

Selective Use of Low Dose Tranexamic Acid in Orthopedic Surgery

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Tranexamic acid, a synthetic derivative of lysine, is the most commonly used antifibrinolytic agent to reduce blood loss associated with surgical procedures. The regimens and routes used are highly variable. There is a current shift from systemic (intravenous) use towards topical instillation and periarticular injections. We aimed to analyze the efficacy and safety for selective use of low dose tranexamic acid in major orthopedic surgery. The use of tranexamic acid (Exacyl) was retrospectively reviewed from our Hospital's electronic database. Over a period of 12 months, a number of 46 surgeries in 45 patients were identified, with a mean age was 66 years old. An average of 1.17 units of tranexamic acid (500mg/5mL) were used per case (range 1-3). The drug was administered immediately postoperatively and if necessary repeated once after 8-24 h. The maximum dose per administration was 10mg/kg body weight, with a mean of 7.3 (SD 1.92). The average drop in hemoglobin (from preoperative to lowest consecutive postoperative) was 2.55 (range 0.1-5.8, median 1.3). 22/46 of surgeries required transfusions, with an average of 1.8 red blood cell mass per case (range 1-4). The average duration of postoperative hospital stay was 13 days (range 7-25). There were no complications directly related to tranexamic acid administration. Even in low dose, postoperative intravenous administration of tranexamic acid reduces total blood loss and requirements for transfusion.

Key words: tranexamic acid, total knee arthroplasty, hip replacement, blood loss

Tranexamic acid is a synthetic derivative of the amino acid lysine that reversibly binds to plasminogen, blocks the interaction with fibrin and inhibits clot breakdown. It is currently the most commonly used antifibrinolytic agent to reduce blood loss for a variety of surgical procedures. For major orthopedic surgery in particular, it significantly reduces total blood loss and the need for transfusion. It is inexpensive, well tolerated and does not increase the risk of deep vein thrombosis and pulmonary embolism [1].

The regimens and routes used to administer tranexamic acid are highly variable. There is a current shift from systemic (intravenous) use towards topical instillation and periarticular injections. The per dose amount ranges from 10 to 15mg/kg and the number of doses range from 1 to 3. The timing is either preoperative, before Tourniquet deflation, postoperative or a combination. The effects and potential cautions are dose dependent [2].

Experimental part

We aimed to analyze the efficacy and safety for selective use of low dose tranexamic acid in major orthopedic surgery.

The use of tranexamic acid (Exacyl) was retrospectively reviewed from our Hospital's electronic database. Over a period of 12 months, a number of 46 surgeries in 45 patients were identified: 22 patients were male and 23 female. The mean age was 66 years old (range 36-78). We extracted pre and postoperative hemoglobin (Hb) levels, comorbidities, adverse events and length of hospital stay (fig. 1a,b). All knees had cemented implants and passive drains, clamped for 2 h. Most primary and all revision hips were uncemented. Approximately one third of the primary hips were performed via a posterior approach, while the rest via a modified lateral (Hardinge). None of the trauma cases had cement augmented fixation of the fractures [3].

Results and discussions

An average of 1.17 units of Exacyl (500mg/5ml) were used per case (range 1-3). The drug was administered immediately postoperatively and if necessary repeated once after 8-24 h. The maximum dose per administration was 10mg/kg body weight, with a mean of 7.3 (SD 1.92). The intent was to complement transfusions in cases where

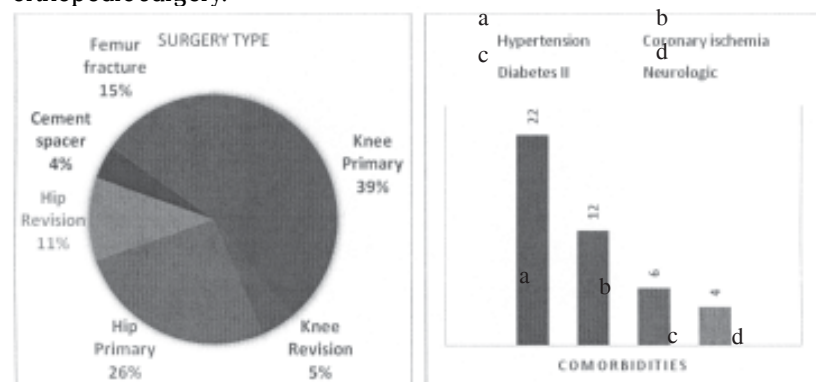


Fig. 1a, b. Distribution of surgery types and associated diseases among patients who received tranexamic acid

