Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2024i1.1389
*Biol. Clin. Sci. Res. J., Volume, **2024**: 1389*
Original research article

PROSPECTIVE RANDOMIZED EVALUATION OF THE IMPACT OF MULTIMODAL ANALGESIA AND TRANEXAMIC ACID ON POSTOPERATIVE PAIN AND BLOOD LOSS IN KNEE ARTHROPLASTY PATIENTS

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(Received, 27th August 2024, Revised 20th December2024, Published 30th December 2024)

Abstract: *The most prevalent type of arthritis and a major contributor to disability is osteoarthritis. One of the most successful surgical treatments is total knee arthroplasty (TKA), which improves function and relieves pain in most patients.* ***Objectives:*** *The aim of this study is to evaluate the effects of intra-articular tranexamic acid and multimodal cocktail on postoperative blood loss and pain in patients undergoing total knee replacement.* ***Methods:*** *Enrolled were ninety-six male or female individuals with knee osteoarthritis who intended to have a total knee replacement. Group A received conventional anaesthetic medications only; tranexamic acid was not administered. Patients in Group B received an intraarticular injection of tranexamic acid weighing three grammes. Patients in Group C received a multimodal cocktail consisting of bupivacaine, tramadol, and ketorolac. Following TKA, patients had a 72-hour follow-up period. For 72 hours, blood loss and a pain score were recorded every 24 hours.* ***Results:*** *Patients in the cocktail group were 50.22±9.63 years old, those in the TXA group were 52.31±14.69 years old, and those in the control group were 48.92±13.22 years old. In three groups, the male-to-female ratios were, respectively, 11:21, 14:18, and 10:22. Within the first 72 hours, the control group lost 1030.1±177.27ml of blood, the TXA group lost 453.7±80.4ml, and the cocktail group lost 607.7±122.5ml. There was a significant difference ($p<0.05$) between TXA and cocktail groups and in all three groups. In the control group, the mean postoperative pain score was 4.4±2.3, in the TXA group it was 2.4±1.5, and in the cocktail group, it was 1.8±1.0 over the first 72 hours. The TXA and cocktail groups showed negligible differences ($p>0.05$), whereas the three groups showed substantial differences ($p<0.05$).* ***Conclusion:*** *Compared to the control group, the use of an intraarticular TXA injection was found to be effective in lowering blood loss. Although the multimodal cocktail allowed for better pain management than the other two groups.*

Keywords: Post-operative blood loss, Intra-articular injection, tranexamic acid, cocktail, total knee replacement.

Introduction

Because pain is the main symptom of osteoarthritis, it is the most prevalent kind of arthritis and a major global source of disability. Osteoarthritis in the knee causes pain that gradually changes from sporadic weight-bearing pain to a more chronic, ongoing pain. 1 In the entire sample, the overall prevalence of self-reported osteoarthritis was 14.8%, with 10.5% of people reporting knee osteoarthritis and 8.5 per cent reporting hip osteoarthritis. There were differences in the prevalence of hip and knee osteoarthritis between males and females in different age groups. 2

The articular cartilage softens, ulcerates, and focally disintegrates in the late stage of osteoarthritis (OA). Although non-inflammatory arthritis is the term used to describe it, synovial inflammation can also exist in chronic cases. Clinical symptoms often consist of discomfort, especially after extended exertion and weight-bearing, and stiffness following inactivity. It is sometimes referred to as degenerative arthritis, and it typically affects the spine, hands, feet, and big weight-bearing joints like the knees and hips. 3

