Drug that prevents clot breakdown could save thousands of accident victims worldwide

June 14 2010

a cheap, widely available and easily administered drug which reduces the rate of blood-clot breakdown—could save the lives of thousands of accident victims worldwide. The CRASH-2 study, published Online First and in an upcoming *Lancet*, also concludes that TXA should now be included on the WHO list of essential medicines. The Article is written by Professor Ian Roberts and Dr Haleema Shakur, London School of Hygiene and Tropical Medicine, UK, and colleagues from the CRASH-2 consortium.

Injuries are major causes of death worldwide. Every year, more than a million people die as a result of road traffic injuries around the world. Road traffic injuries are the ninth leading cause of death globally, and such injuries are predicted to become the third leading cause of death and disability by 2020. About 1.6 million people die as a result of intentional acts of interpersonal, collective, or self-directed violence every year. More than 90% of trauma deaths occur in low-income and middle-income countries. Furthermore, haemorrhage is responsible for about a third of in-hospital trauma deaths and can also contribute to deaths from multi-organ failure.

Part of the response to surgery and trauma is stimulation of clot breakdown (fibrinolysis). TXA works by inhibiting the enzyme which carries out fibrinolysis. The authors proposed that TXA might reduce mortality due to bleeding in trauma patients; however, until now there have been no randomised trials of this drug in such patients. Thus in CRASH-2, the authors assessed the effects of the early administration of

a short course of TXA in trauma patients.

The trial was funded by England's National Institute for Health Research (NIHR) Health Technology Assessment programme and was a large, randomised trial involving over 20,000 adult patients in 274 hospitals across 40 countries. Participants received either one gram of TXA by injection, followed by another one gram in a drip over the following eight hours, or a matching placebo. The researchers studied the numbers of deaths in hospital within four weeks of injury.

TXA reduced the risk of death by any cause by 10% compared with placebo, with 14•5% of patients in the TXA group dying versus 16.0% in the placebo group. Looking specifically at the risk of death due to bleeding, TXA reduced the risk of death by 15% compared with placebo, with 4.9% of patients in the TXA group dying versus 5.7% in the placebo group. Although the research team was concerned that TXA might increase the risk of complications, such as heart attacks, strokes and clots in the lungs, the results of CRASH-2 show that TXA reduces death from bleeding without any increase in these complications.

Professor Roberts says*: "Each year about 600,000 injured patients bleed to death worldwide. Injuries may be accidental, for example road traffic crashes, or intentional, such as shootings, stabbings or land mine injuries and the majority of deaths occur soon after injury. Although most deaths from injuries are in developing countries, injury is a leading cause of death in young adults throughout the world."

He adds*: "It's important to remember that deaths from injuries are increasing around the world and that they usually involve young adults, often the main breadwinner in the family. The impact on the family is devastating."

The researchers estimate that TXA could prevent up to 100,000 deaths

per year across the world. In India it could save about 13,000 lives each year, with about 12,000 lives saved in China. The drug would also save lives in developed countries, around 2,000 each year in the USA and more in Europe. About 1800 people die from bleeding after injury each year in the UK and TXA could cut this figure by about 280.

Furthermore, the researchers are excited about other potential future applications of TXA, such as reduction of brain bleeds after brain injury, for which new studies are needed. TXA could also be used for reduction of postpartum haemorrhage in women worldwide, which causes around 100,000 deaths each year. A large trial to assess TXA for this purpose is in progress.

The authors conclude: "Tranexamic acid could be given in a wide range of health-care settings, and safely reduced the risk of death in bleeding trauma patients in our study. The option to use tranexamic acid should be available to doctors treating trauma patients in all countries, and this drug should be considered for inclusion on the WHO List of Essential Medicines. On the basis of these results, tranexamic acid should be considered for use in bleeding trauma patients."

In an accompanying Comment, Dr Jerrold H Levy, Emory University School of Medicine, Atlanta, GA, USA; and Cardiothoracic Anesthesiology and Critical Care, Emory Healthcare, Atlanta, GA, USA, says: "Today's study shows that inhibition of fibrinolysis with tranexamic acid after major trauma is an important mechanism to reduce mortality... However, caution is needed before extrapolation of the results of CRASH-2 to other antifibrinolytic agents until they have been studied in a similarly robust manner."

Provided by Lancet