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The effect of cardiopulmonary bypass on hemogram parameters in patients operated for tetralogy of Fallot

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Abstract

Background: Tetralogy of Fallot (TOF) constitutes 10% of congenital heart diseases. Cardiopulmonary bypass (CPB) is a procedure where the heart pump function and the lungs' gas exchange function are temporarily suspended, and circulation is carried out by the heart-lung machine. Blood is exposed to abnormal physical and chemical trauma during cardiopulmonary bypass. In this study, we aimed to determine the duration of cardiopulmonary bypass on hemogram parameters in patients undergoing corrective surgery for tetralogy of Fallot.

Material and Method: Age, sex, operative time, cardiopulmonary and cross-clamp time, length of stay in hospital and intensive care unit, mortality rate, and blood parameters of patients operated for tetralogy of Fallot were retrospectively evaluated. A total of 28 patients were included in the study.

Result: There was a significant difference between the preoperative and postoperative neutrophil lymphocyte levels ($p<0.001$, $p<0.001$, respectively). There was a significant difference between the Neutrophil/Lymphocyte ratios and Platelet/Lymphocyte ratios measured at different times at the preoperative and postoperative periods ($p=0.001$, $p=0.029$). The analysis of the distribution of the N/L ratio at the preoperative and postoperative periods showed that the N/L first increased and then decreased. The P/L ratio was measured at 54.1 (34.1-67.3) during the preoperative period; the highest P/L ratio was measured at 67 (46.5-11.3) at the 48th hour of the postoperative period.

Conclusion: The results of this study demonstrated statistically significant differences between WBC, hemoglobin, hematocrit, neutrophil, lymphocyte, N/L and P/L ratio, urea, creatinine, CRP, lactate values measured in the preoperative period and postoperative 24, 48 and 72 hours

Keywords: Cardiopulmonary bypass, Tetralogy of Fallot, Neutrophil/Lymphocyte ratio, Platelet/Lymphocyte ratio.

INTRODUCTION

Tetralogy of Fallot (TOF) constitutes 10% of congenital heart diseases. It is the most common cyanotic heart disease [1]. Eighty-five percent of patients undergoing total correction surgery reach adulthood. Operative mortality has dropped to as low as 3-5% thanks to advances in the field of cardiac surgery [2].

Cardiopulmonary bypass (CPB) is a procedure where the pump function of the heart and the gas exchange function of the lungs are temporarily suspended, and circulation is carried out by a device called the heart-lung machine. Since one of the most important causes underlying the complications of CPB is the changes in tissue oxygenation, it is evident that monitoring and controlling tissue oxygenation during CPB is of paramount importance. Blood is exposed to abnormal physical and chemical trauma during cardiopulmonary bypass. Altered platelet number and function is the most prominent hematological abnormality during CPB [3].

Hypoxia is the main cause of hematological disorders in patients with TOF. The objective of medical treatment is to relieve hypoxia and prevent hypoxic spells. In order to prevent the occurrence of hypoxic spells, patients should be protected against polycythemia and dehydration, and iron deficiency, when present, should be treated. Another problem in these patients is the hyperviscosity syndrome. Phlebotomy should be performed in symptomatic patients with a hematocrit level of 65% or higher. A great majority of patients with TOF undergo corrective surgery in the first year of life. The main factor determining the operative approach is the site and degree of pulmonary artery stenosis. Corrective surgery performed at an early stage protects many tissues, including the heart, lungs, brain, and kidneys, from the detrimental effects of hypoxia. Among cyanotic congenital heart diseases, TOF represents a condition that is amenable to complete correction. Therefore, complications related to hypoxia improve after corrective surgeries [4,5].

In this study, we aimed to determine the duration of cardiopulmonary bypass during heart surgery on hemogram parameters in patients undergoing corrective surgery for tetralogy of Fallot.

MATERIAL AND METHOD

Age, sex, operative time, cardiopulmonary and cross-clamp time, length of stay in hospital and intensive care unit, mortality rate, and blood parameters of patients operated for tetralogy of Fallot at Diyarbakır Gazi Yaşargil Training and Research Hospital between 01 January 2021 and 31 December 2022 were retrospectively evaluated.

