International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 13, No. 12, December 2024 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_13.12.2024.162

Original Research

Change in haemoglobin levels and reduce pain after subperiosteal injection of tranexamic acid and bupivacaine cocktail in unilateral total knee arthroplasty

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Received Date: 19 November, 2024 Accepted Date: 29 December, 2024

Abstract

Background: Total knee arthroplasty (TKA) is a common surgical procedure for treating end-stage knee osteoarthritis. However, excessive blood loss and postoperative pain are significant concerns. **Objectives:** To compare the efficacy of intravenous (IV) versus topical with IV tranexamic acid (TXA) and Bupivacaine in reducing perioperative blood loss and pain after TKA. **Methods:** This prospective, randomized study included 70 patients undergoing unilateral TKA. Patients were randomized into two groups with 35 patients in each group: IV TXA (Group 1) and IV plussubperiosteal administration of TXA and Bupivacaine cocktail (Group 2). The primary outcomes were change in hemoglobin levels and postoperative pain assessed using Visual Analog Scale (VAS) scores. **Results:** The results showed that Group 2 had lower drain collection and required fewer blood transfusions compared to Group 1. The IV+Subperiosteal group maintained higher hemoglobin levels throughout the study period. Additionally, Group 2 consistently showed lower VAS scores compared to Group 1 at all timepoints, indicating reduced pain levels. **Conclusion:** The study demonstrates that topical cocktail with IV TXA is more effective than IV TXA alone in reducing perioperative blood loss and pain after TKA. The findings suggest that topical cocktail of TXA and Bupivacaine can enhance the efficacy of IV TXA in reducing blood loss and pain.

Keywords: Tranexamic acid, Bupivacaine,Total knee arthroplasty, blood loss, pain, Visual Analog Scale scores.

Introduction

Total knee arthroplasty (TKA) is the most cost-effective[1] and efficacious way for treating patients with end-stage knee osteoarthritis suffering from severe pain, activity limitation and in whom conservative treatment has been unsuccessful.[2] However, TKA is a procedure which is subject to a series of postoperative complications; excessive blood loss because of extensive soft tissue release and bone cuts being one of the main complications.[3]

Tranexamic acid (TXA) is a multifaceted agent that not only inhibits fibrinolysis but also activates plasminogen. Its efficacy in reducing blood loss after total knee arthroplasty (TKA) has been well established. Despite its widespread use, the optimal method of administering TXA remains a topic of debate.[4] Research has shown that intravenous administration of TXA results in limited bioavailability, with only a small fraction of the drug reaching the target site.[5] The mechanism of TXA's action is thought to involve the inhibition of tissue fibrinolysis, which leads to the stabilization of clots. Furthermore, TXA has been shown to accumulate in tissues for up to 17 hours, suggesting that alternative methods of administration could potentially enhance its efficacy.[6] Therefore, there is a need for more efficient and advanced methods of TXA application to optimize its benefits in reducing blood loss after TKA.

TXA is commercially available in different forms: intravenous (IV.), topical and oral. Each form needs different time to reach maximum plasma levels (5-15 min for IV. injection, 30 min for intra- muscular injection and 2hr oral administration).[7]

Bupivacaine is a local anaesthetic agent of amino-amide group which binds with voltage gated sodium channels and preventsdepolarisationIt is available in different concentrations as 0.25%, 0.50% and 0.75% in different brands and post effect lasts upto 48 to 72hours.

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Hence, the present study was carried with aim to compare the efficacy and safety of intravenous versus topical with intravenous tranexamic acid in reducing peri-operative blood loss in total knee arthroplasty.

Materials and Method

The present study was conducted a prospective, randomised study in 70 patients presenting with unilateral arthritis of the knee scheduled for TKR in Rama medical college and Research center, Hapur. The study was conducted in the duration from March 2022 to September 2023. The study was carried out after theapproval of the institutional ethics committee. A well-informed written consent was takenfromall subjects beforeenrolment in the study.

The inclusion criteria comprised of adult patients between the ages of 55 and 70 years who presented with advanced arthritis of the knee joint and were scheduled to undergo total knee replacement (TKR) surgery. Patients were excluded from the study if they had a history of allergic reaction to tranexamic acid or bupivacaine. Additionally, patients with a history of venous or arterial thrombosis, acute renal failure, or those with a hemoglobin level (HB) less than 12g/dL were also excluded from the study.

