Research Article

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Title: Effect of peroperative local tranexamic acid admistration on bleeding in total knee arthroplasty performed with general or spinal anesthesia.

Short title: Tranexamic acid in knee arthroplasty: anaesthetic impact.

Abstract

Purpose: This retrospective study focused on a comparative examination of the effect of local tranexamic use on postoperative bleeding in TKA surgery performed with general or spinal anaesthesia.

Materials and methods: This study analysed the postoperative bleeding amounts in 95 knees with primary osteoarthritis that underwent TKA between January 2017 and 2023. Patients undergoing TKA under general or spinal anaesthesia were separated into four groups based on whether or not local tranexamic acid was given perioperatively. Patients who underwent total knee arthroplasty under general anaesthesia were divided into two groups: group 1 if local tranexamic acid was applied, and group 2 if tranexamic acid was not applied. Patients who underwent total knee arthroplasty under spinal anaesthesia were divided into two groups: group 3 if local tranexamic acid was applied, and group 4 if tranexamic acid was not applied. Tranexamic acid administration was performed locally as 1 g injection into the surrounding soft tissues after knee arthroplasty. The postoperative hemogram alterations, drainage volume, and transfusion needs of these patients were assessed.

Results: Group 4 saw a significantly higher decline in haemoglobin levels within the first twenty-four hours following surgery, distinct from groups 1-3 (p1:0.001; p2:0.000; p3:0.001, $p<0.05$). There was no notable variance in third-day haemoglobin control values (HG3) between groups 1-4 ($p>0.05$). Postoperative haemoglobin values in Group 3 were statistically significantly higher than in Groups 1, 2, and 4 (p1:0.019;

p2:0.003; *p*<0.05). Group 4 showed considerably higher drainage values compared to groups 1-3 (*p=0.000*; *p*<0.05). The drainage values in group 1 were statistically substantially lower than those in groups 2, 3, and 4 (p1: 0.001; p2: 0.032; *p*<0.05). When evaluating a replacement threshold of 2 units (6.1%), group 3 had considerably lower blood replacement rates than group 1 (26.7%), group 2 (45.5%), and group 4 (25%) (p1:0.002; p2:0.000; *p*<0.05).

Discussion: Our study found that administering local tranexamic acid during TKA surgery, whether under general or spinal anaesthesia, has a substantial impact on postoperative bleeding and transfusion requirements. Overall, these findings suggest that local use of TXA during TKA surgery can effectively reduce postoperative bleeding, maintain haemoglobin levels, reduce drainage amounts, and reduce transfusion rates, thus potentially reducing bleeding-related complications and contributing to cost savings.

Keywords: Tranexamic acid, knee arthroplasty, blood transfusion, anesthesia, surgical drain.

Makale başlığı: Genel veya spinal anestezi ile yapılan total diz artroplastisinde peroperatif lokal traneksamik asit uygulamasının kanamaya etkisi.

Kısa başlık: Diz artroplastisinde traneksamik asit: anestezi tiplerinin etkisi.

Öz

Amaç: Bu retrospektif çalışma, genel veya spinal anestezi ile yapılan Total diz artroplastisi cerrahisinde lokal traneksamik kullanımının postoperatif kanamaya etkisinin karşılaştırmalı olarak incelenmesine odaklanmıştır.

Gereç ve yöntem: Bu çalışmada Ocak 2017-2023 tarihleri arasında TDA uygulanan primer osteoartritli 95 dizdeki postoperatif kanama miktarları analiz edildi. Genel veya spinal anestezi altında TDA uygulanan hastalar perioperatif olarak lokal traneksamik asit verilip verilmediğine göre dört gruba ayrıldı. Genel anestezi altında total diz artroplastisi yapılan hastalarda lokal traneksamik asit uygulandıysa grup 1, traneksamik asit uygulanmadıysa grup 2 olarak gruplara ayrılmıştır. Spinal anestezi altında total diz artroplastisi yapılan hastalarda lokal traneksamik asit uygulandı ise grup 3, traneksamik asit uygulanmadıysa grup 4 olarak gruplara ayrılmıştırr. Traneksamik asit uygulaması diz artroplastisi uygulandıktan sonra çevre yumuşak dokulara enjeksiyon şeklinde 1 g lokal olarak yapılmıştır. Bu hastaların postoperatif hemogram değişiklikleri, dren miktarı ve transfüzyon miktarları değerlendirildi.

