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Percutaneous Nephroscopic Surgery: Using Tranexamic Acid To Prevent Intraoperative Bleeding.

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ABSTRACT

At the present stage Percutaneous nephrolithotomy is the most rational method to treat large high-density stones that resist distant lithotripsy, multiple stones in pyelocaliceal system and staghorn calculus of complex configuration. The accumulation of experience in this field and the improvement of technology implementation in operating endoscopic interventions led to the expansion of indications for percutaneous nephrolithotomy and reduced the number of intra- and postoperative complications. One option to prevent bleeding complications during surgery is the use of tranexamic acid in the preoperative period. Comparative clinical analysis of two groups of patients who underwent percutaneous nephrolithotomy showed that the results of surgical treatment of patients with nephrolithiasis after administering tranexamic acid are different from patients that did not receive this drug. Thus, the use of tranexamic acid has a perspective in percutaneous nephrolithotomy as a drug that greatly reduces the risk of intraoperative bleeding and the need for blood transfusions.

Keywords: nephrolithiasis, percutaneous nephrolithotomy, treat large high-density stones, prevent bleeding complications, tranexamic acid, risk of intraoperative bleeding.

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INTRODUCTION

In the structure of urological diseases nephrolithiasis takes the third place, standing behind urinary tract infections and prostate pathology. Global incidence of urolithiasis varies from 1.0 to 15.0% of the population (1,2). In Kazakhstan, the incidence of urolithiasis is 73,4 per 100 000 population (2013)(3,4).

Minimally invasive techniques, such as shock wave lithotripsy, PCNL (percutaneous nephrolithotomy), retrograde introrenal surgery, that have emerged in the past decade, allowed to abandon open surgical procedures, even for the removal of large stones (5-6).

Percutaneous nephrolithotomy at the present stage is the most rational method to treat large high-density stones that resist distant lithotripsy, multiple stones in pyelocaliceal system and staghorn calculus of complex configuration (1-4).

The accumulation of knowledge and experience in this field and the improvement of technology implementation in operating endoscopic interventions led to the expansion of indications for percutaneous nephrolithotomy and reduced the number of intra- and postoperative complications.

Despite this, the risk of complications, like intraoperative bleeding, remains relevant. Thus, according to a number of major studies, the need of blood transfusion is almost 10% and selective embolization for bleeding of arteriovenous fistula or pseudoaneurysm is at least 1%. (7-8).

One option to prevent bleeding complications during surgery is the use of tranexamic acid in the preoperative period (9-10).

Tranexamic acid is antifibrinolytic drug. The active ingredient of the drug slows fibrinolysis due to specific inhibition of activation of plasminogen conversion to plasmin. Tranexamic acid has local and systemic hemostatic effects (11-13).

MATERIALS AND METHODS

The basis of the present study was a prospective clinical observation of 164 patients with nephrolithiasis, undergoing percutaneous nephrolithotomy (PCNL) for the period from January 2013 to June 2015.

All patients were randomly divided into 2 equal groups of 82 persons depending tranexamic acid injection. Group I (experimental group) - patients that received the drug - tranexamic acid in a volume of 10 ml to 200.0 saline solution intravenously immediately before surgery. Group II (control group) - patients that did not receive the drug.

The age of patients observed in both groups ranges from 18 to 75 years. Table 1 shows the distribution of patients by age, sex, side of surgery, body mass index, calculus area in mm^2, which calix provided access to cavity system of the kidneys, the presence or absence of external drainage of the kidneys in both groups and ASA Physical Status of patients. The average age of patients in group I was 47,3±1,4 years (95% CI = 44,4-50,3 years) and in group II - 45,8±1,5 years (95% CI = 42,8-48,7 years). The difference was not statistically significant ($p > 0.05$), their 95% confidence intervals overlapped. The two groups did not differ statistically ($p > 0.05$) based on sex, there was no evidence. The right-side access to the kidney in the group I – 44 (54%) patients, left-side -38 (46%), in the group II, right-side - 42 patients (51%), left-side- 40(49%). No statistical difference was found between the groups ($p > 0.05$). Body mass index also was not statistically different in both groups. In the group I the mean value equaled to 29,4±0,6 (95% CI = 28,1-30,7), group II - 27,9±0,6 (95 CI 26,7-29,1) (Table 1).

