The Effect of Tranexamic Acid and Gender on Intraoperative Bleeding in Orthognathic Surgery—A Randomized Controlled Trial

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Purpose: The purpose of this randomized trial was to measure the effect of intravenously administered tranexamic acid (TXA) on intraoperative blood loss (IOB) in patients undergoing bimaxillary orthognathic surgery (OS).

Materials and Methods: The authors designed and implemented a double-blinded placebo-controlled trial composed of patients eligible for OS at the Hospital of South West Denmark (Esbjerg, Denmark) from August 2014 through September 2016. The primary predictor variable was a single intravenous dose of TXA 1 g administered preoperatively or an equivalent saline placebo. The primary outcome was IOB determined by milliliters of blood in the suction canister and gauzes deducted from the volume of saline used intraoperatively.

Results: The study population consisted of 96 patients. The TXA group (n = 51) and the placebo group (n = 45) showed a median IOB of 275 and 403 mL (P = .005), respectively. A significant effect of TXA was detected in women (median IOB, 153 mL [96 to 233 mL] in TXA group vs 329 mL [185 to 582 mL] in placebo group; P < .001), whereas no significant effect of TXA on IOB was detected in men (median IOB, 367 mL [275 to 472 mL] in TXA group vs 429 mL [275 to 655 mL] in placebo group; P = .23). No correlations were found between IOB and procedure length, procedure type, or hematologic markers (platelets, hemoglobin, and hematocrit).

Conclusion: In contrast to other studies, this double-blinded randomized controlled trial found a hemostatic effect of TXA in women and none in men who underwent bimaxillary OS. To focus on the specific effect of TXA in men, future studies should include larger male samples.

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Orthognathic surgery (OS) carries an innate risk of intra- and postoperative bleeding because of the richly vascularized tissues of the facial skeleton involved in such surgery. Blood transfusions are performed from time to time, although increasingly infrequently in OS because of hemostatic advancements and

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optimized surgical protocols.[1] Because OS consists of an elective group of procedures, and morbidity can increase from anemia and allogenic blood transfusions,[2] procedures that aim to decrease surgical bleeding are clinically relevant.[3] Hypotensive anesthetic regimes, surgical techniques, and the use of antifibrinolytics, including tranexamic acid (TXA), are the methods of choice.[4-9]

TXA is a synthetic lysine analogue with antifibrinolytic abilities because of its reversible binding to lysine-binding sites on plasminogen molecules. By this binding, plasminogen cannot bind to the fibrin clot, thereby decreasing the subsequent activation of plasminogen to plasmin induced by tissue-type plasminogen activator[10] (Fig 1). The decreased fibrinolytic susceptibility of the clot lessens bleeding. The clinical effect of TXA is well documented and meta-analyses have shown TXA decreases overall intraoperative bleeding (IOB) by one third across various surgeries, including cardiac, orthopedic, head and neck, obstetrics and gynecology, urologic, breast cancer, and OS.[11,12] Similar decreases in IOB have been reported in OS, but the total number of trials is limited.[7,13-17] Furthermore, no information exists on the effect of TXA according to patient gender within the respective patient populations.[12] Most previous OS studies focused on the intravenous (IV) administration of TXA,[7,13-15] although decreased bleeding by topically administered TXA has been reported.[16]

The length and extent of surgery and the experience level of the surgeon are other factors influencing IOB in OS,[4] whereas gender and age have not been considered relevant in these instances.[12] However, recent research by the authors showed a gender-specific variation in IOB during bimaxillary OS performed without TXA. In that study, men displayed markedly higher IOB levels compared with women, which correlated to an increased fibrin turnover in women.[18]

The primary aim of the present trial was to test the effect of IV-administered TXA compared with saline placebo on IOB in patients undergoing bimaxillary OS and secondarily to investigate the effect of gender on IOB.

To address this matter, the following null hypothesis was investigated: administering IV TXA or saline in patients undergoing to bimaxillary OS would result in no meaningful difference in IOB.

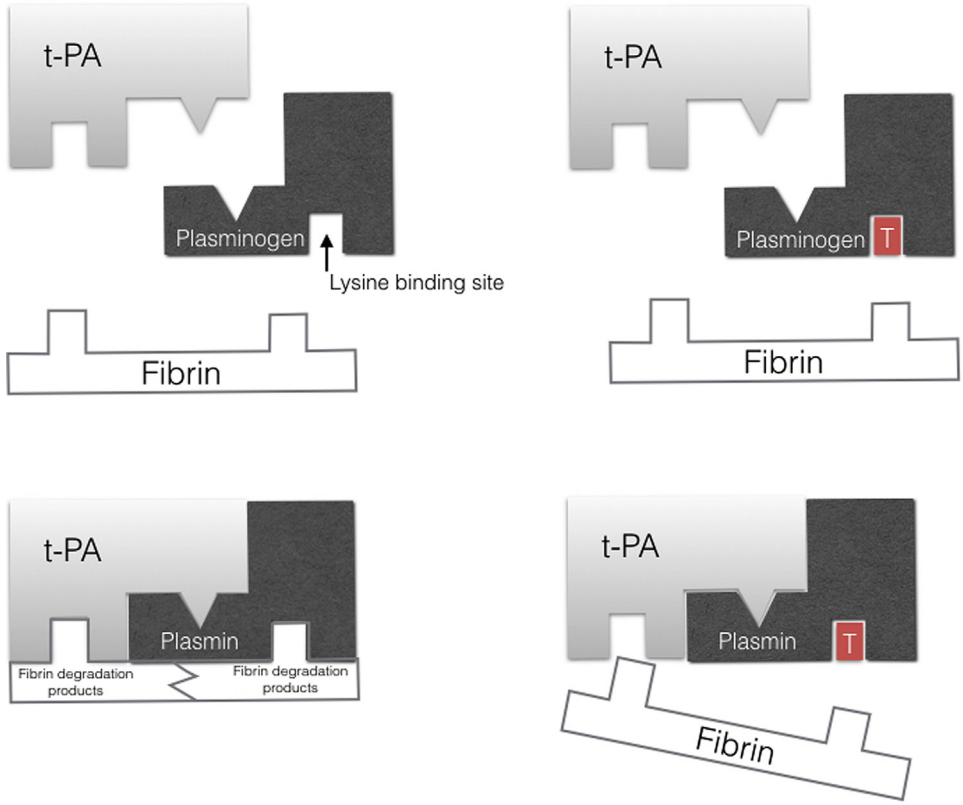

FIGURE 1. Theoretical model of the antifibrinolytic action of tranexamic acid. T, tranexamic acid; tPA, tissue plasminogen activator. Adapted from Dunn and Goa.[10] Q6 Q3

Secher et al. Tranexamic Acid and Intraoperative Bleeding. J Oral Maxillofac Surg 2017.