

OUR EXPERIENCE IN THE CORRECTION OF VENOUS THROMBOEMBOLISM IN BARIATRIC SURGERY UNDER THE CONTROL OF THROMBOELASTOGRAPHY

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НАШ ДОСВІД КОРЕКЦІЇ ВЕНОЗНОЇ ТРОМБОЕМБОЛІЇ В БАРІАТРИЧНІЙ ХІРУРГІЇ ПІД КОНТРОЛЕМ ТРОМБОЕЛАСТОГРАФІЇ

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Вступ. У світі від ожиріння і його ускладнень щорічно помирає близько 2,8 мільйона людей. Ожиріння є незалежним фактором ризику венозної тромбоемболії (ВТЕ), оскільки воно втручається у внутрішні та зовнішні шляхи коагуляції, а також в антикоагулянтні механізми, що призводить до стану гіперкоагуляції. Зменшення надлишкової маси тіла в пацієнтів із морбідним ожирінням за допомогою бариатричної хірургії стає все більш популярним, оскільки барієва терапія є ефективним засобом лікування ожиріння та супутніх захворювань. Переваги бариатричної хірургії незаперечні, як і ризики. Незважаючи на численні дослідження згортання крові, випадки тромбоемболії у таких пацієнтів почастишали, особливо в разі оперативних втручань і в післяопераційний період, враховуючи те, що операція є тригерним фактором розвитку тромбоемболії.

Матеріали та методи. Досліджено систему гемостазу в 63 пацієнтів з ІМТ > 35 кг/м². Усі пацієнти були розділені на 3 групи: 1-ша група (n = 20) – хворі, які отримували комбіновану терапію, а саме еноксапарин натрію 0,1% 0,2 мл/кг 2 рази на добу кожні 12 годин і пентоксифілін 100 мг 2 рази на добу кожні 12 годин; 2-га група (n = 17) – хворі, які отримували еноксапарин натрію 0,1% по 0,2 мл/кг 2 рази на добу кожні 12 годин; до 3-ї групи (контрольної) увійшли 26 осіб з ожирінням, ІМТ > 35, які не підлягали бариатричній хірургії. Дослідження системи гемостазу проводили методом низькочастотної п'езоелектричної тромбоеластографії (ТЕГ) відразу після госпіталізації та на 1-шу, 3-тю, 5-ту добу після бариатрії. Перевіряли такі константи згортання крові: інтенсивність контактної коагуляції; інтенсивність коагуляційного приводу; максимальну щільність грона; фібринолітичну активність, що є показником ретракції та лізису тромбу.

Результати. У пацієнтів 1-ї групи (антикоагулянти + антиагреганти) ризик тромботичних ускладнень нижчий, оскільки ця терапія знизила значення на всіх етапах гемокоагуляції до референтних значень. У хворих 2-ї групи (антикоагулянти), незважаючи на нормалізацію коагуляційної одиниці, спостерігалось підвищення показників агрегації та фібринолізу відносно норми, що означає високий ризик тромботичних ускладнень.

Висновки. Інструментальний метод ТЕГ дав змогу адекватно оцінити систему гемокоагуляції в динаміці у хворих на патологічне ожиріння з ІМТ ≥ 35 кг/м². Ця категорія пацієнтів продемонструвала високий ризик ВТЕ; Доведено, що

для адекватної профілактики ВТЕ у пацієнтів з ожирінням, які перенесли бариатричну хірургію, комбінація антикоагулянтів і антиагрегантів є більш ефективною, ніж монотерапія антикоагулянтами.

Ключові слова: ожиріння, тромбоз, гемостаз, еноксипарин, пентоксифілін.

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Introduction. In the world of obesity and its complications annually dies about 2.8 million people. Obesity is an independent factor of the risk of venous thromboembolism (VTE), as it interferes with the internal and external pathways of coagulation, as well as in anticoagulant mechanisms, which leads to a hypercoagulation state. Reducing excess body weight in patients with morbid obesity by bariatric surgery is becoming increasingly popular, as bariatric surgery is an effective means of treating obesity and related concomitant diseases. Advantages of bariatric surgery are undeniable, as well as risks. Despite many blood coagulation studies, cases of thromboembolism in such patients are becoming more frequent, especially during surgical interventions and in the postoperative period, given that the operation is a trigger factor in the development of thromboembolism.

