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Is there a difference between tranexamic acid application routes in hip hemiarthroplasty?

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ABSTRACT

Objectives: This study aimed to define the optimal efficacy route of tranexamic acid treatment given during hemiarthroplasty after femoral neck fracture.

Methods: This study examined the files of patients with hip fractures over 65 years of age and treated surgically in our clinic between 2017 and 2019. Patients included in these files were grouped as non-tranexamic acid and topical and systemic tranexamic acid. Then, the demographic information, height and weight of the patient files, haemoglobin and hematocrit levels before and after the surgery, bleeding profiles, tranexamic acid dose and the route of administration, complications in postoperative follow-up, the amount of fluid coming from the drain and duration of drainage, postoperative intensive care follow-up duration of hospitalisation was investigated.

Results: A total of 100 patients, 50 of whom were in the control group, 25 of whom were treated with topical tranexamic acid, and 25 of whom were treated with intravenous tranexamic acid, were included in this study. Postoperative blood transfusion was applied to 60% (n = 30) of the control group, 20% (n = 5) of the topical group, and 24% (n = 6) of the intravenous group. When compared statistically, it was found that topical and intravenous groups were lower than the control group ($p = 0.001$ and $p = 0.002$, respectively), but there was no significant difference between them ($p = 0.759$). When the blood loss calculations made by the Gross method were examined, the average of the control group was 1011.5 ml (179-1837 ml), the topical group was 695.7 ml (11-2503 ml), and the intravenous group was 710.9 ml (173-11315 ml) calculated as. When analysed statistically in terms of blood loss, it was found that the control group was significantly higher than the topical and intravenous groups, but there was no significant difference between the topical and intravenous groups ($p = 0.002$).

Conclusions: Tranexamic acid applied to reduce blood loss during arthroplasty surgery can be used effectively either by topical or systemic methods.

Keywords: Femoral neck fracture, hip hemiarthroplasty, tranexamic acid

The number of hip fractures due to osteoporosis increases in the ageing world population [1]. A femoral neck fracture is a common type of hip fracture in ageing populations and is most effectively managed with hemiarthroplasty, which is reported to have relatively good outcomes [2, 3].

One of the complications of hip hemiarthroplasty in the perioperative period is bleeding [4]. Especially

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bleeding complications may cause additional problems as the patient affects early mobilisation. Due to blood loss, the postoperative blood transfusion rate is estimated to be about 18% for total hip arthroplasty (THA). Intra-operative blood loss from THA can range from 700 to 900 ml [5, 6]. In recent years, many methods have been tried to prevent this loss of blood in arthroplasty surgeries and reduce the number of allogeneic blood transfusions [7-9]. Tranexamic acid (TA), an antifibrinolytic agent, is one of these methods. TA is a small molecule that inhibits plasminogen activation and plasmin activity. In recent years, there have been publications on the use of TA during the surgical treatment of hip fractures. However, these are studies with different treatment methods or in which only TA is applied in one way [10-15]. A study comparing hemiarthroplasty with local and systemic applications with the diagnosis of femoral neck fracture could not be seen in the literature. We hypothesise that TA reduces blood loss in hip hemiarthroplasty regardless of the route of administration. This study aimed to compare TA's topical and systemic application with each other and with the control group in terms of blood loss.

METHODS

The study was approved by the local institutional review board (date – number: 18/12/2018 - 1069) and performed under the ethical standards laid down in the Declaration of Helsinki. All patients provided written informed consent before their inclusion in the study. In the study, the files of patients treated with a diagnosis of femoral neck fracture between 2017 and 2019 were retrospectively analysed. Patients over 65 years of age who underwent cemented hemiarthroplasty with the diagnosis of displaced femoral neck fracture were included in the study. From the patient files examined; patients with a pathological femoral neck fracture, history of anticoagulant and antiaggregant treatment, history of a bleeding disorder, history of ischemic heart disease, history of cerebrovascular disease, stage IV and V Chronic renal failure, non-surgical treatment, cases undergoing osteosynthesis, under 65 years of age were excluded. In the analysis based on inclusion and exclusion criteria, the data of 25 patients who were administered topical and systemic TA were obtained. In order to compare the treatment groups, the data of 50 patients with the same characteristics, who were not administered TA by any means, were examined.

All patients underwent hip hemiarthroplasty with a posterolateral approach under spinal anaesthesia in the lateral decubitus position. Antibiotic prophylaxis (2 g cefazolin) was administered to all patients an hour before the incision. A cemented femoral stem (TST®) was performed by three senior surgeons for all patients included in the study. If tranexamic acid was administered intravenously to the patient, it was administered in 100 ml saline at a 10 mg/kg dose 10 minutes before the start of surgery. Topical TA was applied to the group after capsule repair, followed by fascia repair and 2 g/50 ml TA under the fascia. All patients underwent wound drain located under the fascia for postoperative follow-up. The drain was activated 1 hour after surgery. Complete blood count and biochemical values were checked daily at postoperative 2nd hour, 6th hour and postoperative hospital stay. Allogeneic blood transfusion was performed in patients with control haemoglobin values < 8 g/dl or who developed signs of anaemia (chest pain, tachycardia and orthostatic hypotension not responding to fluid resuscitation). It was removed if the drain was below 50 cc on the first postoperative day. On the second postoperative day, the patient was mobilised under the supervision of a physiotherapist.

