The Approach to Managing the Patients with Idiopathic Thrombocytopenic Purpura: A Case-Control Study

Gaybulla Mustafakulov[1], Ulug'bek Ergashev[1], Aminjon Kuryazov[1], Davron Yakubov[1], Fotima Atakhadjaeva[1]

[1]Associate Professor, Tashkent Medical Academy, Tashkent Uzbekistan

Abstract

In this study, we present the results of treatment of 224 patients with idiopathic thrombocytopenic purpura (ITP). In this study, we present the comparative results of treatment with inhalation and traditional method by glucocorticoid hormones and splenectomy (SE). It was established that the usage of glucocorticosteroid hormones in the manner of cold doses inhalation was more effective in 87, (2%) of patients in comparison with traditional method of treatment – 75,(7%) and in this way the remission of disease approaches on 6,3 days earlier. For the treatment of these patients we used splenectomyand created new approach to the operation. This method, which was executed in the early post operational period, was more effective in 96, (9 %) of cases compared with traditional approach.

Keywords: *Thrombocytopenia, glucocorticoids, splenectomy, complications, prophylaxis, hormone inhalation.*

Introduction

Idiopathic thrombocytopenic purpura (ITP) is one of the common forms of hemorrhagic diathesis[1]. It is known that the basis of the pathogenesis of ITP is an autoimmune process from any cause which result in the synthesis of antiplatelet autoantibodies with an antimegakaryocytic orientation occuring in the human body[2].

ITP is not a rare disease in the structure of hematological pathology. So, for example, in Uzbekistan ITP is registered among children with a frequency of 1.5 - 2.0 cases per 100 000people[2,3].

The pathogenetic treatment of ITP is the use of glucocorticoid (GCS) hormones, however, taking per os hormones often gives gastrointestinal complications[4].

Given the pronounced side effects with prolonged use of corticosteroids, especially when taken per os[5], other method of corticosteroid administration are being sought to reduce or prevent complications of corticosteroids[6]. In this regard, the inhalation method of administering GCS hormones to patients with ITP is noteworthy[7], although in the available literature we could not find works devoted to the study of the use of GCS hormones in the form of inhalations in patients with ITP[8].

When performing splenectomy (SE), various method of mobilizing the spleen and processing the elements of its gates areused[9]. Bleeding during SE and after surgery is from 300 ml to 1 litre, postoperative pancreatitis occurs up to 6% and has no tendency to decrease[10]. Complications associated with the technique of surgery adversely affect the results of treatment[11].

Therefore, the improvement of both conservative and surgical treatment of ITP is undoubtedly of great scientific and practical interest for modern hematology and surgery[12].

Materials and Method

Patients Data: This case-control study retrospectively recruited 224 consecutive patients with a diagnosis of «ITP» in the surgical and pediatric wards of the clinic Scientific-research institute ofHematology and blood transfusion, Ministry of Health, Republic of Uzbekistan Among patients with ITP with a chronic form was 187, with an acute form was 37. Men were 88 and women were 136. Only 95 patients (42.4%) received the hormonal treatment: - including traditional

treatment - 48 patients (men –18 (37.5%), women –30 (62.5%), inhaled hormonal treatment of 47 patients, 22 (46.8%) of them were men, and 25 women (53.2%). SE was performed in 129 (57.6%) of patients with chronic ITP (of these, 40(31.1%) of men and 89 (68.9%) of women). The traditional method of SE was performed in 65 (50.4%) patients; we proposed this method in 64 (49, 6%).

To verify ITP, the following criteria were used below (except for complaints, medical history and objective examination):

1. Thrombocytopenia (platelets $<150x10^9$/L) in the absence of other abnormalities in the calculation of blood cells.
2. The absence of clinical and laboratory signs of the disease in blood relatives.
3. Normal - or increased number of megakaryocytes in the bone marrow.
4. The absence of clinical manifestations of other diseases or factors that can cause thrombocytopenia in patients.
5. The effect of corticosteroid therapy.

During SE, the amount of blood loss was determined by weighing the operating dressings - balls, before and after the operation, and blood loss after the operation from the drainage tube entering the dishes with a mark. In addition, patients with ITP underwent ultrasound for examination of internal organs, electrocardiography, and, according to indications, an endoscopic examination of the gastrointestinal tract.