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Table 1 - Distribution of patients by age, sex, side of surgery, body mass index, calculus area, ASA Physical Status, puncture access, presence or absence of nephrostomy tube and pre-operative urine cultures.

Indicator	Group I	Group II	p	p-value
Age	47,3±1,4 (CI=44,4-50,3)	45,8±1,5 (CI=42,8-48,7)	1,22	p>0,05
Sex: male, female	35 (43%) 47 (57%)	47 (57%) 35 (43%)	3,51	p>0,05
Side of surgery: right, left	44 (54%) 38 (46%)	42 (51%) 40 (49%)	0,098	p>0,05
Body mass index (kg/m^2)	29,4±0,6 (CI=28,13-30,77)	27,9±0,6 (CI=26,7-29,1)	1,77	p>0,05
Calculus area (mm^2)	662,14±66,5 (CI=531,7-792,5)	522±45,9 (CI=431,8-612,1)	1,73	p>0,05
ASA: Class I Class II Class III Class IV	40(49%) 22(27%) 19(23%) 1(1%)	43(52,5%) 27(33%) 11(13,5%) 1(1%)	0,22 0,72 2,61 1,0	p>0,05 p>0,05 p>0,05 p>0,05
Puncture access: Upper callix Middle callix Lower callix	 15 (18%) 14 (17%) 53 (65%)	 28 (34%) 9 (11%) 45 (55%)	 5,67	 p>0,05
With nephrostomy tube, Without nephrostomy tube	37 (45,2%) 45 (54,8%)	36 (44%) 46 (56%)	0,025	p>0,05
Pre-operative urine cultures: positive negative	27(33%) 55(67%)	23(28%) 59(72%)	0,46	p>0,05

CI- confidence interval.

In the group I (percutaneous nephrolithotomy + tranexamic acid), the average calculus area was 662,14±66,5 mm^2 (95% CI = 531,7-792,5mm^2). In the group II the average calculus area was 522±45,9 mm^2 (95% CI = 431,8-612,1mm^2) (Table 1). The American Society of Anesthesiologists (ASA) Physical Classification System was used for comorbidities in the compared groups. In the Group I -40 patients(49%) related to the class I, 22 patients (27%) – class II, 19 patients(23%) – class III, and 1 patient (1%) related to the class IV. In the Group II 43 patients (52.5%) were assigned to the class I, 27 patients (33%) – class II, 11 patients (13.5%) – class III, and 1 patient (1%) related to the class IV. The Groups did not have statistically significant difference as related to the severity of condition and the presence of comorbidities. Puncture Access to kidney cavity system in group I was more often made through the lower callix - 53 (65%) patients, through the upper callix - 15 (18%), and the least often, through the middle callix - 14 (17%) patients. In group II access was also often carried through the lower callix of the kidney - 45 (55%) patients, through the upper callix - 28 (34%) patients, and less often - through the middle callix - 9 (11%) patient. An analysis of contingency tables (2 × 3) showed no statistically significant difference between the groups (p> 0,05). In group I nephrostomy tube was not used in 45 (54,8%) patients, and in 37 (45,2%), the surgery ended leaving nephrostomy tube. In group II, surgery for 46 (56%) patients ended without external drainage, and with nephrostomy tube for 36 (44%) patients (p> 0.05). Bacteriological diagnostic of urine in group I in 27 (33%) seeded positive flora, in 55 (67%) negative. In group II in 23 (28%) patients positive urine flora, while 59 (72%) - negative. Statistically significant differences between groups were not found (p> 0,05).

In group I, staghorn calculus was observed in 43 patients (52,5%), in the renal pelvis – 21 patients (26%), lower callix - 6 patients (7%), proximal ureter - 4 patients (5%), pelvis + calyx - 6 patients (7%) and middle calyx -2(2,5%). In group II staghorn calculus was observed in 37 patients (45,5%), renal pelvis in 28 patients (34%), upper ureter 7 patients (8,5%), lower calyx of the kidney in 3 patients (3,5%), pelvis + calyx - 4 patients (5%), and upper calyx – 3(3,5%) (Table 2). When comparing the groups based on calculus localization in cavity system no statistically significant difference was revealed (p> 0,05).

