Tranexamic Acid *vs* Autologous Reinfusion Drain in Primary HIP Arthroplasty

A retrospective cohort study

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Management of blood loss in primary hip arthroplasty is a controversial topic. Although the efficacy of tranexamic acid has been proven, there is still controversy regarding the efficacy of autologous reinfusion drains. The purpose of this study was to compare the efficacy of these two methods. We retrospectively reviewed a total of 246 randomized patients who underwent primary hip arthroplasty. The patients were divided into three groups: TNX group: single preoperative tranexamic acid dose and postoperative hemovac drain, ABRD group: did not receive tranexamic acid, but received a reinfusion drain, and C group: did not receive tranexamic acid but had a hemovac drain used postoperatively. The data collected for analysis were: demographic data, hemoglobin (Hb) variation preoperatively and at 12 and 24 h postoperatively, number of red blood cell units administered postoperatively, and postoperative complications. The mean Hb levels 12 h postoperatively decreased significantly in all groups ($p = 0.001$), without significant differences ($p = 0.093$). The mean Hb levels at 24 h postoperatively decreased significantly in all groups compared with the preoperative ones ($p = 0.001$), a significantly lower mean level being recorded in TNX compared to C or ABRD groups ($p = 0.001$). Our results showed a lower efficacy of ABRD compared to C ($\Delta Hb_{24\ C} = 3.1$mg/dL compared to $\Delta Hb_{24\ ABRD} = 3.33$ mg/dL, $p = 0.001$)($\Delta Hb_{24\ ABRD} = 3.33$ mg/dL and $\Delta Hb_{24\ C} = 3.1$mg/dL, respectively). The administration of a single tranexamic acid dose of 15 mg/kg one hour before incision is more effective than reinfusion drains in reducing postoperative allogeneic blood use in patients who underwent primary hip arthroplasty.

Keywords: tranexamic acid, arthroplasty, hip, autotransfusion, efficacy study

Tranexamic acid (TNX) is an antifibrinolytic agent, a synthetic derivative of lysine who act by blocking the binding of lysine to plasminogen that plays an important role in fibrin degradation. Tranexamic acid (TNX) is the most commonly used antifibrinolytic agent to reduce intra- and postoperative blood loss in orthopaedic and trauma surgery.

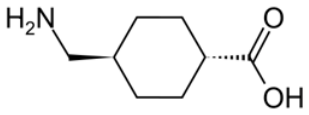

Fig. 1. Chemical structure of tranexamic acid

Hip arthroplasty has become a commonly used surgical technique that is often accompanied by substantial blood loss. The increasing number of arthroplasties resulted in an increase in blood transfusion rate due to the intra- and postoperative blood loss.

To prevent blood loss many methods are used, such as allogeneic blood transfusions, preoperative autologous donation, intraoperative and postoperative blood salvage, deliberate hypotension, patient position, regional anesthesia, erythropoietin, etc. [1-3].

Allogeneic blood transfusions carry significant risks, such as the transmission of infections, immunological reactions, volume overload, renal failure, altered mental status, increased mortality, longer rehabilitation and higher hospital costs [4].

Even though reinfusion drains do not have the above-mentioned disadvantages, their use remains controversialin terms of their efficacy in restoring the hemodynamic balance [5].

Current studies bring into question the use of antifibrinolytic agents to control bleeding, their advantage being a minimal thromboembolic risk and low price [4, 6-8]. Although the effectiveness of tranexamic acid in reducing the need for perioperative transfusion has been proved, controversy in its administration route continues [4, 8, 9].

The study goal was to evaluate the effectiveness of two *blood salvage* methods (preoperative single dose tranexamic acid administration and use of reinfusion drains) on allogeneic blood transfusions in primary hip arthroplasty.

Experimental part

We retrospectively reviewed all cases of primary hip arthroplasty performed by the same team in the interval June 2013 to June 2015. In all patients the lateral approach was used; antibiotic and thromboembolic prophylaxis was done according to the local protocol with third-generation cephalosporin and an aminoglycoside for 3 postoperative days and a LMWH over a period of 35 postoperative days. Tranexamic acid (TNX) was administered in a single dose one hour before surgery.

