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Pharmacokinetic characteristics of topical and intravenous tranexamic acid administration in primary unilateral total knee replacement

Background:

Tranexamic acid (TXA), an antifibrinolytic drug, is usually administered intravenously; however, topical administration has recently been proven to be as effective as intravenous administration. Limited information regarding the pharmacokinetics (PK) of TXA after topical administration has been reported. We studied the PK of TXA administered as a single topical dose and as two intravenous doses.

Methods:

This was a phase I, randomized, open-label, single-period, parallel-group clinical trial in adult patients who underwent primary unilateral total knee replacement (TKR). Patients were randomized to receive 1 g/10 mL (concentration of 100 mg/mL) of TXA applied directly to the surgical field (topical administration) before wound closure, or 2 g (two doses of 1 g) of intravenous TXA as two 30-min infusions of 1 g each of TXA diluted in 1000 mL of saline solution. The first dose was administered 15–30 min before the pneumatic tourniquet was inflated, and the second dose was administered

at the end of surgery, when the pneumatic tourniquet was deflated (between 90 and 140 min).

For intravenous TXA administration, we measured its plasmatic concentration from blood samples collected before starting the surgical procedure, at the end of the first 30-min infusion and at 0.5, 0.75, 1, 2, 4 and 6 h after starting the second infusion. For patients receiving topical treatment, the determinations were just before starting the surgical procedure and at 0.5, 1, 1.5, 2, 2.5, 3, 4, 6 and 8 h post-dose. We compared bleeding between treatment groups calculating mean total blood loss by Nadler formula [1].

Results:

Twenty-four patients were included, 12 in each group, 83% were female, mean age was 73.7(5.6) years. The disposition of TXA was best described as a two-compartment model with clearance dependent on kidney function. The estimated bioavailability for topical administration was 81%. Based in blood concentrations, topical administration would produce complete inhibition of fibrinolysis in only 12% of patients compared with 72.5% with intravenous administration. Mean total blood loss was 692 (244) mL for intravenous TXA and 455 (201) mL for topical TXA ($p = 0.019$).

Conclusions:

A single dose of high-concentration, low-volume topical TXA can achieve antifibrinolytic plasma concentrations of the drug, providing both local and systemic effects in patients undergoing TKR. TXA administration to the surgical field could be an alternative to the intravenous route for patients undergoing TKR.

[1] Nadler SB, Hidalgo JU, Bloch T. Prediction of blood volume in normal human adults. Surgery. 1962;51:224‑32.