International Journal of Orthopaedics Sciences

E-ISSN: 2395-1958
P-ISSN: 2706-6630
IJOS 2021; 7(1): 528-532

www.orthopaper.com
Received: 18-10-2020
Accepted: 27-11-2020

Dr. Gagan Khanna
MBBS, MS orthopaedics professor, Sri Guru Ramdas University Of Health Sciences, Amritsar, Punjab, India

Dr. Jaskaran Singh Bajwa
Junior Resident Orthopaedics, Department of Orthopaedics, Sri Guru Ram Das University of Health Sciences, Sri Amritsar, Punjab, India

Dr. Rohit Sharma
MBBS, DNB orthopaedics, Professor Sri Guru Ramdas University of Health Sciences, Amritsar, Punjab, India

Corresponding Author:
Dr. Rohit Sharma
MBBS, DNB orthopaedics, Professor Sri Guru Ramdas University of Health Sciences, Amritsar, Punjab, India

The role of tranexamic acid in decreasing intraoperative and postoperative blood loss in patients undergoing total hip replacement

Dr. Gagan Khanna, Dr. Jaskaran Singh Bajwa and Dr. Rohit Sharma

DOI: https://doi.org/10.22271/ortho.2021.v7.i1i.2535

Abstract
We investigated 60 patients undergoing Total hip arthropasty in a prospective, interventional and randomized study. Here, patients were divided alternatively into two groups of 30 patients each, in group A and group B.
Group A will receive intravenous infusion of tranexamic acid at dose of 15mg/kg and same will be given 3hrs after the first dose, while in group B no drug will be given. Direct and Indirect blood loss is calculated. Hence, direct blood loss is less (p value=0.000) in tranexamic group compared to control group i.e988 vs 1295 ml. Indirect blood loss, is also significantly lower in patients receiving drug as compared to placebo group. i.e (1018.87±160.76 vs 1335.2±194.4 ml) None of the patient in our study in either group developed any complication. In conclusion, we found Tranexamic acid, administrated before surgical incision, to be efficient in reducing Direct and Indirect blood loss during Total hip arthroplasty.Thus, we conclude that Tranexamic acid administration is an effective, safe and cheap method for reducing total blood loss, drain output, and hemoglobin drop without any increase in thromboembolic complications.

Keywords: Total hip arthroplasty (THA), tranexamic acid (TXA), avascular necrosis of hip (AVN)

Introduction
Total hip arthroplasty (THA) has become an excellent treatment method for pain relief and functional improvement in patients with degenerative hip joint disease. Osteoarthritis (OA) is one of the most common chronic conditions, particularly in elderly populations, which leads to pain and loss of function [1, 2]. Total hip arthroplasty (THA) is a surgical intervention that is carried out in end-stage arthritis patients. Total hip arthroplasty (THA) has been termed the operation of the century. In patients with end-stage refractory hip arthritis or other hip problems, THA provides significant reduction in pain, improves function and quality of life, which are the main reasons why patients undergo this procedure [3, 4]. Although the most common indication for hip arthroplasty is a diagnosis of osteoarthritis, approximately 5%-18% are performed in the setting of avascular necrosis (AVN) of the femoral head(late stages most commonly in stage 3 and 4), whereas joint sparing procedures are becoming less common.[5] However, THA is associated with increased blood loss, ranging from 1188 to 1651 ml and the transfusion rate is 16 to 37%, which often resulting in postoperative blood transfusions subsequently [6]. Perioperative blood loss is an important concern in patients undergoing total hip arthroplasty, upto 37% of patients require blood transfusions for postoperative anemia. The average amount of blood loss during primary THA is between 1000and 2000ml.[7] Hence, blood loss is most common complication encountered in THA. Extensive blood loss is associated with extra risk to patients due to severe anaemia until replaced with blood transfusion [8].
Blood transfusion is associated with complications which include transmission of infectious agents, hemolytic transfusion reaction, and short-term mortality. It endangers transfusion related lung injury, fluid overload, immunological adverse effects which are severe enough to cause multiple organ failure and even mortality. There is also risk of transmission of various infectious diseases like HIV and hepatitis. Furthermore, it also delays rehabilitation, prolongs stay in the hospital and thus increase medical expenses.

