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Comparison of IL-6 and IL-10 Trombosite and Soluble Levels in Thrombocytopenia Post-transfusion Thrombopheresis

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Abstract

Thrombocytopenia can occur due to tumors in the bone marrow, spleen, or both. Other factors such as myeloablative and non-myeloablative chemotherapy, drugs, dosage, and the number of therapeutic cycles and immune disorders. Platelet transfusion is indicated to prevent or treat bleeding due to thrombocytopenia. This study aims to analyze the relationship between thrombocyte posttransfusion platelet levels with IL-6 and IL-10 levels in thrombocytopenia patients. Respondents consisted of 14 patients who were measured platelet levels pre and posttransfusion with a hematological analyzer and IL-6 and IL-10 levels by the ELISA method. The difference in the number of pre and post-transfusion platelet platelets with mean pre-transfusion platelet levels is 12,937 cells / µl, and the average post-transfusion platelet level is 80,062 cells / µl. Posttransfusion thrombogenesis decreased IL-6 levels with a minimum level of 12.487 pg/ml and a maximum level of 161.325 pg/ml and posttransfusion IL-10 levels decreased with a minimum level of 7,431 pg/ml and a maximum cadr of 55.868 pg/ml. The results showed an increase in platelet levels accompanied by decreased levels of IL-6 and IL-10 showed a reduction in inflammatory reactions caused by platelet function in improving the immune response.

Keywords: thrombocytopenia; platelet transfusion; IL-6, IL-10.

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1. Introduction

Blood transfusion is the process of transferring blood or blood components from the donor to the recipient (patient). Blood from a donor can be processed into several components, namely; Red cell concentrate (Packed red cells), Thrombocyte concentrates, Fresh frozen plasma (FFP), Cryoprecipitate, Leucocyte depleted RBC concentrate, Granule oocyte concentrate, Single plasma donor, Fibrinogen concentrate, and Factor VIII concentrate [1]. Blood transfusion is a form of transplantation in which all blood cells or blood components of one or more individuals are transferred intravenously into another individual's circulation. Blood transfusion is done to replace blood loss due to bleeding or repair defects due to inadequate blood cell production, which may occur in various diseases. The main obstacle to the success of the blood transfusion process is the presence of an immune response to different cell surface molecules between individuals. The most essential alloantigen system in blood transfusion is the ABO system. ABO antigens are expressed on the surface of red blood cells. Individuals who lack specific blood group antigens produce natural IgM antibodies against the antigen. If the individual is given a blood cell that expresses the target antigen, preexisting antibodies bind to the transfused cell, activate complement, and cause a transfusion reaction, which can be life-threatening [2]. Platelet transfusion is indicated for the treatment or prevention of bleeding in patients with low platelet counts (thrombocytopenia) or platelet dysfunction. Adult therapeutic dose (ATD) for platelets is> 240 × 109 per transfusion. Platelets have ABO antigens on their surface and can cause a rejection reaction if they are transfused into ABO receptors that are not appropriate. Anti-A or anti-B antibodies in the platelet component plasma rarely cause receptor erythrocyte cell hemolysis, especially in infants and young children [3]. Platelet Activation After activation, platelets are able to secrete the immunomodulatory chemokine secretion contained in granules a, including platelet factor 4 (PF4), RANTES, and CXCL7. Post degranular, transmembrane proteins from granules appear on the surface of platelets, including molecular P-selectin adhesion which facilitates platelet interactions with endothelium, monocytes, neutrophils, and lymphocytes. By removing soluble and platelet-bound CD40L microparticles, platelets can also stimulate monocyte dendritic cell maturation, B cell proliferation, differentiation, and class switching. Gerdes and his colleagues (2011) found that platelets can increase the production of proinflammatory cytokines TNF-a and the regulation of IL-10 in purified CD4 + cells, which depend on the action of PF4 [4]. This study aims to analyze the relationship between thrombocyte posttransfusion platelet levels with IL-6 and IL-10 levels in thrombocytopenia patients.

2. Material and Methods

This study used blood samples from patients who had thrombocytopenia due to hematologic malignancy, namely acute leukemia and impaired blood formation (aplastic anemia) and required platelet transfusion. A total of 14 patients participated in this study. The study sample was venous blood collected before and after the administration of a thrombopoiesis transfusion. Every blood sample is routinely examined for platelet levels using a hematology analyzer and measuring IL-6 and IL-10 levels using the ELISA method, respectively, before and after the transfusion of 1 bag of thrombopheresis.

3. Results

The research sample consisted of 16 groups of children. Consists of 14 men and 2 women. All samples were diagnosed with hematological abnormalities. Based on the presence or absence of a post-transfusion thrombopheresis reaction, all respondents did not experience a transfusion reaction.

