq potassium per litre of blood and was prepared at 35-37°C; the dose used was 10 ml/kg. Antegrade normothermic blood cardioplegia was provided as a single dose after aortic clamp was placed, and an additional dose of 5 ml/kg was administered when the cardiac arrest duration exceeded 15 minutes. Topical heart-cooling methods were not used.

The results of the patients were included in the study by retrospectively obtaining them from the hospital information system, and the SPSS v23 (Statistical Package for the Social Sciences for Windows, version 23.0) program was used to evaluate the results.

Akdeniz University Clinical Research Ethic Commitee approval was taken for the study (Decision number and date: 316, 02.05.2018).

RESULTS

The mean age of the 62 patients who were included in the study was 7.6±4.6 years and mean body weight was 27.09 ± 18.4 kg. ASD types were “low venosum” type in 8 patients and “secundum” type in 54 patients. The average Qp / Qs value was 2.57±1.2; mean pulmonary artery pressure values were systolic, 31.88 ± 6.6 mmHg, diastolic 11.0±2.6 mmHg and general mean 18.54±3.8 mmHg respectively. All patients had a Basic Aristotle score of 3 due to being diagnosed with ASD without additional pathology, but the mean level of Aristotle complexity was 1.5 as they were operated with a 3/4 partial upper mini sternotomy and mini skin incision.

Fifty-one patients who underwent surgery were found to have a primary closure and 11 patients a fresh pericardial patch closure. Mean CPBP and aortic clamp times were 26.04±10.8 minutes and 15.38±8.2 minutes, respectively. Repeated normothermic blood cardioplegia (5 ml/kg) was given in 19 patients who had aortic clamping time over 15 minutes. Of these 19 patients whose aortic clamp time exceed 15 minutes, 8 patients underwent fresh pericard closure and 6 patients had 'low venosum type' ASD. After removal of the aortic clamp, spontaneous sinus rhythm resumed in 46 patients while 16 patients required defibrillation. During CPBP termination, positive inotropic support was required in 2 patients and the preferred inotropic agent was dobutamine (10 mcg/kg/min). In a patient with inotropic need, very extensive secundum ASD was present, the duration of aortic clamp was 20 minutes and the duration of CPBP was 35 minutes. Pulmonary artery systolic pressure was 40 mmHg after weaning from bypass; inotropic support was initiated and then terminated after 12 hours postoperatively. In the other patient, the duration of aortic clamping was 20 minutes and the duration of CPBP was 30 minutes. Inotropic support was terminated within 6 hours postoperatively.

Twenty-eight patients were extubated in the operating room, and only one of these patients had fresh pericardial patch closure while the others had primary closure of ASD. Mean extubation time of 34 patients who were extubated in the Pediatric Intensive Care Unit was 3.02±2.9 hours. Mean drainage volume of the patients was 58.95±44.3 ml and there was no patient who needed a blood product transfusion in the postoperative period. Mean intensive care stay duration was found to be 1.3±0.4 days Table I.

In the postoperative period, there was no need for early reoperation due to bleeding or other reasons. In the follow up period, only one patient had a pericardial effusion (10 mm) which regressed without need of any surgical and medical treatment. On postoperative follow-up echocardiography, all defects were found to be closed. Mean duration of hospital stay was 4.3±1 days. There was no morbidity and mortality in the early postoperative period. Mean follow-up period of the patients was 18.4±9.3 months (range 2 to 36 months). No rehospitalizations and additional mortality were observed during follow-up. Late pericardial effusion was detected in one patient and was controlled by medical treatment.

DISCUSSION

Studies have revealed many negative effects of hypothermic CPBP especially in the last 25 years and hypothermic CPBP has been replaced by normothermic CPBP in many clinics (3-7). More than 10.000 pediatric operations have been performed using normothermic CPBP throughout Europe (8). Some centers still use normothermic CPBP in operations with a short aortic clamp time and use moderate hypothermia in operations with a long aortic clamp time expectancy (6, 8). In cases that required short aortic clamp and CPBP, we decided to use normothermic CPBP and normothermic blood cardioplegia in our clinic in accordance with the congenital heart surgery program that was launched in 2014.

Table I: Results.