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The inclusion criteria for the study were: primary hip arthroplasty, lateral approach, same surgeon, spinal anesthesia. The exclusion criteria were: chronic ischemic heart disease and heart failure, chronic renal disease, viral liver disease, coagulopathy, history of thromboembolic events and chronic administration of steroids.

The analyzed data included: demographic data, hemoglobin (Hb) levels preoperatively and 12 hours and 24 hours after surgery, postoperative hemoglobin variation at 12 (ΔHb12) and 24 h (ΔHb24), number of red blood cell transfusion (RBCT) units administered postoperatively, and postoperative complications.

A total of 295 primary hip arthroplasties were identified. Forty-nine patients did not meet the inclusion criteria: heart failure = 21, kidney disease = 5, liver disease = 12, coagulopathy and history of thromboembolic events = 8, pulmonary embolism = 1, not discotinuing steroid use before surgery = 2.

Included in the study were 246 patients: 152 patients received tranexamic acid (TNX), in 45 patients autologous blood reinfusion drains (ABRD) were used, and 49 patients who received neither TNX nor ABRD formed the control group (C).

The first group (TNX) received 15 mg/kg TNX 1 h before surgery and a hemovac drain was used postoperatively. The second group (ABRD) did not receive TNX, but a reinfusion drain (CBCII ConstaVac™ Blood Conservation System) was used to reinfuse the postoperatively collected blood. The third group (C) did not receive TNX but had a hemovac drain used postoperatively.

The local blood transfusion protocol was used at Hb levels less than 8 mg/dL or when the patients had symptoms of anemia.

For the analysis of blood samples the GEM Premier 3000 testing unit was used.

For the descriptive statistical analysis IBM SPSS 18.0 was used. Student t-test and $\chi 2$ test were analyzed. Frequency distributions were analyzed using Kruskal-Wallis test. Linear and multiple regressions were used to determine the relationship between variables. Statistical significance was set at $p<0.005$.

Results and discussions

Descriptive statistics showed a slightly higher frequency of male cases (53.7%, sex ratio 1.15/1). Kruskal Wallis test revealed the gender homogeneity of the study groups (Chi-square = 2.40, df = 2, p = 0.301). In the groups receiving transfusion there was a slightly higher percentage of male subjects, 57.2% in the TNX group and 51.1% in the ABRD group compared to 44.9% in the control group, but the difference was not statistically significant. With a variance of 20%, patients' age ranged from 21 to 90 years, with a mean of 62.38 ± 12.35 years and a median of 63 years.

The study groups were homogeneous with respect to mean age (p = 0.059), although it was slightly lower in the groups receiving transfusion compared to controls (61.89 years - TNX; 60.18 years- ABRD *vs* 65.90 years - C). By age groups, most patients receiving transfusion were aged 60-69 years (29.6% TNX and 33.3% ABRD), while most controls were 70-79 years of age (44.9%).

Depending on diagnosis, the number of RBCT units administered after surgery was significantly higher in patients with trochanteric fractures (TF) and femoral neck fractures (FNF),40 and 20.6%, respectively. Of the patients with aseptic necrosis of femoral head (ANFH) and hip osteoarthritis (HO) 64.4% and 38.9%, respectively did not receive RBCT (Chi-square = 15.55, df = 3, p = 0.001).

Depending on the surgical maneuver, postoperative RBCT was significantly more frequently administered in patients with cemented total hip arthroplasty (CTHA) - 22.5%, bipolar hemiarthroplasty (BH) and Austin-Moore arthroplasty (AMA) -19.2%. No RBCT received 45.8% of patients who underwent uncemented total hip arthroplasty (UCTHA) and 66.7% of those who underwent CTHA (Chi-square = 7.0, df = 3, p = 0.03).

Kruskal Wallis test showed that a higher number of RBCT units were significantly more frequently administered postoperatively in group C (Chi-square = 28.70, df = 2, p = 0.001) compared to TNX and ABRD groups. Comparing the frequency distributions of RBCT administration, significantly higher percentages in the ABRD group compared with TNX group were found (Chi-square = 4.04, df = 2, p = 0.045).