Bulgular: Grup 4'te, grup 1-3'ten farklı olarak ameliyattan sonraki ilk yirmi dört saat içinde hemoglobin düzeylerinde anlamlı düzeyde daha yüksek bir düşüş görüldü (p1:0,001; p2:0,000; p3:0,001, *p*<0,05). Üçüncü gün hemoglobin kontrol değerlerinde (HG3) grup 1-4 arasında kayda değer bir farklılık yoktu (*p*>0,05). Grup 3'te ameliyat sonrası hemoglobin değerleri Grup 1,2 ve 4'e göre istatistiksel olarak anlamlı derecede yüksekti (p1:0,019; p2:0,003; *p*<0,05). Grup 4'te grup 1-3'e göre anlamlı derecede yüksek dren hacimleri görüldü (*p*=0,000; *p*<0,05). Grup 1'deki drenden gelen miktarları grup 2-4'e göre istatistiksel olarak anlamlı derecede düşüktü (p1:0,001; p2:0,032; *p*<0,05). 2 ünite (%6,1) replasman miktarı değerlendirildiğinde, grup 3'te kan replasman oranları grup 1 (%26,7), grup 2 (%45,5) ve grup 4'e (%25) göre oldukça düşüktü (p1:0,002; p2: 0,000; *p*<0,05).

Tartışma: Çalışma, ister genel ister spinal anestezi altında olsun, TDA ameliyatı sırasında lokal traneksamik asit uygulamasının postoperatif kanama ve transfüzyon gereksinimleri üzerinde önemli bir etkiye sahip olduğunu buldu. Genel olarak bu bulgular, TDA ameliyatı sırasında traneksamik asitin lokal kullanımının postoperatif kanamayı etkili bir şekilde azaltabileceğini, hemoglobin düzeylerini koruyabileceğini, dren miktarlarını azaltabileceğini ve transfüzyon oranlarını azaltabileceğini, dolayısıyla potansiyel olarak kanamayla ilişkili komplikasyonları azaltabileceğini ve maliyetlerin azalmasına katkıda bulunabileceğini göstermektedir.

Anahtar kelimeler: Traneksamik asit, diz artroplastisi, kan transfüzyonu, anestezi, cerrahi dren.

Introduction

One of the orthopaedic surgical procedures that is most frequently carried out is total knee arthroplasty (TKA). The necessity of TKA increases throughout various nations as the population ages. TKA is performed to increase function and decrease pain in patients with end-stage gonarthrosis**.** Blood loss during and after this surgical procedure is a serious problem. In total knee arthroplastic surgery, the percentage of transfusions ranged from 18% to 68% [1]. Allogenic blood product transfusions increase the risk of morbidity. Several studies have identified causes that increase the risk of transfusion-related mobiditis, such as allergic reactions, hemolytic reactions, disease transmission, surgical area infection, and venous thromboembolism [1-4]. Various strategies have been developed to limit peroperative

and postoperative blood loss. The use of tourniquets, autologous blood transfusion, surgical clamping of the drain, controlled hypotensive anaesthesia, and the use of various drugs such as tranexamic acid can be examples of these strategies [5, 6]. Tranexamic acid (TXA) is an amino acid derivative of synthetic lysine that has been found in numerous studies to minimise bleeding and blood transfusions after total knee arthroplasty [7, 8]. The use of spinal anaesthesia in total knee arthroplasty has been associated with lower complication rates [9]. However, the relationship between these benefits and the type of anaesthetic should be studied further. The purpose of this study is to determine whether the local use of TXA during total knee arthroplasty (TKA) under various forms of anaesthesia leads to significantly different outcomes in terms of bleeding volume and transfusion requirements.

Materials and methods

The patient information from the hospital's data system is for patients who underwent total knee arthroplasty due to gonarthrosis between January 2017 and January 2023. Ethics committee approval was received for the study. The investigation was conducted at a single location and followed a retrospective technique.