A detailed history and clinical examination were conducted for all patients. Patients were randomized into group 1 and group 2 with 35 patients in each group. Patients in Group 1 received intravenous tranexamic acid (TXA) as part of their treatment protocol. The dosage administered was 1g, given 20 minutes prior to the inflation of the tourniquet. This timing allowed the TXA to take effect before the surgical procedure began. Additionally, a repeat dose of TXA was administered 3 hours post-surgery to ensure continued efficacy in reducing blood loss.

In contrast, patients randomized to Group 2 received a combination of intravenous TXA and subperiostealcocktail of TXA and Bupivacaine. The intravenous TXA was administered in the same manner as Group 1, with a dosage of 1g given 20 minutes prior to tourniquet inflation. However, Group 2 also received an additional dose of cocktail of TXA and Bupivacaine via subperiosteal administration. This involved applying 3g of TXA and 0.5% of 5 ml Bupivacaine in 50ml of normal saline directly to the surgical site for a duration of 5 minutes before closing the incision. This localized administration of TXA aimed to provide an additional layer of hemostasis and reduce blood loss at the surgical site.

Subsequently, patients underwent total hip arthroplasty (THA) surgery.

The variables collected were entered in Microsoft Excel (Office 2013) and was analyzed using SPSS (version 20). The data obtained at various stages of the study was compared using parametric and non-parametric tests and a possible correlation was attempted to establish the relationship between the various parameters studied taking into account the specific objectives of the study as well as the type of the data. P-value <0.05 was considered as a significant.

Results

The patient demographics and perioperative outcomes of two groups, intravenous (IV) and intravenous plus subperiosteal (IV + Subperiosteal) are reported in table 1. The age range of patients in both groups was 55-70 years, with no significant difference ($p = 0.622$). The gender distribution was also similar, with 10 males and 25 females in the IV group, and 13 males and 22 females in the IV + Subperiosteal group ($p = 0.361$).

In terms of diagnosis, the IV group had a higher incidence of right osteoarthritis (OA) of the knee, while the IV + Subperiosteal group had a higher incidence of left OA of the knee ($p = 0.006$). Similarly, the IV group underwent more right total knee replacements (TKR), while the IV + Subperiosteal group underwent more left TKR ($p = 0.052$).

The body mass index (BMI) was similar in both groups, with a mean value of around 23.8 ($p = 0.056$). Hemodynamic parameters, including heart rate, systolic blood pressure, and diastolic blood pressure, were also comparable between the two groups.

However, significant differences were observed in perioperative outcomes. The IV + Subperiosteal group had lower drain collection on postoperative days 1, 3, and 5 compared to the IV group ($p = 0.020$, 0.024, and 0.031, respectively). Additionally, the IV + Subperiosteal group required fewer blood transfusions, with 6 patients requiring transfusion compared to 15 in the IV group. The preoperative hemoglobin (Hb) levels were slightly higher in the IV group compared to the IV + Subperiosteal group ($p = 0.047$).

A comparative analysis of the two groups, IV and IV+Subperiosteal, was conducted to evaluate the change in hemoglobin levels over time. The results, presented in Table 2, demonstrate the mean and median hemoglobin values for both groups at various time points, including pre-operative, post-operative day 1, day 3, and day 5. The data reveals that the IV+Subperiosteal group maintained higher hemoglobin levels throughout the study period. Specifically, the pre-operative hemoglobin levels were 12.35 g/dl and 12.81 g/dl for the IV and IV+Subperiosteal groups, respectively. On post-operative day 1, the hemoglobin levels decreased to 10.95 g/dl in the IV group, whereas the IV+Subperiosteal group showed a relatively smaller decrease to 11.80 g/dl. This trend continued on post-operative days 3 and 5, with the IV+Subperiosteal group consistently demonstrating higher hemoglobin levels compared to the IV group.

A comparative analysis of the change in hemoglobin levels from pre-operative to post-operative timepoints was conducted between the IV and IV+Subperiosteal groups. The results, presented in Table 3, demonstrate

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the mean absolute change and percentage change in hemoglobin levels at 1, 3, and 5 days post-operatively. The data reveals that the IV+Subperiosteal group experienced a smaller decline in hemoglobin levels compared to the IV group at all timepoints. Specifically, on post-operative day 1, the IV group showed a mean absolute change in hemoglobin of -1.40 g/dl, corresponding to a 10.13% decrease from pre-operative levels. In contrast, the IV+Subperiosteal group demonstrated a mean absolute change of -1.01 g/dl, representing a 7.35% decrease. This trend continued on post-operative days 3 and 5, with the IV+Subperiosteal group consistently showing smaller declines in hemoglobin levels compared to the IV group.