One of the most successful surgical treatments is total knee arthroplasty (TKA), which improves function and relieves pain in most patients.
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The production of suitable interposition materials, clinical application of knee biomechanics, and utilisation of dependable and safe component fixation techniques are the hallmarks of TKA advancement. Considerable advancements and noteworthy inventions have been made since the advent of polycentric and geometric knees, as well as resection and interposition arthroplasty techniques. 5Soft tissue balance is essential to TKA effectiveness. To produce a rectangular flexion joint gap, the femoral component must rotate. 6 When a patient is significantly bleeding and needs extensive transfusion protocols, or when hyper-fibrinolysis is evident, intravenous tranexamic acid is frequently employed. When given within three hours of the injury, tranexamic acid was proven to increase survival in a patient population experiencing substantial haemorrhage. Note that tranexamic acid is not a pro-coagulant; rather, it is an anti-fibrinolytic. 7, 8: In orthopaedic, spinal, and cardiac surgery, tranexamic acid has been utilised to lessen blood loss and the ensuing requirement for transfusion. Although orthopaedic surgery can cause severe bleeding, it is unclear if it is effective in this situation. 9

TXA is a synthetic, reversible competitive inhibitor that works with the plasminogen's Lysine receptor. When this receptor binds, plasmin—the plasminogen that has been activated—is unable to attach to the fibrin matrix and

[Citation: Raza, S.A., Saifullah., Minhas, N.M., Haider, S.I., Bajwa, S.H., Ahmad, S., Ashraf, U., Azam, W., Masood, F., Iqbal, M., (2024). Prospective randomized evaluation of the impact of multimodal analgesia and tranexamic acid on postoperative pain and blood loss in knee arthroplasty patients. *Biol. Clin. Sci. Res. J.*, **2024***: 1389*. doi: https://doi.org/10.54112/bcsrj.v2024i1.1389]

eventually becomes stabilised. When TXA is used to treat hereditary angioedema, complement activation is indirectly decreased. It decreases the amount of C1 esterase inhibitor consumed by decreasing plasmin activity. 10

Therefore, the goal of this research is to determine the best treatment plan for minimising blood loss and postoperative pain following total knee arthroplasty. There hasn't been much research on this topic, either domestically or internationally, and no study comparing TXA to a combination of ketorolac, tramadol, and bupivacaine has been found. Thus, this study may provide more information about the effectiveness of various regimens.

OBJECTIVE: To compare postoperative blood loss and pain with or without Intra-articular tranexamic acid and a multimodal cocktail in patients undergoing total knee replacement.

Methodology

This randomized controlled trial was conducted in the Department of Orthopedic Surgery at Mayo Hospital, Lahore, over two years, from June 2022 to June 2024.

The primary objective was to evaluate the effectiveness of different treatments in reducing blood loss and pain in patients undergoing total knee replacement (TKR) for knee osteoarthritis.

A total of 96 patients were included in the study, divided equally into three groups, each comprising 32 subjects. The sample size was determined based on a 95% confidence level and 80% power of the study, referencing mean blood loss volumes of 1131±336ml without tranexamic acid (TXA) and 921±252ml with TXA in similar patients.

Patients were selected using a non-probability consecutive sampling technique.

Participants aged 30-70 years, of any gender, with an American Society of Anesthesiologists (ASA) status of I or II and diagnosed with knee osteoarthritis, scheduled for TKR, were included. Exclusion criteria were extensive, ruling out patients with previous TKR on the same side, an INR>2 or PT>15sec, bleeding disorders, statin or aspirin usage, cardiac diseases, Systemic lupus erythematosus, anaemia (hb<10g/dl), ASA 3 & 4 status, history of IV drug or alcohol use, conditions like thalassemia or leukaemia, thrombocytopenia, idiopathic thrombocytopenic purpura, any local or systemic infection, or those undergoing radiotherapy, chemotherapy, or immunosuppression.

Eligible patients from the Department of Orthopedic Surgery, Mayo Hospital, Lahore, were enrolled after obtaining informed consent. They were randomly divided into three groups. Group A received standard anaesthesia drugs; Group B was administered a 3gm intra-articular injection of TXA; Group C received an intra-articular cocktail comprising ketorolac, tramadol, and bupivacaine. All surgeries were performed under general anesthesia by the same surgical team, with the assistance of a blinded researcher. Post-surgery, patients were transferred to the post-surgical care unit for a 72-hour follow-up. Blood loss and Visual Analogue Scale (VAS) pain scores were recorded every 24 hours by a blinded member of the research team.