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Table 2 - Distribution of patients by calculus localization in the kidney cavity system.

Calculus localization	Group I	Group II	p	p-value
Pelvis	21 (26%)	28 (34%)	0,026	p>0,05
Lower calyx	6 (7%)	3 (3,5%)	1,05	p>0,05
Pelvis + calyx	6 (7%)	4 (5%)	0,42	p>0,05
Proximal ureter	4 (5%)	7 (8,5%)	0,87	p>0,05
Upper calyx	2(2,5%)	0	0,24	p>0,05
Middle calyx	0	3(3,5%)	0,24	p>0,05
Staghorn calculus	43 (52,5%)	37 (45,5%)	0,87	p>0,05
Total	82 (100%)	82 (100%)		

Thus, based on age, sex, side of surgery, body mass index, calculus area, ASA Physical Status of patients, puncture access, presence or absence of nephrostomy tube and pre-operative urine cultures in both groups no statistically significant difference was found (p> 0,05). Number of staghorn calculi and stone area were greater in group I, but compared with the group II, the difference was not statistically significant (p> 0,05).

All patients were clinically examined in the preoperative period. Laboratory methods included clinical blood and urine analysis, blood group and Rh factor, coagulation group, biochemical blood tests (including urea, creatinine, electrolytes), liver function test, markers of hepatitis, microreaction and HIV. Bacterial method included urine culture with antibiotic susceptibility. Radiological methods included ultrasound investigation of kidneys, plain and excretory urography, and multispiral computed tomography with contrast.

Blood for clinical analysis was taken from all the patients before the surgery and 24 hours after the surgery (9). Ultrasound investigation of kidneys and plain urography were performed the next day after surgery to avoid the presence of residual stones.

Percutaneous nephrolithotomy surgeries were performed in position on the abdomen under general anesthesia, with pre-ureteral catheterization to administer contrast agent. Percutaneous puncture in kidney cavity was performed under X-ray control, followed by administration of a hydrophil guide and fistula canal bougienage with plastic, flexible dilators «Amplatz» 30 Ch. Calculus fragmentation was carried out by a pneumatic lithotripter. The surgery was completed by the mandatory installation of ureteral stent and nephrostomy tube if necessary. The decision to use external drainage system of the kidney was taken by an operating surgeon intraoperatively and depended on several factors: the presence of large residual calculi and the development of intraoperative complications (14).

Statistical analyses were conducted by using SPSS® for Windows (version 22.0). T- test, the Pearson chi-square test, the Fisher's exact test were used as appropriate. P-values of less than 0.05 were considered significant.

RESULTS OF THE STUDY

The main criteria for comparative clinical evaluation between two groups of patients during and after percutaneous nephrolithotomy were the following:

- The number of patient days after surgery;
- The duration of the surgery;
- The presence of residual stones;
- Postoperative complications;
- The level of hemoglobin and red blood cells before and after surgery.

Patient days (day spent in hospital by patients) after percutaneous nephrolithotomy for the Group I equaled to 9,14±0,3 days (95% CI = 8,4-9,8days) and 10,08±0,5days (95% CI = 8,9-11,1days) for the Group II patients on average. The difference was not statistically significant (p> 0.05) as 95% CI overlap (Table 3). The average duration of surgery after percutaneous nephrolithotomy in the Group I was 107±5,4 minutes (95% CI =

96,8-118,0min), and 119,6±5,3 minutes (95% CI = 109,1-129,9 min) in the Group II. Differences between treatment groups was not statistically significant (p> 0.05).

Table 3 - Distribution of patients according to the number of patient days after surgery, duration of surgery, and presence of residual stones.

Treatment criteria	Group I	Group II	p	p-value
Patient days	9,14±0,3 (CI =8,4-9,8)	10,08±0,5 (CI =8,9-11,1)	1.61	p>0.05
Duration of surgery (min)	107±5,4 (CI =96,8-118,0)	119,6±5,3 (CI =109,1-129,9)	1.61	p>0.05
Residual calculi	21 (25,5%)	25 (30,5%)		
Stone free rate	61 (74,5%)	57 (69,5%)	0.48	p>0.05

CI- confidence interval.

