



## Comparative study between the effect of systemic use versus local use of tranexamic acid on blood loss and transfusion requirement in knee joint replacement.

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### Abstract

Blood loss during total knee replacement (TKR) remains a significant concern. The purpose of this study is to compare the effect of systemic use versus local use of tranexamic acid on blood loss and transfusion requirements in total knee replacement. Tranexamic acid (TXA) is an effective hemostatic agent used for the reduction of blood loss and transfusion. However, the safety profile of TXA remains in question due to a potential increased risk of venous thrombosis.

**Patients and methods:** In this study, 80 patients underwent TKR, and were divided into two groups based on whether they received a systemic tranexamic acid intra-operatively, or a local infiltration of tranexamic acid. Groups were then compared for mean calculated total blood volume (TBV) loss, transfusion rates, and knee range of movement.

**Results:** The groups were compared after TKA, and the results showed that Mean TBV loss was similar between groups: systemic tranexamic acid use mean was 705 ml (281 to 1744), local use mean was 712 ml(261 to 2308) ( $p = 0.929$ ).

**Conclusions:** no statistical difference between the two groups on decreasing blood loss and transfusion requirement in TKA.

### INTRODUCTION

TKA is an effective treatment of severe osteoarthritic knee and other types of knee arthritis. After TKA, joint pain can be relived and restoration of most of knee function and range of motion <sup>(1)</sup>. One of the most important issues of TKA is blood loss. Some studies reported that the average amount of blood loss in primary TKA can reach 1471 ml. allogenic blood transfusion carries risks of blood grouping incomparability, increases risk of infection, fluid overload and increase hospital stay. Preoperative donation of autologous blood prior to TKA had been shown to decrease the risks of allogenic blood transfusion to some extent, yet not all patients require transfusion of their blood during or after surgery and 45% may be wasted <sup>(2,3)</sup>. So many efforts were done to minimize blood loss intraoperatively. One of them was systemic injection of tranexamic acid which is antifibrinolysis during the procedure of TKA, but it may lead to thromboemboli disorders like DVT, PE and cerebrovascular disorders <sup>(4)</sup>. The local application of tranexamic acid into the knee joint could potentially have the same beneficial effects but without the systemic complications of thrombotic events <sup>(5,6,7,8)</sup>. The aim of our study is to compare the results of local infiltration of tranexamic acid versus the systemic use of tranexamic acid in minimizing blood loss in TKA.

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### PATIENTS AND METHODS

This is a prospective interventional study of 80 patients was done at Elmabarah and Zagazig university hospitals from April 2017 to April 2019. Inclusions criteria were patients undergoing primary TKA with Hb>11 and coagulation profile within normal limits. Exclusion criteria were patients with bleeding disorders, thromboembolic episodes, rheumatoid arthritis, revision and bilateral primary cases. Patients were divided into two groups each group was 40 patients, group A patients received systemic tranexamic acid and group B patients received local of tranexamic acid. All TKA were done by the same surgeon and under tourniquet. In group A systemic tranexamic acid was given half an hour before tourniquet inflation in dose of 10mg per Kg with the second dose was given three hours after first dose 2mg per Kg. group B given local tranexamic acid infiltration after implantation of the final prosthesis and before closure of arthrotomy. In the two groups suction drains were put and left closed for an hour then were opened. All patients underwent the same technique by the same surgeon. A compressive bandage was applied after closing the wound in layers and a vacuum suction drain was inserted before tourniquet deflation. Whole blood was administered if the blood loss was more than 15% of the body weight or postoperatively haemoglobin (Hb) was <8 g/dl or haematocrit<30%. Intra-operative and postoperative blood loss was estimated by two different methods. The first was a standard clinical method where approximate blood loss was taken as volume of blood recovered in the suction apparatus, drains and calculation of blood loss from sponges used during surgery. Each half soaked sponge was calculated as 25 ml of blood, and a fully soaked one as 50 ml. The second method was based on changes in Hb level. Assuming that blood volume (BV) on the fifth day after surgery was the same as that before surgery, we calculated the loss of Hb using the formula.

$$\text{Hb loss} = \text{BV} \times (\text{Hbi} - \text{Hbe}) \times 0.001 + \text{Hbt}$$

N B: Hbi – Hb concentration before surgery; Hbe – Hb concentration on the fifth day after surgery; Hbt – total amount of allogenic Hb transfused; BV – blood volume taken as 7% of total body weight of the patient. A unit of banked blood was considered to contain 52 g.

