

Tranexamic Acid: A Recipe for Saving Lives in Traumatic Bleeding

I Roberts

Using kitchen scales, carefully weight out four kilograms of rice and pour it into a deep saucepan. Now put your hands into the rice and let the grains run between your fingers. Contemplate carefully each grain. The number of grains (about 140 000) is approximately the number of lives that could be saved each year world-wide if all hospitalized trauma patients with significant bleeding were treated with tranexamic acid (TXA) within three hours of injury. TXA is cheap and widely available. All that is needed to reap these human benefits is that doctors use it.

That TXA is a potent inhibitor of fibrinolysis was first reported by Shosuke and Utako Okamoto in *The Keio Journal of Medicine* in September 1962.¹ Since then, TXA has been widely used to treat heavy menstrual bleeding and to reduce blood loss in elective surgery where it reduces blood transfusion by about one-third.² The CRASH-2 collaborators hypothesized that TXA might also reduce bleeding in trauma patients. The CRASH-2 trial was a UK government funded randomized trial of the effects of the early administration of TXA on death, vascular occlusive events and blood transfusion in bleeding trauma patients.

A total of 20 211 adults with significant traumatic bleeding were randomized to receive either TXA or matching placebo, with 99.6% follow-up. The risk of death due to bleeding was significantly reduced

with TXA. If TXA is given within three hours of injury, it reduces the risk of bleeding to death by nearly one-third (relative risk: 0.72 [95% CI: 0.63–0.83], $p < 0.001$). All cause mortality was also significantly reduced.^{3,4} The large numbers of patients studied in a wide range of different health care settings help these results to be generalized widely. On the basis of the results of the CRASH-2 trial, TXA has been included in the World Health Organization (WHO) list of essential medicines.⁵ Giving TXA to bleeding trauma patients within three hours of the injury could save over 100 000 lives per year world-wide. Giving TXA to bleeding trauma patients is highly cost-effective in high-, middle- and low-income countries.⁶ It is essential that all doctors who treat trauma patients are aware of the results of the CRASH-2 trial.

TXA should be given to all adults with significant hemorrhage (systolic blood pressure less than 90 mm Hg, heart rate more than 110 beats/min) or those considered by the clinician to be at risk for significant hemorrhage. Because the effect of TXA on death due to bleeding depends significantly on the time interval between the injury and the onset of treatment, it should be given as early as possible and within three or four hours of the injury as it is unlikely to be effective if given later than this.

References

1. Okamoto S, Okamoto U. Amino-methyl-cyclohexane-carbolic acid: AMCHA. A new potent inhibitor of fibrinolysis. *Keio J Med* 1962;**11**:105-15.

Editor, Cochrane Injuries Group, Clinical Co-ordinator CRASH-2 trial



Correspondence to
Ian Roberts, MB, BCH,
MRCP, PhD, FFPH
Editor, Cochrane Injuries Group,
Keppel Street, London
WC1E 7HT
Tel : +20-7958 8128
Fax: +20-7299 4663
E-mail: ian.roberts@lshtm.ac.uk

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2. Henry DA, Carless PA, Moxey AJ, *et al.* Anti-fibrinolytic use for minimising perioperative allogeneic blood transfusion. *Cochrane Database Syst Rev* 2007;**4**:CD001886.
3. The CRASH-2 Collaborators. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomized, placebo-controlled trial. *Lancet* 2010;**376**:23-32.
4. The CRASH-2 Collaborators. The importance of early treatment with tranexamic acid in bleeding trauma patients: an exploratory analysis of the CRASH-2 randomised controlled trial. *Lancet* 2011;**377**:1096-101.
5. Department of Essential Medicines and Pharmaceutical Policies. Essential medicines selection: 18th Expert Committee on the Selection and Use of Essential Medicines. Available from www.who.int/selection_medicines/committees/expert/18/en/index.html (Accessed July 20, 2011).
6. Guerriero C, Cairns J, Perel P, *et al.* Cost-effectiveness analysis of administering tranexamic acid to bleeding trauma patients using evidence from the CRASH-2 trial. *PLoS ONE* 2011;**6**:e18987. doi:10.1371/journal.pone.0018987

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