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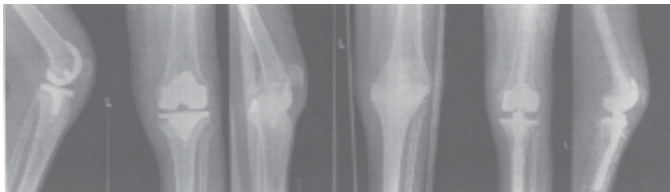


Fig.2. AP and lateral x-ray views of a total knee arthroplasty: significant lysis around the tibial component due to latent infection, 7 months after index surgery; the patient had the implant removed followed by thorough debridement, lavage, iv antibiotics and insertion of a cement spacer; after 6 weeks a semi constrained prosthesis was inserted

higher than usual bleeding was expected, even if no major coagulopathy was present. It was also preferentially administered to cases with blood types that are less compatible and make it more difficult to find donors (O and Rh negative).

The average drop in hemoglobin (from preoperative to lowest consecutive postoperative) was 2.55mg/dL (range 0.1-5.8, median 1.3). 22/46 of surgeries required transfusions, with an average of 1.8 red blood cell mass per case (range 1-4). The average duration of postoperative hospital stay was 13 days (range 7-25).

There were no complications directly related to tranexamic acid administration. All that occurred were associated with cases who had multiple surgeries. A patient with recurrent dislocation of total hip replacement and hyper tonicity due to Parkinson's disease developed a postoperative hematoma after revision for periprosthetic fracture dislocation. A patient with septic loosening of a total knee arthroplasty had ischemic coronary episode after implant removal, cement spacer insertion and tranexamic acid administration. The incident was considered to be caused by transient hypotension.

The incidence of deep vein thrombosis and pulmonary embolism are very low [2]. These potential complications cause less concern compared to risks related to erythropoietic stimulating agents. The effects on myocardial and cerebral ischemia require further evaluation of safety. Tranexamic acid has been extensively used in cardiac surgery and presently the only significant caution for administration is recent history of ischemic stroke [1,4, 5].

Apart from tranexamic, epsilon-aminocaproic acid and aprotinin have also been intensively studied. The effect of epsilon-aminocaproic acid is much lower than for tranexamic. Aprotinin has the strongest effect on containing perioperative blood loss but increased risk of thrombotic – ischemic events stopped its use [6,7].

Both topical and systemic administration reduce blood loss after arthroplasty, but the effects are dependent on dose and timing. For hip replacements, systemic administration seems to be more efficacious. Nonetheless, decreased blood loss is seen primarily in the immediate postoperative period and the total amount is less reduced comparative to knee arthroplasty [8, 9]. In our series, all primary knees were performed under Tourniquet which is known to enhance local fibrinolysis [10]. Future directions in knee surgery should be aimed towards limiting invasive techniques such as intramedullary reaming and focus on cartilage preservation, protection and replacement [11 - 13].

Recent systematic reviews found a 0.52-0.62 decrease in the risk for transfusion. Our series had reduced transfusion requirements, comparable to reports from the literature: 1-3.1 mean transfused units, accounting for a mean of 130-920mL of blood in 20-96% of patients. One of the main limitation of our series is that we were not able to determine the total blood loss. Reports in the literature range between 690-1510mL [1,4, 5,10]. Our average hemoglobin decrease is higher than expected (1.6-2mg/dL) [Seo 2013]. The two main reasons are unsystematized postoperative determinations and high percentage of

revision, septic and complex cases which take longer to perform and require extensile approaches [15,16].

Even in low dose, postoperative intravenous administration of tranexamic acid reduces total blood loss and works to complement transfusions for patient homeostasis.

