

**BLOOD-SAVING EFFECT OF AMINOCAPROIC ACID
IN TOTAL KNEE JOINT REPLACEMENT**

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Цель. Оценить эффективность применения аминокaproновой кислоты для снижения периперационной кровопотери при первичном тотальном протезировании коленного сустава.

Материал и методы. В исследование включено 82 пациента, которым было выполнено тотальное протезирование коленного сустава. В исследуемой группе (42 пациента) применяли парентеральное введение аминокaproновой кислоты (5% раствор) в дозировке 100 мг/кг до наложения жгута, с повторным введением рассчитанной дозы препарата через 4 часа. Пациентам контрольной группы (40 человек) не проводилось введение аминокaproновой кислоты. В группах проводили сравнительную оценку следующих показателей: концентрации гемоглобина, количества эритроцитов, гематокритного объема эритроцитов до операции и в послеоперационном периоде (5 сутки). Выполняли учет величины кровопотери по дренажу в течение 24 часов после операции.

Результаты. Выявлено значительное сокращение объема кровопотери по дренажу в исследуемой группе (300; 200-350 мл (Me; 25%; 75%)) по сравнению с контрольной (600; 525-725 мл (Me; 25%; 75%)), $p < 0,001$. Среднее значение показателей крови в послеоперационном периоде в исследуемой группе (гемоглобин 118; 105-124 г/л, эритроциты 3,95; 3,7-4,2 $\times 10^{12}$ /л, гематокрит 36,55; 32,8-39,6 (Me; 25%; 75%)) было достоверно выше, чем в группе контроля (гемоглобин 105,5; 95-119 г/л, эритроциты 3,45; 3,1-3,9 $\times 10^{12}$ /л, гематокрит 30,95; 29,65-34,05 (Me; 25%; 75%)), $p < 0,05$. В контрольной группе 11 пациентам (27,5%) проводилось переливание эритроцитарной массы. Переливания компонентов донорской крови пациентам исследуемой группы не проводили. Не было каких-либо осложнений, связанных с применением аминокaproновой кислоты.

Заключение. Применение аминокaproновой кислоты позволяет повысить эффективность лечения пациентов с дегенеративно-дистрофическими заболеваниями коленного сустава за счет исключения необходимости переливания донорской крови при тотальном эндопротезировании коленного сустава, а также снижения экономических затрат на обеспечение данного оперативного вмешательства.

Ключевые слова: протезирование коленного сустава, кровопотеря, ингибиторы фибринолиза, аминокaproновая кислота, гемотрансфузия, экономическая эффективность, оперативное вмешательство

Objectives. To evaluate the effectiveness of aminocaproic acid for reducing the perioperative blood loss in primary total knee joint replacement.

Methods. The patients (n=82) with the total knee joint replacement were included in the study. In the study group (n=42) parenteral administration of aminocaproic acid (100 mg/kg, 5% solution) was administered before applying the tourniquet, with repeated administration of the calculated dose of the drug in 4 hours. Patients of the control group (n=40) did not receive aminocaproic acid. The following indicators were compared: hemoglobin concentration, erythrocyte count, hematocrit volume of red blood cells prior to surgery and in the postoperative period (5 days). Drainage blood was recorded within 24 hours after the operation.

Results. In the study group blood loss/drainage volume was significantly reduced (300, 200-350 ml (Me 25%, 75%)) compared to the control group (600, 525-725 ml (Me, 25%, 75%)), $p < 0,001$. In the postoperative period the drainage blood loss and calculated blood loss volumes were significantly higher for the control group (mean value of blood indicators in the study group: hemoglobin 118, 105 – 124 g/l, erythrocytes 3,95, 3,7 – 4,2 $\times 10^{12}$ /l, hematocrit 36,55, 32,8 – 39,6 (Me 25%, 75%) and mean value of blood indicators: hemoglobin 105,5, 95 – 119 g/l, erythrocytes 3,45, 3,1 – 3,9 $\times 10^{12}$ /l, hematocrit 30, 95, 29,65 – 34,05 (Me, 25%, 75%)), $p < 0,05$, respectively. In the control group, 11 patients (27,5%) were subjected to massive red blood cell transfusion. Donor blood component transfusion was not performed in the patients of the study group. No complication associated with aminocaproic acid application was registered.

Conclusion. The use of aminocaproic acid has proved to be an efficient and practical method of treatment patients with degenerative dystrophic diseases of the knee joint by eliminating the need for surgical blood transfusion in the total knee joint replacement, as well as by decreasing reimbursement for surgical procedures.