Moreover, blood is not prepared artificially, it has to be provided from donors so it has limited availability [9].

One of approach to reduce bleeding during surgery is administration of anti-fibrinolytic agent such as Tranexamic Acid (TXA) which peri operative stabilize the multiple micro-clots that form within the surgical wound. TXA is a synthetic derivative of the amino acid lysine (4-aminoethyl cyclohexane carboxylic acid), which exerts its antifibrinolytic effect through the blockade of lysine binding sites on plasminogen molecules reversibly, hence reduces the conversion of plasminogen to plasmin [10] It will further inhibit the conversion of fibrin to its end products, thus increasing clot formation and decreasing blood loss. Various pharmacologic agents have been tried, Out of which some drugs enhance thrombogenesis while others reduce fibrinolysis.

Recombinant Activated Factor VII is used in patients with hemophilia and congenital factor VII deficiency but can increase the number of thromboembolic events. Prothrombin complex containing factor II, VII, IX, X and some preparations with heparin and C-S protein complex are used as prophylactic treatment in patients with coagulation factor deficiency and Vitamin K deficiency to decrease intra operative bleeding. Major limiting factor in both the therapies is cost. The use of antifibrinolytic agents is based on the fact that surgical trauma besides promoting clot formation by activating the intrinsic and extrinsic coagulation cascades also leads to a concomitant activation of plasminogen, inducing a state of hyperfibrinolysis accelerating clot degeneration and increasing surgical site bleeding.

Action and indications of use of Epsilon-Aminocaproic Acid (EACA) is similar to Tranexemic acid. It preserves platelet function by avoiding the degradation of the platelet glycoprotein 1b receptor. Desmopressin, an analogue of vasopressin has hemostatic effect through induction and expression of endothelial Von Willebrand factor. It is useful in reducing bleeding in patients of hemophilia A and functional platelet defects. Aprotinin is a direct inhibitor of the fibrinolytic enzyme plasmin and is the only FDA approved drug reported to minimize transfusion requirements in coronary bypass surgery.

TXA is significantly more effective than EACA and achieves higher synovial concentrations. Therefore, it's use in orthopedic surgery is becoming more popular. Aprotinin was found to be more effective than tranexemic acid and epsilon aminocaproic acid in reducing blood loss but it was banned because of the risk of serious side effects associated with its uses in the form of renal failure, myocardial infarction, cardiac failure [11].

Various analysis on efficacy and safety of TXA, aprotinin, epsilon aminocaproic acid in decreasing surgical blood loss and improving blood transfusion rate have shown lower efficacy of EACA and more side effects of apportion than TA. Interestingly TXA was also the most cost effective out of three [12].

Material and Methods

The study will be conducted in Orthopaedic Department of Sri Guru Ramdas University of Medical Sciences after taking approval from ethics committee.

Inclusion Criteria

1. Patients with severe osteoarthritis and RA (unremitting pain and irreversibly damaged joints)
2. Skeletally mature patients.
3. Minimum accepted hemoglobin: 10 g/dL.
4. Both genders.
5. Patients with full informed written consent.

Exclusion criteria

1. Patients with ischaemic heart disease and low ejection fraction.
2. Patients with history of stroke or chronic kidney disease (creatinine clearance less than 60 mL/min m^2) Bleeding disorders or thrombophilia, Low platelet count (preoperative platelet count less than 150 000), chronic anemia (preoperative hemoglobin less than 10 g/dL)
3. Patients in whom tranexamic acid is contraindicated (hypersensitivity to TA or active intravascular bleeding)