1. Comparison of pre and post platelet transfusion platelet levels

In general, there is an increase in platelet levels after administration of a platelet transfusion of 1 bag. The mean pre-transfusion platelet level was 12,937 cells / µl (2000 cells / µl - 43,000 cells / µl). The mean post-transfusion platelet level is 80,082 cells / µl (7,000 cells / µl - 246,000 cells / µl).

Table 1: Comparison of platelet levels of pre and post-transfusion Thrombosferesis

Platelet level	Min	max	Mean
Pretransfusion	2.000	43.000	12.937
Posttransfusion	7.000	246.000	80.062

Increased platelet levels after transfusion of thrombopheresis, on average more than 50%, even some samples showed an increase in platelet levels to more than 4 times the platelet levels before transfusion.

2. Comparison of levels of soluble interleukin 6 (IL 6) pre and post-transfusion thrombopheresis

Serum IL 6 levels of thrombocytopenia patients show a decrease in post-transfusion thrombopheresis. The minimum level of IL 6 pre-transfusion was 115.167 pg/ml and the maximum level was 185.818 pg/ml. While the minimum level of IL 6 post-transfusion is 12.487 pg/ml and the maximum level is 161.325 pg/ml. The highest post-transfusion IL 6 level difference was 169,593 pg/ml and the lowest was 4,711 pg/ml.

Table 2: Comparison of soluble levels IL 6 Pre and Post transfusion Thrombopheresis

Soluble IL 6 levels	Minimal	Maximum
Pre-transfusion	119,935 pg/ml	185,818 pg/ml
Post-transfusion	12,487 pg/ml	161,325 pg/ml
Difference	4,711 pg/ml	169,593 pg/ml

3. Comparison of levels of soluble interleukin 10 (IL 10) pre and post transfused thrombopheresis

The level of interleukin 10 (IL 10) in serum which is an anti-inflammatory cytokine is assessed before and after administration of transfused thrombopheresis. It was found that the highest IL level of 10 pre-transfusion

samples was 93.154 pg/ml and the lowest level was 56.913 pg/ml. The administration of a thrombopheresis transfusion caused a decrease in IL 10 levels, where the lowest IL 10 post-transfusion value was 7,431 pg/ml and the highest value was 55,868 pg/ml. Changes in IL 10 levels pre and post-transfusion vary from the lowest value of 1.045 pg/ml and the highest value of 75.966 pg/ml.

Table 3: Comparison of soluble IL 10 levels of Pre and Post-transfusion Thrombopheresis

Soluble IL 10 levels	Minimal	Maximum
Pretransfusion	56,913 pg/ml	93,154 pg/ml
Posttransfusion	7,431 pg/ml	55,868 pg/ml
Difference	1,045 pg/ml	75,966 pg/ml

4. Discussion

Blood transfusion is an action in the management of patients which is only given on the right indication. Blood and blood products play an important role in health care. Availability, safety, and ease of access to blood and blood products must be guaranteed. The security of blood transfusion services must be carried out starting from the process of taking blood, processing blood to the distribution of blood, both for complete blood and blood components and apheresis [5]. The American Association of Blood Banks (AABB) recommends prophylactic platelet transfusion to reduce the risk of spontaneous bleeding in adult patients hospitalized with thrombocytopenia with platelet counts of 10 × 109 cells/liter or less to reduce the risk of spontaneous bleeding. Transfusion can be given with 1 unit of thrombopheresis or platelets from complete blood (6-10 units). Larger doses are not always effective and lower doses or half of 1 apheresis unit provide the same effectiveness. One bag of thrombopheresis usually contains 3-4 x 1011 platelet cells [6].

A. Effect of platelet transfusion on increasing platelet levels

In this study, all samples received 1 unit thrombopheresis transfusion (1 bag). After administration of 1 bag of thrombopheresis an increase in the number of platelets of patients varies. The highest increase in platelet count was pretransfusion of 7,000 cells / µl and posttransfusion of 1 bag of thrombopheresis 246,000 cells / µl. The difference in increase in posttransfusion platelet count can be influenced by various factors, namely age, sex, BMI, diagnosis of the disease, or the length of the course of the disease and other treatments given to patients. Several criteria for evaluating the effectiveness of platelet transfusion have been tested such as posttransfusion platelet count, bleeding events, CCI (corrected count increment), transfused platelet dose, ABO compatibility, platelet processing and storage [7]. In this study the increase in the number of platelet post-transfusion thrombopheresis in general was more than 109, unless one patient had an increase in platelet counts of less than 109 ie only 108. The increase in platelet counts that were lacking in these patients might have been caused by the patient suffering from aplastic anemia. Transfusion administration in patients with aplastic anemia may have

to be done every day to maintain platelet counts of more than 20,000 / mm3. Transfusion administration should use cellular blood products that are irradiated and with very high leukocyte levels (leukocyte filters). Retrieval of thrombopheresis uses leukocyte filtration method so it is suitable for patients with aplastic anemia [8]. This is in line with the research of Pickard SA and his colleagues who found that transfusion in patients with severe aplastic anemia requires routine transfusion to improve quality of life and administration of drugs such as immunosuppression can reduce the frequency of monthly transfusion [9].

