International Journal of Psychosocial Rehabilitation, Vol.24, Issue 09, 2020
ISSN: 1475-7192

The study of the relationship of indicators of immune status and serum ferritin in patients with thalassemia.

[1] U. U. Rakhmanova, [2] D.N. Suleymanova, [3] M.I. Shamsutdinova, [4] I.Yu. Masharipova, [5] N.H. Ishchanova

Abstract: *Data on increased susceptibility to infections with thalassemia have generated interest in studying the immune status of patients with beta-thalassemia. The state of cellular and humoral immunity and the amount of iron-containing ferritin protein were studied in 200 patients, girls and boys with various forms of thalassemia. The indicators of humoral immunity, immunoglobulins A, M, G, as well as some indicators of cellular immunity CD3+, CD4+, CD8+, CD16+ were determined. Determination of immunoglobulins A, M, G was carried out by enzyme-linked immunosorbent assay on an apparatus of Human GmbH (Germany). Indicators of humoral immunity show a decrease in immunoglobulin A, but immunoglobulins M and G are elevated. Normally, ferritin is -10-120 ng / ml, and according to the results of our study, the content of serum ferritin is -1513.1 ng / ml, this indicator is 12.6 times higher, which indicates a risk of developing hemosiderosis of internal organs.*

Keywords: *hemosiderosis, hemolysis, humoral immunity, immunoglobulin, cellular immunity, ferritin*

Introduction

β-thalassemia is a hereditary disease caused by mutations in the β-globin locus on the 11th chromosome, which cause a violation of the synthesis of β-chains of the hemoglobin molecule. Heterozygous inheritance from one of the parents of the abnormal gene leads to the development of a small form of β-thalassemia (thalassemia minor), in which there is a decrease in the synthesis of β-chains.
With this form of β-thalassemia, treatment is not required in most cases. When an abnormal gene is inherited from both parents - homozygous β-thalassemia (thalassemia major, Cooley anemia) - mutations in the coding zone lead to a decrease in the synthesis of β-chains (β + thalassemia) or to its complete stop (β0-thalassemia). The severity of anemia is directly dependent on the degree of accumulation of α-chains. The following forms of homozygous β-thalassemia are distinguished:
• severe, ending with the death of the patient in the first months of life;

• moderate, in which patients live up to 6-9 years;

• intermediate - patients live to adulthood.
Currently, there are more than 100 variants of hemoglobin gene mutations that can lead to beta-thalassemia. Until recently, lifelong blood transfusion therapy with its uncontrolled negative effect on the immune and coagulation systems of blood was the practically and only main way to correct anemia in thalassemia [3,4]. The danger was that regular blood transfusions lead to immunosuppression and iron accumulation in tissues and, as a result, to the addition of an intercurrent infection and immunization of the patient with antigens that are absent in him, with difficult to predict consequences.

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[1]Basic doctoral student of the Department of Hematology, Transfusiology and Laboratory Affairs of the Tashkent Medical Academy. Uzbekistan
[2] Doctor of medical sciences, professor, head of the anemia center of the Scientific Research Institute of Hematology and Blood Transfusion of the Republic of Uzbekistan
[3] Doctor of medical sciences, associate professor of the Department of Hematology, Transfusiology and Laboratory Affairs of the Tashkent Medical Academy. Uzbekistan
[4] Hematologist, assistant of the department of faculty and hospital therapy of the Urgench branch of Tashkent Medical Academy.
[5] Hematologist, assistant of the department of faculty and hospital therapy of the Urgench branch of Tashkent Medical Academy.Uzbekistan

Patients with thalassemia have an increased susceptibility to various infections [1,7]. According to the results of multicenter studies conducted in Italy, infections are the second most common cause of death in thalassemia after heart complications [1,5]. Therefore, it is necessary to determine the main plasma protein of serum ferritin, an indicator of hemosiderosis of internal organs.

Despite the fact that short duration of the achieved effect is characteristic for blood transfusions, this procedure in beta-thalassemia is still dangerous by the development of progressive post-transfusion hemosiderosis, with damage to vital organs and systems. Cardiac complications associated with hemosiderosis are the main cause of death in patients with β-thalassemia.

The listed complications explain the need to search for new safe therapies for β-thalassemia. In recent years, in the Republic of Uzbekistan, a number of targeted national programs have been implemented to strengthen reproductive health of the population, protection of motherhood and childhood, and a concept has been developed for the development of the healthcare system of the Republic of Uzbekistan for 2019-2025. At the same time, there are problems that require strengthening measures for early diagnosis and treatment of orphan and other hereditary - genetic diseases in children, which include thalassemia. Data on increased susceptibility to infections with thalassemia have generated interest in studying the immune status of patients with beta-thalassemia

Material and methods of research

At the Research Institute of Hematology and Blood Transfusion of the Republic of Uzbekistan, 200 patients examined at the hematologist with a diagnosis of thalassemia aged 1 year to 27 years were examined. The state of cellular and humoral immunity and the amount of iron-containing ferritin protein were studied in 200 patients, girls and boys with various forms of thalassemia.All patients were registered and received treatment of the underlying disease from a hematologist. We used a set of diagnostic methods for determining cellular and humoral immunity, which was determined by the enzyme-linked immunosorbent assay using special tests - systems that are highly sensitive. The indicators of humoral immunity, immunoglobulins A, M, G, as well as some indicators of cellular immunity CD3+, CD4+, CD8+, CD16+ were determined. Determination of immunoglobulins A, M, G was carried out by enzyme-linked immunosorbent assay on an apparatus of Human GmbH (Germany). Indicators of cellular immunity CD3+, CD4+, CD8+, CD16+ were determined by the enzyme-linked immunosorbent assay using special tests - systems that are highly sensitive.Data were presented as mean values and their standard deviation. The critical level of significance (p) when testing statistical hypotheses was taken equal to 0.05. Statistical processing of the obtained data was carried out using the software packages «MS-WORD» and «MS-EXCEL»

Research results

Of the study The most informative indicator of the body's iron supply is serum ferritin, the content of which rises much earlier than the iron content in serum. Normally, it is -10-120 ng / ml, and according to the results of our study, the content of serum ferritin is -1513.1 ng / ml, this indicator is 12.6 times higher, which indicates a risk of developing hemosiderosis of the internal organs.