Keywords: knee joint replacement, blood loss, fibrinolysis inhibitors, aminocaproic acid, blood transfusion, economic costs, surgical intervention

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Blood-saving Effect of Aminocaproic Acid in Total Knee Joint Replacement

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Introduction

Total knee joint replacement is one of the most effective and dynamically developing technologies of current orthopedics. In the whole world, including the orthopedic clinics in Belarus, the incidence of arthroplasty operations performed annually has increased [1, 2]. However, the unsolved problems of this type of surgical interventions enable to effect significantly on the outcomes of treatment remain. One of these unsolved problems is perioperative hemorrhage, the volume of which, according to various sources, can be up to 1500 ml. As a rule, endoprosthetics of the knee joint is performed using a pneumatic tourniquet, which minimizes the blood loss directly during the operation. But after removal of the tourniquet, diffuse bleeding from periarticular tissues intensifies due to reflex vasoplegia and activation of the fibrinolysis system. The total postoperative volume of blood lost includes blood from drains as well as the "hidden" volume, represented by interstitial and intraarticular hematomas. [3, 4, 5].

Significant blood loss accompanying such surgeries, leads to the development of post-operative anemia, increases the risk of infectious complications and duration of treatment in a hospital [6]. Donor red blood cell and plasma transfusions is most often used to treat and prevent the postoperative anemia. The average incidence rate of the postoperative blood transfusions is about 45% [7]. This method of blood loss compensation is expensive, and is at risk of developing various (including severe) complications [8].

Nowadays in the Republic of Belarus there is no single protocol for reducing the perioperative blood loss in the replacement of the knee joint. Known technologies and algorithms of blood saving are diverse, not standardized and differ significantly in orthopedic clinics [9].

One of the ways to prevent the perioperative blood loss is considered to be used inhibitors of fibrinolysis. Their effectiveness, safety, significant reduction in economic costs in comparison with other methods is confirmed by many studies [10, 11]. Tranexamic acid is most often used in world clinical practice. Many authors position this drug as the "strongest" inhibitor of fibrinolysis [3, 12, 13]. This

group of drugs also includes aminocaproic acid, which is cheaper and more affordable, but, at the moment, unlike tranexamic acid has no wide application and evidence base for endoprosthetics of large joints [14].

Objectives. To evaluate the effectiveness of aminocaproic acid for reducing perioperative blood loss in primary total knee joint replacement.

Methods

A prospective open study of the patients (n=82) who underwent a primary unilateral total knee joint replacement for gonarthrosis, grade III in the clinic of traumatology and orthopedics on the basis of Vitebsk Regional Clinical Hospital were enrolled. Prior to operation the patients were informed in details and the protocol of voluntary consent for participation in this study was drawn up.

The criteria for inclusion in the study were: the age of patients (40-80 yrs), prior to operation hemoglobin values of less than 120 g/l (men) and 110 g/l (women). The criteria for excluding patients from the study were: thrombosis (deep vein thrombophlebitis, thromboembolic syndrome, myocardial infarction), varicose veins of the lower limbs, cerebral circulation disorders, coagulopathy, kidney disease with the impaired function, hypersensitivity to aminocaproic acid.

In accordance with the objectives of the study, as well as depending on the treatment performed, patients were divided into 2 groups. The groups were comparable in age, height, weight (Table 1).

The study group included patients who were parenterally administered aminocaproic acid (5% solution) at a dosage of 100 mg / kg before applying the tourniquet with repeated administration of the calculated dose of the drug after 4 hours. Patients of the control group did not receive aminocaproic acid.

All patients underwent a standard preoperative examination. In the case of necessity the consultations of such specialists as cardiologist, endocrinologist were appointed. Aspirin, non-steroidal anti-inflammatory drugs were abolished 3 days prior to the surgery. The majority of patients had concomitant pathology: arterial hypertension, ischemic heart disease, bronchial asthma, diabetes mellitus, alimentary obesity.

Table 1

Comparative characteristics of groups of patients (M±SD)

Parameter	Values of parameters in groups		p
	Study group, n=42	Control group, n=40	
Average age (years)	62,7±7,6	61,4±7,5	p>0,1*
Average height (cm)	165,2±8,6	164,1±9,7	p>0,1*
Average weight (kg)	86,6±12,1	82,1±12,2	p>0,1*
Number of men/women	13/29	10/30	p>0,1**

Note: * – Student's t-test; ** – criterion χ^2 .

Spinal anaesthesia is considered to be the technique with an average volume of infusion therapy (1500 ml). Surgical interventions were performed by one surgical team according to a standard technique with medial arthrotomy and using a pneumatic tourniquet. Bicondylar models of endoprostheses with preservation of the posterior cruciate ligament without replacing the articular patellar surface with rotational or fixed liners were used. The drainage was placed after inserting the components of the endoprosthesis, the wound was sutured layer by layer; the pressure bandage was applied. Draining of the operating wound was carried out within 24 hours. Medication prophylaxis of thromboembolic complications was performed according to the current clinical protocols for the treatment and prevention of venous thromboembolism of the Ministry of Health of the Republic of Belarus. Mechanical prophylaxis was carried out by early mobilization of the patient, as well as the use of elastic bandage of the lower limbs in the postoperative period.