The demographic characteristics of patients will be reviewed retrospectively. The study comprised individuals aged 60 to 90 who received total knee arthroplasty for primary gonarthrosis. During surgery, patients were separated into two groups: general anaesthesia and spinal anaesthesia. In addition, patients were separated into two subgroups: those who got 1 gr of local tranexamic acid during surgery and those who did not. Tranexamic acid administration was performed locally as 1 g injection into the surrounding soft tissues after cemented total knee arthroplasty. The incision site was then sutured according to the anatomical plan by applying a surgical drain. Intravenous tranexamic acid was not administered to the patients. Patients under 60 and over 90 who had received total knee arthroplasty were eliminated from the research. Patients who underwent revision arthroplasty due to reasons such as infection, trauma, and aseptic loosening were elininated from the research. Additionally, patients with rheumatologic and systemic diseases involving joint issues were also dismissed from the research. The preoperative and postoperative hemogram results, amount of bleeding from drains, drain durations, and blood transfusion requirements of patients who had total knee arthroplasty surgery in our clinic will be compared. In total knee arthroplasty, the effect of local tranexamic acid

on bleeding and the requirement for transfusions in the postoperative phase will be studied in connection with the present anaesthesia type. Patients undergoing total knee arthroplasty had their hemograms taken preoperatively and on the first, third, and fifth days following surgery.

A tourniquet was applied to all patients during the surgery. Surgical drains were applied to all patients, and the volumes of drainage were recorded from medical records. The surgical drains were extracted at the 24th postoperative hour. Bleeding volumes from the drain and transfusion amounts were obtained from patient records. Two methods were evaluated in the study. Group 1: 1 g of tranexamic acid was applied locally to the knee joint after cemented TKA with general anesthesia. Group 2: local tranexamic acid was not applied to the knee joint after cemented TKA with general anesthesia. Group 3: 1 g of tranexamic acid was applied locally to the knee joint after cemented TKA with spinal anesthesia. Group 4: Local tranexamic acid was not applied to the knee joint after cemented TKA with spinal anaesthesia.

Statistical analysis

The study's findings were analysed using the IBM SPSS Statistics 22 (IBM SPSS, Turkey) statistical analysis programme. The Shapiro-Wilk test was used to determine whether the parameters had a normal distribution. A One-Way ANOVA test was employed to compare statistical methods such as mean, standard deviation, and frequency, as well as groups with normally distributed parameters, in the study data evaluation. For comparisons between groups with non-normally distributed parameters, the Kruskal-Wallis test and Dunn's test were utilised to identify the group responsible for the differences. The Wilcoxon signed-rank test was used to analyse non-normally divided parameters within groups. To analyse qualitative data, we employed the Fisher-Freeman-Halton and Chi-square tests. A *p*-value of <0.05 indicated the significance level.

Results

The research included 95 patients who underwent TKA between January 2017 and January 2023. The patients were between 50 and 89 years of age, with an average of 67.78±8.23. 17.9% of cases were male, and 82.1% were female. 51.57% of patients have been operated on with gonarthrosis on the right and 48.42% on the left (Table 1). In the study, they were examined in 4 groups: 15 patients (15.8%) in Group 1, 11 patients (11.6%) in Group 2, 33 patients (34.7%) in Group 3, and 36 patients (37.9%) in Group 4. The first 24 hours of haemoglobin (HG) decrease (the

change in HG1 compared to HG0) ranges from -0.1 to 4.8 g/dl, with an average of 1.69±1.13 g/dl and a median of 1.5 g/dl. Total HG decrease (variation in HG4 compared to HG0) range from 0 to 5.7 g/dl, with an average of 2.81±1.33 g/dl and a median of 2.9 g/dl. (Table 2). The blood loss from the drain ranges from 40 to 220 ml, with an average of 95.11±32.55 ml and a median of 90 ml. 50.5% of patients were given peroperative local tranexamic acid, while 49.5% were not given tranxamic acid. 27.4% of the patients received general anaesthesia and 72.6% test spinal anaesthesia. In 54.7% of patients, no blood replacement was performed, in 22.1% 1 unit, in 21.1% 2 units, and in 2.1% 3 units (Table 3). There were no statistically notable variations between the groups in terms of average age or gender distribution (p>0.05).