The collected data were analyzed using SPSS Version 25. The mean and standard deviation were calculated for age, blood loss, and pain. Gender, diabetes, and hypertension were presented as frequencies and percentages. An Analysis of Variance (ANOVA) test was used to compare mean blood loss and pain scores across the three groups, with a p-value of ≤0.05 considered statistically significant.

Results

Patients in the cocktail group were 50.22±9.63 years old, those in the TXA group were 52.31±14.69 years old, and those in the control group were 48.92±13.22 years old. In three groups, the male-to-female ratios were, respectively, 11:21, 14:18, and 10:22. The patients' mean BMIs were 30.25±12.36 kg/m2, 28.56±9.41 kg/m2, and 27.44±5.69 kg/m2, in that order. In the control group, there were 27 (84.4%) hypertension patients, 24 (75.0%) in the TXA group, and 29 (90.6%) in the cocktail group. Twenty-four (75.0%) diabetic patients were in the control group, twenty-one (65.6%) were in the TXA group, and twenty-five (78.1%) were in the cocktail group. (Table 1)

In the control group, the mean blood loss over the first 24 hours was 320.1±25.97ml; in the TXA group, it was 147.2±23.2ml; and in the cocktail group, it was 203.6±33.6ml. There was a significant difference ($p<0.05$) between TXA and cocktail groups and in all three groups. 489.7±88.4 ml of blood were lost on average in the control group, 210.9±49.6 ml in the TXA group, and 296.3±79.1 ml in the cocktail group within the first 48 hours. There was a significant difference ($p<0.05$) between TXA and cocktail groups and in all three groups. The control group saw a mean blood loss of 220.3±62.9ml, the TXA group 95.6±7.6ml, and the cocktail group 107.8±9.8ml within the first 72 hours. There was a significant difference ($p<0.05$) between TXA and cocktail groups and in all three groups. In the control group, the mean total blood loss over the first 72 hours was 1030.1±177.27ml; in the TXA group, it was 453.7±80.4ml; and in the cocktail group, it was 607.7±122.5ml. There was a significant difference ($p<0.05$) between TXA and cocktail groups and in all three groups. In the control group, the mean postoperative pain score was 1.9±0.4, in the TXA group, 0.6±0.2, and in the cocktail group, 0.5±0.1 within the first 24 hours. There was a significant difference ($p<0.05$) between TXA and cocktail groups and in all three groups. After 48 hours, the control group's mean postoperative pain score was 3.2±1.4, the TXA group's was 2.1±1.1, and the cocktail group's was 1.7±0.8. The TXA and cocktail groups showed negligible differences ($p>0.05$), whereas the three groups showed substantial differences ($p<0.05$). In the control group, the mean postoperative pain score was 4.4±2.3, in the TXA group it was 2.4±1.5, and in the cocktail group, it was 1.8±1.0 after 72 hours. The TXA and cocktail groups showed negligible differences ($p>0.05$), whereas the three groups showed substantial differences ($p<0.05$). (Table 2)

Table 1: Demographics of patients

	Control	TXA	Cocktail
N	32	32	32
Age (years)	48.92±13.22	52.31±14.69	50.22±9.63

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Male	11 (34.4%)	14 (43.8%)	10 (%)
Female	21 (65.6%)	18 (56.2%)	22 (%)
BMI	30.25±12.36	28.56±9.41	27.44±5.69
Hypertension	27 (84.4%)	24 (75.0%)	29 (90.6%)
Diabetes	24 (75.0%)	21 (65.6%)	25 (78.1%)

