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Research Article

Topical Tranexamic Acid Reduces Postoperative Blood Loss in Patients Undergoing Primary Total Hip Arthroplasty with the Drain-Clamping

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Abstract

Purpose: To evaluate the effect of topical epinephrine and tranexamic acid (TXA) with the drain-clamping protocol on postoperative blood loss and the frequency of allogenic blood transfusion (ALBT) after primary total hip arthroplasty.

Methods

We retrospectively reviewed the consecutive case series which included three groups: TXA with epinephrine (R), TXA (T) and saline (S).

Results: Mean drain bleeds of groups R, S, and T were 287 ml, 367 ml, and 268 ml, respectively. The difference between the values of groups S and T was significant. Mean decreases in the haemoglobin (Hb) level of groups R, S, and T were 1.94 g/dL, 2.80 g/dL, and 2.39 g/dL, respectively. The difference between the values of groups R and S was significant. There was no significant difference between the values of groups R and S. No ALBT was executed and no complications were associated with TXA in this series.

Conclusions: The overall results indicated that topical TXA with drain clamping was effective and safe for reducing postoperative blood loss after THA, but the effect of additive epinephrine was not evident.

Keywords: *Arthroplasty; Replacement; Hip; Tranexamic Acid; Postoperative Haemorrhage*

Introduction

Although the estimated risk of transfusion-associated disease has decreased recently [1], allogenic blood transfusion (ALBT) is still a concern for patients undergoing orthopaedic surgeries. As operative techniques for total hip arthroplasty (THA) have evolved and peri operative blood management has improved, the necessity of ALBT has decreased in primary THA. Blood management methods include pre donated autologous blood transfusion (PR-ABT), intraoperative autologous blood transfusion (IE-ABT), controlled hypotension, and the administration of tranexamic acid (TXA). TXA reportedly decreases bleed in various surgeries, particularly joint Arthroplasties [2,4]. Many recent reports have indicated that a topical dosage of TXA is useful [5,6]. The topical administration of TXA may be safer than intravenous (IV) administration because it reduces potential systemic risks and allows higher drug concentration at the site [2]. The drain-clamping technique has been recognised as useful and is commonly used because it keeps local drug concentrations high, and the drain clamp itself may suppress bleeding [7,8]. Topical epinephrine is also confirmed as useful for providing a haemostatic effect via shrinkage of the peripheral artery; in total knee arthroplasty (TKA), epinephrine with drain clamping was reportedly effective [7,8]. At first, we utilized the drain-clamping concomitant to the retrograde injection of antibiotics solution through the drain for hemostasis and the prevention of periprosthetic joint infection. Then we added TXA and epinephrine to gain further hemostatic effect. To evaluate the effect of topical epinephrine and TXA dosage with the drain-clamping protocolon the reduction of blood loss and frequency of ALBT, we retrospectively reviewed the consective case series of three groups (TXA with epinephrine, TXA, and saline).

Methods

Ninety consecutive primary THA cases performed between April 2012 and July 2014 by one surgeon at our hospital were included and assessed. Surgeries were performed with a minimally invasive minitrochanteric direct lateral approach [9] in a lateral decubitus position. The solution described below was retrogradely injected into the joint space through the drain after closure of the deep fascia.

Our routine postoperative management protocol was as follows: We clamped the drain for 1 hr and then opened the clamp with atmospheric pressure, removed the drain on the first day postoperatively, and measured the total blood loss. We performed blood tests including haemoglobin (Hb) on the first and seventh days. Postoperative gait exercise started on the second day postoperatively with full weight bearing allowed in all cases. To prevent deep venous thrombosis (DVT), mechanical prophylaxis, including pneumatic compression with foot pumps, was applied to every case, and no chemical agents were used.

The consective case series included three groups as follows: Thirty cases in which a 30-cc solution composed of 1 g TXA, 1 mg epinephrine, and saline was injected were allocated to group R. Thirty cases in which a 30-cc solution composed of 1 g TXA and saline were allocated to group T. Lastly, thirty cases in which 30-cc of saline was injected were allocated to group S. Amikacin sulphate (200 mg) was mixed into the solution in all cases.

We performed PR-ABT of 400 cc for patients who consented, had > 40 kg in body weight (BW) and had a preoperative blood haemoglobin (PB-Hb) of > 11 g/dL. Blood was transfused after blood tests on the first day postoperatively. For patients who did not undergo PR-ABT, IE-ABT was usually performed unless patients had enough blood volume with a PB-Hb > 14 g/dL and BW > 60kg.