The correlation between the number of TNX vials administered preoperatively and the number of RBCT units was indirect, moderate, statistically significant, which allows the extrapolation of results to the general population (r = -0.341; R2 = 0.1163; p = 0.001). In over 34% of patients, the preoperative TNX administration decreased the postoperative blood requirements.

RBCT	HO		ANFH		FNF		TF	
(unit)	n	%	n	%	n	%	n	%
0	65	38.9	29	64.4	8	27.6		
1	78	46.7	12	26.7	15	51.7	3	60.0
2	17	10.2	4	8.9	5	17.2	2	40.0
3	7	4.2			1	3.4		

Table 1
DISTRIBUTION OF CASES ACCORDING TO DIAGNOSIS AND REQUIRED RBCT UNITS

RBCT	UCTHA		CTHA		BH/AMA	
(unit)	n	%	n	%	n	%
0	81	45.8	12	27.9	9	34.6
1	75	42.4	21	48.83	12	46.2
2	15	8.5	9	21.0	4	15.4
3	6	3.4	1	2.32	1	3.8

Table 2
DISTRIBUTION OF CASES ACCORDING TO SURGICAL MANEUVER AND RBCT

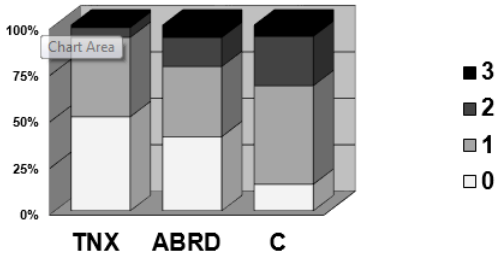

Fig 2. Distribution of the number of RBCT units by study groups

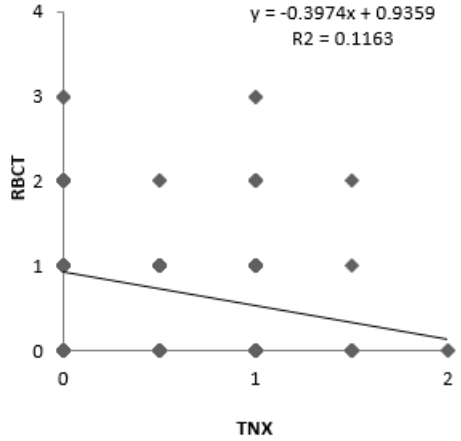

Fig 3. Correlation between the number of TNX vials and RBCT units (r= -0.341; R^2=0.1163; p=0.001)

Preoperatively, Hb level ranged from 8.20 mg/dLin TNX group to 17.20 mg/dLin group C. In ABRD (13.87 mg/dL) and TNX (13.74 mg/dL) groups significantly higher mean Hb levels compared to group C (13.09 mg / dL) (p = 0.015) were recorded. The mean Hb levels at 12 h postoperatively (ΔHb12) decreased significantly in all groups (p = 0.001), without significant differences (p = 0.093). The mean Hb levels at 24 h (ΔHb24) decreased significantly in all groups compared to those recorded preoperatively (p = 0.001), with a mean level significantly lower in the TNX group compared to groups ABRD and C groups (p = 0.001).

Our results show a lower efficacy of ABRD compared to C ($\Delta Hb_{24\,C}$ = 3.1mg dL compared $\Delta Hb_{24\,ABRD}$ = 3.33 mg/dL, p = 0.001), table 3.

No postoperative thromboembolic events were recorded

Postoperative bleeding is a factor of major importance that has an immediate impact on mortality and morbidity after hip arthroplasty. M*aintaining Hb levels in* elderly patients is an important goal because of the many associated comorbidities. It is known that postoperative blood transfusion increases by 1.5 times the risk for thromboembolic events [10]. A variety of blood salvage techniques have been used, with various administration methods and complication rates [9, 11, 12]. According to Fiona E. Ralley [13], there is a trend toward increasing use of antifibrinolytic agents as a method of blood salvage (from 0 to 11.2% in the past 7 years). Studies have shown that the use of TNX in primary hip arthroplasty causes a smaller, statistically significant decline in Hb level compared to the control group [4, 7, 8, 13, 14-19].