Type of study – interventional randomized controlled study

- This study will be conducted on 60 patients scheduled for THR alternatively dividing the patients into two groups of 30 patients each, group A (study group) and group B (control group). After getting medical fitness, a written informed consent will be taken. Surgery will be conducted under regional anaesthesia. Group A will receive intravenous infusion of TXA at dose of 15mg/kg and same will be given 3hrs after the first dose, while in group B no drug will be given. Standardized procedure of THR through postero-lateral approach (modified Gibson approach) will be performed. A vacuum suction drain will be placed and compression bandage will be applied after closing the wound in layers. Direct blood loss will be estimated by measuring the differential weight of all surgical swabs and dressing used during operation and quantity of blood recovered in suction bottles (subtracting the volume of saline used). Post operatively the amount of blood in the drain will be measured using a beaker after 48 hours when drain is removed. In case of drain failure or where drain is not put, here blood loss will be calculated by estimating weight of soaked dressings.
- i.e. ($W=W_A - W_B$)
- Here, W_A - wt of soaked dressing
- W_B -wt of clean dressing
- Indirect blood loss will be estimated based on changes in hb levels. Hb will be recorded before surgery and then on 4^{th} post-operative day assuming that it takes 4 days for decline of hb to reach its nadir in the human body.[13]

Haemoglobin Balance method is used to estimate blood loss.[14]

Hb loss=BV X{(Hb(i)-Hb (e)} X 0.001+Hb (t)

$Hb_{loss\ total}$ (g): The loss volume of Hb

Hb_i (g/L): The Hb value before surgery

Hb_e (g/L): The Hb value after surgery;

Hb_t (g): The total volume of blood transfusion

BV(blood volume) will be estimated using NADLER'S FORMULA[15], which takes into account gender, weight and size of the patient.Therefore,formula is different for males and femalesThe formula is

MALE: $604+0.0003668 \times (size\{cm\})^3+32.2 \times wt(kg)$

FEMALE: $183+.000356 \times (size\{cm\})^3+33 \times wt(kg)$

Where hb_i is Hb value before surgrey. Hb_e is hb value 4^{th} post op day. HB_t is total volume of blood transfusion done. BV is calculated using nadler formula.A unit blood banked blood is considered to contain 52g of hb.

(Indirect blood loss =1000xhb loss/hb_i) [14]

Total blood loss(direct and indirect) will be estimated in group A and group B. Result obntained by both the methods will be tabulated, analyzed, and compared using student T paired test.

After assesing vitals, blood loss and general condtion, the blood wiil be infused and number of transfusions given will be recorded. Blood will be administerd if postoperatively haemoglobin is less than 9g/dl.Patient will be monitored for deep vein thrombosis, pulmonary embolism or any thromboembolic event throughout their post operative stay. Their hospital stay will also be recorded.

Results

The present study of "Role of tranexamic acid in reducing intra and post operative blood loss in patients undergoing total hip replacements" was undertaken on 60 patients in orthopedics department of SGRDIMSAR. They were divided into two groups, Group A (Study group) and Group B (control group) of thirty patients each. In Group A (study group), 15 mg/kg of tranexamic acid (TXA) was given by slow intravenous injection 30 minutes prior to incision and the same dose was repeated approximately 3 hours postoperatively when the patient was shifted to the ward while in Group B (control group) TXA was not given.

Table 1 shows mean age of patients in Group A and Group B was 58.33±10.58 and 54.73±12.23 respectively. 37% of patients in group A and 40% patients in group B are female.

Table 1: Shows mean age of patients in Group A and Group B

Age	Group A (n=30)	Group B (n=30)
<40	2(6.67)	4(13.33)
41-50	5(16.67)	4(13.33)
51-60	13(43.33)	11(36.67)
61-70	9(30)	8(26.67)
>70	1(3.33)	3(10)
Mean age in Years	58.33±10.58	54.73±12.23
p value	0.228	

Table 2 shows mean weight (in kgs)of patients in Group A and Group B are 76.6±12.72 and 78.7±9.97 respectively and mean height (in cms) in Group A and Group B are 169.2±9.31 and 170.4±8.68 respectively.