The postoperative pain assessment of patients in Group 1 and Group 2 was evaluated using Visual Analog Scale (VAS) scores at 1, 3, and 5 days after surgery. The results, presented in Table 4, demonstrate that Group 2 consistently showed lower VAS scores compared to Group 1 at all timepoints, indicating reduced pain levels. Specifically, on postoperative day 1, the VAS scores for Group 1 were 0.98 ± 0.25 in the static state (A1) and 1.67 ± 0.64 in flexion and extension (B1), whereas Group 2 showed VAS scores of 0.86 ± 0.56 (A1) and 1.12 ± 0.58 (B1). This trend continued on postoperative days 3 and 5, with Group 2 consistently demonstrating lower VAS scores in both static and dynamic states. The differences in VAS scores between the two groups were statistically significant at all timepoints ($p < 0.05$).

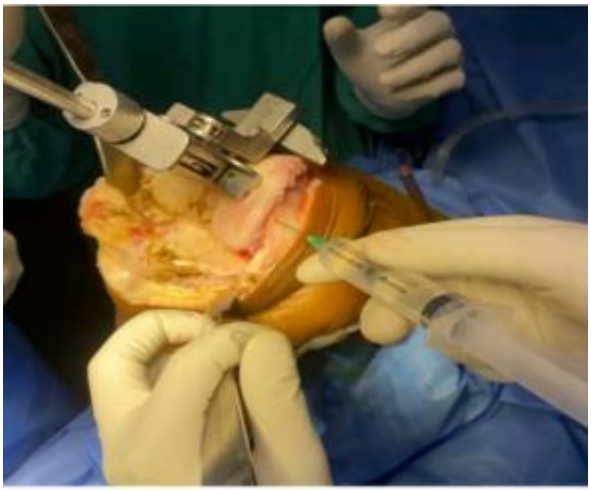

Figure 1: TXA via subperiosteal administration

Table 1: Patient demographics: intravenous (IV) vs intravenous + subperiosteal (IV + subperiosteal)

Parameters	IV	IV+Subperiosteal	P Value
Age	55-70	55-70	0.622
Gender Male Female	 10 25	 13 22	 0.361
Diagnosis Left OA Knee Right OA Knee	 21 14	 17 18	0.006
Surgery Lt TKR Rt TKR	 21 14	 17 18	0.052
Body Mass Index	23.83+/-2.64	23.85+/-2.66	0.056
Heart Rate (mp)	82.4	79.7	0.443
Systolic BP (mmHg)	133.3	130.5	0.094
Diastolic BP (mmHg)	85.2	81.8	0.341
Duration of Surgery Drain collection (ml) on postop day 1 Drain collection on postop day 3 Drain collection on postop day 5	 216.5 125.1 58.1	 160.4 89.7 24.8	 0.020 0.024 0.031
Blood Transfusion (Required)	15	6	-
Hb (g/dL) (Pre-operative)	12.5	12.3	0.047

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Table 2: Comparison of the two groups in terms of change in hemoglobin (g/dl) over time (N=20)

Hemoglobin	IV		IV+Subperiosteal	
	Mean(SD)	Median(IQR)	Mean(SD) (IQR)	Median
Pre-Operative	12.35	12.04	12.81	12.64
Post-Operative Day 1	10.95	10.82	11.80	11.71
Post Operative Day 3	10.45	10.36	11.13	11.02
Post Operative Day 5	10.32	10.27	10.90	10.86

Table 3: Comparing change in hemoglobin (g/dl) from pre-operative to post-operative timepoints-iv vs. iv + subperiosteal

Time point Comparison	Change in Hemoglobin (g/dL) from Pre-Operative to follow up time points			
	Group: IV		Group: IV+Subperiosteal	
	Mean (SD) of Absolute change	Mean(SD) of % Change	Absolute change	Change
1 Day post-operative – pre-operative	-1.40	-10.13%	-1.01	-7.35%
3 Day post-operative – pre-operative	-1.90	-13.95%	-1.68	-12.81%
5 Day post-operative – pre-operative	-2.03	-14.70%	-1.94	-14.08%