Residual stones in the Group I were abandoned in 21 patients (25.5%) and in the Group II - 25 (30,5%). Accordingly, the absence of calculus in the Group I was observed in 61 patients (74.5%) and in 57 patients (69.5%) in the Group II. The groups did not have statistically significant difference (p>0.05).

For visual display of the degree and the number of complications in the two groups, we used the International Classification of complication of surgery by Clavien, et al. (15). In Group I, there were no complications in 61 patients out of 82 accounting for 74,3%; in Group II there were no complications in 54 patients, respectively 65,8%. The statistical comparison shows there was no difference between the groups (p>0.05). Grade I complications in the Group I were observed as follows: fever more than 38.0 - in 12 patients (14.6%), increased creatinine in postoperative period – in 1 patient (1.2%), postoperative bleeding without blood transfusion - in 1 patients (1.2%). In the Group II: fever was observed in 12 patients (14.6%), increased was creatinine - in 1 patients (1.2%), active bleeding without blood transfusion - in 12 patients (14.6%). Here we can see a clear statistically significant differences between the groups (p <0,05). Grade II complications in the Group I were observed as follows: blood transfusion – in 2 patients (2.4%), and 1 patient (1.2%) developed lower lobe pneumonia. In the Group II- 10 patients (12%) developed massive bleeding that required blood transfusion. We can see a clear statistically significant differences between the groups (p <0,05). Grade IIIa complications in the Group I - 2(2,4%) developed hemothorax, followed by pleurocentesis, 2 (2,4%) - restenting due to poor performance of the stent, one patient (1,2%) - replacement of nephrostomy tube due to its inadequate work. The groups did not have statistically significant difference (p>0.05).

Table 4 - Intra - and postoperative complications in the patient groups (classification by Clavien).

Complications by Clavien	Group I	Group II	p	p-value
Grade 0: no complications	61 (74,3%)	54 (65,8%)	1,4	p>0,05
Grade I: Fever greater than 38,0°C	12 (14,6%)	12 (14,6%)	1,0	p>0,05
Increased creatinine	1 (1,2%)	1 (1,2%)	1,0	p>0,05
Bleeding without transfusion	1 (1,2%)	12 (14,6%)	10,1	p<0,05
Total:	14 (17%)	25 (30,5%)	4,5	p<0,05
Grade II: Blood transfusion	2 (2,4%)	10 (12%)	5,7	p<0,05
Uroplania (less than 12h)	0	0		
Wound infection	0	0		
Pneumonia	1(1,2%)	0	0,5	p>0,05
Total:	3 (3,6%)	10 (12%)	4,0	p<0,05
Grade IIIa: Hemo\hidrotorax	2 (2,4%)	1 (1,2%)	0,34	p>0,05
Stenting in case of uroplania for more than 12h	2 (2,4%)	4 (4,8%)	0,69	p>0,05
Stenting in case of pelvis and ureteropelvic junction injure	0	1 (1,2%)	0,5	p>0,05
Embolization	0	1 (1,2%)	0,5	p>0,05
Obstruction and colic because of clot	0	0		
Nephrostomy	1 (1,2%)	0	0,5	p>0,05
Total:	5 (6%)	7 (8,5%)	0,36	p>0,05

Grade IIIb: AV fistula	0	1 (1,2%)	0,5	p>0,05
Isthmus stricture	0	0		
Ureter stricture	0	0		
Perinephric abscess	0	1 (1,2%)	0,5	p>0,05
Haematoma with intervention	0	1 (1,2%)	0,5	p>0,05
Stones in ureter and urinary bladder	0	0		
Conversion	0	0		
Total:	**0**	3 (3,6%)	0,24	p>0,05
Grade IVa: Contiguous organ dysfunction				
Myocardial infarction	0	**0**		
Nephrectomy	0	**0**		
Cardiopulmonary decompensation	0	**1(1,2%)**	0,5	p>0,05
Acute Cerebrovascular Event	0	**0**		
Total:	0	**1 (1,2%)**	0,5	p>0,05
	0	**2 (2,4%)**	0,49	p>0,05
Grade IVb: Urosepsis	0	0		
Multiorgan failure	0	0		
Grade V: Death	0	0		

In the Group II grade IIIa complications: 1 (1,2%) patient - hemothorax, followed by pleurocentesis; 4 (4,8%) patients required restenting, в следствие затека мочи, 1 (1.2%) – restenting due to perforation of the renal pelvis, and in 1case (1,2%) – there was an attempt of angiographic embolization. The groups did not have statistically significant difference (p>0.05).