The following intergroup indicators were compared: hemoglobin concentration, erythrocyte count, hematocrit volume of erythrocytes prior to surgery and in the postoperative period (5 days). The blood counts were taken on the 5th day. According to the opinion of some authors by this time the volume of circulating blood had been recovered and the results obtained most accurately reflect the total blood loss in comparison with the baseline level. [15]. The total estimation of blood loss/drainage volume occurred over 24 hours. The results were processed using Microsoft Office Excel 2010 and STATISTICA 10.0 package.

The Shapiro-Wilk criterion was used for testing hypotheses regarding the distributional form. In the case of a normal distribution the Student's t-test was used. In the distribution different from normal, the nonparametric methods were used and the Mann-Whitney test was used. The data of the studies are presented as mean value, standard deviation ($M \pm SD$) for values of signs subjected to normal distribution and median (Me), interquar-

Table 2
Comparative characteristics of groups of patients ($M \pm SD$)

Volume discharged by the drainage (ml)		
Study group, n=42	Control group, n=40	p
300 [200-350]	600 [525-725]	p<0,001

Note: p – Mann-Whitney test.

tile interval [25%; 75%] for those, not subjected to normal distribution of values. For categorical data analysis the criterion 2 was used. The level of statistical significance was assumed to be p<0,05.

Results

The account of intraoperative blood loss was not carried out since in all cases blood volume was insignificant due to a pneumatic tourniquet application.

A significant decrease of this parameter in the study group was established by the comparative evaluation of the amount discharged by the drainage (Table 2).

The groups were statistically comparable according to the initial data of hemoglobin concentration, the number of erythrocytes and the hematocrit volume of erythrocytes. When assessing the indicators of hemoglobin, erythrocyte, hematocrit, with subsequent comparison between the baseline values and obtained on the 5th day from the onset of surgical intervention, a reliable intergroup difference was revealed (Table 3).

When red blood cell transfusion was administered, not only the level of hemoglobin and the hematocrit volume of erythrocytes were taken into account, but also the presence of the circulatory disorders. A reduction of hemoglobin level of less than 80 g/l was considered to be an indication for blood transfusion. In patients with concomitant ischemic heart disease, a decrease of hemoglobin concentration of less than 100 g/l was considered to be an indication for red blood cell transfusion. Based on this, 11 patients of the control group (27,5%) were transfused the erythrocyte mass (2 units). On

Table 3
Comparative characteristics of indicators of hemoglobin concentration, the number of erythrocytes and the hematocrit volume of erythrocytes (Me [25%; 75%])

Indicator	Research group, n=42	Control group, n=40	p
Hemoglobin concentration before surgery (g/l)	142,5 [135-149]	142 [132,5-146]	p=0,42
Hemoglobin concentration on the 5 th day from the surgery (g/l)	118 [105-124]	105,5 [95-119]	p<0,05
The number of erythrocytes before surgery ($10^{12}/l$)	4,75 [4,6-5,0]	4,8 [4,25-5,05]	p=0,27
The number of erythrocytes on the 5 th day from the surgery ($10^{12}/l$)	3,95 [3,7-4,2]	3,45 [3,1-3,9]	p<0,05
The hematocrit volume of erythrocytes before surgery (%)	45,1 [41,0-46,9]	44,1 [38,95-45,75]	p=0,1
The hematocrit volume of erythrocytes on the 5 th day from the surgery (%)	36,55 [32,8-39,6]	30,95 [29,65-34,05]	p<0,05

Note: p – Mann-Whitney test.

the evening of surgery for total knee replacement only in 6 patients of the study group hemoglobin level was less than 100 g/l, in 1 – less than 90 g/l. There was no need for allogeneic blood transfusion in the patients of the study group.

Discussion

Prosthetics of large joints of the lower extremity may be accompanied by clinically significant blood loss. The results of the study demonstrate the effectiveness of using the fibrinolysis inhibitor (aminocaproic acid) in total knee joint replacement concordant with the data of a few pilot studies [14].

A significant reduction of the amount of drainage content to be discharged in the case of using aminocaproic acid in recommended doses in comparison with control group was found out. The post-operative average volume of blood lost from drains in the control group (600 ml) was comparable to those results of other clinical studies that performed similar measurements [4, 13, 15]. No drug -related complications had been documented. Also none of the patients had clinical signs of deep vein thrombosis and / or thromboembolic complications in the early postoperative period. Taking into account the age of patients and the concomitant pathology, minimization of blood loss has promoted early active rehabilitation, as well as the reduction in hospitalization terms of patients.

A significant reduction of the postoperative blood loss while using aminocaproic acid is comparable to that of other similar studies in which tranexamic acid was used as the inhibitor of fibrinolysis [3, 6, 11, 13, 15]. The lower price of aminocaproic acid, as well as the presence of a domestic manufacturer, determines the rationality and prospects of using this drug.

Conclusions

1. Aminocaproic acid has a pronounced blood-saving effect in performing total knee replacements.

2. Parenteral administration of aminocaproic acid prior to operation is considered to be a safe method, permitting increase the effectiveness of treatment in patients with degenerative dystrophic diseases of the knee joint by eliminating the need for donor blood transfusion in the total knee replacement and also reducing the economic costs for providing this surgical intervention.

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