BMJ

BMJ 2012;344:e3665 doi: 10.1136/bmj.e3665 (Published 23 May 2012)

EDITOR'S CHOICE

Are we nearly there with tranexamic acid?

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It's the week of the annual BMJ Group Improving Health Awards (http://groupawards.bmj.com). By the time you read this we'll know who has won which of the 12 awards and why. Last year we awarded research paper of the year to the CRASH trialists for their large multicountry placebo controlled randomised trial of tranexamic acid after trauma (*Lancet* 2010;376:23-32). They found a significant reduction in bleeding and mortality in patients given the drug. At the awards event one of the senior authors, Ian Roberts, told me of his frustration that, despite cumulative evidence of the effectiveness of tranexamic acid in reducing the need for blood transfusion in a range of surgical procedures, the drug was not as widely used or available as it should be. As a sign of continuing clinical uncertainty, small trials in various types of surgery continued to be done, he said.

Now he and colleagues have put this frustration to work in the best possible way. Their systematic review and cumulative meta-analysis of trials of tranexamic acid in surgical patients is published in the *BMJ* this week (doi:10.1136/bmj.e3054). It finds that the scientific uncertainty about the effects of tranexamic acid on blood transfusion during and after surgery was resolved over a decade ago. However, it also shows that uncertainties remain about the drug's effects on thromboembolic events and mortality. Figures 2-4 in the full paper on bmj.com tell the story. All 36 trials with adequate allocation concealment were small, with tens or hundreds rather than thousands of patients. Over the past 10 years or so, the cumulative evidence of benefit is clear for blood loss, with narrow confidence intervals favouring tranexamic acid, but less clear for thromboembolic events and mortality.

So what will be learnt from the 14 mainly small ongoing trials in a range of surgical procedures? Not a great deal it seems, since 12 of them have blood transfusion, not mortality, as the main outcome. The review's authors point out that only half of the published trials make reference to available systematic reviews and only two carried out their own systematic review, suggesting that many trialists aren't taking proper account of the existing evidence when they embark on their own research.

Even a small increase in rates of thromboembolism could outweigh the benefits of reduced blood loss, and the ultimate arbiter must be the effect of this drug on mortality—an outcome that the CRASH trial did evaluate, but in patients with trauma. The authors call for all ongoing and future trials in surgical patients to monitor thromboembolic events and mortality so these data can be included in prospective meta-analyses. They also call for a large pragmatic clinical trial of the effects of routine use of tranexamic acid in a heterogenous group of surgical patients.

It's nice to think that the BMJ Group award may have helped to get tranexamic acid on to WHO's essential medicine's list at the end of last year (www.who.int/selection_medicines/committees/expert/18/applications/tranexamic/en). Let's hope that this latest systematic review will inspire researchers to collaborate and resolve these remaining uncertainties. Because patients are waiting.

Cite this as: *BMJ* 2012;344:e3665

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