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Topical tranexamic acid for prophylaxis of bleeding

OPINIONS

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The author has completed the ICMJE form and declares the following conflicts of interest: She has received an open research grant from Pfizer, the manufacturer of the tranexamic acid Cyklokapron.

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Uncertainty surrounding possible thromboembolic events may prevent widespread use of tranexamic acid in surgery. Topical application may be an alternative.

Tranexamic acid is an antifibrinolytic drug used routinely by intravenous administration in cardiac surgery and orthopaedics, but uncertainty surrounding the risk of thrombosis has prevented general use in soft tissue surgery. In a randomised placebo-controlled trial from The New England Journal of Medicine, intravenous tranexamic acid or placebo were administered to prevent bleeding in 9,500 patients at increased risk of bleeding who were predominantly undergoing soft tissue surgery (1). The primary outcome 'major bleeding complication' occurred less frequently in the tranexamic acid group ($p < 0.001$), but a very small increase in thromboembolic events ($p = 0.04$) was also seen in this group. Therefore, it is unclear whether the trial will contribute to a change in practice in soft tissue surgery. The trial supports the prophylactic systemic administration of tranexamic acid in patients at increased risk of bleeding, but provides no basis for advocating general systemic prophylaxis in patients at low risk of bleeding and in surgical procedures rarely associated with major bleeding complications.

Topical (local) application of tranexamic acid on surgical wound surfaces is an alternative with a presumed reduced risk of systemic adverse effects. Although systemic administration at the start of the procedure makes most sense if major perioperative bleeding is expected, topical application at the end of the procedure can be a good alternative to reduce postoperative bleeding in particular. Topical application is not yet a formally approved method of administration, but a reduction in bleeding equivalent to systemic administration has been demonstrated in literature in the orthopaedic and cardiac surgery fields particularly (2).

Research into topical application

Plastic surgery wound surfaces are large and easily accessible. In 2012, we wanted to investigate whether moistening the wound surface with tranexamic acid could reduce bleeding. There was little documentation regarding potential toxicity with topical application, and we designed a procedure based on practical considerations: We diluted a 5 ml ampoule of 100 mg/ml tranexamic acid with 15 ml physiological saline. This produced 20 ml of 25 mg/ml tranexamic acid, which provided a sufficient volume to moisten even large wound surfaces (3).

Our first randomised placebo-controlled pilot trial was conducted in 28 patients with bilateral reduction mammoplasty (4). Each patient was treated with active medicinal product and placebo, and less drain fluid production was recorded from the breast moistened with tranexamic acid ($p < 0.05$). We subsequently collaborated with the breast surgeons in Trondheim and Ålesund. In a study including 202 mastectomy patients, drain fluid production was reduced by 33 % in those who received tranexamic acid ($p < 0.001$) (5).

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In our two studies into reduction mammoplasty/mastectomy involving 258 breast procedures, there were ten rebleeding episodes requiring surgery, nine of which were in the placebo group. We measured systemic concentrations after topical application to the large wound surfaces in abdominoplasties, and investigated the potential impact on wound healing with topical application (6, 7). Our findings to date indicate that the application of 25 mg/ml tranexamic acid on wound surfaces is both effective and safe. In our studies, we diluted tranexamic acid with saline, but in everyday clinical practice we dilute it in local anaesthetic with added adrenaline because we consider vasoconstriction and pain relief to be potentially beneficial adjunctive effects at the wound surface.

Benefits beyond plastic surgery?

Topical application of tranexamic acid is now widespread in the international plastic surgery field, and retrospective review articles into bleeding before and after the introduction of tranexamic acid crop up regularly in plastic surgery journals. However, there is no reason why the effect should only apply to wound surfaces in plastic surgery.

We have published a systematic literature review of randomised controlled trials into the effect of topical tranexamic acid in soft tissue surgery (8). In addition to our own published material, we found studies involving adenoidectomy, pacemaker implantation, skin excisions, blepharoplasty, lung decortication, prostatectomy, myomectomy and hysterectomy. Efficacy of topical application generally seems to be equivalent to systemic administration. There are many indications that topical tranexamic acid also prevents rebleeding episodes requiring intervention, but evidence needs to be obtained in a large prospective randomised trial with sufficient power.

The optimal concentration and method of administration for topical application is unclear, and the lowest effective concentration is unknown (8). It is likely that the method of administration can be adapted to the surgical specialty, including pouring or spreading the drug on the wound, using it to moisten dressings and adding it to the irrigation fluid or local anaesthetic. Inadvertent intrathecal administration of tranexamic acid can trigger generalised and potentially fatal seizures (9), and therefore topical application is inappropriate in all neurosurgery.

In our opinion, topical application of tranexamic acid is a simple, inexpensive and effective method of reducing bleeding, and its use could be explored in several specialties.

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