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Optimizing effectivity of tranexamic acid in bilateral knee arthroplasty — A prospective randomized controlled study

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ABSTRACT

Introduction: Tranexamic acid (TEA) is used in reducing surgical blood loss. Literature shows no optimal regimen recommended for Bilateral Total Knee Arthroplasty (TKA). We evaluated three TEA regimens differing in dosage, timing and mode of administration in bilateral TKA to identify the most effective regimen to reduce blood loss.

Methods: We prospectively studied three TEA regimens (25 patients each) as follows: (1) two intraoperative, intravenous doses (IOIO), (2) two intraoperative local applications (LALA), and (3) one preoperative plus two intraoperative, intravenous doses (POIOIO). Two independent parameters of drain loss and total blood loss, calculated by the hemoglobin balance method were statistically evaluated.

Results: Mean drain loss was least (412.9 ml) in the POIOIO group, greatest (607.2 ml) in the IOIO group and LALA group in between (579.4 ml), with a statistically significant difference among them ($p = 0.0022$). On paired evaluation, the drain loss in the POIOIO group was significantly less as compared to the other two groups, whereas the difference between IOIO and LALA was not significant.

Mean total blood loss was least in the POIOIO group (1207 ml) and greatest in LALA group (1270 ml). The difference among the groups was not statistically significant ($p = 0.80$). There was no incidence of any thromboembolic phenomenon. On correlation with our study on Most Effective Regimen in Unilateral TKA, both results were found to substantiate each other.

1. Introduction

Simultaneous bilateral total knee arthroplasty (TKA) is associated with greater blood loss and greater requirement of blood transfusions compared to unilateral TKA. Blood loss in bilateral TKA is estimated to be between 1000 ml to 3400 ml [1] as compared to 800 to 1800 ml in unilateral TKA [2,3,4,5,6].

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Tranexamic acid (TEA) is a synthetic analog of the amino acid lysine which inhibits fibrinolysis locally without any effect on the fibrinolysis in the plasma from peripheral venous circulation [7]. A previous study established the need for a therapeutic plasma concentration of 10 ng/ml for TEA and an 80% reduction in the activity of plasminogen activator for adequate suppression of fibrinolysis in tissues [8]. An intravenous dose of 10 mg/kg of TEA maintains such a plasma concentration for approximately three hours [8]. Evidence suggests that intravenous TEA reduces surgical blood loss (by 40 to 50%) and the requirement of blood transfusions [9]. Topical application of TEA has also been shown to be very effective [10].

Multiple previous studies have shown a reduction in blood loss and post-operative transfusion requirement with the use of TEA in patients undergoing unilateral TKA [11,12]. In our previous study on use of TEA in unilateral TKA, we have concluded that a regimen containing one pre-operative dose before tourniquet inflation, one intra-operative dose before tourniquet deflation and a post-operative dose (POIOPO), three hours after the second dose is the most effective regimen [13]. In patients undergoing simultaneous bilateral TKA, there is no ideal regimen of TEA recommended in literature.

We started using TEA in bilateral TKA in July 2010 and observed a dramatic reduction in blood loss which prompted us to undertake this study. The aims of this study were, (1) to identify the most effective TEA regimen in bilateral TKA for reducing blood loss. Outcome parameters of drain collection and total blood loss by Hemoglobin Balance Method (Nadler's formula) [14,15] were estimated, (2) to compare the incidence of post-operative thromboembolic events among different regimens of TEA, and (3) to correlate with results of regimens evaluated in our Unilateral TKA study.

2. Patients and methods

The study was approved by the (Lilavati hospital and research centre Ethics Committee). The study was conducted from August 2010 to April 2013. From August 2010, we prospectively assessed 97 consecutive patients with the diagnosis of bilateral osteoarthritis who were scheduled to have simultaneous bilateral TKA for inclusion in our study. We assumed a difference of 300 ml of total blood loss between groups to be clinically significant since this would equate with need for one unit of blood transfusion. Considering a power of 80% at a significance level of five percent, Stata 8.2 software (Stata Corp, College Station, TX, USA) gave a sample size of 24 per group, which we rounded to 25. The exclusion criteria were, (1) a known allergy to TEA, (2) preoperative hepatic or renal dysfunction, (3) serious cardiac or respiratory disease, (4) congenital or acquired coagulopathy, (5) deranged coagulation profile (platelet count, prothrombin time, partial thromboplastin time, and international normalized ratio) and (6) history of thromboembolic disease. Patients taking antiplatelet agents were asked to stop them at least seven days before surgery.

Of these 97 evaluated patients, eight had to be excluded because antiplatelet agents were not stopped seven days prior to surgery and six other patients declined to participate (Figure 1). The selected patients were randomized into three regimen groups as follows: (1) two intra-operative IV doses (IOIO): first intra-operative dose of 10 mg/kg, 15 min before deflation of tourniquet on the first side, and second intra-operative dose of 10 mg/kg 15 min before deflation of tourniquet on the second side; (2) two intra-operative local applications (LALA): three grams of TEA diluted in 100 ml normal saline applied locally to the whole synovium after cementing the implant and before tourniquet release on first side, and also three grams diluted in

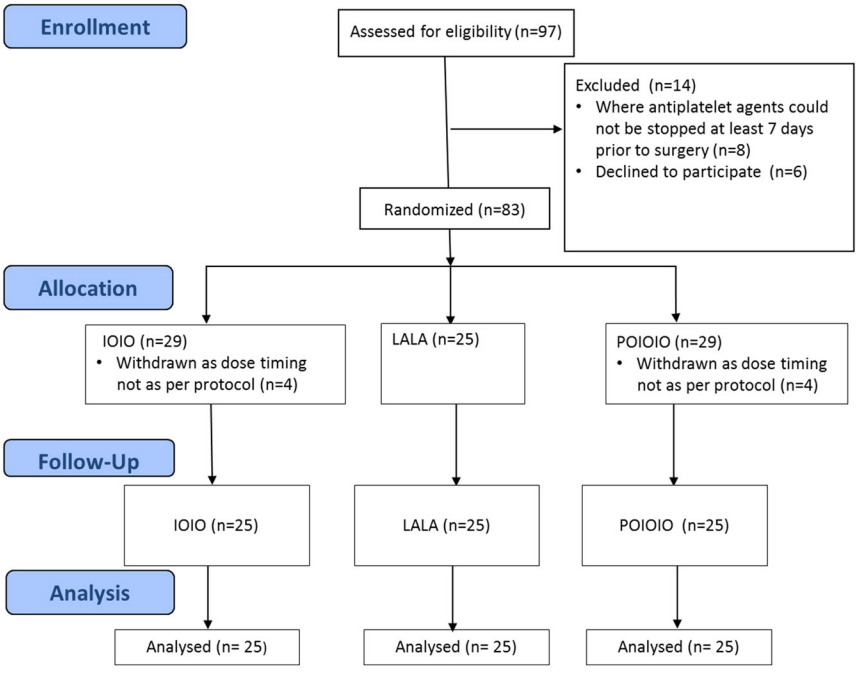

Figure 1. Flow diagram indicating the number of patients assessed and included at each stage of the trial.

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