Materials and methods. A hemostasis system was studied in 63 patients with BMI > 35 kg/m². All patients were divided into 3 groups. 1 group (n=20) – patients who received combined therapy: Enoxaparin sodium 0.1% 0.2 ml/kg 2 times a day every 12 hours and Pentoxifylline 100 mg 2 times a day every 12 hours. The 2nd group (n = 17) – patients treated with: Enoxaparin sodium 0.1% 0.2 ml/kg 2 times daily for every 12 hours. Group 3 (control): 26 people with obesity, BMI > 35, not subject to bariatric surgery. The study of the hemostasis system was carried out using low-frequency piezoelectric thromboelastography (LPTEG) immediately after hospitalization and on 1,3,5 days after bariatry. The following blood coagulation constants were checked: Contact Coagulation Intensity; intensity of coagulation drive; maximum bunch density; Fibrinolytic activity is the index of retraction and lysis of the clot.

Results. In patients of group 1 (anticoagulants + antiplatelet agents) the risk of thrombotic complications is lower, since this therapy has reduced the value at all stages of hemocoagulation to the reference values; Patients in group 2 (anticoagulants), despite the normalization of the coagulation unit, had an increase in the values of aggregation and fibrinolysis, relative to the norm, which means the risk of thrombotic complications remains high.

Conclusions. The instrumental method of NPTEG allowed to adequately estimate the system of hemocoagulation in dynamics in patients with morbid obesity, with BMI ≥ 35 kg/m²; This category of patients has shown a high risk of VTE; It has been proved that for an adequate prevention of VTE in obese patients undergoing bariatric surgery, the combination of anticoagulants and antiplatelet agents is more effective than monotherapy with anticoagulants.

Key words: obesity, thrombosis, hemostasis, enoxiparin, pentoxifylline.

Introduction. Annually from obesity and complications of it die about 2.8 millions of the patients. In some countries, the percentage of people who are overweight or

obese exceeds 50%. In European countries from obesity suffers from 15 to 25% of the adult population [3]. In Ukraine, the problem of obesity is no less relevant than in the whole world. According to the Ministry of Health of Ukraine, 50.5% of men, 56% of women and 10% of children are overweight, and 16% of men and 26% of women are obese [3, 4].

Obesity can be considered as a prothrombotic condition. The proposed mechanism thrombi formation in obesity by L. Freeman, 2010, shows the disorders in the hemostatic system, and confirms it. These include: increased platelet activity (leptin and adiponectin, insulin resistance, blood stasis, inflammation), procoagulation state (increased production of thrombin, increased levels of tissue factor, fibrinogen, factor VII and factor VIII), and impaired fibrinolysis (excess production of an inhibitor-1 plasminogen activator and thrombin activated fibrinolysis inhibitor), as well as activation of endothelial cells due to tissue hypoxia [5; 6; 7]. Thus, the obesity interfering with the internal and external pathways of coagulation, as well as in anticoagulant mechanisms, which leads to an hypercoagulable state.

Bariatric surgery aimed at reducing excess body weight in patients with morbid obesity is becoming more popular, because it has been proved that this is an effective method of treating obesity and related diseases [15].

Indications for bariatric surgery: Patients from 18 to 60 years old: with BMI ≥ 40 kg/m²; with BMI = 35–40 kg/m² and with concomitant illness (metabolic disorders, cardiovascular diseases, respiratory diseases, severe joint diseases, obesity-induced severe psychological problems); patients over 60 years, where the main goal is to improve the quality of life. The benefit should be higher than the potential risks, so the indications for surgery should be individualized.