The Gross method was used to measure the amount of blood loss [16]. Nadler Formula was used to calculate the blood volume required for the method [17]. This formula;

Blood volume (l) = height (m) 3 x k1 + body weight (kg) x k2 + k3

The fixed values in the formula are for female gender; k1: 0.356, k2: 0.033, k3: 0.183 for the male gender as k1: 0.367, k2: 0.032, k3: 0.604 were taken as. After calculating the blood volumes of all patients, preoperative and postoperative blood losses were calculated.

The formula of the Gross method is

$V_{\text{total blood loss}}$ (ml) = Blood volume x ($Hct_{\text{preop}} - Hct_{\text{postop}}$) / Hct_{average}

Patients included in the study; demographic characteristics (age, sex, height, weight, laterality), hospitalisation and intensive care unit stay, usage and doses of tranexamic acid during surgical treatment, haemo-

globin, hematocrit, INR, PT, aPTT values, amount of fluid from surgical drains, allogeneic blood transfusion rates and amounts in postoperative follow-up, and postoperative deep vein thrombosis and periprosthetic infection complications were evaluated.

Statistical Analysis

SPSS (Statistical Package for the Social Sciences) 25.0 package program and Microsoft Excel 2016 programs were used for statistical analysis. Assuming an α error of 0.05 and 1 minus β of 0.80 when calculating power, we assumed that the mean change in haemoglobin level in patients undergoing hip fracture surgery would be 4 g/dl (standard deviation [SD] 1 g/dl). Assuming a 20% reduction in blood loss would be clinically significant (i.e. 8 g/dl), 25 patients in each group would be required to detect a change. Shapiro-Wilk test was used to determine whether or not it was in a normal distribution. These findings were compared between the independent groups using student t-test or ANOVA. The Chi-square test was used for categorical variables between independent groups. The significance limit for all statistical tests was $p = 0.05$. Results will be analysed based on a 95% confidence interval.

RESULTS

A total of 100 patients were included in this study, including 25 patients receiving topical tranexamic acid, 25 patients receiving intravenous administration, and

Table 1. Demographic data of patients

	Control	Topical	Intravenous	*p* value
Gender, n				0.079*
Female	27	20	17	
Male	23	5	8	
Age (year)	80.1 ± 8.4	79.4 ± 8.5	78.7 ± 9.6	0.807**
Laterality				0.503*
Right	19	8	13	
Left	31	17	12	
Hospitalization time (day)	11.5 ± 5.1	10 ± 3.4	9.6 ± 3.5	0.167**
Height (m)	1.64 ± 0.08	1.63 ± 0.07	1.62 ± 0.06	0.540**
Weight (kg)	68.5 ± 11.5	64.9 ± 9.9	64.9 ± 12.8	0.309**
Surgery time (min)	85.2±15.1	87.4±13.2	86.7±14.3	0.845**
Preoperative Hgb (g/dL)	11.5 ± 1.2	11.3 ± 1.2	11.8 ± 0.9	0.267**
Preoperative Hct (%)	35.8 ± 3.3	34.2 ± 3.2	35.2 ± 2.7	0.130**
Preoperative PT (sec)	12.2 ± 1.1	11.8 ± 0.8	11.7 ± 1.4	0.152**
Preoperative aPTT (sec)	27.2 ± 3.2	26.6 ± 3.9	26.7 ± 2.7	0.731**
Preoperative INR	1.05 ± 0.08	1.06 ± 0.09	1.06 ± 0.1	0.813**
Postoperative (2nd day) Hgb (g/dL)	9.6 ± 1.3	9.8 ± 1.3	9.9 ± 1.2	0.570**
Postoperative (2nd day) Hct	29.2 ± 3.9	29.7 ± 3.6	29.8 ± 3.7	0.771**
Postoperative (2nd day) PT (sec)	13.7 ± 1.6	13.4 ± 1.3	13.1 ± 1.6	0.310**
Postoperative (2nd day) aPTT (sec)	29.8 ± 4.5	28.5 ± 3.9	28.7 ± 2.0	0.331**
Postoperative (2nd day) INR	1.19 ± 0.15	1.16 ± 0.13	1.16 ± 0.13	0.680**

Hgb = hemoglobin, Hct = hematocrit, aPTT = activated partial thromboplastin time, PT = prothrombin time, INR = international normalized ratio
* Kruskal Wallis test
** Oneway ANOVA test

50 patients who had never received topical tranexamic acid. 64 (64%) of the patients were female, 36 (36%) were male, and the mean age was 79.6. Trauma causing fracture was found to be a simple fall in all patients. Forty (40%) of the fractures are right, and 60 (60%) are left femoral neck fractures. The distribution of some sociodemographic and fracture characteristics of the patients is shown in Table 1. As indicated in the table, no statistically significant difference was found between the patients divided into three groups in terms of gender, age, laterality, hospitalisation time, height and body weight. Blood samples taken before and after surgical treatment were examined in all patients. No significant difference was observed among the groups (Table 1).