Table 2: Comparison of outcomes in groups

Outcome	Control	TXA	Cocktail	p-value
N	32	32	32	
Blood loss (ml)				
24 hour	320.1±25.97	147.2±23.2*	203.6±33.6	<0.0001
48 hour	489.7±88.4	210.9±49.6*	296.3±79.1	<0.0001
72 hour	220.3±62.9	95.6±7.6*	107.8±9.8	<0.0001
Total blood loss (ml)	1030.1±177.27	453.7±80.4*	607.7±122.5	<0.0001
Pain score (VAS)				
24 hour	1.9±0.4	0.6±0.2*	0.5±0.1	<0.0001
48 hour	3.2±1.4	2.1±1.1!	1.7±0.8	<0.0001
72 hour	4.4±2.3	2.4±1.5!	1.8±1.0	<0.0001

Discussion

One of the most popular orthopaedic surgeries is TKA. The number of people undergoing joint replacement surgery has been rising over the last few decades, and this trend is expected to continue into the foreseeable future due to factors such as population ageing, longer life expectancies, and our improved ability to manage comorbidities during the perioperative period. It is projected that by 2030, there will be about 3.5 million complete knee arthroplasties performed annually, only in the US. 11

Patients undergoing TKA have been treated with intrathecal morphine, epidural or femoral nerve block, intraarticular drug infusion, and periarticular multimodal drug injection, among other analgesic treatments (anaesthetic cocktail).

The use of periarticular multimodal medication injection is increasing, as evidenced by multiple studies that demonstrate its potential to minimise narcotic use, diminish adverse effects connected to narcotic usage, and offer postoperative pain control. 12

There have been several "cocktails" proposed for the local injections. Most contain a long-acting local anaesthetic in addition to corticosteroids, different antibiotics, opioids or ketorolac, and other ingredients. 13-15 Prior studies with minimally invasive total knee arthroplasty (TKA) patients demonstrated a 15% blood conservation level following intravenous TXA delivery. 16 It is yet unknown, nevertheless, how well topical TXA administration can reduce blood loss in patients undergoing minimally invasive total knee arthroplasty. Furthermore, the majority of the patients in the studies that examined the impact of topical TXA treatment on blood conservation in TKA did not have access to contemporary oral anticoagulants for thromboprophylaxis.17

Ten per cent of packed red blood cell transfusions are administered following orthopaedic surgery; however, the frequency of utilisation varies greatly throughout institutions and surgeons. Systemic problems from transfusions can include infections, graft-versus-host disease, allergic reactions, acute lung injury related to transfusions, and circulatory overload associated with transfusions. TXA is a revolutionary, reasonably priced blood management technique that lowers the need for transfusions and blood loss during total joint arthroplasty. Transfusions are not warranted for haemoglobin levels greater than 8 g/dL in the absence of symptoms, according to current clinical data. Research has additionally validated the application of this trigger in individuals with a history or potential for cardiovascular disease. 18

In our study, the average blood loss in the first 24 hours was 320.1±25.97 millilitres for the control group, 147.2±23.2 millilitres for the TXA group, and 203.6±33.6 millilitres for the cocktail group. There was a significant difference ($p<0.05$) between TXA and cocktail groups and in all three groups. 489.7±88.4 ml of blood were lost on average in the control group, 210.9±49.6 ml in the TXA group, and 296.3±79.1 ml in the cocktail group within the first 48 hours. There was a significant difference ($p<0.05$) between TXA and cocktail groups and in all three groups. The control group saw a mean blood loss of 220.3±62.9ml, the TXA group 95.6±7.6ml, and the cocktail group 107.8±9.8ml within the first 72 hours. There was a significant difference ($p<0.05$) between TXA and cocktail groups and in all three groups. In the control group, the mean total blood loss over the first 72 hours was 1030.1±177.27ml; in the TXA group, it was 453.7±80.4ml; and in the cocktail group, it was 607.7±122.5ml. There was a significant difference ($p<0.05$) between TXA and cocktail groups and in all three groups.