Statistical Analysis

The study data were analyzed using SPSS 26 (Chicago, IL, USA) software package. The results were expressed as percentage for categorical variables. Continuous variables were presented as mean± standard deviation or median [Q1-Q3] as appropriate. Non-normally distributed variables were divided into four equal

parts, with the first quartile (25%) being designated as Q1, and the third one as Q3. The relation between categorical variables was tested using $\chi 2$ test. Normality of data distribution was tested with the Kolmogorov Smirnov and Shapiro Wilk tests. Accordingly, variables that did not have a normal distribution (N/L ratio, P/L ratio, CRP) were analyzed using the Friedmann test while those with normal distribution were analyzed using the ANOVA test for repeated measurements. Multiple comparisons between normally distributed variables were carried out with the Bonferroni test.

RESULTS

A total of 28 patients were included in the study. The mean age of the patients was 11.50 (8.2-29.7) months. Thirteen (46.4%) patients were female. The mean operative time was 235±62 minutes. Cardiopulmonary cross time was 173±44 minutes, and cardiopulmonary bypass time was 134±39 minutes. The mean length of hospital stay was 15 (10.2-21) days, while the mean length at the intensive care unit was 7(6-16) days. None of our patients who were operated on for TOF and followed up died (Table 1).

Table 1. Clinical Features of Operated Fallot Patients

Variables	Patients n: 28
Ages, month, median(Q1-Q3)	11.50(8.2-29.7)
Gender, female, n(%)	13(46.4)
Surgery time, min, mean±SD	235±62
Cardiopulmonary cross time, min, mean±SD	173±44
Cardiopulmonary bypass Time, min	134±39
Hospitalization day, median(Q1-Q3)	15(10.2-21)
Intensive care day, median(Q1-Q3)	7(6-15)
Mortality	0

Table 2. Distribution of Preoperative and Postoperative Blood Parameters

Variables	**Preoperative**	**postoperative First day**	**postoperative Second day**	**Postoperative Third day**	***p* value**

White Blood Cell	12.1±3.0	12.9±4.6	14.6±4.2	15.7±6.2	**0.004**
Neutrophil	4.7±2.7	9.3±3.9	10.9±3.7	11.4±4.9	**<0.001**
Lymphocyte	6.2±3.4	2.8±1.5	2.2±1.0	3.4±1.7	**<0.001**
N/L ratio median(Q1-Q3)	0.67(0.3-1.34)	3.0(2.0-5.9)	4.6(3.3-8.7)	3.2(2.2-5.7)	**0.001**
Hematocrit	43.8±9.3	38.5±4.7	38.2±4.0	37.0±4.9	**<0.001**
Hemoglobin	14.0±2.8	12.6±1.4	12.5±1.2	12.0±1.7	**0.001**
Platelet	302.8±127.7	128.8±51.8	154.4±52.9	125.6±42.4	**<0.001**
P/L ratio median(Q1-Q3)	54.1(34.1-67.3)	40(25-81.9)	67(47.5-11.3)	40.3(28-58.5)	**0.029**
Urea	25.1±10.0	24.4±7.4	31.7±14.2	33.1±17.1	**0.010**
Creatinine	0.47±0.12	0.54±0.12	0.50±0.11	0.47±0.10	**0.002**
C Reaktive Protein median(Q1-Q3)	2(2-2.3)	2(2-8.2)	44.7(39.7-82.1)	95.2(68.5-140-9)	**<0.001**
Blood gas					
pH	7.32±0.13	7.40±0.09	-	-	0.059
PCO2	39.2±10.8	33.9±8.3	-	-	0.107
HCO3	20.7±2.7	20.6±2.0	-	-	0.977
Lactate	1.9±1.6	3.3±2.8	-	-	**0.013**
Base defisite	4.6±2.4	3.1±2.6	-	-	0.023
N/L ratio: Neutrophil/Lymphocyte ratio, P/L ratio: Platelet/Lymphocyte ratio, RDW: Red					

Cell Distribution Width,

An analysis of Table 2 shows a significant difference between WBC levels measured at differentiation times before and after surgery (p=0.004). Accordingly, the mean WBC level at the preoperative period was 12.1±3.0 g/dl; the highest mean WBC was 15.7±6.2 g/dl at the 24th hour of the postoperative period. An analysis of the preoperative and postoperative distribution of WBC levels revealed that WBC levels increased over time. There was a significant difference between the preoperative and postoperative neutrophil levels (p<0.001). Accordingly, the mean neutrophil level at the preoperative period was 4.7±2.7 g/dl; the highest was measured at 11.4±4.9 g/dl at the 72nd hour of the postoperative period. When the distribution of the preoperative and postoperative neutrophil levels was analyzed, it was found that neutrophil levels increased over time.