Age (year)	7.6±4.6
Body Weight (kg)	27.09±18.4
Qp/Qs	2.57±1.2
Systolic MPAP (mmHg)	31.88±6.6
Diastolic MPAP (mmHg)	11±2.6
MCPBP Time (minute)	26.04±10.8
MAC Time (minute)	15.38±8.2
MDV (ml)	58.95±44.3
MIC Stay Duration (Day)	1.3±0.4
MH Stay Duration (Day)	4.3±1

MPAP: Mean Pulmonary Artery Pressure, **MCPBP:** Mean Cardiopulmonary Bypass, **MAC:** Mean Aortic Clamp, **MDV:** Mean Drainage Volume, **MIC:** Mean Intensive Care, **MH:** Mean Hospitalization.

In CPBP, whole body hypothermia is used for organ protection, especially in the brain, kidneys, lungs and heart by reducing metabolic activity and reducing the oxygen requirement (1, 2). Decreased brain blood flow and autoregulation during hypothermia have been shown to cause changes in neural tissue oxygen and glucose uptake, cellular membrane stability, and the use and production of ATP (1). It was determined that there was no increase in the probability of a neurological disorder with normothermic CPBP in the brain tissue that was protected by hypothermia and autoregulation was preserved (1). No cerebrovascular event was detected in the early postoperative period or in the follow-up period in the patient group included in the study. The increase in plasma viscosity and decrease in erythrocyte elasticity during hypothermic CPBP and the increase in hemoglobin oxygen affinity with hypothermia decrease oxygen delivery at the tissue level, which leads to increased circulatory disturbance at the microcapillary level (1). Both the direct effect of hypothermia and the temporary deterioration that occurs in NO synthesis at the endothelium level and the increase in serum norepinephrine level lead to an increase in peripheral vascular resistance, which increases the afterload of the heart and results in further deterioration of peripheral vascular circulation (1). In the study group, the need for positive inotropic support in only 2 patients at low dose and short duration, and no need for inotropic support in 60 patients, can be attributed to protection from the increase in cardiac afterload that is known to be caused by hypothermia. There is also a known possibility of deterioration in renal function with the result of vasoconstriction, and no renal dysfunction has been observed in any of the operated patients (1, 2). In addition, surgical hypothermia was found to be associated with a higher rate of surgical wound infections but none of the patients had any surgical site infection (1). It is also known that hypothermic perfusion is associated with increased blood loss and increased blood product replacement. The mean amount of surgical drainage detected was 2 ml per kilogram in the patients, and there was no need for postoperative blood product replacement, similar to the literature (1). The mean duration between aortic clamp time and CPBP time of the patients who underwent surgery was 10 min. Normothermic CPBP does not require additional time for systemic warming and allows the total CPBP duration to be shortened. The most important clinical positive effects of normothermic CPBP are short CPBP duration, spontaneous sinus rhythm after aortic clamp removal, more stable hemodynamics in the postoperative period, early extubation, and short intensive care and hospital stay (1). Twenty-eight of the patients were extubated on the operation table and mean extubation time of the patients who were extubated in the intensive care unit was 3.02±2.9 hours. Moderate hypothermia (32°C) was used in ASD surgeries performed by Zeng-Shan et al. with a total thoracoscopic approach; the mean extubation time was 0.7±1.1 hours, intensive care time was 10±5.1 hours, and mean hospital stay was 4.5 days. Compared with this study in which the thoracoscopic procedure and the ASD surgery in the beating heart were associated with a short hospital stay, the study group found that the duration of hospital stay of 4.3 days correlates with the literature reporting that normothermic CPBP is associated with a short hospital stay, while the short extubation time and short intensive care period of 1.3 days in the study support the literature (9, 10).

Surgical techniques that can be performed without an aortic clamp for ASD surgery are found in the literature, but the lack of aortic clamping carries the risk of systemic air embolism. Systemic air embolism has been reported in multiple articles that published the results of ASD surgery without an aortic clamp, although the results were not statistically significant. Some surgical teams such as Thapmongkol et al. have abandoned ASD surgeries without aortic clamping because of the systemic air embolism (10). Because of the presence of a cerebrovascular event, aortic clamping in ASD surgery has been preferred in our clinic. Cerebrovascular events were not detected in early and late postoperative period in 62 patients. Another method used for ASD surgery in the beating heart is the surgical technique performed by maintaining the antegrade flow in the coronary arteries under the aortic clamp as in the study of Ma and his colleagues. Although no cardiac arrest was induced, the myocardial protection of antegrade 4-5 ml/kg/min perfusion was controlled by ECG change only and the use of the method was not deemed appropriate due to the lack of objective data on the extent of preservation of the myocardium.

