Josh's Corner

Articles that shaped my practice

Subject: Tranexamic

Article 1 –

CRASH-2 trial collaborators, Shakur H, Roberts I, Bautista R, Caballero J, Coats T, Dewan Y, El-Sayed H, Gogichaishvili T, Gupta S, Herrera J, Hunt B, Iribhogbe P, Izurieta M, Khamis H, Komolafe E, Marrero MA, Mejía-Mantilla J, Miranda J, Morales C, Olaomi O, Olldashi F, Perel P, Peto R, Ramana PV, Ravi RR, Yutthakasemsunt S. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. Lancet. 2010 Jul 3;376(9734):23-32. doi: 10.1016/S0140-6736(10)60835-5. Epub 2010 Jun 14.

Synopsis –

20127 patients were enrolled and analyzed in a double blinded randomized controlled trial upon arrival to the respective hospital to either receive 1 g of tranexamic acid over 10 minutes followed by a second 1 g of tranexamic acid over 8 hours versus placebo. Inclusion criteria included all traumatically injured patients who could have an intervention within 8 hours of injury with either a systolic blood pressure less than 90, a heart rate greater than 110 beats per minute, or physician discretion. Patients were excluded if there was a clear indication or contraindication to the use of tranexamic acid. There was a 1.5% reduction in absolute risk of mortality. There was no change in mortality from vascular occlusion or multi-organ failure. There was no change in amount of units transfused.

Details –

The study was funded by UK NIHR Health Technology Assessment programme, Pfizer, BUPA Foundation, and J P Moulton Charitable. The study occurred in 40 countries with the vast majority of the study sites being in countries that may or may not have modern trauma systems/protocols.[1] Patients were randomized by a central computer and communicated to centers over telephone. 84 patients were excluded. 99.1% completed the loading dose and 94.2% of the patients completed the maintenance dose. Outcomes were only recorded if they occurred within 28 days. Only 3076 patients died (35% on the day of randomization) and of the 20127 patients, only 1063 of the patients died from hemorrhage (60% on the day of randomization). Less than half of the patients met inclusion criteria by heart rate and less than half of the patients met inclusion criteria by blood pressure. 13 patients in the tranexamic acid arm received recombinant factor VIIa while only 4 in the placebo group. The benefit of tranexamic acid was only seen if given within 3 hours of the injury, while there was an increase in mortality if given afterwards. Patients with a systolic blood pressure

≤ 75 or had penetrating trauma were also more likely to have a benefit from receiving tranexamic acid.

Questions raised –

If this study were to be repeated in countries with modern trauma systems and protocols, would the effect size be as large? Do patients with hyperfibrinolysis have the greatest improvement in outcomes? What happens after 3 hours that increases mortality when administering tranexamic acid? If you used modern surveillance techniques, would you find an increase in thrombotic complications with administration of tranexamic acid?

References –

1.) Napolitano LM, Cohen MJ, Cotton BA, Schreiber MA, Moore EE. Tranexamic acid in trauma: how should we use it? J Trauma Acute Care Surg. 2013 Jun;74(6):1575-86. doi: 10.1097/TA.0b013e318292cc54.