In the placebo group, the mean blood loss was 1131±336 ml; for intravenous TXA, it was 921±252 ml; and for topical TXA, it was 795±231 ml (Yen et al., 2014). There was a significant difference ($p<0.01$). The authors conclude that in minimally invasive TKA patients receiving rivaroxaban for thromboprophylaxis, TXA is as effective in conserving blood either applied topically or intravenously. 17

In the first 24 hours following surgery, the control group's mean postoperative pain score was 1.9±0.4, the TXA group's was 0.6±0.2, and the cocktail group's was 0.5±0.1. There was a significant difference ($p<0.05$) between TXA and cocktail groups and in all three groups. After 48 hours,

the control group's mean postoperative pain score was 3.2±1.4, the TXA group's was 2.1±1.1, and the cocktail group's was 1.7±0.8. The TXA and cocktail groups showed negligible differences ($p>0.05$), whereas the three groups showed substantial differences ($p<0.05$). After seventy-two hours, the average postoperative pain score for the control group was 4.4±2.3, 2.4±1.5 for the TXA group, and 1.8±1.0 for the cocktail group. The TXA and cocktail groups showed negligible differences ($p>0.05$), whereas the three groups showed substantial differences ($p<0.05$).

Systemic TXA therapy has not been associated with an increased risk of thromboembolic events or renal failure, according to recent reviews and meta-analyses.

19 Poeran et al. have published the largest analysis of this kind in orthopaedic patients. Perioperative intravenous TXA administration was not linked to an increased risk of complications, including a composite of thromboembolic complications, acute renal failure, cerebrovascular events, myocardial infarction, and in-hospital mortality, in a retrospective cohort study that included over 870,000 cases of elective total knee or hip arthroplasty in 510 US hospitals. This study is noteworthy not only for providing more proof of the safety of TXA use in orthopaedic patients, but also for grouping patients receiving intravenous TXA based on dose categories (none, ≤1,000, 2,000, and ≥3,000 mg). The use of TXA was dramatically linked to a lower need for autologous or allogeneic blood transfusions [odds ratio (OR) varying from 0.31-0.38 by dose category], as well as an allogeneic blood transfusion requirement (OR, 0.29-0.37). There was also no significantly higher risk of thromboembolic complications (OR, 0.85-1.02), acute renal failure (OR, 0.70-1.11), combined complications (OR, 0.75-0.98), and admission to an intensive care unit (OR, 0.73-1.01). According to the authors' findings, 2,000 mg of TXA appeared to have the best safety and efficacy profile. 20

The effect of TXA on blood loss was examined in a recently published meta-analysis of 14 randomised controlled trials. It was found that, when indirect comparisons of placebo-controlled trials of topical and intravenous TXA are made, topical administration is even better than the intravenous route, with no discernible difference in complication rates. 21

A single topical dose of TXA proved to be more effective than a single systemic dose, according to Maniar and colleagues' findings from a prospective randomised controlled research that looked into several TXA dosage regimens and modes of administration. The most effective TXA dosing regimen, according to the same study, is two intravenous doses—one administered before surgery and one administered during it. 22

A further RCT was conducted in 2013 by Kim et al. to examine the effectiveness of TXA in lowering blood loss and transfusion rates following unilateral and bilateral TKA. Among them were 146 patients who had bilateral TKA and 180 patients who had unilateral TKA. The transfusion rate dropped when TXA was used during bilateral TKA, but there was no effect during unilateral TKA, according to the results, which also showed that TXA use reduced overall blood loss. However, its effects on the transfusion rate may differ. 23

Similar to Kim et alstudy, 's Kakar et alstudy .'s involved 26 patients who had bilateral TKA and 24 patients who had unilateral TKA. This is different from Kim et alconclusion, 's which only showed this decrease in patients who had the bilateral operation. The sample size may have an impact on this discrepancy. There were notable variations in the TXA application and dose protocols throughout the studies. 24

A study by Shi et al. compared the effects of TXA by itself to a combination of 3g TXA and 0.25mg diluted epinephrine; 1:200,000. It was shown that applying cocktail wine topically considerably decreased both overall blood loss ($P = 0.007$) and blood loss ($P = 0.000$). As a result, topical TXA + diluted epinephrine had a superior hemostatic effect than TXA alone. Combining them can be a useful strategy to lessen blood loss following TKA because it does not result in serious side effectss. 25.