Patients in the Group I had no grade IIIb complications. In the Group II - 3 patients had grade IIIb complications: 1 patient developed AV fistula which led to an attempt of embolization and a following nephrectomy 1 patient - perinephric abscess in the postoperative period, which led to repeated surgery with incision and drainage of an abscess; 1 patient - hematoma in the lower pole of the kidney, followed by opening and drainage of perirenal hematoma. The groups did not have statistically significant difference (p>0.05).

Patients in the Group I had no grade 4a complications. One patient (1,2%) in the Group II had grade 4a complication in the postoperative period - in the form of acute cerebrovascular event and 1 patient (1.2%) underwent nephrectomy due to a developed fistula, and an unsuccessful attempt of angiographic embolization which was mentioned above. The groups did not have statistically significant difference (p>0.05). Grade 4b and 5 complications were not observed.

Key indicators that demonstrate the extent of intraoperative blood loss is to compare the level of hemoglobin and red blood cells before and after surgery (9). When comparing the groups based on the average level of hemoglobin before surgery, one can see that they are almost identical. The level of red blood cells in the Group I before the surgery was 137±2,02 g\l (95% CI = 133,3-141,2g\l), and in the Group II it was equal to 139,2±2,1 g\l (95% CI = 135,1-143,4 g\l); and the difference was not statistically significant (p> 0,05) (Table 5). When comparing hemoglobin levels after the surgery in the two groups it can be seen that it equals to 126,0±2,15 g\l (95% CI = 121,8-130,2g\l) in the Group I, and 116,5±3,04 g\l (95% CI = 110,5-122g\l) in the Group II. Therefore, level of hemoglobin reduced more in the patients of the Group II compared to the Group I, and the difference of these parameters was statistically significant **(p <0 05)**. Comparing the differences of hemoglobin levels decrease, in the Group I the difference was 11,42±0,15 g\l (95% CI = 11,12-11,73g\l), and in the Group II, it was equal to 22,76±3,7 g\l (95% CI = 15,51-30,02g\l). This shows that the level of hemoglobin decreased more in the Group II, and the difference of these parameters was statistically significant **(p <0 05).**

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Table 5 - Distribution of patients by the level of hemoglobin and red blood cells before and after surgery.

Indicator	Group I	Group II	p	p-value
Hemoglobin before surgery	137±2,02 (CI =133,3-141,2)	139,2±2,1 (CI =135,1-143,4)	0,76	p>0,05
Hemoglobin after surgery	126,0±2,15 (CI =121,8-130,2)	116,5±3,04 (CI =110,5-122)	2,55	**p<0,05**
Hemoglobin difference	11,42±0,15 (CI =11,12-11,73)	22,76±3,7 (CI =15,51-30,02)	3,06	**p<0,05**
Red blood cells before surgery	4,7±0,06 (CI =4,58-4,85)	4,7±0,09 (CI =4,59-4,95)	0,09	p>0,05
Red blood cells after surgery	4,3±0,07 (CI =4,17-4,45)	3,9±0,12 (CI =3,67-4,16)	2,88	**p<0,05**
Red blood cells difference	0,4±0,05 (CI =0,29-0,51)	0,85±0,08 (CI =0,69-1,01)	4,10	**p<0,05**

CI- confidence interval.