Table 2: Shows mean weight (in kgs) of patients in Group A and Group B

	Group A (n=30)	Group B (n=30)	p value
Mean weight in Kg	76.6±12.72	78.7±9.97	0.480

Direct blood loss (DBL) was estimated by measuring the differential weight of all surgical swabs and dressings used during the operation and quantity of blood recovered in the suction bottles (subtracting the volume of saline solution used). Post operatively the amount of blood in the drain was measured using a beaker after 48 hours when the drain was removed. As shown in table 3 Direct blood loss was recorded in both Group A and Group B. Direct blood loss in Group A and Group B are 988.67±142.6 and 1295±172.22, for which p value is 0.000.(i.e statistically significant).

Table 3: Direct blood loss was recorded in both Group A and Group B

	Group A (n=30)	Group B (n=30)	P Value
DBL	988.67±142.6	1295±172.22	0.000

As shown in table 4 the mean pre-operative haemoglobin in group A and group B are 119.5±14.24 and 123.5±16.5 (gm/l) respectively. The mean post-operative Hb on day 4 in Group A and Group B are 99.6±9.92 and 96.6±8.41 respectively. The mean difference of Hb in group A and Group B are 19.9 and 26.6, which is statistically significant as its p value is 0.000.

Table 4: As shown in table 4 the mean pre-operative haemoglobin in group A and group B

	Group A (n=30)	Group B (n=30)	p value
Preoperative Hemoglobin	119.5±14.24	123.5±16.5	0.319
Hb on 4th postoperative day	99.6±9.92	96.6±8.41	0.211
Mean Difference	19.9	26.9	
p value	0.000	0.000	

As shown in table 5 mean hemoglobin loss in Group A and Group B was 121.4±24.17 and 165.71±35.67 respectively and it was statistically significant. (p< 0.001). As shown in table 6, when Indirect blood loss (IDBL) calculated based on Hb balance, it was also higher in Group B 165.71±35.67 than Group A 121.4±24.17and it was statistically significant (p= <0.001).

Table 5: As shown in table 5 mean hemoglobin loss in Group A and Group B

	Group A (n=30)	Group B (n=30)	p value
Hb Loss	121.4±24.17	165.71±35.67	0.000

Table 6: As shown in table 6, when Indirect blood loss (IDBL

	Group A (n=30)	Group B (n=30)	P Value
IDBL	1018.87±160.76	1335.2±194.94	0.000

Discussion

The primary surgical treatment for patients with osteoarthritis hip and in late stages of AVN hip with chronic pain and disability despite maximum medical therapy is replacement of the joint with prosthesis. Total Hip Replacement (THR) is one of the most common orthopedic procedures performed. It is considered to be an effective surgical option for an end stage arthritis and millions of patients across procedure, the focus of attention has increased from techniques of surgery to others problems like perioperative blood loss with subsequent need for blood transfusion and associated complications like delayed recovery, increased length of stay in the hospital and higher rates of morbidity and mortality.

Horrow JC *et al.* [16] found that 15mg/kg was the minimum dosage needed to obtain the desired anti hemorrhagic effect. Mean duration of effect of TA is around 3 hours so second dose was given after this period to prolong the effect of TA over the first 6 hours when most bleeding occurs. Hence, we also used the same dosage in our investigation so as to have maximum effect with minimal side effects.

A study conducted by Kazemi *et al.* [17] where dose of 15 mg/kg body-weight of either tranexamic acid or placebo was given intravenously shortly before giving incision. Nisakanen *et al.* [18] conducted a study in which 10-mg/kg bolus of TXA was administered before surgery, with two additional 10-mg/kg boluses administered at 8-hour intervals.

Sadigursky D *et al.* [19] divided the patients into two groups. Group A, which comprised patients who used 10mg/kg IV TA after cementation of the components, and had the dose repeated 3h after the first dose. Group B, formed by patients who did not use TA.