Contraindications to bariatric surgery: Lack of effort to lose weight after appropriate non-surgical medical treatment; psychic disorder, severe depression, disorders of personality; alcohol and/or drug addiction; life-threatening diseases (in the short term); patients that cannot take care of themselves; patients with very high or unacceptable risk for anesthesia.

The benefits of bariatric surgery are undeniable, as are the risks [15]. Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and its complication, pulmonary embolism (PE), is a common cause of morbidity and mortality after bariatric surgery. However, the postoperative VTE frequency varies widely: from 0.2% to 1.3% within 30 days [9; 10; 11] to 0.42% within 90 days [12]. Fatal postoperative episodes of pulmonary embolism were also not uncommon. The following postoperative risk factors for VTE in patients with morbid obesity who were subject to bariatric surgery are: type of surgery (high risk with open surgery compared to laparoscopic surgery and high risk of RYGP compared with adjustable gastric bandage) [9; 10; 11], age over 50 years, postoperative leakage of anastomosis, history of smoking, as well as previous VTE [9]. Despite many studies of the blood coagulation system, cases of thromboembolic complications in these patients are becoming more frequent, especially during surgical interventions and in the postoperative period, given that it is the intervention that is the trigger factor in the development of thromboembolism. Perioperative factors for the development of thromboembolic complications include the expansion of the volume of surgical intervention, the duration of the operation, postoperative immobilization, and the use of general anesthesia.

Pharmacological prophylaxis of VTE. The preemptive use of low molecular weight heparin (LMWH), Enoxyparin Sodium reduces the likelihood of VTE by 45–63% in all patients, including surgical patients, compared with those patients who have not been given prophylaxis [14]. While the pharmacological dosage of these agents has been well characterized for patients with normal body weight, the dosage in obese patients presents a number of problems due to changes in both the redistribution of drugs and their pharmacokinetics. Patients with morbid obesity have an increased percentage of fat relative to total body weight, but at the same time, rather low vascularization of adipose tissue, which on the one hand leads to an increase in the redistribution of lipophilic drugs, and on the other hand, can lead to an overdose of them. Many recommendations for the prevention of VTE in patients with a moderate and high risk of thrombotic complications in general surgery, including bariatric surgery, describe the use of UFH, LMWH and fondaparinux for the prevention of thrombosis. So, in relation to therapy with Enoxyparin Sodium 0.1%, dosing by body weight (Mt) is offered. In patients with MT < 50 kg, Enoxyparin is prescribed at 20 mg 1 p/d; Mt = 50–100 kg – 40 mg 1 p/d; Mt = 100–150 kg – 40 mg 2 p/d; Mt > 150 kg – 60 mg 2 p/d [6; 14; 15].

However, the category of obese patients (BMI \geq 30), including patients with morbid obesity (BMI \geq 40), poorly represented in the aspect of adequate and effective preventive and/or corrective therapy VTE. Despite the proven high risk of thromboembolic events for obese patients, including patients, are subject to bariatric interventions, treatment method of choice are still questionable. For example: Is the dose of anticoagulant adequately selected? Is monotherapy for LMWH sufficient? Is it possible to use a combination of drugs for the prevention of VTE, if so, which ones? Is prophylaxis possible with a combination of LMWH with antiplatelet agents? How effective is this combination? But to answer these questions, we must understand the functional condition of the platelet-vascular component, coagulation link of the system of hemostasis and fibrinolysis in these patients. For objectification, the thromboelastography method has been increasingly used recently. Low frequency piezoelectric thromboelastography (LPTEG) is the most effective method for studying hemostatic potential (GP), it is able to objectively display the vascular-platelet component, the coagulation link of the hemostasis system and fibrinolysis. The device provides the calculation of the relevant parameters displayed in the form of a graph (Fig. 1; Fig. 2) and a table with digital values: A0 – initial indicator of the state of aggregation of blood ; R (t1) is the time of the contact phase of coagulation; ICC – the intensity of contact coagulation; CTA – constant thrombin second activity; CT – coagulation time; ICD – coagulation drive intensity; IPC – the intensity of the polymerization of the clot; MA — maximum clot density ; T is the time of formation of the fibrin-platelet structure of the clot (time of total blood coagulation) ; And IRLC – the intensity of retraction and lysis of the clot [16; 17].