Indicators of red blood cells prior to surgery did not have statistically significant difference between the groups. In the Group I it was average to 4,7±0,06 ×10^12 (95% CI = 4,58-4,85×10^12), and in the Group II - 4,7±0,09 ×10^12 (95% CI = 4,59-4,95×10^12), p value > 0,05. Level of erythrocytes after the surgery in the Group I decreased to 4,3±0,07 ×10^12 (95% CI=4,17-4,45×10^12), and in the Group II it decreased to 3,9±0,12×10^12 (95% CI=3,67-4,16×10^12), that was much greater than in the Group I, statistically significant difference existed between the groups (p<0,05). When comparing differences in reducing erythrocytes before and after the surgery, where in the Group I the level of erythrocytes reduced to 0,4±0,05 ×10^12 (95% CI=0,29-0,51×10^12), while in the Group II - to 0,85±0,08×10^12 (95% CI=0,69-1,01×10^12). Here we can see a clear statistically significant differences between the groups (p <0,05).

DISCUSSION

Percutaneous nephrolithotomy is the best treatment for large (greater than 2 cm), high density and staghorn calculus. Despite the huge experience in PCNL accumulated over many years, as well as the improvement of methods of access to the cavity system and dilation of the puncture channel, complications such as the intraoperative bleeding remain very relevant. This way, according to several studies the frequency of blood transfusion needed after surgery, ranged from 6% to 20%, and selective embolization of the blood vessels in the kidneys at developed arteriovenous fistula is about 1% (1,2,16). The intensity of the bleeding proved a significant decrease in the level of hemoglobin in the postoperative period, which fell by 2.1 to 3.3 gm/dl.. This fact was noted in multiple scientific studies (7).

The effectiveness of using tranexamic acid as the drug reducing the intensity of intraoperative bleeding has been proven in many branches of medicine: trauma (11,12), cardiology (17.18), gynecology (19), neurosurgery (20-21), and others.

In urology the drug has been widely studied during trans ureteral resection (TUR) at benign prostatic hyperplasia (BPH) and radical prostatectomy, where tranexamic acid has proven its clinical effectiveness as a drug that significantly reduces the intensity of intraoperative bleeding (22,23). The use of tranexamic acid in the performance of percutaneous nephrolithotomy is described in a single work (9, 24).

We have conducted a comparative analysis of our research with other similar research by S.Kumar (9), studying the use of tranexamic acid in the performance of percutaneous nephrolithotomy (table 6).

In our work, length of patient stays in hospital after the surgery had almost equal values in two groups. In the Group I it averaged to 9,14 days, and in the Group II patients stayed on average 10,08 days. Patients spent less patient days in the group using tranexamic acid, but no statistically significant difference. When comparing these figures with the other study (9), these figures were much lower, 2.74 days and 4.67 days. It should be noted that patients in our hospital staied until external drainage was completely removed and post-surgery complications were completely relieved. In our clinic, we adhere to the following tactics of

removing drainage: nephrostomy tube is usually removed in 3-5 days after the surgery, or longer, in case of any complications. Urethral catheter is removed in 5-7 days after the surgery. This was reflected in the length of hospital stay.

Table 6 - Compare the results of our work with the S.Kumar's work.

	S.Kumar (%)			Our work (%)		
Group	I	II	**p-value**	I	II	**p-value**
Length of patient stays in hospital after the surgery	2,74	4,67	**p<0,0001**	9,14	10,08	p>0,05
Length of PCNL	48,3	70,8	**p<0,0001**	107	119,6	p>0,05
Stone free rate	91	82	p>0,05	74,5	69,5	p>0,05
Hemoglobin decrease (gr\dl)	1,39	2,31	**p<0,0001**	1,14	2,27	**p<0,05**
Total number of patients (N)	100	100		82	82	

The mean length of PCNL surgery in Group I was 107 minutes and 119,6 minutes in the Group II, there were no statistically significant difference. In the study by Kumar S this indicator was equal to 48.3 in the first group and 70.8 min in the second group. In our study the difference between the groups is small, in contrast to other studies, where surgeries with tranexamic acid were much shorter than surgeries without hemostatic. It should be noted that in both groups the number of coral calculi was greater in our study and our patient population was more difficult as related to these parameters. Time of the surgeries in the Group I for both studies was shorter, this is due to better visualization with reduced bleeding during treatment with hemostatic. Также The duration of the surgery, in the observed patients depended on the size, density and location of calculus, efficiency of lithotripsy, anatomical features of kidney structure and the presence of intraoperative complications (25).