Table 4: Postoperative Pain Assessment using Visual Analog Scale (VAS) Scores at 1, 3, and 5 Days After Surgery

Variables	Group 1	Group 2	P Value
Post Operative Day A1	0.98+/-0.25	0.86+/-0.56	<0.05
Post Operative Day B1	1.67+/-0.64	1.12+/-0.58	<0.05
Post Operative Day A3	1.18+/-0.32	1.01+/-0.41	<0.05
Post Operative Day B3	1.95+/-0.69	1.53+/-0.47	<0.05
Post Operative Day A5	1.87+/-0.72	1.32+/-0.54	<0.05
Post Operative Day B5	1.91+/-0.66	1.45+/-0.39	<0.05

[VAS score with A is in static state, VAS score with B is in in flexion and extension]

Discussion

Our study showed that patients who were given IV+Subperiosteal TXA compared to patients who were given only IV TXA showed higher hemoglobin levels at 1 day, 3 days and 5 days post TKR. Though these findings were not statistically significant, they show early evidence in that combining IV and subperiosteal TXA may have an additive effect that presents hematological benefits.

The mean pre-operative Hb in our study was 11.75 in Group IV and 12.24 in the IV + Subperiosteal group which were comparable to studies conducted on the Indian population, When compared to studies done in the more developed nations, the pre-operative Hb values tended to be higher as compared to our studies.

The post-operative Hb in our study was calculated post-op Day 1, Day 3 and Day 5 in both the groups and their mean was considered as the post-operative Hb value. This was reported as 10.51 g/dL in Group IV and 11.39 g/dl, in Group IV+Subperiosteal. Our results are in concordance with other studies. **Kushwaha NS et al[8]** reported that administration of TXA (1.5 g) significantly lowers blood loss without increasing problems, which can eliminate concerns about intravenous TXA use. The post-op Hb value of Group iv was comparable to studies like Gautam PL et al 11.1 g/dL, **Yuan et al[9] 10.33 g/dL.**

In our study population, the Group IV and subperiosteal combined when compared to studies conducted by **Gautam PL et al[10] and Yuan et al[9]** all of which evaluated the role of IV TXA alone, appeared to fare better with a post-operative HB value of 11.39 g/dL as compared to a Hb value of 9.96g/dL, 11.1 g/dL and 10.33 g/dL respectively.

The postoperative pain levels of patients in group 1 in which given intravenous tranexamic acid (Dose-1g) 20 minutes before inflation of tourniquet and a repeat dose 3 hours post-surgery and Group 2 in which combination of intravenous TXA as well as subperiostealtranexamicacid were assessed using Visual Analog Scale (VAS) scores at 1, 3, and 5 days after surgery. Group 2 exhibited consistently lower VAS scores compared to Group 1 at all evaluated timepoints, indicating a significant reduction in pain levels. On postoperative day 1, Group 1 reported VAS scores of 0.98 ± 0.25 in the static state and 1.67 ± 0.64 in flexion and extension, whereas Group 2 reported lower scores of 0.86 ± 0.56 and 1.12 ± 0.58, respectively. This trend persisted on postoperative days 3 and 5, with Group 2 demonstrating lower VAS scores in both static and dynamic states. Notably, the differences in VAS scores between the two groups were statistically significant at all timepoints ($p < 0.05$), highlighting the effectiveness of the treatment approach used in Group 2. In a similar study conducted by **Singh H et al.[11]** assessed postoperative pain using the Visual Analog Scale (VAS) score in patients undergoing knee surgery. The results showed

DOI: 10.69605/ijlbpr_13.12.2024.162

that the mean VAS score in the study group was significantly lower, with scores ranging from 1.27 to 2.55, during the first 24 hours postoperatively. In contrast, the control group had higher VAS scores, ranging from 3.8 to 5.8, during the same period. The study found a statistically significant reduction in mean VAS scores in the study group compared to the control group until 24 hours ($p < 0.001$) and at 48 hours ($p = 0.033$) postoperatively. However, the difference in VAS scores between the two groups at 72 hours was not statistically significant ($p = 0.097$). Similarly, lower postoperative VAS scores for pain during the first 48 hours was also reported by **Vendittoli PA et al[12] ($p = 0.01$) and Kelly TC** et al[13] ($p = 0.023$).