Johansson *et al.* [20] conducted study in which before the start

of the operation, the patients received a bolus infusion of TA (15 mg/kg) mixed in 100 mL normal saline, or the same volume of saline in placebo group. Regarding the amount of bleeding in the THR procedure, the patients who received tranexamic acid (TXA) bled less. The total blood loss was on average 0.97 L in the TXA group and 1.3 L in the placebo group. ($p< 0.001$)

In our study the DBL (direct blood loss) in pts receiving TXA i.e Group A is 988.67±142.6 and in other Group where drug was not given, blood loss is 1295±172.22, which is statistically significant. (p value-0.000)

Similar results were observed in study conducted by Kazemi *et al.* [17] where intra operative blood loss in patients given TXA is less 1024±544 ml as compared to pts in whom drug was not given i.e., 1399±587.Niskanen and Korkala [18] investigated the use of TXA in cemented THA and observed that Total blood loss (Direct blood loss =IOBL+ drain volume (after 24hrs)) was significantly lower in the TXA group than in the control group (792 mL versus 1,102 mL; $P = 0.03$)

Post operatively, intra-articular drain was applied and connected to a high-vacuum drain bottle. Post-operative drainage was measured and removed after 48 hours of surgery. It was 356.33±60.88 and 532.33±65.32 in Group A and Group B respectively, which is statistically significant. (p value=0)

Hiippala S *et al.* and Benoni G *et al.* [21] were the pioneers to publish the blood conservative properties of TA in orthopedics. Hiippala *et al.* observed that Total blood loss was 847 (356) ml in the tranexamic acid group and 1549 (574) ml in the placebo group ($P< 0.001$).

Johansson *et al.* [20] concluded that IOBL was 534 ml in (TXA+) pts and 612 in placebo group. Total drain volume is 350 ml in TXA group and 528 ml in placebo group.

Zhou *et al.* [22] conducted study in which patients receiving TXA have total (DBL) blood loss is 1196 ml and in placebo group, DBL is 1470 ml. Husted *et al.* [23] performed study in which patients receiving tranexamic acid had a mean intra - operative blood loss of 480 mL versus 622 mL in patients receiving placebo (p = 0.3), a postoperative blood loss (blood in drain) of 334 mL versus 609 mL (p = 0.001), a total blood loss (Direct blood loss) of 814 mL versus 1231 mL (p = 0.0)

Clayes *et al.* [24] conducted study in which patients Postoperative blood loss (blood in drain), and total blood loss (direct blood loss) were significantly less in the TA group: 352 vs 524 ml (p = 0.013), and 801 vs 1038 ml (p = 0.013), respectively.

In our study we recorded significant Hb loss in Group B (149.13±36) as compared to Group B (80.43±21) in g/l. Total Indirect blood loss calculated depending upon Hb drop is significantly more in group B (1335.2±194.94) as compared to Group A. (1018.87±160.76)

Similar report was published by Panchmatia JR *et al.* [25] after his experience on 273 patients. He concluded that the mean post-operative blood loss with tranexamic acid was less than half the blood loss in the placebo group (272 vs. 685; $P< 0.001$). The total measured blood loss was significantly lower in the tranexamic acid group (443 vs. 985; $P< 0.001$). The above findings were mirrored by a significant difference in mean calculated blood loss using the Hb loss formula (427 vs. 911; $P< 0.001$).

Chang *et al.* [26] conducted study in pts undergoing THR found out the pts in whom TXA was administered has lower hb loss post-operatively as compared to pts in whom drug was not given, (1.87 ± 1.10 vs 2.20 ± 1.36) in g/dl respectively.

Johansson *et al.* [20] concluded that Indirect blood loss was calculated using Hb balance method, which is (969 vs 1324 ml) in TXA group and placebo group respectively.

None of the patient in our study in either TA + group or TA - group developed any complication. Moreover, previous research on tranexamic acid and thrombosis have failed to show any thrombogenic effect, even in patients who were treated for several days or even weeks. This may be due to the fact that fibrinolytic activity in vain walls is not affected by tranexamic acid.