Furthermore, there was little change in the distribution of operated sides across groups 1-3, and 4 (p>0.05) (Table 4).

There were substantial distinctions between groups in terms of HG1 (haemoglobin control value at 24th hours) (p=0.002; p<0.05). Binary comparisons revealed that Group 4 had significantly lower HG1 values compared to Groups 1-3 (p1:0.018; p2:0.046; p3:0.000; p<0.05). Nevertheless, there were not any significant differences in HG1 values between the other groups (p>0.05) (Table 5). There was no statistically important difference between groups 1-4 in terms of HG3 (haemoglobin control value on day 3) (p>0.05). There were important distinctions comparing each group in terms of HG5 (the 5th day haemoglobin control value) (p=0.010; p<0.05). Binary comparisons revealed that Group 3 had considerably higher HG5 values than Groups 1, 2, and 4 (p1:0.019, p2:0.003, p<0.05).

There is not a significant variation in HG5 readings between the other groups (Groups 1, 2, and 4) (p>0.05) (Table 5).

In groups 1-4, the decreases in HG1, HG3, and HG5 levels were statistically significant for HG0 (preoperative haemoglobin) (p<0.05) (Figures 1 and 2). The first 24-hour decreases in haemoglobin (HG) levels differed significantly between groups (p=0.000; p<0.05). Comparisons were made to determine from which group the differences stems. In group 4, the first 24 hours of HG decreases were statistically significantly higher compared to groups 1-3 (p1:0.001; p2:0.000; p3:0.001, p<0.05). The first 24-hour haemoglobin (HG) declines did not differ significantly from the other groups (Groups 1-3; p>0.05) (Table 6).

There are numerically significant variations between the groups in terms of total haemoglobin (HG) reductions (p=0.007; p<0.05). Pairwise comparisons revealed that

Group 4 experienced a substantially larger total HG drop than Groups 1-3 (p1:0.002; p2:0.014; $p<0.05$). Although no statistically significant difference in overall HG reduction values was seen between the groups ($p>0.05$) Table 6).

Drain values differed significantly between groups ($p=0.000$; $p<0.05$). Pairwise comparisons were used to identify the source of these differences. Drain values in group 4 were substantially higher compared to groups 1-3 ($p=0.000$; $p<0.05$). Conversely, in group 1, the drain values were statistically significantly lower than in groups 2, 3, and 4 (p1:0.001; p2:0.032; $p<0.05$). Drain values did not differ significantly across the other groups ($p>0.05$) (Table 7).

There were substantial differences in blood replacement distribution rates between the groups ($p=0.002$; $p<0.05$). Pairwise comparisons were used to identify the source of these differences. Group 3 had significantly lower blood replacement rates compared to group 1 (26.7%), group 2 (45.5%), and group 4 (25%) at a replacement level of 2 units (6.1%) (p1:0.002; p2:0.000; $p<0.05$). There were insufficiently significant variations in blood replacement distribution rates among the other groups ($p>0.05$) (Table 7).

Discussion

The results of our study showed a significant decrease in haemoglobin levels in the first twenty-four hours after surgery in the group that underwent total knee arthroplasty with spinal anaesthesia and did not receive local tranexamic acid (Group 4). There was no significant difference between the groups in haemoglobin control values on the third day. Postoperative haemoglobin values in the group that underwent total knee arthroplasty with spinal anaesthesia and local tranexamic acid was not administered (group 3) were statistically significantly higher than the other groups. Group 4, in which total knee arthroplasty was performed with spinal anaesthesia and local tranexamic acid was not administered, had significantly higher drain volumes compared to groups 1-3. The drain volumes in group 1 were statistically significantly lower than the other groups. When 2 units (6.1%) replacement amount was evaluated, blood replacement rates in group 3 were significantly lower than the other groups.

Total knee arthroplasty (TKA) serves as an effective solution for restoring function and alleviating pain in patients with advanced arthritis. It is estimated that approximately 700,000 cases are documented annually in the United States [10]. As

the number of total knee arthroplasty procedures increases, various strategies are being explored to mitigate bleeding-related complications. Among these strategies, studying the relationship between the use of tranexamic acid and the type of anaesthesia is likely to help progress these approaches.

