CRASH

Clinical Randomisation of an
Antifibrinolytic in Significant Head Injury

Tranexamic acid for the treatment of traumatic brain injury: an international randomised trial

DISSEMINATION STRATEGY

Dissemination strategy

1. Background

Each year, world-wide, about 27 million people (95% CI 24 - 30 million) will experience a traumatic brain injury (TBI). About 2 million people will die but many millions will live with a TBI related disability. Road traffic crashes and falls are the leading causes. TBI is a major public health problem everywhere regardless of country income or level of development. Although the risk of TBI seem to be greatest in high income countries, this may be an artefact due to the lack of reliable data from low and middle income countries. Nevertheless, the number of cases of TBI is greatest in low and middle income countries because they have a much larger population. The incidence of TBI increases with age. With increasing use of motor vehicles and population ageing, the global incidence of TBI is expected to increase.

2. The CRASH-3 trial

The CRASH-3 trial is an international, multi-centre, randomised trial of the effects of early administration (within 3 hours of injury) of tranexamic acid on death and disability in TBI patients. Adults with TBI within 3 hours of injury, with any intracranial bleeding on CT scan or who have a GCS of 12 or less, and no significant extra cranial bleeding are eligible. We hope that tranexamic acid will reduce death and disability after TBI by reducing the extent of bleeding into the brain or into the skull which may cause death or disability by exerting pressure on the brain.

The time window for eligibility was originally within 8 hours of injury but in 2016 we changed the protocol to limit recruitment to patients who are within 3 hours of injury. This was done in response to accumulating evidence that the TXA treatment is unlikely to be effective when given beyond 3 hours of injury and might even do more harm than good. We recruited nearly 13,000 patients from hospitals world-wide. The primary outcome is head injury death in hospital within 28 days of injury in patients treated within 3 hours of injury but we will also asses and report on levels of disability.

3. Objectives of dissemination

3.1 Make the results clear and explain the biological mechanisms

The first objective is to make the result clear. TXA is a drug that reduces bleeding by inhibiting fibrin clot breakdown, a process called fibrinolysis. Most head injury patients are managed by neurosurgeons who have only a rudimentary understanding of haematology. One of the main obstacles to implementing the results of the CRASH-2 trial of TXA in extra-cranial bleeding was that emergency physicians knew very little about fibrinolysis. Indeed, shortly after publication of the CRASH-2 trial results, an US doctor posted a highly viewed video explaining the trial results.

https://www.youtube.com/watch?v=YXPU_MEd5vg

Whilst reasonably accurate, it could have been better and we should have done this. The general level of haematology understanding should be higher now as a result of the CRASH-2 trial, but we must not overestimate neurosurgeons knowledge about fibrinolysis and need to prepare media that explain the results. We must also bear in mind that doctors understanding of epidemiology and biostatistics is extremely limited and that pathophysiological explanation is much more important. You may have a highly statistically significant benefit from a large randomised trial but the results will not be implemented unless doctors understand the mechanism of action. Biological mechanism is narrative and narrative is the only thing that is memorable.

3.2 Make sure that we have everything that journalists need for publication day.

We need patient stories about the impact of TBI on the lives of patients and their families. Ideally, we would have this for high (UK) and middle income countries (e.g. Pakistan). We don't know what the results show yet but we are reasonably sure that any treatment effect will be time dependent in that earlier treatment will be most effective and late treatment least effective. Our film footage should therefore emphasise time to treatment and the need for urgency. We need to identify patients who are willing and able to talk about the results to the media on the day of publication. We need to identify some authoritative independent experts (possibly including WHO) willing to discuss the trial results in the media. We should liaise with the funders (NIHR, MRC, DFID, Wellcome) to make sure they know the results are coming and to link in with their press offices.

3.3 Make sure that we meet the publication deadline.

We have been invited to present the trial results at two large international meetings that are happening at the same time: The World Congress on Intensive Care (https://www.worldcongressintensivecare2019.com/) in Melbourne which IR will attend and the Neuro-critical Care Society Annual Meeting in Vancouver which HS will attend (https://www.neurocriticalcare.org/events/annualmeeting). Ideally, we would time the publication of the trial results to coincide with these presentations. The meetings would be a good dissemination opportunity.

3.4 Engage with stakeholders in advance of the results being published

Although the burden of death and disability from TBI is far greater than for PPH, there is much less global coordination of treatment policy decision making and far fewer "authoritative" bodies. Nevertheless, we should engage with key stakeholders and leaders (including patient organisations of which Headway is the most important in the UK). We need to build a database of key stakeholders as we did for the Woman trial and let them know about the trial well in advance of publication and the trial results just before publication.

3.5 Help our collaborators to disseminate the results in their respective countries.

Develop dissemination tools that collaborators can use for national and international audiences. We need to upgrade our trial website and make sure that it hosts all of the trial dissemination materials that can be downloaded and used locally. We need to help national co-ordinators to achieve press coverage in their respective countries. Unlike the Woman trial there will be no focus countries since TBI is a major public health issue in every country of the world. However, we will focus our efforts where we have good contacts. Making an impact in the UK will be important since this influences treatment decisions in other countries.

Specific outputs:

1. Short videos that explain the trial procedure and the results in pathophysiological terms

2. Authoritative explanation of the results from respected neurosurgeons that have contributed importantly to the trial (e.g. Prof Rashid Jooma in Pakistan and Prof Tony Belli in the UK). Membership of the trial steering committee is shown below.

3. One page infographic that summarises the trial and the results that can be disseminated similar to the one prepared for the woman trial.

4. Film footage of victim experiences from UK and Pakistan

5. Film footage that emphasise urgency and the importance of reducing treatment delay

6. Identify victims of TBI who are prepared to talk to the media (consider approaching Headway and RoadPeace for this). https://www.headway.org.uk/

7. Identify independent experts who are prepared to talk to the media

8. Co-ordinate the dates of the publication to the world congresses.

9. Build a database of key stakeholders and provide advance warning of the results.

10. Upgrade the trial website – make sure that it hosts trial related materials that can be downloaded by investigators and others and used for dissemination.

11. Photography – we need high resolution still photos from the film

12. Social media toolkit to share with partners and stakeholders so that everyone has content and messaging to share via their channels

13. Media plan and materials – specifics will depend on results, but may include a press release(s) for examples, and media pitches for specific outlets, plus case studies.