Patients complained of hemorrhagic syndrome: petechiae and ecchymoses on the skin, nasal, uterine bleeding, bleeding from the gums and the gastrointestinal tract, which often appeared with platelet counts <20.5 - 30.0 x 109/L. The duration of the disease at the time of the first visit to the hospital ranged from 3 days to 5 months in acute ITP. In the anamnesis, the duration of the disease ranged from 6 months to 20 years with a chronic form of ITP and during this time patients received hormones in tablets from 2 to 10 times.

GCS was prescribed in the traditional treatment of 2.0-2.5 mg/kg in the acute form, 1.0-1.5 mg/kg in the chronic form of ITP per os and parenterally. Inhalation (solution of prednisolone and dexamethasone) was carried out on a nebulizer inhalation device “Boreal” (manufactured in Italy) at a dose of 1.0-2.0 mg/kg. In addition, patients received fibrinolysis inhibitors, vascular wall protectors, biological membrane stabilizers and topical treatment for nasal and gingival bleeding. Red blood cell mass was transfused for patients with severe anemia.

In 50 (52.6%) patients with ITP, gastrointestinal complications were revealed; gastroduodenitis in 21, gastric ulcer in 6, duodenal ulcer in 5, colitis in 2, gastrointestinal discomfort in 11, stomach pain in 5.

SE was performed in 129 patients with ITP. For 64 patients of the experimental group, splenectomy was performed by the method we proposed - during revision of the spleen, its mobility and connection with the circumference were assessed, its posterior surface was separated from the parenteral peritoneum by hemostasis in the direction of the pedicle and posterior surface of the stomach.

Then the spleen was easily dislocated into the wound, starting from the lower pole, it was freed from the ligaments and previously bandaged; two clamps were applied over the ligature, then dissected between the clamps and the stump was stitched. Next, a window of 0.5 x 0.5 cm in size was opened in the anterior sheet of the peritoneum from the upper pole of the spleen and the gastro-splenic ligament was ligated in the aforementioned manner.

If the width of the leg is large, more tissue is taken when the poles are highlighted. The front sheet of the peritoneum in the leg area does not open, this preserves the integrity of the tissue and hemostasis. The next stage of the operation is the preliminary ligation of the spleen leg with catgut over the capsule of the pancreas, under the control of the back surface, so as not to damage the tail of the pancreas. At the same time, all the elements of the spleen leg are assembled into a single stem with a straightened axis, which greatly improves subsequent clamping over the ligature.

This, in turn, is the prevention of bleeding. Subsequently, 2-3 clamps are applied over the ligature, and the spleen is removed. The stump is bandaged and stitched. Performing SE in this way prevents damage to the tail of the pancreas, creates reliable hemostasis, maintains the integrity of adjacent tissues

Results

Inhalation was carried out at a dose of 1.0 to 2.0 mg/kg per day. Of 18 patients with ICU, a clinical and hematological effect (CGE) was obtained in 13 (72.2%) patients, an average of 6.5 days, a clinical effect (CE) in 2 (11.1%) patients, on average for 5.5 days. Clinical and hematological effect (K and KGE) were obtained in 15 (83.3%) patients, on average for 6 bed days. In 3 (16.7%) patients, the effect was not obtained. In patients with CITPwho received inhaled therapy of corticosteroid hormones, the hemorrhagic syndrome began to disappear by days 3 and 4, the platelet count began to rise from days 5 and 6 of treatment. 19 patients (adults - 9, children - 10) with ICU, starting from the first or second day of admission, received hormones (prednisone and dexamethasone) in tablets and injections at a dose of 1.5 - 2.0 mg/kg with other HA drugs per day. The results of traditional hormone therapy in adults and children with ICU have shown that CGE was obtained in 13 (68.4%) patients, on average for 9.8 bed days. CE was obtained in 2 (10.5%) patients, an average of 16.5 hospital days. K and CGE was obtained in 15 (78.9%) patients, on average, for approximately 11 bed days. In 4 (21.1%) patients, the effect of hormone therapy was not obtained even after carrying out hormonal treatment for more than 3-4 weeks they were ineffective.