Studies in the literature have revealed that women have a higher incidence and that the prevalence increases with age [11-13]. In our study, 82.1% of the patients were female, which aligns with findings in the literature indicating a higher prevalence of total knee arthroplasty among women. Pierson et al. [14] reported that patients who underwent TKA had an average decrease in haemoglobin levels of 3.8 g/dL. In our study, changes in the patients' haemoglobin values on the 1st, 3rd, and 5th days were evaluated. The average haemoglobin (HG) decrease in the first 24 hours is 1.69±1.13 g/dl. The average total HG reduction was 2.81±1.33 g/dl. We examined the dynamics of haemoglobin decline and postoperative bleeding following total knee arthroplasty (TKA). The data demonstrated that a significant amount of total haemoglobin drop occurred within the first 24 hours after surgery, highlighting the importance of early postoperative blood loss. This finding is consistent with prior studies, which found a considerable drop in haemoglobin levels within the first three days after TKA [15, 16].

In our study, haemoglobin levels dropped dramatically in the first few days, and the average haemoglobin values on the fifth day were comparable to those on the third day. In our study, the haemoglobin decrease in the early period (first day) after total knee arthroplasty was highest in Group 4. In our opinion, the main explanation for this could be a lack of local tranexamic acid administration.

Another possibility is that spinal anaesthesia may have a longer-term effect on peripheral vascular dilatation. Sympathetic nervous system blockade after spinal anaesthesia application It causes hypotension by reducing venous return and systemic vascular resistance [17]. Venous dilatation is more effective than arterial dilatation in the formation of hypotension [18]. However, no significant difference in hemoglobin decline was observed between the groups by the 3rd postoperative day. Interestingly, haemoglobin values were notably higher in Group 3 by the 5th postoperative day, suggesting reduced blood loss compared to other groups in the late postoperative phase. In group 1, TKA was administered under general anaesthesia, while group 3 had spinal anaesthesia. Tranexamic acid was administered to both groups. However, the amount of bleeding in group 3 on the 5th postoperative day was significantly lower than in group 1, suggesting that spinal

anesthesia may have an effect on bleeding in the late period. A definitive judgement cannot be reached. However, the effect of anaesthesia type on late bleeding in total knee arthroplasty needs to be investigated with further studies. Additionally, when the preoperative haemoglobin amounts were compared with the postoperative 1st, 3rd, and 5th days in each group, the haemoglobin amounts decreased significantly. There are studies in the literature supporting that haemoglobin values decrease for more than 3 days after total knee arthroplasty [19].

Blood loss from the drain ranged between 40 and 220 ml, with a mean of 95.11±32.55 ml. The quantity of blood emanating from the drain was observed to be consistent with what is reported in the literature [20]. Our study compared the amount of bleeding from the drain. There were statistically significant variations between the groups in the drain values. The amount of bleeding from drain in group 4 was statistically significantly higher compared to groups 1-3. In group 1, the amount of bleeding from drain was statistically significantly lower than in groups 2, 3, and 4. The literature supports that the admission of tranexamic in total knee arthroplasty reduces the amount of bleeding [7, 21-23]. The amounts of blood coming from the drain between groups 1 and 3, where tranexamic acid was applied, and groups 2 and 4, where tranexamic acid was not applied, are significantly different. It shows that the type of anaesthesia is also effective, as is the effect of tranexamic acid.

In one of the oldest systematic reviews, Rodgers et al.'s [24] study evaluating complications related to general anesthesia and regional anaesthesia found that regional anaesthesia had a lower transfusion requirement. Our study also evaluated the amount of blood transfusion between groups. The rate of 2 units of blood transfusion was significantly lower in Group 3, where spinal anaesthesia and local tranexamic acid were administered.

This significant value suggests that tranexamic acid and spinal anaesthesia have a bleeding-reducing effect. In a meta-analysis comprising 12 studies with 1189 patients, Yue et al. [25]. They found that local tranexamic acid (TXA) decreased blood loss by an average of 280.65 mL, leading to a decrease in the need for blood transfusion. In the study by Chapman et al. [26], regional anaesthesia was associated with a decreased likelihood of perioperative blood transfusion compared to combined anaesthesia and general anaesthesia. However In the study of Lee et al. [27], they did not find any difference in transfusion rates between patients receiving general and spinal anaesthesia during total knee arthroplasty.