For each case, we measured Hb on the first and seventh days. If the postoperative Hb level decreased to < 8.0 g/dL each time, ALBT was usually planned. Finally, five cases (one in group R, 2 in group S, and 2 in group T) were excluded from this study because the postoperative protocol was not properly adhered to, thus 85 cases were enrolled in this study. Of 85 cases, 59 received PR-ABT of 400 cc. For 20 patients who did not undergo PR-ABT and 2 who did undergo PR-ABT, IE-ABT was performed. We did not perform PR-ABT or IE-ABT for six cases; these included four cases with a PB-Hb > 14 g/dL and BW > 60 kg, one case in which the patient rejected transfusion for religious reasons and one case in which the device for IE-ABT did not function. We used PR-ABT and IE-ABT simultaneously in one case from group T, in which the patient's BW was 40 kg and PB-Hb was 11.7 g/dL and in one rheumatoid arthritis case from group S, in which the patient's BW was 54 kg and PB-Hb was 11.4 g/dL.

We measured the allogenic transfusion rate, blood loss from the drain and Hb changes among three time points (preoperatively, the first day postoperatively and the seventh day postoperatively). In addition, to evaluate the influence of PR-ABT and IE-ABT, we divided patients into four groups. We defined group A as patients with PR-ABT without IE-ABT. Group B included those with IE-ABT without PR-ABT, Group C included those without PR-ABT and IE-ABT, and group D included those with PR-ABT and IE-ABT (Table 1). We compared the decreased Hb level and blood loss from the drain among groups. More than two-thirds of patients underwent PR-ABT without IE-ABT (group A) so we also compared the decreased Hb level and mean blood loss from the drain in that group.

PR-ABT / IE-ABT	Do	Do not
Do not	A (n= 57)	C (n= 6)
Do	D (n= 2)	B (n= 20)

Table 1: *Combination of preoperative blood preservation (PR-ABT) and intraoperative auto transfusion (IE-ABT) in study groups A, B, C, and D.*

Furthermore, to exclude the influence of the surgical technique in each group, cases of hybrid THA using the same implant were extracted and compared among the three groups (R, S, and T). One-way analysis of variance with a posthoc Tukey honest significant difference test and chi-square test were used to analyse differences among the three groups. The level of significance was set at $p< 0.05$.

Results

Patients background (age, sex, height, weight, body mass index [BMI], presence of hip disease, approach of the operation, type of implant, and preoperative Hb) did not have a significant difference among the three groups (R, T, and S). The operative time and amount of bleeding during surgery also did not have a significant difference (Table 2). There were no peri or postoperative complications such as infection, pulmonary embolism, dislocation or symptomatic DVT in this series. No patients Hb level was < 8.0 g/dL so we did not perform ALBT in any case. Regarding drain bleeding, the S group had 367 ml, which was more than that in the R (287 ml) and T groups (268 ml) on average. The difference between drain bleeding in the S and T groups was significant (Table 3). The postoperative decrease in the Hb level did not have significant differences on the first day, but that of the S group was significantly higher than that of the R group on the seventh day. Drain bleeding and the decreased Hb level on the seventh day were not different among the A, B, C, and D groups, whereas the decreased Hb level of group A (PR-ABT) was more than that of group B (IE-ABT) (Table 4). Among the cases in group A, there was a tendency for group S to have a larger decrease in the Hb level and drain bleeding, but this was not significantly different (Table 5).

	R (n=29)	S (n = 28)	T (n=28)	p-value*
Age	63.1 ± 11.7	63.7 ± 12.4	63.3 ± 9.8	0.98
Sex (female/male)	22/7	23/5	24/4	0.63
Height (cm)	156.6 ± 9.2	154.7 ± 9.5	154.9 ± 9.3	0.71
Weight (kg)	57.4 ± 11.8	58.5 ± 12.1	57.6 ± 13.9	0.94
BMI (kg/m^2)	23.3 ± 3.6	24.3 ± 3.2	23.8 ± 4.1	0.6
Hip disease	OA 24 ANF 5	OA 23 ANF 4 RA 1	OA 27 ANF 1	0.29
Implant	cemented4 cementless4 hybrid20	cemented2 cementless6 hybrid20	cemented3 cementless5 hybrid20	0.94
Pre operation Hb (g/dL)	12.5 ± 1.7	13.3 ± 1.4	13.0 ± 1.0	0.12
Operative time (min)	121 ± 18	120 ± 27	123 ± 22	0.89
Bleeding during operation (ml)	172 ± 105	219 ± 169	190 ± 105	0.39
Transfusion pattern				
A	21	12	24	0.032#
B	6	12	2	
C	2	3	1	
D	0	1	1	

Abbreviations: SD: Standard deviation; BMI: Body mass index; OA: Osteoarthritis; ANF: Avascular necrosis of femoral head; RA: Rheumatoid arthritis; Hb: Haemoglobin

* One-way analysis of variance or chi-square test was performed.