Conclusion

The administration of intraarticular TXA injection was found to be more advantageous in minimising blood loss than the control group. A combination of tramadol, bupivacaine, and ketorolac helped regulate pain better. In the future, the TXA can be used in conjunction with a cocktail (ketorolac, tramadol, and bupivacaine) to effectively relieve post-operative pain and reduce blood loss per procedure as well as in draining after surgery.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate.

Approved by the department Concerned. (IRBEC-MYOE-092/20)

Consent for publication

Approved

Funding

Not applicable

Conflict of interest

The authors declared an absence of conflict of interest.

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References

1. Neogi T. The epidemiology and impact of pain in osteoarthritis. Osteoarthritis Cartilage 2013;21(9):1145-53.

2. Plotnikoff R, Karunamuni N, Lytvyak E, Penfold C, Schopflocher D, Imayama I, et al. Osteoarthritis prevalence and modifiable factors: a population study. BMC Public Health 2015 2015/11/30;15(1):1195.
3. Pal C, Singh P, Chaturvedi S, Pruthi K, Vij A. Epidemiology of knee osteoarthritis in India and related factors. Indian Journal of Orthopaedics [Original Article] 2016 September 1, 2016;50(5):518-22.
4. Schroer WC, Berend KR, Lombardi AV, Barnes CL, Bolognesi MP, Berend ME, et al. Why Are Total Knees Failing Today? Etiology of Total Knee Revision in 2010 and 2011. The Journal of Arthroplasty 2013 2013/09/01/;28(8, Supplement):116-9.
5. Makridis K, Karachalios T. A Brief History of Total Knee Arthroplasty. In: Karachalios T, editor. Total Knee Arthroplasty: Long Term Outcomes. London: Springer London; 2015. p. 1-6.
6. Itokazu M, Minoda Y, Ikebuchi M, Mizokawa S, Ohta Y, Nakamura H. Anatomical landmarks of the distal femoral condyles are not always parallel to the tibial bone cut surface in flexion during total knee arthroplasty. The Knee 2016;23(4):725-9.
7. Vernon T, Morgan M, Morrison C. Bad blood: A coagulopathy associated with trauma and massive transfusion review. Acute medicine & surgery 2019 Jul;6(3):215-22.
8. Kodali S, Holmes CE, Tipirneni E, Cahill CR, Goodwin AJ, Cushman M. Successful management of refractory bleeding in liver failure with tranexamic acid: Case report and literature review. Research and practice in thrombosis and haemostasis 2019;3(3):424-8.
9. Choi WS, Irwin MG, Samman N. The effect of tranexamic acid on blood loss during orthognathic surgery: a randomized controlled trial. Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons 2009 Jan;67(1):125-33.
10. Pandove PK, Singla RL, Mittal P, Mahajan N, Kumar A. Role of Tranexamic Acid on Blood Loss in Laparoscopic Cholecystectomy. Nigerian Journal of surgery : official publication of the Nigerian Surgical Research Society 2017 Jul-Dec;23(2):111-4.
11. Oremus K. Tranexamic acid for the reduction of blood loss in total knee arthroplasty. Ann Transl Med 2015;3(Suppl 1):S40-S.
12. Tammachote N, Kanitnate S, Manuwong S, Yakumpor T, Panichkul P. Is pain after TKA better with periarticular injection or intrathecal morphine? Clinical orthopaedics and related research 2013;471(6):1992-9.
13. Dalury DF. A state-of-the-art pain protocol for total knee replacement. Arthroplast Today 2016;2(1):23-5.
