The CRASH trial: The first large-scale randomized controlled trial in head injury

The Medical Research Council CRASH Trial (Corticosteroid Randomization After Significant Head injury) is a large-scale randomized controlled trial, among adults with head injury and impaired consciousness, of the effects of a short term infusion of corticosteroids on death and neurological disability. Following a successful pilot phase that included over 1000 randomized participants, the main phase of the trial is now under way. Over the next five years the trial aims to recruit a total of 20 000 patients. Such large numbers will only be possible if doctors and nurses worldwide join the trial and help to make it a success (www.crash.lshtm.ac.uk).

There are many reasons for conducting the CRASH trial now: (i) results from animal studies show that high dose methylprednisolone (MP) can reduce post-traumatic neuronal degeneration;¹² (ii) 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 in sensation to pinprick and touch;³⁴ (iii) there are wide variations within and between countries in the use of corticosteroids in head injury;⁵ (iv) a meta-analysis of randomized trials of corticosteroids in head injury shows that existing trials are too small to demonstrate or 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 disability following significant head injury. Head injured adults with impaired consciousness are eligible for inclusion in the trial if the treating doctor is for any reason substantially uncertain whether or not to use corticosteroids. These patients 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 the consent of the relatives can be obtained. Hence, the doctor in-charge should take responsibility for entering such patients into the trial, 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. Randomization involves calling a 24-hour free phone service. The call should last only a minute or two, at the end of which the service will specify to the caller which numbered treatment pack to use. If, for any reason, telephone randomization is not feasible, it can also be carried out by fax. The outcome measures are death from any cause within 2 weeks of injury, and death or dependence at 6 months. In-hospital deaths, complications and short term recovery are recorded on a single-sided outcome form that can be completed entirely from hospital notes without any extra tests. Long term recovery is assessed at 6 months either by a simple postal questionnaire, sent directly to each trial participant from the national coordinating centre or by telephone interview, and does 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.⁷ Road traffic accidents account for most of the deaths and cars are being increasingly used in many countries. It is estimated that by 2020, road traffic accidents will have moved from the ninth to the third place in the world disease burden ranking, as measured in disability-adjusted life-years, and to the second in developing countries. The identification of effective treatments for head injury is of global health importance. The CRASH trial is already the largest randomized controlled trial in head injury ever conducted, but it will only be possible to reach the recruitment target of 20 000 patients if doctors and nurses worldwide join the trial and help to make it a success (www.crash.lshtm.ac.uk). If you would like to take part, please register your interest via the trial website or write to the CRASH Trial Coordinating Centre and we will send you everything you need to participate.
REFERENCES


IAN ROBERTS
On behalf of the CRASH trial management group
CRASH Trial Coordinating Centre
London School of Hygiene and Tropical Medicine
49–51 Bedford Square
London
UK
crash@lshtm.ac.uk

The National Medical Journal of India is now covered in Current Contents: Clinical Medicine, Science Citation Index, SciSearch and Research Alert.
—Editor