Wound drainage was applied to all patients after routine surgical treatment. The drain was recorded as a mean of 246.5 ml (50-650 ml) in the control group, 124 ml (5-250 ml) in the topical group and 101.4 ml (20-250 ml) in the intravenous group. When compared statistically, it was found that topical and intravenous groups were lower than the control group ($p < 0.001$), but there was no significant difference between them ($p = 0.487$). Allogeneic blood transfusion was applied to the patients who developed anaemia during clinical follow-up. It was observed that transfusion was applied to 60% of the patients in the control group (n = 30, 1 unit of erythrocyte suspension in 6 patients, two units of erythrocyte suspension in 21 patients, three units of erythrocyte suspension in 2 patients, and four units of erythrocyte suspension in 1 patient were replaced.), 20% of the patients in the topical group (n = 5, 1 unit of erythrocyte suspension in 2 patients, and two units of erythrocyte suspension in 3 patients were replaced.), and 24% of the patients in the intravenous group (n = 6, 1 unit of erythrocyte suspension in 2 patients, and two units of erythrocyte suspension in 4 patients were replaced.) (Table 2).

Blood loss and haemoglobin differences of all patients included in the study were calculated. While calculating the haemoglobin difference, the lowest postoperative blood and preoperative blood results were used. The mean difference in haemoglobin values before and after surgery in the control group was calculated as 2.3 g/dL (0.1- 4.5 g/dL). The haemoglobin difference of patients in the topical group is 1.6 g/dl (0.1- 4.7 g/dl); patients in the intravenous group were calculated as 1.8 g/dL (0.1-3.9 g/dL). When the calculated values were analysed statistically, it was found that haemoglobin decrease significantly decreased (Table 2).

When the blood loss calculations made by the Gross method were examined, the average of the control group was 1011.5 ml (179-1837 ml), the topical group was 695.7 ml (11-2503 ml), and the intravenous group was 710.9 ml (173-11315 ml) calculated as. When analysed statistically in terms of blood loss, it was found that the control group was significantly higher than the topical and intravenous groups, but there was no significant difference between the topical and intravenous groups ($p = 0.002$) (Table 2).

In the postoperative follow-up of the patients, deep vein thrombosis (DVT) was observed in 4% (n = 2) of the control group. Similarly, when the topical and intravenous groups were examined, this complication was observed in one patient in both groups. When analysed statistically, it was calculated that there was no significant difference ($p > 0.99$) (Table 3).

Patients included in the study were examined in terms of periprosthetic infection. As a result of this examination, no complication was encountered in any patient in groups treated with topical and intravenous

Table 2. Fluid amount from patients' drains, blood transfusion rates, haemoglobin difference and blood loss

	Control	Topical	Intravenous	*p* value
Drain (ml)	246.5 ± 1.2	124 ± 83	101.4 ± 77	**< 0.001***
ABT* **	60% (n = 30)	20% (n = 5)	24% (n = 6)	**0.001****
Hgb difference (g/dL)	2.3 ± 1.12	1.6 ± 1.01	1.8 ± 1.2	**0.031***
Blood loss (ml)	1011.5 ± 419	695.7 ± 478	710.9 ± 374	**0.002***

ABT = Allogeneic blood transfusion, Hgb = hemoglobin
*Oneway ANOVA test
**Chi-square test

Table 3. Complication and mortality rates of patients

	Control	Topical	Intravenous	*P* value
DVT	4% (n = 2)	%4% (n = 1)	4% (n = 1)	> 0.99*
Periprosthetic joint infection	10% (n = 5)	0% (n = 0)	0 (n =0)	0.074* **0.028****
30-day mortality	12% (n = 6)	24% (n =6)	16% (n = 4)	0.409*
90-day mortality	20% (n = 10)	28% (n =7)	16 (n = 4)	0.564*
1-year mortality	44% (n = 22)	28 (n = 7)	24 (n = 6)	0.161*

DVT = deep vein thrombosis
*Chi-square test
**Fisher'sExact test

tranexamic acid. Periprosthetic infection developed in 10% of the patients in the control group, and a second surgical intervention was required. Allogeneic blood transfusion was applied to all of these cases during the perioperative period. When analysed statistically, no significant difference was found when the three groups were compared (p = 0.074). However, it was calculated that the infection rate was higher in the control group than patients who used tranexamic acid regardless of the route of administration (p = 0.022) (Table 3).

