

Complex Correction of Thrombohemorrhagic Disorders in Patients with Giant Uterine Myoma

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Abstract

Actuality: Typical clinical manifestations of growth and development of uterine myoma is often accompanied by an increasing menstrual blood loss, and sometimes uterine bleeding, which some researchers consider “dysfunctional”, and mainly dependent “neuroendocrine disorders”. Thus, intraoperative blood loss, can act as an aggravating factor during the perioperative period. Reduced blood loss is an urgent problem in patients with uterine cancer, which is planned surgery.

The aim of the study was to reduce perioperative blood loss in patients with giant uterine myoma.

Materials and Methods: Examined the results of surgical treatment of 114 patients with a diagnosis of giant uterine myoma. Research conducted at the Department of Gynecology and intensive therapy Odessa Regional Hospital in 2014 - 2017. The average age of patients with uterine myoma was $44,31 \pm 5,35$ years. Blood clotting system was investigated using low-frequency piezoelectric thromboelastography.

Patients were divided into two groups depending on the type of correction hemocoagulation disorders. 35 patients of 1 group received in complex correction epidural anesthesia at the level of L2-L3 7-12 ml of 0.5% bupivacaine and 10 mL of 0.5% bupivacaine in the first postoperative day fractionally. Anticoagulant therapy was bemiparin 2500 IU in the first post-operative day and for 7 days after. Antifibrinolytic therapy in these patients has not been evaluated. 39 patients of second group had complex correction which included epidural anesthesia at the level of L2-L3 7-12 ml of 0.5% bupivacaine and 10 mL of 0.5% bupivacaine in the first postoperative day fractionally. Anticoagulant therapy was bemiparin 2500 IU in the first post-operative day and for 7 days after. Patients in this group was assigned tranexamic acid for 30 minutes prior to surgery in a dose of 20 mg/kg, and followed infusion - 5 mg/kg per hour for the first postoperative day.

Statistical analysis was provided using the methods of parametric and non-parametric analysis (software Statistica 6.0 (StatSoft Inc., USA).

Results: In the preoperative period in patients with giant uterine myomas was found activation of fibrinolysis, increasing of platelet aggregation and hypercoagulability. Patients with uterine cancer had structural and chronometric activation of vascular-platelet hemostasis with an increased generation of thrombin and the activation of the fibrinolytic activity of the blood.

As a result of studies have provided evidence that the use of antifibrinolytic therapy as intravenous infusion of tranexamic acid for 30 minutes before the surgery in a dose of 20 mg/kg followed by infusion of 5 mg/kg per hour for the first postoperative day, helped to reduce perioperative blood loss by 29%. Hemoglobin level was higher by 10% ($p < 0.05$), blood loss was lower by 29% ($p < 0.05$), the length of stay in hospital was reduced by 24% ($p < 0.05$) in patients of the second group on the second postoperative day.

Keywords: Giant Uterine Myoma; Blood Loss; Fibrinolysis

Introduction

The uterine myoma is the most common benign tumor of the reproductive system, which is diagnosed in 20 - 30% of women of reproductive age. Giant uterine fibroids include tumors weighing over 11.4 kg [1,2]. The maximum mass described in the literature of the giant fibromyoma 40 kg [3,4]. Giant-sized fibroids can be represented as a single tumor, and a conglomerate with a multitude of tumorous nodes.

Typical clinical manifestations of the growth and development of uterine fibroids are often accompanied by an increase in menstrual blood loss and sometimes uterine bleeding, which some researchers consider to be “dysfunctional”, and are largely dependent on “neuroendocrine disorders” [5]. Other researchers attributed the origin of the pathological blood loss primarily with the growth and localization of the nodes of the tumor, as well as neuroendocrine and humoral shifts, causing severe metabolic disturbances [6,7]. Post bleeding that does not stop after repeated visco uterine mucous membranes, hormone therapy and other conservative treatments often cause prob-

lems for both the patient and the physician. Replacement abundant blood loss is often associated with submucosal or interstitial myoma and requires surgical treatment, despite the fact that the uterus may not be achieved the clinicians consider this an indication for urgent surgical treatment [8]. Chronic post-hemorrhagic anemia is indicative of surgical treatment in more than 70% of patients suffering from myoma [9].