In our study, the transfusion rates in group 4, where spinal anaesthesia was administered without local tranexamic acid, were found to be comparable to the other groups where general anaesthesia was utilised. Our study's weaknesses include its limited sample size and retrospective nature. The study's strength is that it examines the effect of local tranexamic acid usage on bleeding in total knee arthroplasty against general or spinal anaesthesia.

The findings of this study hold potential significance for clinical practice. They are consistent with prior studies demonstrating the usefulness of local tranexamic acid administration in minimising bleeding and the need for blood transfusions in total knee arthroplasty. However, more research is needed to determine the effect of anaesthesia types in relation to local TXA on bleeding in total knee arthroplasty.

In conclusion, our study emphasises the importance of local tranexamic acid administration in managing blood loss during TKA, particularly in mitigating early postoperative decreases in haemoglobin and reducing the need for blood transfusions. Understanding the interplay of anaesthesia types and tranexamic acid application contributes valuable insights to optimising perioperative care in TKA procedures.

Conflict of interest: No conflict of interest was declared by the authors.

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Ethics committee approval: Permission was received for the study from the Health Sciences University Şişli Hamidiye Etfal Training and Research Hospital SUAM Clinical Research Ethics Committee (permission date: 13/06/2023, and permission number: 3971).

Authors' contributions to the article

B.B. created the main idea and hypothesis of the study. B.B. and E.I. developed the theory and edited the materials and methods section. I.T. evaluated the data in the results section. Discussion section of the article written by B.B. Reviewed, edited and approved by E.I. Additionally, all authors discussed the entire study and approved the final version.

Table 1. Distribution of general features

		Min-Max	Mean±Sd (median)
Age		50-89	68.78±8.23
		n	**%**
Gender	**Male**	17	17.9
	Female	78	82.1
Side	**Right**	49	51.57
	Left	46	48.42

Table 2. Information on HG levels

	Min-Max	Ort±SS (medyan)
HG0	10-15.8	13.11±1.18 (13.1)
HG1	8.6-15.2	11.42±1.3 (11.4)
HG3 (n=94)	8.2-14.3	10.5±1.38 (10.2)
HG5 (n=90)	7.6-14.2	10.25±1.27 (10.1)
HG decreases in the first 24 hours	(-0.1)-4.8	1.69±1.13 (1.5)
Total HG decrease	0-5.7	2.81±1.33 (2.9)

Table 3. Distribution of operating parameters

		Min-Max	Mean±Sd (median)
The amount of the drain (ml)		40-220	95.11±32.55 (90)
		n	**%**
Tranexanic acid usage	**TXA unused**	47	49.5
	TXA used	48	50.5
Type of Anesthesia	**General**	26	27.4
	Spinal	69	72.6
Blood replacement	**0**	52	54.7
	1	21	22.1
	2	20	21.1
	3	2	2.1

Table 4. Evaluation of general characteristics between groups

	General anesthesia Txa used Group 1	General anesthesia Txa unused Group 2	Spinal anesthesia Txa used Group 3	Spinal anesthesia Txa unused Group 4	*p*
	(Min-Max)-(Median±SD)	**(Min-Max)-(Median±SD)**	**(Min-Max)-(Median±SD)**	**(Min-Max)-(Median±SD)**	
Age	(57-84)-(68.87±7.36)	(57-76)-(66.36±6.34)	(55-89)-(69.85±9.06)	(50-86)-(68,5±8.43)	[1]**0.678**
	n (%)	**n (%)**	**n (%)**	**n (%)**	
Gender					
Male	1 (6.7%)	0 (0%)	9 (27.3%)	7 (19.4%)	[2]**0.150**
Female	14 (93.3%)	11 (100%)	24 (72.7%)	29 (80.6%)	
Side					
Right	11 (73.33%)	5 (45.45%)	16 (48.48%)	17 (47.22%)	[3]**0.770**
Left	4 (26.66%)	6 (54.54%)	17 (51.51%)	19 (52.77%)	