Conclusion

To conclude, we observed that supplementing intravenous tranexamic acid with subperiostealtranexamic acid yields added advantages, including an improved hematological profile and a reduced likelihood of requiring transfusions. However, it's important to note that the scope of our analysis was constrained by a limited sample size. Conducting additional studies with larger cohorts could enhance the robustness and generalizability of our results. Although our findings are preliminary, they suggest a potential avenue for healthcare teams to consider standardizing the concurrent use of subperiostealTranexamic acid for patients undergoing Total Knee Replacement in the future. Incorporating an analgesic such as bupivacaine into this combination has proven to be efficacious for postoperative pain relief, resulting in a reduced need for analgesia.

References

1. Chen AT, Bronsther CI, Stanley EE, Paltiel AD, Sullivan JK, Collins JE, Neogi T, Katz JN, Losina E. The Value of Total Knee Replacement in Patients With Knee Osteoarthritis and a Body Mass Index of 40 kg/m^2 or Greater : A Cost-Effectiveness Analysis. Ann Intern Med. 2021 Jun;174(6):747-757.
2. Losina E, Walensky RP, Kessler CL, Emrani PS, Reichmann WM, Wright EA, Holt HL, Solomon DH, Yelin E, Paltiel AD, Katz JN. Cost-effectiveness of total knee arthroplasty in the United States: patient risk and hospital volume. Arch Intern Med. 2009 Jun 22;169(12):1113-21.
3. Maccagnano G, Pesce V, Noia G, Coviello M, Vicenti G, Vitiello R, Ziranu A, Spinarelli A, Moretti B. The effects of a new protocol on blood loss in total knee arthroplasty. Orthopedic Reviews. 2022;14(5).
4. Ishida K, Tsumura N, Kitagawa A, Hamamura S, Fukuda K, Dogaki Y, Kubo S, Matsumoto T, Matsushita T, Chin T, Iguchi T, Kurosaka M, Kuroda R. Intra-articular injection of tranexamic acid reduces not only blood loss but also knee joint swelling after total knee arthroplasty. IntOrthop. 2011 Nov;35(11):1639-45.
5. Ralley FE, Berta D, Binns V, Howard J, Naudie DD. One intraoperative dose of tranexamic acid for patients having primary hip or knee arthroplasty. ClinOrthopRelat Res. 2010;468:1905–1911.
6. Mannucci PM. Hemostatic drugs. N Engl J Med. 1998;339:245–253.
7. Georgiev GP, Tanchev PP, Zheleva Z, Kinov P. Comparison of topical and intravenous administration of tranexamic acid for blood loss control during total joint replacement: Review of literature. J OrthopTranslat. 2018 Jan 20;13:7-12.
8. **Kushwaha NS, Singh S, Kumar S, Singh A, Abbas MB, Deshwal S, Agarwal R. Local Versus Systemic Tranexamic Acid in Total Hip Arthroplasty in Young Adults. Cureus. 2023 Mar 16;15(3):e36230.**
9. **Yuan ZF, Yin H, Ma WP, Xing DL. The combined effect of administration of intravenous and topical tranexamic acid on blood loss and transfusion rate in total knee arthroplasty: combined tranexamic acid for TKA. Bone & joint research. 2016 Aug 1;5(8):353-61.**
10. **Gautam PL,**Katyal S, Yamin M, Singh A. Effect of tranexamic acid on blood loss and transfusion requirement in total knee replacement in the Indian population: A case series. Indian journal of anaesthesia. 2011 Nov 1;55(6):590-3.
11. Singh H, Agarwal KK, Tyagi S, Makadia P, Oza B, Jain P, Patel M. Peroperative Intra-Articular Infiltration of Tranexamic Acid and Ropivacaine Cocktail in Patients Undergoing Total Knee Arthroplasty: A Randomized Controlled Trial. Cureus. 2022 Mar 12;14(3):e23091.
12. Vendittoli PA, Makinen P, Drolet P, Lavigne M, Fallaha M, Guertin MC, Varin F. A multimodal analgesia protocol for totalkneearthroplasty. A randomized, controlled study. J Bone Joint Surg Am. 2006;88:282–289.
13. Kelley TC, Adams MJ, Mulliken BD, Dalury DF. Efficacy of multimodal perioperative analgesia protocol with periarticular medication injection in total knee arthroplasty: a randomized, double-blinded study. J Arthroplasty. 2013;28:1274–1277.