The leading role in solving thrombotic process, and then DIC-syndrome in women with benign tumor diseases of the reproductive system, is confirmed by the logical finding in many cancer patients of a significant increase in blood plasma, both tissue thromboplastin and f. Villa According to some reports, when the myomas of the uterus, the coagulating activity of the blood plasma is elevated, fibrinolysis is inhibited, the functional activity of the platelets without any features. With tumor lesions of female genital organs of different localization, the system of hemostasis changes in the direction of activation [9].

Operative intervention enhances this combination of hemostasis disorders in patients with tumors of the body of the uterus, increasing the risk of developing thrombotic complications in the postoperative period [9].

Thus, intraoperative blood loss may act as a burden during the perioperative period. Reducing blood loss is a topical issue in patients with uterine myoma, which is scheduled for surgical treatment.

Materials and Methods

The results of surgical treatment of 114 gynecological patients diagnosed with giant uterine myoma have been investigated. The research was conducted on the basis of departments of gynecology and intensive care of the Odessa Regional Clinical Hospital in 2014 - 2017.

The average age of patients with myoma in the uterus was $44,31 \pm 5,35$ years. Among the concomitant pathologies, cardiovascular pathology prevailed, among which hypertension was determined - 40.5%, ischemic heart disease - 36.48%, and heart failure I - II A st. - 18.91%. Much less frequently was diagnosed gastritis - 6.75%, housing and communist housing - 4,05%, chronic bronchitis - 4,05%, chronic pancreatitis - 2,7%, ulcer illness - 1.35%. There were also obese patients - 4,05%, diabetes - 8,1%.

The system of blood coagulation was investigated using low-frequency piezoelectric thromboelastography (LPTEG) on the hardware-software complex ARP-01M "Mednord". The following parameters were studied: the initial indicator of the aggregate state of blood A0, the amplitude of the contact phase of coagulation (A1), the time constant of the contact phase of coagulation (R (t1)), the intensity of the coagulation drive (IDD), the constant of thrombin activity (CTA), the intensity of the contact phase of coagulation ICC), time of blood coagulation (PSC), intensity of polymerization of the clot (IOP), maximum clot density (MA), intensity of retraction and lysis of the clot (IRCL). Blood collection was performed prior to the operation, after the onset of surgical intervention, after the surgery, and for 1, 2, 3 days after the operation. The subjects were divided into two groups, depending on the type of correction of hemocoagulation disorders. Group 1 consisted of 55 patients, in whom the complex correction scheme included prolonged epidural anesthesia at the L2-L3 level of 7-12 ml 0.5% bupivacaine and 10 ml 0.5% bupivacaine during the first postoperative days of fine. Anticoagulant therapy was performed with enoxaparin 2500 IU from the first postoperative days and for 7 days. Antifibrinolytic therapy for these patients was not performed. The 2nd group consisted of 62 patients, in whom the complex correction scheme included prolonged epidural anesthesia at the L2-L3 level of 7-12 ml 0.5% bupivacaine and 10 ml 0.5% bupivacaine during the first postoperative days of fine. Anticoagulant therapy was performed with ENOXYPARIN 2500 IU from the first postoperative days and for 7 days. Patients in this group were prescribed tranexamic acid 30 minutes prior to surgery in a dose of 20 mg/kg followed by infusion of 5 mg/kg/hour during the first postoperative days.

For statistical analysis, the methods of parametric and nonparametric analysis were used (Statistica 6.0 (StatSoft Inc., USA). To judge the validity of differences, in the case of distribution close to normal, Student's t-criterion was used, otherwise, Mann Whitney's non-parametric criterion was used Differences were considered to be significant at $p < 0.05$. To compare the risk of developing complications, the definition of relative risk (RR) was used.

Results

In the preoperative period, the activation of the vascular-platelet component of hemostasis was detected in patients of both groups. Thus, the index of ICC increased in group 1 - by 46.18% and in group 2 - by 42.79%, the index A0 increased in group 1 by 39.63% and in group 2 by 40.54%, the indicator R (t1) is reduced in group 1 by 77,38% and in group 2 - by 75,11% in comparison with the norm. Also, at the preoperative stage, the indicators characterizing the coagulation link of hemostasis have been changed. In relation to the norm, the following indicators were elevated: CTA in group 1 on 87.64% and in group 2 - by 82.91%, IDU in group 1 by 72.45% and in group 2 - by 70.11%, IDUs in group 1 by 88,58% and in group 2 - by 72,52%, MA in group 1 by 44,04% and in group 2 - by 42,65%. These changes, as well as the reduction of PSC in group 1 by 49.28% and in group 2 - by 52.49% and the time of fibrin formation - the platelet structure of the clot - T in group 1 - by 49.97% and in group 2 - by 52.73% in relation to the norm testify to hypercoagulability. Also activation of fibrinolysis was revealed - an increase in the IRLC in group 1 by 63.16% and in group 2 by 67.91% in relation to the norm (Table 1).