Study objectives. The aim of this study is to improve the effectiveness and determine the extent thrombotic danger using LPTEG, and minimization of the risk of the development of thromboembolic complications in patients, which is subject to whether the surgical treatment by bariatric surgery; optimization of the methods of the diagnostic of the system of hemostasis; targeted selection of the prophylaxis and correction methods of VTE by rational anticoagulant and antiplatelet therapy.

Materials and research methods. The hemostatic system was studied in 63 patients with a BMI > 35 kg/ m², who received treatment at the clinics of Odesa. All patients were divided into 3 groups. Patients who underwent surgical treatment by bari-

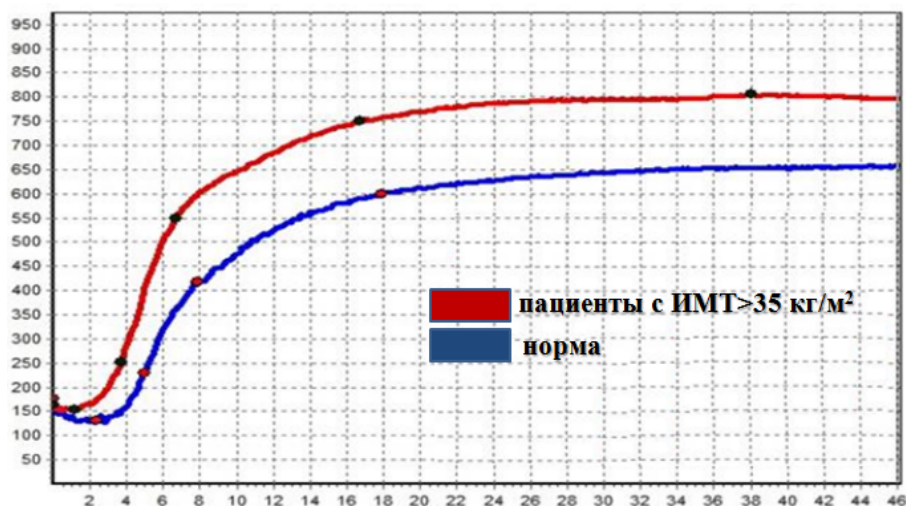


Fig. 1. Integral thromboelastogram according to the results of studies of the hemostatic system in a group of healthy volunteers and obese patients

atric surgery were divided into 2 groups, depending on the type of therapy. Group 1 consisted of 20 patients who underwent combination therapy: Enoxaparin sodium 0.1% 0.2 ml sc 2 times a day every 12 hours and Pentoxifylline 100 mg 2 times a day every 12 hours; Group 2 consisted of 17 patients who underwent treatment: Enoxaparin sodium 0.1% 0.2 ml sc 2 times a day every 12 hours. Control group: 26 people with obesity, with a BMI > 35, which are not subject to bariatric intervention, without regard to gender and associated pathologies.

The study of the hemostasis system was carried out using low-frequency piezoelectric thromboelastography (LPTEG), immediately after hospitalization and on 1,3,5 days after bariatrics. Blood was taken for examination under identical conditions according to the standard technique from the cubital vein.

The following blood coagulation constants have been tested:

- Intensity of Contact Coagulation (ICC).
- Intensity of Coagulation Drive (ICD).
- Maximum clot density (MCD).
- Fibrinolytic activity is an index of retraction and clot lysis (IRLC).

Results. In both groups of patients with morbid obesity, with a BMI of ≥ 35 kg/m², who were subject to bariatric surgery, before therapy: ICC was increased by 23.57%, ICD by more than 32.68%, MCD was increased by 74.52 %, IRLC – 91.18% above normal.