When the 30-day, 90-day and 1-year mortality rates of the patients included in the study were examined, it was calculated as 12%, 20% and 44% in the control group, respectively. In the topical group, these rates are 24%, 28% and 28%; in the intravenous group, it was observed as 16%, 16% and 24%. When analysed statistically, no significant difference was observed between the groups (Table 3).

DISCUSSION

Arthroplasty is used in the current treatment of hip fractures which are increasingly observed in the elderly. Blood loss during and after arthroplasty can reach up to 1800 ml [10, 18-20]. At the same time, allogenic blood transfusion rates in these patients have been reported in the literature between 20% and 60% [9, 18]. In this case, both haemorrhage amount and high blood transfusion rates may cause multiple complications [21]. Hemodynamic instability can cause severe complications in these patients whose general condition is fond [22]. This study found more blood loss and blood transfusion rates in patients in the group that we did not apply TA. Regardless of the method of administration, its application significantly reduced the need for blood transfusion.

It is available in the literature that TA used during hemiarthroplasty reduces the amount of haemoglobin decrease [10, 11]. It has also been shown that different TA administration route does not provide any advantage [23]. It has been shown that there is no difference between the method of TA application and the complication rates [23]. In this case, it may be an appropriate strategy to reduce the amount of bleeding while performing hemiarthroplasty in femoral neck fractures. The route of administration can be left to the surgeon's preference.

Emara *et al*. [23] reported in their study that the drain follow-up of control groups and tranexamic acid-treated groups decreased by approximately 50%. In our study, when we compared the control group with both the topical group and the intravenous group, half of the reduction in fluid from the drain was found. There was a difference of approximately 20 ml between the groups in which TA was applied in this study, and no statistically significant difference was found.

Our study showed a more significant decrease in blood transfusion rates in TA groups than in the literature [24, 25]. In fact, in these two studies, 15 mg/kg tranexamic acid was used as two intravenous doses, and in our study, the intravenous dose was applied as 10 mg/kg. In their studies, Kang *et al*. [12] reported that they topically applied 3 g TA and decreased the blood transfusion rate by 25%. In our study, we applied 2 gr TA and detected a 66% reduction in blood transfusion rate. Achieving the same effect with a lower dose can help reduce complications after sur-

gery.

Vascular embolism and thrombosis are the most severe complications reported after tranexamic acid administration [26]. In the literature, although it has been reported that there is no increase in complications and mortality rates of TA application in orthopaedic procedures, studies are showing that topical application may be safer [5, 10, 11, 20, 25]. There may be no difference between the application route and the possibility of developing complications in hemiarthroplasty patients. Even so, the possibility of complications associated with the use of tranexamic acid can be reduced by appropriate patient selection and appropriate administration.

Considering the data on the duration of hospitalisation, it has been reported that the administration of tranexamic acid did not significantly reduce these times. In their study, Liu *et al*. [10], the meantime of hospitalisation was 5.5 days, Lee *et al*. [11], while it was found to be approximately 20 days in their study, this average was 10.6 days in our study. This difference may have resulted from countries' health systems and sociocultural differences.

Limitations

The main limitations of our study are that the research was conducted retrospectively and a single surgeon could not perform the surgical treatments of the patients included in the study. The small number of samples included in the study, different surgical techniques and approaches are not included, and the effect of reducing bleeding on functional results is unknown. This situation can only be demonstrated by randomised controlled prospective studies with many cases.

CONCLUSION

As a result of our study to evaluate the effectiveness of tranexamic acid administration during partial arthroplasty application as a surgical method in femoral neck fractures. It has been concluded that both topical and systemically used tranexamic acid reduces blood loss and reduces blood transfusion rates.

Authors' Contribution

Study Conception: MY, Yİ, HÇ, SSD, AY, TOB, NE, HG; Study Design: MY, Yİ, HÇ, SSD, AY, TOB, NE, HG; Supervision: MY, Yİ, HÇ, SSD, AY, TOB, NE, HG; Funding: MY, Yİ, HÇ, SSD, AY, TOB, NE, HG; Materials: MY, Yİ, HÇ, SSD, AY, TOB, NE, HG; Data Collection and/or Processing: MY, Yİ, HÇ, AY, TOB, NE; Statistical Analysis and/or Data Interpretation: MY, Yİ, HÇ, AY, TOB, NE; Literature Review: MY, Yİ, HÇ, AY, NE; Manuscript Preparation: MY, Yİ, HÇ, AY, NE and Critical Review: MY, Yİ, HÇ, AY, TOB, NE.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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