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15:00-15:45

Room 3C

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The CRASH Trial (Corticosteroid Randomisation After Significant Head injury) is a large-scale randomised controlled trial, among adults with head injury and impaired consciousness, of the effects of a short term infusion of corticosteroids on death and on neurological disability. Following a successful pilot phase that included over 1,000 randomised participants, the main phase of the trial is now underway. Over the next five years the trial aims to recruit a total of 20,000 patients. Such large numbers will only be possible if hundreds of doctors and nurses in emergency departments all over the world can collaborate.

There are many reasons for conducting the CRASH Trial now: (1) Results from animal studies show that high dose methylprednisolone (MP) can reduce post-traumatic neuronal degeneration [1,2]; (2) Patients with spinal cord injury who are treated with corticosteroids rather than placebo within 8 hours of injury appear to have greater improvement in motor function, and sensation to pinprick and touch [3,4]; (3) There are wide variations within and between countries in the use of corticosteroids in head injury [5]; (4) A meta-analysis of randomised trials of corticosteroids in head injury shows that existing trials are too small to demonstrate or to refute the possibility of a moderate but clinically important benefit [6].

The CRASH Trial aims to determine reliably the effects of high dose MP infusion on death and on disability following significant head injury. Head injured adults with impaired consciousness are eligible for inclusion in the trial if the responsible doctor is for any reason substantially uncertain whether or not to use corticosteroids. Patients with head injury and impaired consciousness may be unable to give properly informed consent, and in this emergency situation it may not be appropriate to delay the start of treatment until relatives consent can be obtained. Hence, the doctor in charge should take responsibility for entering such patients, just as they would take responsibility for choosing other treatments. However, the requirements of the relevant research ethics committee must be adhered to.

Numbered drug or placebo packs will be available in each participating emergency department. Randomisation involves calling a 24-hour free phone service. The call should last only a minute or two, and at the end of it the service will specify to the caller which numbered treatment pack to use. If, for any reason, telephone randomisation is not feasible, randomisation can also be carried out by fax. The outcome measures are death from any cause within two weeks of injury, and death or dependence at six months. In-hospital deaths, complications and short-term recovery are recorded on a single sided outcome form that can be completed entirely from the hospital notes and no extra tests are needed. Long term recovery is assessed at six months either by a simple postal questionnaire, sent directly to each trial participant from the national co-ordinating centre, or by telephone interview, and will not involve any additional work for collaborating hospitals.

The global epidemic of head injuries is just beginning. At present, over a million people die each year and a similar number are disabled from brain injuries, often with profound effects on the quality of life of the affected individuals and their carers.<sup>7</sup> Road traffic crashes account for most of the deaths and car use is rapidly increasing in many countries. It is estimated that by 2020 road traffic crashes will have moved from ninth to third in the world disease burden ranking, as measured in disability adjusted life years, and second in developing countries. The identification of effective treatments for head injury is of global health importance. With over 8,000 randomised patients the CRASH trial is already the largest randomised controlled trial in head injury ever conducted but it will only be possible to reach our recruitment target of 20,000 patients if doctors and nurses worldwide join the trial and help to make it a success.

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## REFERENCES

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4. Otani K, et al. Beneficial effect of methylprednisolone sodium succinate in the treatment of acute spinal cord injury (translation of Japanese). *Sekitsui Sekizui J* 1994;**7**:633-47
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