In diagnostic studies, the highest importance is given to immunoglobulins A, M, G. During the studies, their qualitative and quantitative content is determined. The first determines the presence of infection in the blood, the second study determines the level of antibodies in the blood, some infections are not accompanied by an increase in the level of immunoglobulins. Immunoglobulins belong to the local, humoral immunity, which is triggered later than cellular immunity. The main role of immunoglobulin A is to ensure local mucosal immunity. They prevent the attachment of bacteria to the mucous membranes, ensure the transport of polymer immune complexes with immunoglobulin A, neutralize enterotoxin, activate phagocytosis and the complement system. It decreases in the absence of a spleen. Immunoglobulin A was (1.01 g / l) lowered, normal it was 1.25-2.52 g / l, and immunoglobulins M was (1.78 g / l) normal (0.65-1.65 g / l) and G (normal 7.5-15.46 g / l), and according to the results of our research it is increased (16.1 g / l).

This indicates a violation of the immune balance, i.e. an immunodeficiency state. In primary immunity, immunoglobulin M predominates for a longer time; in secondary, immunoglobulin G antibodies are rapidly synthesized and predominate. Immunoglobulin G-plays the largest role in antitoxic immunity, immunoglobulin M in antimicrobial immunity (phagocytosis of corpuscular antigens), and the role of immunoglobulins A in antiviral immunity (phagocytosis of corpuscular antigens).

Immunoglobulin M-increases against the background of acute infectious diseases, autoimmune pathologies and liver disease. The level of immunoglobulin A - deviates from the norm if violations have arisen in internal systems and organs. The results of the study of the immune status indicate that in patients with thalassemia, iron overload is considered the main factor of immune deficiency in thalassemia is a complication of both the disease itself and therapy.

Since iron and its protein compounds have immunoregulatory properties, and therefore, excess iron can adversely affect the immune balance. However, the high plasma ferritin content in patients with thalassemia can cause the formation of antiferritin antibodies, which in turn leads to the formation of circulating immune complexes.The weak ability of lymphocytes to isolate additional iron in ferritin may also help explain the causes of deviations in the immune system in patients with iron overload. The results of the study of the immune status indicate that in patients with thalassemia, the indicator of cellular immunity CD3+ was 39.5%, which is more than normal, normal rates are (23-36%). CD3+ is carried by all mature T-lymphocytes, and immature-in the cytoplasm, provides signal transmission from the T-cell antigen-specific receptor to the cytoplasm. The T-helper CD4+ marker, a receptor, a transmembrane glycoprotein, is involved in the recognition of antigens associated with class II HLA molecules. According to our data, the CD4+ marker was 27.7%, an indicator within the permissible norm, which is 23-49%. The CD8+ marker of the T-suppressor and cytotoxic lymphocytes, has some natural killers, the adhesion structure, is involved in the recognition of antigens with the participation of class I HLA molecules, consists of two chains It is also in the range of normal indicators and amounted to 28.6%, while normal it is 23-36%. CD16-EC, monocytes (weakly) low affinity Fc receptor for immunoglobulin G, an integral membrane protein, is available on natural killer cells and macrophages. According to our analysis results, it amounted to 24.8%, which is a valid indicator of the norm, which is 3-40%, and has no deviations. Iron overload is considered the main factor of immune deficiency in β-thalassemia, it is a complication of both the disease itself and therapy.It was found that iron and its protein compounds have immunoregulatory properties, and therefore excess iron can adversely affect the immune balance. The results of numerous studies indicate a negative effect of excess iron on immunological functions, which include the suppression of phagocytosis of the monocyte-macrophage system, changes in subpopulations of T-lymphocytes, increased secretion of immunoglobulins and suppression of the function of the complement system. It was shown both in vitro and in vivo that iron plays an important role in regulating the expression of surface markers of T lymphocytes, affecting the expansion of various subpopulations of T cells and possibly affecting the functions of immune cells. The weak ability of lymphocytes to isolate additional iron in ferritin may also help explain the causes of deviations in the immune system in patients with iron overload.

Conclusion

After evaluating these results as a whole, we came to two conclusions. First, immunological disorders are associated with immunological stimulation and excess iron, which occur as a result of multiple blood transfusions. Secondly, one cannot exclude the fact that in some patients, immune disorders are innate. Indicators of humoral immunity show a decrease in immunoglobulin A, but immunoglobulins M and G are elevated, which indicates impaired function and liver disease, in particular hemosiderosis as a result of hemolysis and regular blood transfusions. In turn, the results of determining isolated indicators of cellular immunity with the exception of the number of CD3+ cells, as a rule, do not have any special changes. Thus, violations of cellular and humoral immunity in thalassemia require the use of immunocorrection methods in the treatment of this disease.

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