14. Ashraf A, Raut VV, Canty SJ, McLauchlan GJ. Pain control after primary total knee replacement. A prospective randomised controlled trial of local infiltration versus single shot femoral nerve block. The Knee 2013;20(5):324-7.
15. Kurosaka K, Tsukada S, Seino D, Morooka T, Nakayama H, Yoshiya S. Local Infiltration Analgesia Versus Continuous Femoral Nerve Block in Pain Relief After Total Knee Arthroplasty: A Randomized Controlled Trial. The Journal of arthroplasty 2016;31(4):913-7.
16. Lin P, Hsu C, Huang C, Chen W, Wang J. The blood-saving effect of tranexamic acid in minimally invasive total knee replacement: is an additional pre-operative injection effective? The Journal of bone and joint surgery British volume 2012;94(7):932-6.
17. Yen S-H, Lin P-C, Chen B, Huang C-C, Wang J-W. Topical Tranexamic Acid Reduces Blood Loss in Minimally Invasive Total Knee Arthroplasty Receiving Rivaroxaban. BioMed Research International 2017;2017:8.
18. Ponnusamy KE, Kim TJ, Khanuja HS. Perioperative blood transfusions in orthopaedic surgery. The Journal of bone and joint surgery American volume 2014;96(21):1836-44.
19. Henry DA, Carless PA, Moxey AJ, O'Connell D, Stokes BJ, Fergusson DA, et al. Anti-fibrinolytic use for minimising perioperative allogeneic blood transfusion. The Cochrane database of systematic reviews 2011(3):Cd001886.
20. Poeran J, Rasul R, Suzuki S, Danninger T, Mazumdar M, Opperer M, et al. Tranexamic acid use and postoperative outcomes in patients undergoing total hip or knee arthroplasty in the United States: retrospective analysis of effectiveness and safety. BMJ (Clinical research ed) 2014;349:g4829.
21. Alshryda S, Sukeik M, Sarda P, Blenkinsopp J, Haddad FS, Mason JM. A systematic review and meta-analysis of the topical administration of tranexamic acid in total hip and knee replacement. The bone & joint journal 2014;96-b(8):1005-15.
22. Maniar RN, Kumar G, Singhi T, Nayak RM, Maniar PR. Most effective regimen of tranexamic acid in knee arthroplasty: a prospective randomized controlled study in 240 patients. Clinical orthopaedics and related research 2012;470(9):2605-12.
23. Kim TK, Chang CB, Kang YG, Seo ES, Lee JH, Yun JH, et al. Clinical value of tranexamic acid in unilateral and simultaneous bilateral TKAs under a contemporary blood-saving protocol: a randomized controlled trial. Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA 2014;22(8):1870-8.
24. Kakar PN, Gupta N, Govil P, Shah V. Efficacy and Safety of Tranexamic Acid in Control of Bleeding Following TKR: A Randomized Clinical Trial. Indian journal of anaesthesia 2009;53(6):667-71.
25. Shi LJ, Gao FQ, Sun W, Wang WG, Cheng LM, Guo WS. Cocktail therapy reduces hidden blood loss after total knee arthroplasty. Chinese Journal of Tissue Engineering Research 2017;21:329-34.

[Citation: Raza, S.A., Saifullah., Minhas, N.M., Haider, S.I., Bajwa, S.H., Ahmad, S., Ashraf, U., Azam, W., Masood, F., Iqbal, M., (2024). Prospective randomized evaluation of the impact of multimodal analgesia and tranexamic acid on postoperative pain and blood loss in knee arthroplasty patients. *Biol. Clin. Sci. Res. J.*, **2024***: 1389*. doi: https://doi.org/10.54112/bcsrj.v2024i1.1389]