The results of inhalation therapy of sick children and adults with a chronic form of ITP (CITP),inhalation was performed at a dose of up to 2 mg/kg per day. Of the 29 patients who received inhalation therapy, CGE - in 13 (44.8%) patients, an average of 6 bed days, CE in 13 (44.8%) patients received an average of 7 days, 3 (10.4%) - without effect. Twenty-six (89.7%) patients received K and KGE, on average for 7 bed days. Starting from days 2 and 4, in all patients whose hemorrhagic syndrome has subsided.

29 patients with CITP(children - 9, adults - 20) received traditional treatment, including hormones at a dose of 1.0 - 1.5 mg/kg per day as a pathogenetic therapy of HK. From the traditional treatment of HK with hormones, sick children and adults with HITP received CGE of 6 (20.7%) patients, on average, for 9 bed days. Clinical remission (CR) in 15 (51.7%) patients, an average of 11 bed days. K and RAG were obtained in 21 (72.4%) patients, an average of 11 bed days, 8 (27.6%) patients were without effect with the preservation of hemorrhagic syndrome. Hemorrhagic syndromes began to disappear from 3-5 days in patients with remission.

Thus 47 patients withAITP and HITP received dosed cold inhalation of GCS hormones, while in patients with AITP K and RAG were obtained in 83.3% of cases on average in 6 days, on the contrary to traditional treatment 78.9% and 11 days. In patients with HITP K and RAG received in 89.7% of patients, in 6.5 days, on the contrary 72.4% and 10.7 days Of the 47 patients who received inhalation therapy 26 (55.3%) patients with average of 6 bed days admission received a CGE, in 15 (31.9%) with average of 7.0 bed days received a CR and in 41 (87.2%) patients with average of 6 bed days received K and CGE. In 6 (12.8%) patients, the effect was not obtained and they still had skin hemorrhagic diseases, in the form of ecchymoses[14].

ITP splenectomy results for years 2000-2002 in the generally accepted manner, 65 (50.4%) patients with ITP were operated among them: children - 37 (56.9%), adults - 28 (43.1%). Moreover, the total blood loss amounted to between 122.8 - 7980 ml per patient. During the operation, a total of 5590 ml of FFP and 9715 ml of erythrocyte mass were transfused. In total, 235.5-15305 ml were transferred per patient[15].

A complication such as damage to the pancreas during surgery was observed in 12 (18.5%) patients. Days 1 and 2 after surgery, 4 (6.2%) patients had an increase in temperature to 38^0C and 3 (4.6%) patients had complaints on the 2nd day after surgery for pain in the left hypochondrium and lumbar region. From the drainage tube, hemorrhagic discharge amounted to 100.0 ml or more on the 1st and 2nd day. In 50% of patients, the drainage tube was removed on the 1st day after surgery[16].

Relaparotomy for internal bleeding after SE was performed in 2 (3.1%) patients. The immediate postoperative results in patients with ITP with a chronic course of K and RAG amounted to 91.6% of patients. We proposed and performed SE on 64 patients with ITP with a chronic course. Moreover, the total blood loss is estimated to be between 76.8 - 4915 ml per patient. During the operation in 3 (4.7%) patients, the tail of the pancreas on the catgut ligature was damaged, but in the postoperative period, a pancreatitis clinic was not observed[17].

After surgery, hemorrhagic discharge from the drainage tube was up to 30 ml. The immediate postoperative results in patients with ITP with a chronic course of K and RAG were in 96.9% of patients. In 90%

of cases, drainage tubes were removed on the 1st day after surgery. There were no complications during and after the operation[18].

Discussion

Thus, the inhaled method of administering GCS hormones in dosed cold form on the Boreal nebulizer apparatus to patients with acute and chronic ITP is not inferior compared with traditional treatment with oral and parenteral administration of HA and has such positive aspects as;lack of complications from inhalation, good tolerance of the procedure, especially by children; prevention of neurosis, hysteria, pain associated with the manipulation of corticosteroids with hormones in children; lack of withdrawal syndrome; prevention of parenteral infection;economic efficiency by reducing the amount of hormones, blood components, and other drugs introduced by HA; and reducing the number of days. In a comparative aspect, with traditional treatment in acute ITP, 4.4, in chronic ITP 4.2 days earlier, remission was received.

The method we proposed allows us to preserve the integrity of adjacent tissues, prevents damage to the tail of the pancreas, and prevents bleeding during and after surgery. At the same time, the duration of the operation decreased by 10-15 minutes, bleeding during the operation decreased by 45.7 ml in one patient, and after the operation by 2-3 times. Postoperative pancreatitis, relaparotomy, and death were not observed. Erythrocyte mass, blood components and other drugs are saved.