The 2016 study of Bryan S et al. comparing the efficacy of tranexamic acid versus reinfusion drains in primary total joint arthroplasty identified a smaller decline in ΔHb level in patients receiving tranexamic acid (p <0.0001 compared with controls and p <0.0061 compared with ABRD [5], but they used a hip and knee arthroplasty patients cohort.

Many studies have reported different TNX doses administered before surgery [16, 17]. In their analysis, Ralley et al. [20] state that the ideal dose of preoperative TNX bolus in patients with primary hip arthroplasty is in the range 15-35 mg/kg. The dose used in our study was in the above mentioned range and had a statistically comparative effectiveness.

The study has several limitations. We conducted a retrospective database analysis,the accuracy of the obtained results depending on the quality of data collection. To minimize these errors, a single team member was responsible for data collection. However, although the study was nonrandomized, uncontrolled and the study groups did not have the same number of patients, the results are statistically significant, the groups being homogeneous according to Kruskal Wallis test (Chi-square = 2.40, df = 2, p = 0.301).

Study group	N	Mean	Std deviation	Std. error	Confidence interval		Min	Max	ΔHb	p
					- 95%CI	+95%CI				F_{ANOVA} test
Preoperative										
TNX	152	13.74	1.40	.11	13.51	13.96	8.20	16.61		0.015
ABRD	45	13.87	1.47	.22	13.43	14.31	9.00	16.40		
C	49	13.09	1.71	.24	12.60	13.58	8.50	17.20		
Postoperative-12 hours										
TNX	152	10.75*	1.38	.11	10.53	10.97	6.80	14.90	2.99	0.093
ABRD	45	10.65*	1.31	.20	10.25	11.04	7.40	13.30	3.22	
C	49	10.26*	1.33	.19	9.88	10.64	7.60	12.70	2.83	
Postoperative-24 hours										
TNX	152	10.73*	1.17	.10	10.54	10.92	7.10	14.60	3.01	0.001
ABRD	45	10.54*	1.49	.23	10.08	10.99	6.90	13.20	3.33	
C	49	9.99*	1.05	.15	9.69	10.30	7.90	12.70	3.10	

* p=0.001 postoperatively vs preoperatively

Table 3
DESCRIPTIVE STATISTICAL INDICATORS OF Hb (mg/dL) BY STUDY GROUPS

Secondly, in order to assess the need for postoperative blood, Hb levels were used as a marker, although other factors also influence the perioperative decline in Hb level, such as administration of fluids for restoring the electrolyte balance [20].

In the comparative analysis we did not take into account the patients' coagulation profile. All patients in the 3 groups underwent surgical trauma, which does not require coagulation profile testing by measuring the preoperative D-dimer levels [21].

Another limitation may be the use spinal anesthesia, know being the fact that hypotension may minimize blood loss [3], fact contradicted by Zufferey et al. in a meta-analysis [18].

However, our study has several strengths. All patients were operated on by the same technique, *the same* surgical team and the same anesthetist, thus increasing the reproducibility of the study. The patients included in the study groups received different types of implants and the groups were characterized by a wide age range of patients, thus increasing the statistical significance.

According to Fiona E. Ralley [13], TMX use is associated with a lower rate of thromboembolic complications compared to the control group. Similar to Poeran et al. no thromboembolic, cardiac, renal or allergic complications were recorded in the study groups [16, 17, 20, 22-25].

Although the use of reinfusion drains has its proponents [26], recent data show low efficacy compared to TMX [2, 5, 11, 12]. Our results showed that ABRD is less effective in maintaining the ΔHb_{24} levels compared to C (ΔHb_{c} = 3.1mg/dL *versus* ΔHb_{ABRD} 3.33 mg / dL, p = 0.001).

Conclusions

A single tranexamic acid dose of 15 mg/kg administered one hour before incision is more effective than drains in reducing the need for postoperative allogeneic blood transfusion in patients who underwent primary hip arthroplasty (ΔHb_{TNX} = 3.01mg/dL, p = 0.001).

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