# $p < 0.05$.

Table 2: *Background of the R, S, and T groups (mean ± SD).*

	R	S	T	p-value*
Drain bleeding (ml)	287 ± 121	367 ± 170	268 ± 155	0.038[#x]
Hb decrease (day 1) (g/dL)	2.09 ± 0.92	1.94 ± 1.21	2.45 ± 0.92	0.17
Hb decrease (day 7) (g/dL)	1.94 ± 0.98	2.80 ± 1.23	2.39 ± 1.13	0.019[#y]
Hb decrease (day1 to day7) (g/dL)	-0.14 ± 0.84	0.81 ± 1.31	-0.06 ± 1.34	0.0053[#z]

Abbreviation: Hb: Haemoglobin

* One-way analysis of variance was performed.

[#] p< 0.05.

[x] Significant between groups S and T.

[y] Significant between groups S and R.

[z] Significant between groups S and R, and T.

Table 3: *Drain bleeding and decreased Hb level in study groups R, S, and T (mean ± SD).*

	A (n = 57)	B (n=20)	C (n = 6)	D (n = 2)	p-value*
Drain bleeding(ml)	311 ± 163	291 ± 102	278 ± 211	410 ± 170	0.72
Hb decrease(g/dL)	2.40 ± 1.02	2.17 ± 1.49	3.13 ± 0.97	1.05 ± 0.35	0.12

Abbreviation: Hb: Haemoglobin

* One-way analysis of variance was performed.

Table 4: *Drain bleeding and decreased Hb level (mean ± SD) on the seventh day in groups A, B, C, and D.*

	R (n=21)	S (n=12)	T (n=24)	p-value*
Drain bleeding(ml)	299 ± 128	396 ± 203	278 ± 161	0.11
Hb decrease(g/dL)	2.17 ± 0.76	2.96 ± 1.24	2.32 ± 1.04	0.089

Abbreviation: Hb: Haemoglobin.

* One-way analysis of variance was performed.

Table 5: *Drain bleeding and decreased Hb level (mean ± S.D.) on the seventh day in the R, S, and T groups in group A.*

Among the R, S, and T subgroups of the group that underwent hybrid THA using the same implant, drain bleeding was significantly higher in group S than in group T (Table 6).

Overall, there was no significant difference between groups R and T.

	R (n=20)	S (n = 20)	T (n=20)	p-value*
Drain bleeding (ml)	268 ± 97	338 ± 155	243 ± 105	0.048[# x]
Hb decrease (day7) (g/dL)	2.02 ± 0.99	2.53 ± 1.33	2.14 ± 1.09	0.36
Transfusion pattern				

A	14	5	15	0.01#
B	3	10	2	
C	1	2	0	
D	0	1	0	

Abbreviations: Hb: Haemoglobin; THA: Total hip arthroplasty; BMI: Body mass index.

* One-way analysis of variance or chi-square test was performed.

#p< 0.05.

Table 6: *Patients' background, drain bleeding, and decreased Hb level (mean ± SD) of the R, S, and T groups with the hybrid THA using the same implant group.*

Discussion

In our study, drain bleeding was less in groups R and T than in group S. This indicated that bleeding postoperatively was decreased by TXA. The blood volume of those who underwent IE-ABT depended on the volume of bleeding during surgery, whereas in those who underwent PR-ABT, that quantity was fixed at 400 ml. In addition, in those who underwent IE-ABT, blood was transfused immediately postoperatively, whereas blood was transfused on the next day in those who underwent PR-ABT. In this study, IE-ABT was performed more often in group S than in the other groups. Therefore, the decreased Hb level (from day 1 to day 7) of group S was significantly higher than that of the other groups. Because each group had different combinations of PR-ABT and IE-ABT, it seemed difficult to clearly compare the postoperative decreased Hb level among groups R, S, and T (Table 3). However, the difference in the decreased Hb level on the seventh day between groups A and B was relatively small, with an average of 0.23 g/dl (Table 4). Groups A and B included most patients (90.6%). Although the decreased Hb level of groups C and D was quite different from that of groups A and B their influence on the statistics was relatively small. Although group S was mostly included those in group B, which had a smaller decrease in the Hb level on the seventh day, the decreased Hb level on the seventh day in group S was the largest. Thus, it is appropriate to consider that the decreased Hb level on the seventh day was reduced by the administration of TXA, and this is consistent with the lower drain bleeding found in groups R and T (Table 3).