Patients of the 1st group on the 5th day after bariatric surgery, according to the LPTEG (Fig. 2): ICC reduced by 15.22%, compared with the norm; coagulation and fibrinolysis parameters have a reliable tendency to normal values and a decrease in fibrinolysis activity reaches normal values. Patients of the 2nd group, at the same time, the ICC has increased by 12.62%, ICD close to normal values, MCD increased by 18.63% compared with the norm, and the IRLC was increased by 31.17% higher norms.

Results of LPTEG research

		ICC	ICD	MCD	IRLC
Pre-treatment		↑* 23,57 %	↑ 32,68%	↑ 74,52%	↑ 91,18%
5 th day	1 st group	↓ 15,22%	N	↑ 2,31%	↑ 1,17%
	2 nd group	↑ 12,62%	N	↑ 18,63%	↑ 31,17%

Fig. 2. Results of the hemostatic system (LPTEG) in patients with morbid obesity before therapy and 5 days after the intervention.

Note: * ↑ ↓ – increase/decrease relative to normal (N)

In patients of the 1st group (anticoagulants + antiplatelet agents), the risk of thrombotic complications was lower, since this therapy reduced the values at all stages of hemocoagulation to reference values (Fig. 3); patients of the 2nd group (anticoagulants), despite the normalization of the coagulation link, had an increase in the values of aggregation and fibrinolysis, relative to the norm, which means that the risk of thrombotic complications remains high.

Conclusions. As a result of the studies, by using LPTEG a high degree of risk of VTE in patients with morbid obesity, with a BMI ≥ 35 kg/m², was proved.

The instrumental method “low-frequency piezoelectric thromboelastography” made it possible to adequately evaluate the dynamics of hemocoagulation in this category of patients.

In patients with morbid obesity, monotherapy with Enoxaparin sodium 0.1% 0.2 ml sc 2 times a day every 12 hours has low efficiency compared with the combined therapy of Enoxaparin sodium 0.1% 0.2 ml s/c 2 times per day every 12 hours and Pentoxifyl-

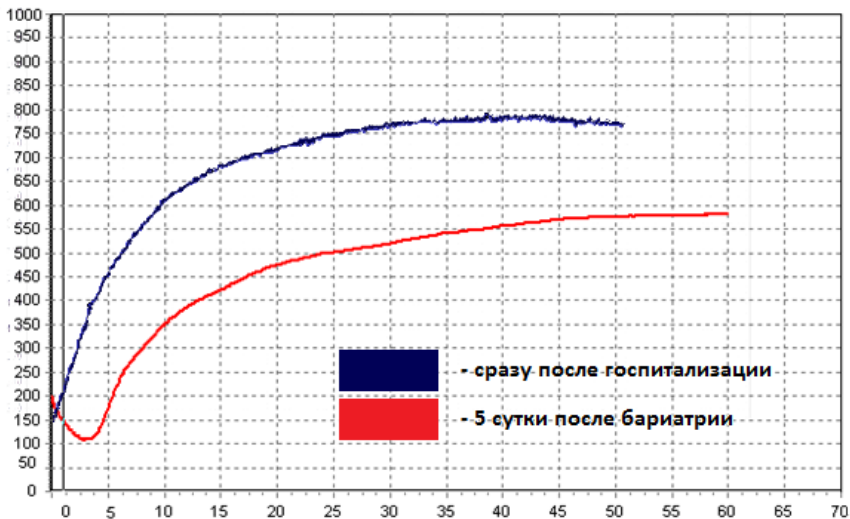


Fig. 3. Comparative thromboelastogram (LPTEG) of the patient 55 y.o. with BMI 48.05 kg/m² (height – 167 cm, weight – 134 kg), immediately after admission and on 5th day after sleeve-gastroplasty. The patient was given combined therapy

line 100 mg 2 times a day every 12 hours, since the indicators of the vascular-platelet component of hemostasis and fibrinolysis remained elevated.

In this category of patients, combined therapy with Enoxaparin sodium 0.1% 0.2 ml sc 2 times a day every 12 hours and Pentoxifylline 100 mg 2 times a day every 12 hours is an effective method for the prevention and correction of thrombotic complications.

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