[1]One-Way Anova Test [2]Fisher Freeman Halton Test [3]Ki-Kare Test

Table 5. Evaluation of Hemoglobin levels between groups

	General anesthesia Txa used Group 1	General anesthesia Txa unused Group 2	Spinal anesthesia Txa used Group 3	Spinal anesthesia Txa unused Group 4	*p*[1]
	(Min-Max)-(Median±SD (median))	**(Min-Max)-(Median±SD (median))**	**(Min-Max)-(Median±SD (median))**	**(Min-Max)-(Median±SD (median))**	
HG0	(10.9-14.9)-(12.9±1.1 (12.9))	(10.5-13.3)-(12.08±1.02 (12))	(10.9-15.8)-(13.36±1.18 (13.4))	(10-15.6)-(13.29±1.11 (13.2))	**0.016***
HG1	(10-13.3)-(11.72±0.88 (11.9))	(9.4-12.7)-(11.01±1.14 (11))	(8.6-15.2)-(11.95±1.29 (12))	(8.9-14.3)-(10.95±1.31 (10.8))	**0.002***
HG3	(8.6-13.2)-(10.74±1.44 (10.5))	(8.8-12.8)-(10.48±1.51 (9.9))	(9.2-14.3)-(10.79±1.31 (10.3))	(8.2-13.5)-(10.16±1.37 (9.9))	**0.117**
HG5	(8.8-12.2)-(10.19±1 (10.3))	(7.7-12.2)-(9.63±1.47 (9.6))	(9.5-14.2)-(10.8±1.2 (10.5))	(7.6-13.4)-(9.9±1.25 (10))	**0.010***
***HG0-HG1 p*[2]**	0,001*	0,004*	0,000*	0,000*	

HG0-HG3 p²	0,001*	0,009*	0,000*	0,000*
HG0-HG5 p²	0,001*	0,018*	0,000*	0,000*

*[1]Kruskal-Wallis Test [2]Wilcoxon Signed Ranks Test *p<0.05*

Table 6. Evaluation of first 24 hours and total Hg decreases between groups

	General anesthesia Txa used Group 1	**General anesthesia Txa unused Group 2**	**Spinal anesthesia Txa used Group 3**	**Spinal anesthesia Txa unused Group 4**	***p***
	(Min-Max)-(Median±SD (median))	**(Min-Max)-(Median±SD (median))**	**(Min-Max)-(Median±SD (median))**	**(Min-Max)-(Median±SD (median))**	
HG decrease in the first 24 hours	(0.1-2.5)-(1.18±0.71 (1.1))	(-0.1-3.6)-(1.06±0.98 (1))	(0.1-4.8)-(1.41±1.06 (1.3))	(0.6-4.7)-(2.34±1.09 (2.3))	**0.000***
Total HG decrease	(0.1-4.4)-(2.66±1.28 (2.6))	(0-5.4)-(1.94±1.66 (1.1))	(0.4-4.6)-(2.56±1.04 (2.7))	(1.1-5.7)-(3.38±1.28 (3.3))	**0.007***

*Kruskal-Wallis Test *p<0.05*

Table 7. Evaluation of the amount of blood coming from the drain and blood replacement parameters between groups

	General anesthesia Txa used Group 1	General anesthesia Txa unused Group 2	Spinal anesthesia Txa used Group 3	Spinal anesthesia Txa unused Group 4	*p*
	(Min-Max)-(Median±SD (median))	(Min-Max)-(Median±SD (median))	(Min-Max)-(Median±SD (median))	(Min-Max)-(Median±SD (median))	
Amount of drain	(40-150)-(66±26.61 (60))	(70-200)-(106.36±40.38 (90))	(50-220)-(84.24±28.59 (80))	(85-160)-(113.75±21.86 (112.5))	[1]**0.000***
	n (%)	**n (%)**	**n (%)**	**n (%)**	
Amount of blood replacement					[2]**0.002***
0	10 (66.7%)	3 (27.3%)	27 (81.8%)	12 (33.3%)	
1	1 (6.7%)	3 (27.3%)	4 (12.1%)	13 (36.1%)	
2	4 (26.7%)	5 (45.5%)	2 (6.1%)	9 (25%)	
3	0 (0%)	0 (0%)	0 (0%)	2 (5.6%)	

*[1]Kruskal-Wallis Test [2]Ki-Kare Test *p<0.05*

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