We extracted the cases of hybrid THA using the same implant. Drain bleeding in group T was significantly less than that in group S, and the decreased Hb level on the seventh day of groups R and T was less than that in S group. By using the same type of implant, there was a significant difference for drain bleeding. The results were compatible with the comparison among the R, S, and T groups in group A.

There are several reports that topical TXA administration reduces blood loss after THA [3,6,10]. Alshryda *et al*. divided 161 THA cases into a topical TXA group and placebo group and performed a double-blind prospective investigation. With TXA, the blood transfusion rate decreased from 32.1% to 12.5%, and drain bleeding decreased from 389 ml to 260 ml on average: regarding the Hb level postoperatively, that of the TXA group was significantly higher [10]. The probability of complications such as DVT in both groups was equal. The mean drain bleeding amounts were close to those in our study.

Yue *et al*. divided 101 THA cases into a topical TXA group and placebo group, and conducted a prospective double-blind study [6]. In the TXA group, the blood transfusion rate decreased to 5.7% from 22.4%, total blood loss calculated by the gross formula decreased to 945 ml from an average of 1,255 ml, and drain bleeding decreased to 217 ml from an average of 296 ml.

Chang *et al*. administered TXA topically to 154 THA patients and retrospectively compared them with 234 patients who underwent THA without the administration of TXA [3]. In the TXA group, the total blood loss calculated with the formula by Nadler decreased to 695 ml from 819 ml, and the blood transfusion rate decreased from 35% to 17%. Although the authors estimated the total blood loss by the formula, we did not estimate it in our study. The reason for this was because blood loss during surgery was not influenced by topical TXA administration from the drain, and the estimated total blood loss was meaningless in this study.

Regarding epinephrine in our study, there was no difference between groups R and T in terms of drain bleeding or the decreased Hb level. Yamada reported that an intra articular dosage of epinephrine and drain clamping after TKA decreased blood loss [8]. They concluded that a 1 hr drain clamp was effective enough, but a 24 hr drain clamp reduced bleeding more effectively. Because the joint space is sealed postoperatively in TKA, a haemostatic effect by the continuous intra articular pressure with the drain clamp may be evident. Unlike TKA, because the joint space cannot be sealed sufficiently after THA, there is a possibility that the haemostatic effect of epinephrine did not occur in this study. It was also supposed that the superior haemostatic effect of TXA may mask the effect of epinephrine. However, all patients avoided ALBT and the drain clamp had enough of a haemostatic effect to avoid ALBT in this study, in which auto transfusion was effectively performed, although scheduled auto transfusion was a self-limiting factor in this study.

Considering that the hip joint space after THA is not sealed, the injected solution may possibly stay in the joint space for a short duration. Why was the intra articular administration of TXA effective in THA? One possible reason was that postoperative bleeding arose from the hip joint space and from the juxtaarticular damaged muscles and thus the space that was sealed via the closure of deep fascia effectively accommodated the injected solution, which resulted in the haemostatic effect of TXA.

Similar to the meta analysis on the IV administration of TXA in cases of THAs reported by Sukeik *et al*. [11] there are many reports demonstrating that IV TXA in THA was effective to reduce blood loss [11,17]. However, few studies have compared local administration with IV administration in arthroplasty. Wei *et al*. compared three groups of THA patients with topical TXA, IV TXA, and without TXA. They reported that dosages of topical and intravenous TXA were equally effective and safe [18]. Regarding TKA, Gomez-Barrena *et al*. compared topical TXA with IV TXA and demonstrated that non inferiority of topical administration [19]. Since the superiority of intravenous TXA has not been demonstrated so far, it is reasonable to apply TXA topically because it can minimise the systemic effect.

Physicians should reduce the probability of ALBT in THA if possible because it causes various complications [20,22]. In this series, allogenic transfusion was not needed in any case. However, ALBT is indispensable in some patients undergoing THA with specific conditions such as preoperative severe anaemia.

There were several limitations in this study: First, the auto transfusion pattern varied, as we performed PR-ABT and IE-ABT on a case-by-case basis. However, detailed comparisons made by dividing patients into subgroups, as described previously (Table 3–5), showed that topical TXA had a certain effect. Second, we only used one amount of TXA and epinephrine so we could not evaluate their quantitative effects. Third, the number of cases enrolled in this study was relatively small, especially in the more unified comparison described in (Table 5–6). However, the results consistently indicated the effect of topical TXA on the reduction of postoperative blood loss and they demonstrate the usefulness of topical TXA administration with drain clamping. The dosage of epinephrine was safe, but it was not clearly effective for reducing blood loss.

Further prospective and retrospective data on topical TXA is still necessary to determine the optimal quantity and method of TXA administration for THA.

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