B. Effects of IL-6 and IL-10 on thrombocytopenia

Aplastic anemia is anemia that is marked by a marked decrease in the number of blood cells or the absence of blood-forming elements so that it manifests peripheral blood pancytopenia with a platelet count of less than 20,000 / ul. Gamma interferon (IFN-γ) plays an important role in the pathophysiology of aplastic anemia. In vitro studies show that T-cells from patients with aplastic anemia release IFN-γ and tumor necrosis factor (TNF). Long-term bone marrow culture has shown that IFN-TN and TNF are inhibitors of both early and slow hematopoietic progenitor cells. Both of these cytokines suppress hematopoiesis which has an effect on the mitotic cycle of the apoptotic mechanism. The mechanism of cell apoptosis involves IFN-γ and TNF, as well as Fas receptors in hematopoietic stem cells. Cytotoxic T cells also secrete interleukin-2 (IL-2), which causes a polyclonal expansion of T-cells. Activation of Fas receptors in hematopoietic stem cells by Fas ligands in lymphocytes leads to apoptosis of targeted hematopoietic progenitor cells. In addition, IFN-γ mediates its hematopoietic suppressant activity through IFN regulatory factor 1 (IRF-1), which inhibits the transcription of cellular genes and their entry into the cell cycle. IFN-γ also induces nitric oxide production, diffusion which causes additional toxic effects on hematopoietic progenitor cells [8]. Transfusion administration in patients with aplastic anemia may have to be done every day to maintain platelet counts of more than 20,000 / mm3. Transfusion administration should use cellular blood products that are irradiated and with very high leukocyte levels (leukocyte filters). Retrieval of thrombopheresis uses leukocyte filtration method so it is suitable for patients with aplastic anemia [8]. Because thrombopheresis in samples with hemolytic anemia is only 1 unit and 1 time giving, the increase in the number of posttransfusion thrombopheresis platelets is not high. This is in line with the study of Pickard SA and his colleagues who found that transfusions in patients with severe aplastic anemia require routine transfusions to improve quality of life and administration of drugs such as immunosuppression can reduce the frequency of monthly transfusion [9]. In this study, the administration of platelet transfusion caused a decrease in serum IL-6 levels, which showed that platelet transfusion could reduce the inflammatory response and activation of platelet cells by IL 6 which also played a role in the immune response. Increased posttransfusion platelet levels and decreased levels of IL 6 are said to be in accordance with the role of platelets in the immune response, so an increase in platelet levels will improve the inflammatory response characterized by a decrease in IL-6 levels. This is also indicated by the correlation of the highest increase in platelet levels and a reduction in the level of soluble IL-6. The results of this study are in line with research by Samuel Diomário da Rosa and his colleagues Which showed an increase in markers of oxidative damage and decreased levels of interleukin-6 after giving patients a transfusion in the ICU [10]. Interleukin 10 as an anti-inflammatory cytokine plays an important role in the regulation of immunity, this role is also found in platelets, especially for modulation of the adaptive immune response. Gerdes and his colleagues found that platelets increase the production of TNF-α proinflammatory cytokines and IL-10 regulation in pure CD4 + T

cell culture [11]. Gudbrandsdottir and his colleagues also found that platelets and dissolved factors released by platelets were able to increase the production of IL-10 Ag-elicited and inhibit the production of TNF-a which was suitable by monocytes [4]. The role of IL-10 in the incidence of transfusion reactions was also investigated by Kapur R and his colleagues (2017) who showed that TRALI was associated with lower IL-10 levels and that increased IL-10 levels gave resistance to TRALI in experimental animals [12]. In this study, patients with thrombocytopenia who were given transfusion of thrombopheresis obtained serum IL-10 levels lower than before transfusion of thrombopheresis. Decreased levels of IL-10 can be caused by emphasis on the inflammatory effect of platelets so that it indirectly decreases IL-10 levels as an anti-inflammatory cytokine [13, 14].

5. Conclusion

Giving thrombopheresis transfusion will increase platelet levels and reduce levels of IL-6 and IL-10 levels of thrombocytopenia patients.

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6. Competing Interest

The authors declare that they have no competing interests.

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