There was a significant difference between the lymphocyte levels measured at different preoperative and postoperative periods (p<0.001). Accordingly, the mean lymphocyte level at the preoperative period was 6.2±3.4 g/dl; the lowest was 2.2±1.0 g/dl at the 48th hour of the postoperative period. When the distribution of the preoperative and postoperative distribution of the lymphocyte level was analyzed, it was found that the lymphocyte level increased over time.

There was a significant difference between the Neutrophil/Lymphocyte ratios and Platelet/Lymphocyte ratios measured at different preoperative and postoperative periods (p=0.001, p=0.029). Accordingly, the mean N/L ratio at the preoperative period was 0.67(0.3-1.34); the highest N/L ratio was measured at 4.6(3.3-8.7) at the 48th hour of the postoperative period. The analysis of the distribution of the N/L ratio at the preoperative and postoperative periods showed that the N/L first increased and then decreased.

The P/L ratio was measured at 54.1 (34.1-67.3) during the preoperative period; the highest P/L ratio was measured at 67 (46.5-11.3) at the 48th hour of the postoperative period. When the distribution of the P/L ratio at the preoperative and postoperative periods was analyzed, it was found that it decreased over time.

A significant difference was found between the hematocrit and hemoglobin levels measured at different times at the preoperative and postoperative periods (p<0.001, p=0.001). The analysis of the preoperative and postoperative distributions of the hemoglobin and hematocrit levels showed that both parameters decreased over time.

A significant difference existed between urea and creatinine levels measured at different preoperative and postoperative periods (p=0.010, p<0.001). The analysis of the distributions of the preoperative and postoperative urea levels revealed that it increased over time. On the other hand, creatinine levels first increased and then decreased.

A significant difference was found between the CRP levels measured at different preoperative and postoperative periods

($p<0.001$). Accordingly, the mean CRP level at the preoperative period was 2(2-2.3) mg/L; the highest mean CRP was 95.2 (68.5-140.9) mg/L measured at the 72nd hour of the postoperative period. The analysis of the CRP levels at preoperative and postoperative periods showed that the CRP level increased over time.

Blood gas analysis showed that the lactate level increased at the 24th hour. Other blood gas parameters had no significant difference (Table 2).

DISCUSSION

Thanks to advances in surgical techniques and postoperative management, it has been reported that children born with TOF have a 90% chance of surviving more than 30 years after surgical repair. Recent studies assessing both the short- and long-term outcomes after TOF surgery have shown that the mortality rate is significantly reduced by early surgical correction performed in the first year of life in many centers [6- 8]. We observed no mortality in our patients who were operated on and followed up for TOF.

In a study by Şaşmazel et al. on patients with TOF who were under 1 year of age, it was found that 48% of patients were female, 52% were male, and the mean age was ten months [9]. In another study conducted in Turkey, 65.9% of patients were male, and 32.9% were female; the mean age of patients was two years in TOF surgery performed with the transannular patch technique [10]. The mean age of our patients was 11.50(8.2-29.7) months. Fifteen (53.6%) patients were male.

In cardiac surgery, cardiopulmonary bypass time and cross clamp time are very important for inflammation and hemostasis balance. When these times are prolonged, severe inflammation is triggered and hemostatic disorders emerge [11]. In a study by Özdem, the mean cross clamp time was 98.57 minutes, the mean cardiopulmonary bypass time 145.90 minutes, and the mean hospitalization time 10.8 days [10]. Another study found a mean cross clamp time of 83.6 minutes, a mean cardiopulmonary bypass time of 100.7 minutes, and a mean length of stay at the intensive care unit of 6.5 days [9]. In our study, the mean operative time was 235±62 minutes. The cardiopulmonary cross time was 173±44 minutes, and the cardiopulmonary bypass time was 134±39 minutes. The mean total length of hospital stay was 15(10.2-21) days, while the mean ICU stay was 7(6-15) days.