In the Group I, residual calculi were left at 21(25.5%) of cases, this means the kidney was cleared of stones completely in 74,5% of cases. In the Group II - residual calculi were left in 25(30,5%) of patients, that is in 69,5% of patients no residual concrements were left in the kidney after the surgery. The groups did not differ statistically. There were less coral calculi in the Group I, but the statistical comparison of groups showed no significant difference based on these indicators. However, there were no statistically significant difference between the two groups. When compared with the other research by S.Kumar, we can see that 91% of patients in group I had no residual calculi after surgery, as well as 82% of patients in group II. The reasons for leaving residual calculi were simultaneous inability to complete disintegration of calculus due to the large size of the calculus, the loss of a stone because of poor visibility on the background of bleeding, migration of calculus to the places impossible to reach by nephroscope (26).

When comparing the reduction of hemoglobin level after the surgery, it decreased on 11,42 g\l (1,14 gr\dl) in the Group I and on 22,7g\l (2,27gr\dl.) in the Group II. In the study by S .Kumar (9) this index decreased on 1.39 and 2.31 g\dl. respectively. In our study, this indicator had statistically significant difference. In the Group I in our study level of erythrocytes after the surgery decreased on 0.4×10^12, and in the Group II - on 0.85×10^12. The difference in erythrocyte level reduction was statistically significant. The study by S.Kumar such a comparison was not conducted. Thus, by comparing the differences in hemoglobin and red blood cells reduction before and after the surgery, statistically significant difference is observed between the groups. Much lower level of reduction of erythrocytes and hemoglobin takes place in the Group II. Given this fact, we can say that tranexamic acid reduces intraoperative bleeding.

In our study, we used the International Classification of surgical complications by Clavien (15). In the comparison with our research work, S.Kumar (9) did not use this classification for complications, so we conducted a comparison of specifically developed complications, and in addition, we compared these data with the European Association of Urology, although there are no trials of tranexamic acid in the PNL (table 7). In our study, 21% of patients in the Group I had complications, and 28% had complications after the surgery in the Group II, there were no statistically significant difference between two groups. The study by S.Kumar and 33% of patients in the Group I and 59% of the patients in the Group II had complications. In our study fever was observed in 14,6% of patients in the Group I and 14,6% of patients in the Group II and the difference was not statistically significant. In the other study (9) fever was observed in 14% of patients in the Group I, and 15% of patients in the Group II in the early postoperative period. According to the literature fever develops in 0-

32,1% (on average 10.8%) of patients after the surgery(2). Bleeding requiring blood transfusion in the Group I was observed in 2(2,4%) patients, and it was present in 10(12%) of patients who needed a blood transfusion in the Group II. In the compared study 2% of patients in the Group I needed a blood transfusion, and 11% of patients in the Group II received a blood transfusion after the surgery. According to the literature transfusion is performed in 0-20% (average 7%) of cases (2). Hemo / hydrothorax, that required pleural puncture, developed in 2(2,4%) of patients in the Group I in our study, and it also developed in 1(1,2%) of patients in the Group II. In the other study (9) no one in the Group I had this complication, and in the Group II pleural puncture was performed due to hemo / hydrothorax in 3% of patients. According to the literature this kind of complications usually develops in 0-11,6% (1.5% average) of patients (2).

Table 7- Comparison of percentage of complications of our work with the work of S.Kumar and results of European Association of Urology.

Complications	S.Kumar (%)			Our work (%)			
Fever							
Nausea							
Urinoma							
Transfusion							
Embolisation							
Thoracic complication							
Pelvic perforation							
Urosepsis							
Clot obstruction							
Organ injury							
Death							
Overall percentage of complications (%)							
Total number of patients (N)							

Restenting was observed in 2(2,4%) of patients in the Group I due to inadequate work of ureteral stent, and in 4(4,8%) of patients in the Group II in postoperative period. In 1(1,2%) of patients in the Group I nephrostomy tube was replaced due to inadequate operation of the tube. In the study by S.Kumar two of the patients in the group with tranexamic acid required the stent to be established in the postoperative period. Angiographic embolization was performed in 1 case (1.2%) in our study in the Group I, the patient developed advanced arteriovenous fistula, embolization was not effective, as a result nephrectomy was performed for this patient. In the study by S.Kumar angiographic embolization was performed in 3% of patients in the Group II. According to EAU- 1%(0-1,5). Urosepsis did not develop in our study in any group; and in the compared study it developed in 1% of cases in the group I and in 3% - in the group II. According to EAU urosepsis develops in 0,5 % (0,3-1,1).