Indicators	Normal	1 st group	2 nd group
A0, RI.	222,25 ± 15,33	310,11 ± 13,12*	312,21 ± 14,33*
R(t1), min	2,36 ± 0,34	1,09 ± 0,3*	1,01 ± 0,31*
ICC, RI.	84,3 ± 10,91	149,72 ± 9,86*	147,84 ± 8,92*
CTA, RI.	15,22 ± 3,46	28,56 ± 3,4*	27,84 ± 3,61*
PSC(t3), min	8,42 ± 1,68	4,15 ± 1,01*	4,45 ± 1,12*
ICD, RI.	21,15 ± 3,70	36,45 ± 3,26*	35,98 ± 3,42*
IOP, RI.	14,45 ± 1,4	27,25 ± 1,29*	24,33 ± 1,42*
MA, RI.	525,45 ± 70,50	756,91 ± 56,49*	749,58 ± 55,71*
T, min	48,50 ± 4,25	24,25 ± 3,9*	25,09 ± 4,1*
IRLC, %	16,45 ± 1,40	26,84 ± 2,14*	27,62 ± 2,73*

Table 1: Status of the system of hemostasis in patients with a giant uterine myoma before surgery ($M \pm m$).

*: $p < 0,05$ - in accordance with norms.

In the preoperative period, patients with a giant uterine myoma have been shown to activate fibrinolysis against the background of increased platelet aggregation and hypercoagulation. From the data obtained, it is clear that in patients with myoma of the uterus on the background of activation of the vascular-platelet linkage of the hemostasis, there is a slight structural (increase in the amplitude of the AMI LPTEG index) and the chronometric (reduction of the IEC, IR, CTA, R (t1) and PCHC NPTEG) hypercoagulation with elevated the generation of thrombin (an increase in the A0, ICC LPTEG) and the activation of fibrinolytic blood activity (IRCL).

The development of the epidural unit and the onset of the operation were activated by fibrinolysis: in group 1, IRLC increased from 26.84 ± 2.14% to 28.61 ± 1.98%, which was 7.14%. In group 2, the rate of IRLC before surgery was 27.67 ± 2.73%, and after the onset of the epidural block and the use of tranexamic acid - 12.21 ± 2.14%, - the decrease in fibrinolysis activity by 55.87% relative to the indicator IRLC to surgery ($p < 0,05$). This value is 42,67% less than IRLC after the onset of the epidural unit in group 1 ($p < 0,05$). This indicated a decrease in the activity of fibrinolysis in patients of the 2nd group against the background of the use of fibrinolytics, despite the activating effect of epidural anesthesia.

As a result of the application of the proposed correction scheme in patients with 2 groups with a violation of hemostasis in the form of hypercoagulation and activation of fibrinolysis, immediately after the onset of surgical intervention, there was a decrease in the IRLC index by 55.87% in relation to the IRLC index to surgical intervention and reduction of manifestations of structural hypercoagulation in the form of positive dynamics of indicators in comparison with preoperative data: an increase in CTA by 57.09%, a reduction in the CHP by 38.36%, an increase in IOP by 51.82%, an increase in IOP by 46.15%, an increase in IA by 41, 39%.

Comparative dynamics of NPTEG indices in patients 1 and 2, reflecting the coagulation link, was characterized by a decrease in the amplitude and lengthening of the time constants of hemocoagulation for the third day in comparison with the norm. Patients in the 1 group noted an increase in CTA at 18.26%, an ICD of 8.22%, a PSC (t3) of 7.24%, an IRCL of 27.11% compared to the norm.

In group 2, on the third day of treatment, there was a decrease in CTA by 9.8%, an IUD by 7.2%, an IU by 11.1%, an IRLs by 10.76%, and an increase in TPCs (t3) by 10.1% compared to the norm. The given data testify to the normalization of coagulation on the third day of treatment for patients with giant uterine myoma 1 and 2 groups. Despite this, there was a difference in the state of the fibrinolytic link: fibrinolysis was continued in group 1, the IRCL index was increased by 27.11% compared with the norm, while in the 2nd group there was a slight suppression of fibrinolysis, the IRCL index was reduced by 10.76% in comparison with the norm.