Hb. The blood loss (ml) was related to the patients' preoperative Hb value (g/l) (blood loss = 1000 × Hb loss/ Hbi). Results were analysed using Student's paired test.

### RESULTS

The demographic profile of the patients and preoperative physical status were comparable in both groups (Table 1)

Table (1) patients characteristics, laboratory and surgical data.

parameters	I.V TXA Group(n=40)	Local TXA Group(n=40)	Significance P value
Age (years)	65.6	68.2	(P>0.05)
Weight (kg)	88.6	89.3	(P>0.05)
Sex (M/F)	16/24	18/22	(P>0.05)
Hb at admission	12.3	12.6	(P>0.05)
Duration of operation	78.5	81.2	(P>0.05)

The mean post-operative blood loss with systemic administration of tranexamic acid was the same as in the locally administrated tranexamic acid group (272 vs. 685; P>0.5). The total measured blood loss was insignificant in both groups. The above findings were mirrored by a significant difference in mean calculated blood loss using the Hb loss formula (427 vs. 911; P>0.5) [Table 2].

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**Table (2)** blood loss in IV TXA and local TXA groups

	<b>I.V TXA Group(n=40)</b>	<b>Local TXA Group(n=40)</b>	<b>Significance P value</b>
Post-operative blood loss	272.3ml	301.5ml	(P>0.05)
Total blood loss(measured)	443.5ml	491.6ml	(P>0.05)
Total blood loss calculated	427.6ml	482.2ml	(P>0.05)

Values are given as mean

The post-operative Hb levels in the systemic administrated tranexamic acid group and the locally administrated group were  $11.51 \pm 1.56$  and  $11.42 \pm 1.44$ , respectively. There was insignificant difference in the change in Hb levels from pre- and post-surgery between the two groups ( $P > 0.5$ ).

Four patients of 40 patients of group A received one unit of blood transfusion and three patients received two units of blood transfusion. Three patients of group B received one unit of blood transfusion and four patients received two units of blood transfusion.

The length of hospital stay between the two groups was statistically insignificant.

In this study systemic use of TXA had one case that developed DVT but was managed medically successfully.

### DISCUSSION

The most important findings of our study is that there are no significant differences in transfusion rates, total blood loss, drain output, the drop of Hb level at day 1, and the incidence of infection and DVT between local and IV TXA for patients with TKA. TXA is a synthetic antifibrinolytic agent and can competitively inhibit fibrinolysis by reversibly blocking the lysine-binding sites of plasminogen, thereby displacing plasminogen from the fibrin surface<sup>(9)</sup>. The trauma of surgery promotes the release of tissue plasminogen activator and the activation of fibrinolysis, so TXA can block the activation process (plasminogen to plasmin) in an earlier stage and thus reduce blood loss postoperatively<sup>(10)</sup>. Various methods of administration of TXA have been used, including oral, intra articular injections, and IV<sup>(10,11)</sup>. However, there remains no consensus regarding the optimal regimen for tranexamic acid administration. The potential advantages of topical application of tranexamic acid are directly targeting of the site of bleeding and preventing of systemic side effects<sup>(11)</sup>. Craik et al<sup>(12)</sup>. conducted a randomised trial using intra-articular tranexamic acid but they did not use suction drains in any of their patients. They reported reduced bleeding through analyzing post-operative Hb and PCV values and concluded that topical tranexamic acid significantly reduces bleeding. Chen et al<sup>(13)</sup>. After reviewing 16 randomized controlled trials with 1,250 patients undergoing TKA and four randomized controlled trials involving 550 patients undergoing THA concluded that there was no significant difference between using topical and IV TXA in reducing blood loss or transfusion rate. Li et al<sup>(14)</sup> evaluated 2056 patients after THA in their systematic review and meta-analysis study and established that topical TXA had a similar efficacy compared with IV TXA. No significant difference was found between topical and IV application of TXA regarding the blood loss, the transfusion rates, the haemoglobin drop and the thrombo-embolic complications. According to these authors, the advantages of topical use of TXA were as follows: easy application, reduced costs, lower systemic absorption and direct effect to the bleeding sites

### CONCLUSION

The topical application of tranexamic acid effectively reduces both transfusion risk and blood loss like IV TXA administration but without risk of thrombo embolic disorders. Topical use of tranexamic acid may soon replace intravenous route as the established mode of delivery to achieve lower bleeding and transfusion rates.

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