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References

- 1.MCCORMACK PL. Tranexamic acid: a review of its use in the treatment of hyperfibrinolysis. *Drugs*. 2012 Mar 26;72(5):585-617.
- 2.KIM TK, CHANG CB, KOH IJ. Practical issues for the use of tranexamic acid in total knee arthroplasty: a systematic review. *Knee Surg Sports Traumatol Arthrosc*. 2013 Mar 31.
- 3.VERMESAN D, PREJBEANU R, HĂRĂGUS H, NITESCU S, BOGDAN C - Polymethylmethacrylate Cement Augmented Fixation of Implants - *Mat. Plast.*, **50**, no. 4, 2013 p 300
- 4.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. *Thromb Res*. 2009 Mar;123(5):687-96.
- 5.KER K, EDWARDS P, PEREL P, SHAKUR H, ROBERTS I. Effect of tranexamic acid on surgical bleeding: systematic review and cumulative meta-analysis. *BMJ*. 2012 May 17;344:e3054.
- 6.ZUFFEREY P, MERQUIOL F, LAPORTE S, DECOUSUS H, MISMETTI P, AUBOYER C, SAMAMA CM, MOLLIEUX S. Do antifibrinolytics reduce allogeneic blood transfusion in orthopedic surgery? *Anesthesiology*. 2006 Nov;105(5):1034-46.
- 7.EUBANKS JD. Antifibrinolytics in major orthopaedic surgery. *J Am Acad Orthop Surg*. 2010 Mar;18(3):132-8.
- 8.YAMASAKI S, MASUHARA K, FUJI T. Tranexamic acid reduces blood loss after cementless total hip arthroplasty-prospective randomized study in 40 cases. *Int Orthop*. 2004 Apr;28(2):69-73.
- 9.WIND TC, BARFIELD WR, MOSKAL JT. The effect of tranexamic acid on transfusion rate in primary total hip arthroplasty. *J Arthroplasty*. 2014 Feb;29(2):387-9.
- 10.HIIPPALA ST, STRID LJ, WENNERSTRAND MI, ARVELA JV, NIEMELÄ HM, MÄNTYLÄ SK, KUISMA RP, YLINEN JE. Tranexamic acid radically decreases blood loss and transfusions associated with total knee arthroplasty. *Anesth Analg*. 1997 Apr;84(4):839-44.
- 11.PATRASCU JM, KRÜGER JP, BÖSS HG, KETZMAR AK, FREYMAN U, SITTINGER M, NOTTER M, ENDRES M, KAPS C. Polyglycolic acid-hyaluronan scaffolds loaded with bone marrow-derived mesenchymal stem cells show chondrogenic differentiation in vitro and cartilage repair in the rabbit model. *J Biomed Mater Res B Appl Biomater*. 2013 Oct;101(7):1310-20.
- 12.VERMESAN D, PREJBEANU R, LAITIN S, GEORGIANU V, HARAGUS H, NITESCU S, TATULLO M, TATTOLI M, CAPRIO M, CAGIANO R. Meniscal tears left in situ during anatomic single bundle anterior cruciate ligament reconstruction. *Eur Rev Med Pharmacol Sci*. 2014 Jan;18(2):252-6.
- 13.DELEANU B, PREJBEANU R, POENARU D, VERMESAN D, HARAGUS H. Reamed versus unreamed intramedullary locked nailing in tibial fractures. *Eur J Orthop Surg Traumatol*. 2014 Jan 3. [Epub ahead of print]
- 14.SEO JG, MOON YW, PARK SH, KIM SM, KO KR. The comparative efficacies of intra-articular and IV tranexamic acid for reducing blood loss during total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc*. 2013 Aug;21(8):1869-74.
- 15.VERMESAN D, PREJBEANU R, HĂRĂGUS H, AHMADI M, DAMIAN G - *Rev. Chim. (Bucharest)*, **63**, no.9, 2012, p 953-5
- 16.DELEANU B, PREJBEANU R, VERMESAN D, HARAGUS H, ICMA I, PREDESCU V. Acute abdominal complications following hip surgery. *Chirurgia (Bucur)*. 2014 Mar-Apr;109(2):218-22

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