Conclusion

Total hip arthroplasty (THA) is one of the most successful procedures in orthopaedic elective surgery for end-stage arthritis diseases of hip. It is estimated that by 2030, the demand for primary THA will grow by 174% to 572,000. They have not only got relieved of pain but have also restored their physical functioning. THR like other major orthopedic surgeries is commonly accompanied with marked blood loss and associated complications, delayed recovery, increased length of stay in the hospital and higher rates of morbidity and mortality in the absence of blood conservative strategies. Out of all antifibrinolytic agents, tranexamic acid (TXA) is preferred as it is cheaper and less allergenic than aprotinin and is ten times more potent than e-aminocaproic acid.

We found that tranexamic acid at a preoperative dose of 15mg/kg followed by second dose three hours post operatively was effective in decreasing not only Direct blood loss (IOBL+Drain volume after 48 hrs) i.e., 988 vs 1295 ml in TXA+ and TXA- groups respectively but also lowers Indirect blood loss (1018 vs 1335 ml) based on the calculation using the haemoglobin balance method. None of the patient in either group developed any thromboembolic complication. Use of tranexamic acid in patients of THR resulted in improving early post-operative ambulation and early discharge from the hospital thus decreasing their cost of treatment and rate of hospital acquired infections and allowing them to return to their daily life expeditiously. Despite meta-analyses supporting its safety, concerns still remain regarding risk of thromboembolic events in high-risk patients with pre-existing comorbidities (such as hypercoaguable stages, previous history of DVT, etc.) However, we believe that TA should be preferably avoided in such a patient population.

Thus, we conclude that TA administration is an effective, safe and cheap method for reducing total blood loss, drain output, and hemoglobin drop without any increase in thromboembolic complications.

References

1. Melo GL, Lages DS, Madureira Junior JL, Pellucci GD, Pellucci JW. The use of tranexamic acid in patients submitted to primary total hip arthroplasty: an evaluation of its impact in different administration protocols. Revista Brasileira de Ortopedia 2017;52:34-9.
2. Baltzer AW, Ostapczuk MS, Stosch D, Seidel F, Granrath M. A new treatment for hip osteoarthritis: clinical evidence for the efficacy of autologous conditioned serum. Orthopedic reviews 2013;5(2).
3. Mosleh-shirazi MS, Ibrahim M, Pastides P, Khan W, Rahman H. An insight into methods and practices in hip arthroplasty in patients with rheumatoid arthritis. International journal of rheumatology 2015, 2015.
4. Singh JA, Lewallen DG. Patients with osteoarthritis and avascular necrosis have better functional outcomes and those with avascular necrosis worse pain outcomes compared to rheumatoid arthritis after primary hip