Conclusion

In summary, the inhalation administration of GCS hormones in dosed cold form on the Boreal nebulizer apparatus to patients with acute and chronic forms of ITP is an alternative to the existing traditional method of conservative treatment. From inhalation administration of HA, in a comparative aspect, with traditional treatment for acute ITP, 4.4, in chronic ITP 4.2 days earlier, a remission was received. It prevents a number of complications of corticosteroids therapy and the transmission of parenteral blood-borne infection. Inhalation administration of corticosteroids hormones in patients with ITP disease is indicated, especially in childhood and in patients with diseases of the gastrointestinal tract. Contraindicated in patients with severe chronic condition against the background of the underlying disease and intolerance to inhaled corticosteroids.The use of an advanced method of splenectomy - this operation is less traumatic, has a milder course of the postoperative period, less blood loss and a minimal number of complications.

The use of an advanced method of splenectomy reduces blood flow during splenectomy by 41.4 ml, furthermore, it reduces the need for blood transfusions by 2-3 times. The proposed method reduces risk of damage to the pancreas by 4 times and the development of postoperative pancreatitis. It also reduces the duration of the operation by 10-15 minutes. A good result in the immediate postoperative period is achieved after splenectomy in the proposed.

Ethical Clearance: No ethical approval is needed.

Source of Funding: Self

Conflict of Interest: Nil

References

1. K.M A. Idiopathic thrombocytopenic purpura. Clinical Hematology. - SPb. 2004;: p. 349-370.
2. U.A A. Thrombocytopenic purpura in the Uzbek SSR: Abstract. dis. cand. honey. sciences. 1984;: p. 25.
3. Cines D.B. CA, SJW. Pathogenesis of immune thrombocytopenia.. PresseMed. 2014; 43(2).
4. E.K D. The current state of the issue of idiopathic thrombocytopenic purpura in children. Pediatrics. 1999; 2(56).
5. Feinstein F.E. KGI, BSM, KMT. Diseases of the blood system. Tashkent. 1980;: p. 583.
6. A.V G. Laparoscopic splenectomy in hematological patients: Abstract. dis. cand. honey.. Sciences.– M. 2004;: p. 25.
7. Bermas H. FME, HW, MJT. Hand-assisted laparoscopic splenectomy: indications and technique. JSLS. 2004; 8910: p. 69-71.
8. A K. Disorders associated with autoimmune thrombocytopenic purpura. Nippon Rinsho. 2003; 61: p. 604-608.
9. Klimansky V.A. SVS. Splenectomy with thoracic access in hematological patients. Khirugiya. 1993; 37(2): p. 42-47.
10. Mazurov A. V. KSG, VSA. Diagnosing Thrombocytopenia. Therapeutic Archive. 2018; 90(7): p. 4-13.
11. R M. The pathogenesis of chronic immune

thrombocytopenic purpura. The Scripps Research Institute, La Jolla, CA. robtmcmillan. 2007; 44.

12. L. MA. Clinical guidelines for the diagnosis and treatment of primary Thrombocytopenic purpura. 2015.
13. A. PK. Clinical case of idiopathic thrombocytopenic purpura disease in a teenage boy, Aliyeva A.A. Ismoilova O. M. 2018.
14. Romanova N.A. CNA, GAV, SNN. Diagnostic and prognostic aspects of ulcerous lesions of the gastrointestinal tract in chronic non-specific lung diseases. 6th national congress on respiratory diseases Sat scientific tr - Novosibirsk. 1996;: p. 32-33.
15. Shavlohov V. S. KSR, EIVao. Splenectomy with transthoracic access. Hematology and transfusiology. 2007; 52(5): p. 50-54.
16. system Tcotmosfdotb. Karagyulyan SR, Grzhimolovsky AV, Danishyan KI, Shavlohov VS and others. Hematology and transfusiology. 2007; 52(1): p. 3-10.
17. A.I. V. Guide to hematology. Moscow publishing house “Newdiamed”. 2005;: p. 31-35.
18. Yu.N Z. Nebulizer aerosoletherapy with the use of the Boreal inhaler: Guidelines for doctors. 2001;: p. 16.