We have compared our study with the fundamental work by CROES PCNL Study Group (27), where classification of complications by Clavien was used, but no tranexamic acid was administered to patients. The study examined complications after PCNL in 5803 patients. It was a multi-center study involving 96 centers in Europe, Asia, North America, South America and Australia. The aim of the study was to examine the indications for PCNL and results of the surgery depending on the complete removal of stone and perform the analysis of complications using the classification of surgical complications by Clavien. Most procedures (85.5%) did not have complications. The main complications included: severe bleeding in 446 patients (7.8%), perforation of the renal pelvis - 191 (3.4%), and hydrothorax 104 (1.8%). Blood transfusion was administered in 328 (5.7%) cases, and fever over 38,5 ° C occurred in 598 patients (10.5%). Based on Clavien classification 79.5% of patients did not have complications.

Table 8 – Comparison of complications PNL our research with the study CROES PCNL Study Group by Clavien classification.

Complications	Our research		CROES PCNL Study Group (%)
	Group I (%)	Group II (%)	
Without complications	74,3	65,8	79,5
I	17	30,5	11,1
II	3,6	12	5,3
IIIa	6	8,5	2,3
IIIb	0	3,6	1,3
IVa	0	2,4	0,3
IVb	0	0	0,2
V	0	0	0,03
Total number of patients (N)	82	82	5803

In our study the level of Grade I complications in в I группе -17%, во II группе 30,5%, and in the compared study CROES PCNL (27) – equal to 11.1%. Grade II complications in the Group I -3,6%, and 12% of patients in the Group II in our study; in the other study (27) 5.3% of patients experienced complications. In our study Grade IIIa complications were observed in 6% of patients in the Group I, and in 8,5% of patients in the Group II; in the compared work - in 2.3% of patients. Grade IIIb complications were not observed in the Group I, and in 3,6% of patients in the Group II; in the compared study Grade IIIb complications were observed in 1.3% of patients. Grade IVa complications were not observed in the Group I and in Group II - 2.4%; in the compared work (27) - 0,3%. Grade IVb complications were not observed in both groups in our study; these complications were present in 0.2% of patients in the study CROES PCNL. Grade V complications were also not observed in both groups; and in 0.03% of patients in the compared study (27).

It should be noted that the Group I had had less complications such as massive bleeding requiring transfusion. Unlike the Group II, 12 patients developed active bleeding, which was removed by conservative interventions, and 10 patients developed massive bleeding requiring blood transfusion. Also the Group I did not have more severe complications such as grades IIIb and IVa, in contrast to the second group.

CONCLUSION

Comparative clinical analysis of two groups of patients who underwent percutaneous nephrolithotomy showed that the results of surgical treatment of patients with nephrolithiasis after administering tranexamic acid are different from patients that did not receive this drug. The difference is expressed as follows 1) based on the number of patient days, the duration of the surgery, the presence of residual stones indicators in the Group I were lower compared to the Group II, (no statistically significant difference); 2) there were less complications developed in the Group I than in the Group II (in particular, intra-operative bleeding in the Group I: one patients had active bleeding, which was eliminated by conservative methods and two patients showed massive bleeding that required blood transfusion; in the Group II: 12 patients had active bleeding without blood transfusion and 10 patients had bleeding requiring a blood transfusion). We can see a clear statistically significant differences between the groups ($p < 0,05$); 3) when

comparing hemoglobin and red blood cells levels, we see much more of a decrease in the Group II, but statistically significant differences between the two groups did not exist. When comparing a difference in reduction of erythrocytes and hemoglobin, groups are statistically differ from each other.

Thus, the use of tranexamic acid has a perspective in percutaneous nephrolithotomy as a drug that greatly reduces the risk of intraoperative bleeding and the need for blood transfusions.

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