Induction of diastolic arrest is a major factor in reducing the metabolic activity of the myocardium and hence the oxygen consumption with electromechanical arrest accounting for 90% of the reduction in oxygen consumption and only 7% of hypothermia (6, 8). The main factor that creates myocardial injury is myocardial ischemia that occurs during the placement of the aortic clamp and the subsequent inflammatory response after reperfusion (6, 8). Cardioplegia solutions in use participate in the formation of cardiac damage by damaging excitatory contraction proteins and temporarily limiting NO bioactivity, and ischemia and reperfusion injury can also trigger apoptosis in cardiomyocytes (1, 11). Guru et al. found that the use of blood cardioplegia in the metaanalysis of 34 studies showed a statistically significant decrease in CK-MB and low cardiac output syndrome (11). Hypothermia is known to increase the oxygen affinity of hemoglobin and it is known that the delivery of sufficient oxygen to the myocardium during the aortic clamp decreases with low hematocrit, which is applied to decrease the blood viscosity caused by hypothermia (4, 6, 11). In addition, hypothermia causes decreased ability of microcapillary circulation due to metabolic acidosis, increased plasma viscosity and reduced erythrocyte deformability. Cold cardioplegia leads to an increase in intracellular calcium, energy expenditure and coronary artery resistance when used in conjunction with topical heart cooling (12). Hypothermia disrupts the lipids, electrical and transport functions of the cell membrane (4, 12). The hypothermia also has effects on the cell ion balance and water homology by influencing the enzymatic activity of the sodium, potassium and calcium channels.

When cardiac arrest is achieved with blood cardioplegia, oxygen can be delivered to the tissue, and intercellular and intracellular fluid balance can be maintained as the plasma oncotic pressure does not change. In addition, with normothermic blood cardioplegia, sufficient oxygen can be supplied to the microcapillary area by the preservation of the oxygen affinity of hemoglobin and preservation of erythrocyte elasticity (11, 12). Moreover, hypothermic coronary vasoconstriction caused by thermal and the negative effect on NO metabolism is not observed in normothermic blood cardioplegia, and the intracellular ion balance and high-energy phosphate levels are maintained by the ion pumps and mitochondrial activity of the myocardium that receive sufficient oxygen and continue to function properly (1, 11, 12).

In addition to hypothermic cardioplegia, topical cardiac cooling methods are used for superficial myocardial cooling, and it is also known that topical cold applications lead to diaphragm paralysis. In this study, diaphragm paralysis was not detected. Normothermic blood cardioplegia may be aspirated into the CPBP unit, and when it is aspirated, the osmotic pressure or temperature of the blood in the CPBP cycle does not change. Normothermic blood cardioplegia has been shown to provide myocardial protection for 15 minutes and intermittent administration is used for 15-25 minutes in many clinics. The cleanliness of the surgical site during surgery also provides comfort in terms of surgery. For this reason, it has been decided to use normothermic blood cardioplegia as intermittant in 15-minute intervals in our clinic. The mean aortic clamp time of the operated patients is 15 minutes on mean and is within the proven duration of myocardial protection of single-dose normothermic blood cardioplegia. Also, there was no intracardiac blood pollution during the aortic clamp. A total of 46 (74%) of 62 patients had spontaneous sinus rhythm after removal of the aortic clamp, and only 2 short term low dose inotropic support was required in 2 patients. Postoperative low cardiac output, hemodynamic instability, atrial and ventricular arrhythmia were not observed. In accordance with the literature, it is thought that the administration of normothermic blood cardioplegia with 15-minute intervals is considered to protect the myocardium by leaving the surgical field clean. The lack of comparisons with hypothermic CPBP, hypothermic blood or crystalloid cardioplegia usage in the study group could be considered as the missing aspect of the study.

The observed results are consistent with the literature about the usage of normothermic CPBP in CPBP-guided surgeries of simple congenital heart diseases, with a decrease in total CPBP duration, low blood product and inotropic use, and a decrease in extubation duration, intensive care and hospital stay, and it is also important that no patients experienced a surgical site infection, which is one of the side effects of hypothermia. For ASD surgery, intermittent application of normothermic blood cardioplegia at intervals of 15 minutes under aortic clamp can both provide adequate surgical site cleaning and also protect the myocardium. The results suggest that normothermic CPBP and normothermic blood cardioplegia may be used safely in ASD surgery in the pediatric age group.

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