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Modern Methods of Treatment of Immune Thrombocytopenia with Recombinant Human Thrombopoietin - Eltrombopag

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Abstract This research aims to determine the effectiveness of "Eltrombopag" in the treatment of immune thrombocytopenia. Materials and methods. Eltrombopag was administered to a group of 30 patients with immune thrombocytopenia, the results were studied every 7 days. When determining the hemogram on the "Sysmex" apparatus, 79% of patients showed an increase in platelets, which made it possible to bring patients out of critical condition. It has also been established that the duration of the disease may affect the results obtained.

Keywords Eltrombopag, Thrombocytopenia, Glucocorticosteroids, Romiplostim, Eltrombopag

1. Introduction

Immune thrombocytopenia - is an autoimmune disease caused by antiplatelet antibodies (AT antibodies) and / or circulating immune complexes (CIC), which usually affect the membrane glycoprotein structures of platelets and cause their destruction by cells of the reticuloendothelial system. In about half of the cases, antiplatelet antibodies are detected in the blood, for example, to glycoprotein IIb-IIIa and Ib -IX. Platelet destruction in ITP is caused by certain plasma factors, later called antiplatelet factors.

Treatment of ITP is usually initiated when platelets fall below $30x10^{9}$/l or when a clinically significant hemorrhagic syndrome occurs, regardless of platelet levels. Systemic glucocorticosteroids (GCS) are the standard first-line therapy. In a randomized trial in 2015, splenectomy, rituximab, fostamatinib, and specific thrombopoietin receptor agonists (romiplostim, eltrombopag) are used in cases of insufficient effectiveness of corticosteroids. New approaches to therapy, such as the use of Eltrombopag in adult patients with ITP, have shown their effectiveness. These data are especially important for those patients who need to delay or avoid splenectomy. Thrombopoiesis factors (AMG531, Eltrombopag) can become a breakthrough in the treatment of ITP, including refractory forms of the disease, due to their high efficiency, shown in the course of studies.

Currently, one of the effective therapeutic approaches in the treatment of chronic ITP is available for the treatment of adult patients, which is based on the use of thrombopoietin receptor agonists, one of them is eltrombopag (Revolade). It is a tablet preparation that acts like thrombopoietin, the main substance that regulates the production of platelets in the body [1,2]. Eltrombopag differs from thrombopoietin in terms of its effect on platelet aggregation. Unlike thrombopoietin, the effect of eltrombopag on healthy human platelets does not increase aggregation under the action of adenazine diphosphate (ADP) and does not stimulate the expression of P- selectin. Eltrombopag does not prevent platelet aggregation under the influence of ADP or collagen.

The purpose of this study was to determine the safety and efficacy of human recombinant thromboietin (rHTP) for the treatment of chronic ITP and the side effects on the body during the use of this drug.

Scientific novelty - based on the use of a new drug from among the thrombopoietin receptor agonists for the treatment of ITP, one of them is eltrombopag (Revolade).

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2. Materials and Methods

The study included patients aged 18 to 55 years with signs of hemorrhagic syndrome and no positive response to corticosteroids. Patients with the following conditions or diagnoses were excluded: virus-induced thrombocytopenia, functional disorders of the heart, kidneys, liver or lungs. All patients received Revolade at a dose of 50 mg per day. The treatment was carried out in both inpatient and outpatient settings. The course of treatment was prescribed for several months. We studied the results of the first two weeks, the period that determines the further tactics of managing patients.

Hemogram control was carried out on the day of treatment and every seven days. The hemogram was performed on the sysmex apparatus.

3. Results and Discussions

In RSSPMC, patients with immune thrombocytopenia, with platelet levels from single to 20.10 ^{9} /l were treated with recombinant thrombopoietin - Revolade 50 mg per day by taking a tablet inside. At the same time, for the relief of hemorrhagic syndrome, patients were prescribed hemostatic therapy. All patients underwent glucocorticoid therapy at different times. Prednisolone or methylprednisolone was most often used, the daily dose was 1-1.5 mg/kg of the patient's body weight. The course of treatment lasted 3-6 weeks. Some patients underwent pulse therapy with methylprednisolone. Almost 80% of patients responded to glucocorticoid therapy. But in the future, these patients experienced a rapid decrease in platelets and frequent relapses. In 20% of patients, an increase in the number of platelets was not observed. Two patients from this group underwent splenectomy a few months ago with a temporary improvement in the first months.

Table 1. Results of ITP treatment with Revolade

PLT - before treatment No.=30	excellent	good	Satisfactory	Not satisfactory	PLT- after treatment No.=30
M-21.9	PLT: 180 and up	PLT: 100-180	PLT: 40-100	PLT: 0-30	M-91.18
m-17.54					m-60.8
Quantity sick	6 patients	5 patients	13 patients	6 patients	
In percentages	20%	16%	43%	20%	

Given the frequent relapses, the ineffectiveness of glucocorticoid therapy, patients in this group were prescribed thrombopoietin receptor agonists, eltrombopag (Revolade). As a result of the use of Revolade 50 mg/day for 14 days, the following results were obtained (Table No. 1.). In 20% of patients, platelets rose above 180 thousand. and more, up to 251.0 thousand. The duration of the disease in this group is from three months to nine months. A good result was shown by 16% of patients. In these patients, platelets increased from 100.0 thousand to 180.0 thousand. The duration of the disease in this group was from 3 months to 18 months. One patient from this group underwent splenectomy 1 year ago. In 13 patients (43%), the platelet count reached from 40.0 to 100.0 thousand. Two patients from this group have been ill for 2.5 years. In 6 patients (20%), platelets in two increased to 30.0 thousand, in four platelets remained single. The results obtained showed that in 79% of patients who took Revolade, an increase in platelets was observed, which made it possible to bring patients out of critical condition. It was revealed that the duration of the disease is to some extent reflected as a result of treatment. In 6 patients with an unsatisfactory result, three were ill for three years or more. This is probably due to the depletion of the bone marrow. Since, with autoimmune aggression against platelets, there is an increased destruction of platelets, and the bone marrow works to compensate for the destroyed platelets. This will lead to depletion of the bone marrow. In this case, there will be no positive result from thrombopoiein-like drugs. In two patients who took the drug from the first days, a subjective disorder of a dyspeptic nature was observed. But the patients continued the course of treatment. We did not observe significant complications associated with taking the drug in this relatively short period of time.

Thus, the use of thrombopoietin receptor agonists, one of them being eltrombopag (Revolade), is an effective and fast-acting treatment for patients with ITP who are refractory to primary therapy.

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