arthroplasty: a cohort study. BMC medicine 2013;11(1):210.
5. Ancelin D, Reina N, Cavaignac E, Delclaux S, Chiron P. Total hip arthroplasty survival in femoral head avascular necrosis versus primary hip osteoarthritis: case-control study with a mean 10-year follow-up after anatomical cementless metal-on-metal 28-mm replacement. Orthopaedics & Traumatology: Surgery & Research 2016;102(8):1029-34.
6. Gilbody J, Dhotar HS, Perruccio AV, Davey JR. Topical tranexamic acid reduces transfusion rates in total hip and knee arthroplasty. J Arthroplasty 2014;29(4):681-4.
7. Blumberg N, Kirkley SA, Heal JM. A cost analysis of autologous and allogeneic transfusions in hip-replacement surgery. American J Surgery 1996;171(3):324-30
8. Gandhi R, Evans HM, Mahomed SR, Mahomed NN. Tranexamic acid and the reduction of blood loss in total knee and hip arthroplasty: a meta-analysis. BMC research notes 2013;6(1):1-4.
9. Glance LG, Dick AW, Mukamel DB, Fleming FJ, Zollo RA, Wissler R *et al*. Association between intraoperative blood transfusion and mortality and morbidity in patients undergoing noncardiac surgery. Anesthesiology: The Journal of the American Society of Anesthesiologists. 2011;114(2):283-92.
10. Shakya R, Xu HL, Lin YC, Ma BB, Qi YM, Li YJ. Application of tranexamic acid in total hip arthroplasty: Current evidences. Ann Trauma Acute Care. 2017;1:1001.
11. Fergusson DA, Hébert PC, Mazer CD, Fremes S, MacAdams C, Murkin JM *et al*. A comparison of aprotinin and lysine analogues in high-risk cardiac surgery. New England Journal of Medicine 2008;358(22):2319-31.
12. Kagoma YK, Crowther MA, Douketis J, Bhandari M, Eikelboom J, Lim W. Use of antifibrinolytic therapy to reduce transfusion in patients undergoing orthopedic surgery: a systematic review of randomized trials. Thrombosis research 2009;123(5):687-96.
13. Chen ZY, Wu HZ, Zhu P, Feng XB. Postoperative changes in hemoglobin and hematocrit in patients undergoing primary total hip and knee arthroplasty. Chinese medical journal 2015;128(14):1977.
14. Gao FQ, Li ZJ, Zhang K, Sun W, Zhang H. Four methods for calculating blood-loss after total knee arthroplasty. Chinese medical journal 2015;128(21):2856.
15. Nadler SB, Hidalgo JH, Bloch T. Prediction of blood volume in normal human adults. Surgery 1962;51:224-32.
16. Horrow JC, Van Riper DF, Strong MD, Grunewald KE, Parmet JL. The dose-response relationship of tranexamic acid. Anesthesiology: The Journal of the American Society of Anesthesiologists. 1995;82(2):383-92.
17. Kazemi SM, Mosaffa F, Eajazi A, Kaffashi M, Besheli LD, Bigdeli MR *et al*. The effect of tranexamic acid on reducing blood loss in cementless total hip arthroplasty under epidural anesthesia. Orthopedics 2010;33(1).
18. Niskanen RO, Korkala OL. Tranexamic acid reduces blood loss in cemented hip arthroplasty: A randomized, double-blind study of 39 patients with osteoarthritis. Acta Orthop 2005;76(6):829-32.
19. Sadigursky D, Andion D, Boureau P, Ferreira MC, Carneiro RJ, Colavolpe PO. Effect of tranexamic acid on bleeding control in total knee arthroplasty. Acta ortopedicabrasileira 2016;24(3):131-6.
20. Johansson T, Pettersson LG, Lisander B. Tranexamic acid in total hip arthroplasty saves blood and money: a randomized, double-blind study in 100 patients. Acta Orthop 2005;76:314-9.
21. Hiippala S, Strid L, Wennerstrand M, Arvela V, Mäntylä S, Ylinen J *et al*. Tranexamic acid (Cyklokapron) reduces perioperative blood loss associated with total knee arthroplasty. British journal of anaesthesia. 1995;74(5):534-7.
22. Zhou XD, Tao LJ, Li J, Wu LD. Do we really need tranexamic acid in total hip arthroplasty? A meta-analysis of nineteen randomized controlled trials. Arch Orthop Trauma Surg 2013;133(7):1017-27.
23. Husted H, Blønd L, Sonne-Holm S, Holm G, Jacobsen T, Gebuhr P. Tranexamic acid reduces blood loss and blood transfusions in primary total hip arthroplasty A prospective randomized double-blind study in 40 patients. Acta Orthopaedica Scandinavica 2003;74(6):665-9.
24. Claeys MA, Vermeersch N, Haentjens P. Reduction of blood loss with tranexamic acid in primary total hip replacement surgery. Acta Chir Belg 2007;107(4):397-401
25. Panchmatia JR, SoudehChegini BA, Charlotte Lobban MB C, Stapleton C, Smallman JM, Rakesh Kucheria MB. The routine use of tranexamic acid in hip and knee replacements. Bulletin of the NYU hospital for joint diseases 2012;70(4):246.
26. Chang CH, Chang Y, Chen DW, Ueng SW, Lee MS. Topical tranexamic acid reduces blood loss and transfusion rates associated with primary total hip arthroplasty. Clinical Orthopaedics and Related Research® 2014;472(5):1552-7.