Clinical confirmation of the received laboratory data is the number of postoperative thrombohemorrhagic complications, hemoglobin levels and the amount of blood loss, as well as the terms of staying in patients in the intensive care unit. The course of postoperative period in patients with 2 groups in comparison with patients in group 1 has the most favorable character: hemoglobin level was significantly higher ($p < 0,05$), as immediately after surgery (group 1 - $85 \pm 3,42$ g/l, group 2 - $93 \pm 3,21$ g/l) and on the first one (group 1 - $81 \pm 3,57$ g/l, group 2 - $91 \pm 2,97$ g/l) and the second one (group 1 $82 \pm 2,87$ g/l, Group 2 - $91 \pm 3,02$ g/l) during the postoperative period.

Blood loss is significantly lower in patients with 2 groups compared to 1 group ($p < 0,05$). Immediately after the operation, the blood loss in patients with the 2nd group was less by 23.37% compared with 1 group, in the 1st day of the postoperative period, the loss of blood loss in patients with the 2nd group was 42.85% less than in group 1 and the second day of blood loss in group 2 was less by 41.66% than in group 1.

The need for transfusion of blood products in the group of patients received in the complex correction of tranexamic acid was 9.28% less ($p < 0.05$) than in group 1.

The terms of stay in the intensity of therapy also in group 2 were significantly less than in group 1.

Thrombosis of the deep veins of the lower extremities was detected in 3-5 days after surgery in 6 women (17.14%) in the 1st group. Four women (10.25%) of group 2 had deep vein thrombosis with a clinically asymptomatic course. The frequency of deep vein thrombosis of the lower extremities tended to decrease from 17.14% to 10.25%, but this was not statistically significant ($p < 0.05$). When comparing the risk of deep vein thrombosis in the lower extremities, the risk was lower (RR = 0.6) in the group of patients with myoma in the uterus who received therapy with anti-fibrinolytics at the perioperative stage.

Discussion

1. In the study of the state of hemostasis in patients with giant myoma of the uterus before the treatment, certain differences in comparison with the norm were established, namely: hyperaggregation in the form of an increase in the intensity of the contact phase of coagulation by 76% ($p < 0.05$), hypercoagulability in the form an increase in the intensity of the coagulation drive by 71% ($p < 0,05$) and activation of fibrinolysis, an increase in the intensity of retraction and lysis of the cluster by 65% ($p < 0,05$).
2. It was found that in patients with giant myoma of the uterus, on the third day after surgery, which did not receive antifibrinolytic therapy at the perioperative stage, the intensity of the contact phase of coagulation was increased by 24%, the intensity of the coagulation drive was reduced by 8% comparing with the norm, indicating the restoration of the coagulation level of the hemostasis system. The indicator of the intensity of retraction and lysis of the bunch, characterizing the state of non-recovering fibrinolysis, was increased by 27% compared with the norm ($p < 0,05$), indicating the preservation of activation of fibrinolysis.

3. It was found that in patients with giant myoma of the uterus who received anti-fibrinolytic therapy at the perioperative stage, on the third day after surgery, the intensity of the contact phase of coagulation was increased by 19%, the intensity of the coagulation drive was increased by 6% compared to the norm, indicating the restoration of the coagulation level of the hemostasis system. The rate of retraction and lysis intensity of the bunch, characterizing the state of fibrinolysis, was increased by 6% ($p < 0,05$) compared to 1 group, indicating the normalization of fibrinolysis.
4. The use of prolonged epidural anesthesia, tranexamic acid and bempiparin is most appropriate for reducing blood loss and restoring reserve capacity of the hemostasis system. In patients of the 2nd group, the hemoglobin level for the second postoperative day was higher by 10% ($p < 0,05$), blood loss was lower by 29% ($p < 0,05$), the need for blood transfusions was reduced by 9,28% ($p < 0,05$), the terms of stay in the intensity of therapy were less by 24% ($p < 0,05$).

Conclusion

The use of antifibrinolytic therapy as intravenous infusion of tranexamic acid for 30 minutes before the surgery in a dose of 20 mg/kg followed by infusion of 5 mg/kg per hour for the first postoperative day, it's totally safe during pre-operative and post-operative periods, and helped to reduce perioperative blood loss by 29%. Hemoglobin level was higher by 10% ($p < 0.05$), blood loss was lower by 29% ($p < 0.05$), the length of stay in hospital was reduced by 24% ($p < 0.05$) in patients of the second group on the second postoperative day.

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