Tetralogy of Fallot causes an increase in hemoglobin and hematocrit levels over time; it also causes a drop in platelet count and disorders of many bleeding tests. In the tetralogy of Fallot, erythrocytes lose their biconcave and flexible structure and membrane, which leads to impaired tissue perfusion [12]. It is clear that congenital heart diseases will mainly affect the hematological and hemostatic systems and many other systems of the human body. Cyanosis observed in tetralogy of Fallot is due to right ventricular outflow tract narrowing and worsens as the degree of narrowing increases. Cyanosis occurs secondary to hypoxia. Hypoxia, however, is the leading cause of hematological disorders in TOF patients. Thus, complications of hypoxia improve after complete corrective surgeries [13]. A review of the literature indicates that similar studies have reported that hemoglobin, hematocrit levels, and platelet count decrease after surgery [14,15]. Our

study also found a similar result. These data support the adaptive changes in hematological mechanisms secondary to hypoxia in patients with congenital heart disease.

Recently, in addition to preoperative white blood cell count, CRP, neutrophil count, and lymphocyte count, neutrophil/lymphocyte and platelet/lymphocyte ratios are also used as inflammatory markers in diseases [18]. In a study on 51 patients who underwent tetralogy of Fallot repair, the mean preoperative neutrophil count was 4.4 10e3/uL, and lymphocyte count and neutrophil/lymphocyte ratio were 3.93, 10e3/uL and 0.87, respectively; at the postoperative period, the mean neutrophil count was 7.8 10e3/uL, and the mean lymphocyte count and neutrophil/lymphocyte ratio were 3.35 10e3/uL and 2.33, respectively; the mean preoperative CRP level was 0.1 mg/dl, and the mean postoperative CRP level was 2.8 mg/dl [19]. Our study determined that WBC, CRP, and N/L levels increased, but lymphocyte and P/L levels decreased postoperatively.

Monitoring renal functions is essential for patient follow-up after TOF surgery [20]. In a study by 15. Patil et al., the mean postoperative urea and creatinine levels were reported as 19.39 mg/dl and 0.44 mg/dl, respectively [15]. Our study detected a statistically significant difference between preoperative urea and creatinine levels and those measured at different times after surgery ($p=0.010$, $p<0.001$). The analysis of the preoperative and postoperative urea levels indicated that they increased over time. On the other hand, creatinine levels first increased and then decreased.

Lactate is one of the most important biochemical markers of cerebral ischemia in cardiac surgery [21]. Lactate production from pyruvate increases in hypoxia. In a study on modest hypothermia in aortic surgery, post-induction lactate levels were 1.44 U/L, and post-pomp 15th-minute lactate levels were 4.72 U/L [22]. Blood gas analysis in our study also indicated that lactate levels similarly increased.

CONCLUSION

The results of this study demonstrated statistically significant differences between WBC, hemoglobin, hematocrit, neutrophil, lymphocyte, N/L and P/L ratio, urea, creatinine, CRP, lactate values measured in the preoperative period and postoperative 24, 48 and 72 hours. It was observed that hemoglobin, hematocrit, and platelet values decreased, WBC, CRP, neutrophil, urea, and lactate values gradually increased, and lymphocyte values decreased after total correction surgery. It was observed that neutrophil/lymphocyte count was at the highest level at the 48th hour after surgery. Creatinine level was highest at the 24th hour after surgery.

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Declaration of conflict of interest

The authors declare that there was no conflict of interest during the preparation and publishing of this manuscript.

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ETHİCAL APPROVAL

The study was approved by the Mardin Artuklu University Noninvasive Clinical Research Ethics Committee (Approval Date:08.06.2023, File/Approval No:2023/6-18).

Author contribution :

Esra Aktiz Bıçak and **Özhan Orhan:** Methodology, Writing- Original draft preparation, Resources; **Eşe Eda Turanlı:** Investigation, Data curation, Resources; **Mustafa Bıçak:** Writing- Original draft preparation**;** Resources **Yiğit Kılıç**: Writing- Reviewing and Editing, Resources.

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