African trial questions emergency treatment of children in shock

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Giving fluids rapidly through a drip into a vein (fluid resuscitation) as an emergency treatment for African children suffering with shock from severe infections does not save lives, according to a major clinical trial funded by the Medical Research Council. The ground-breaking research showed that giving children fluids slowly to replace the needs of a sick child who cannot drink, rather than rapid fluid resuscitation, is safer and more effective in aiding recovery. These findings challenge current World Health Organization (WHO) guidelines on how best to provide fluids to children in Africa with fever and shock caused by malaria, sepsis and other infections.

The trial known as FEAST (Fluid Expansion As Supportive Therapy) involved over 3000 children in six hospitals across Tanzania, Uganda & Kenya. It examined the effectiveness of a long-standing treatment used across the world called fluid resuscitation. This treatment involves giving seriously ill children large volumes or 'boluses' of intravenous fluids quickly through a drip in their first hour at hospital to try to reverse the deadly effects of shock.

The children on the trial were divided randomly into three equally sized groups. Two groups were given emergency boluses of either albumin or saline in the first hour of arriving in hospital. After the first hour, the children were then given fluids slowly, to replace the amounts a sick child should drink. The third group were given fluids slowly from the first hour of admission but no additional bolus treatment.

The trial results showed that children given fluids more slowly did better, with a 48-hour survival rate of 92.7%, compared with 89.4% of those children given boluses. Compared with giving children fluids slowly, fluid resuscitation caused three additional children to die out of every hundred treated.

The trial was stopped early because the independent committee overseeing safety saw that giving boluses was unsafe. However, all children who took part in FEAST had a better chance of survival than is normally the case in Africa, in part due to extra training given to hospital staff to give emergency treatments, such as oxygen and providing medicines for malaria and other infections.

Professor Kathryn Maitland, the Chief Investigator for FEAST, Imperial College London and KEMRI-Wellcome Trust Program said: "This is the first time anywhere in the world that fluid resuscitation has been evaluated for safety and effectiveness in such a large trial, even though it has been standard treatment for the last two decades in the United States, Europe and Australasia. The FEAST trial was set up with the hope that fluid resuscitation would help the many African children with malaria and septicemia. Around one in ten children in Africa admitted to hospital with these deadly infections are in a state of shock. Although there are effective medicines for these illnesses, too often children arrive in hospital already very sick, with many children dying within hours of admission. Large-scale clinical trials of this nature carried out to the highest levels are crucial if we are to find new ways to keep children alive when they come into hospital. Disappointingly, across all parts of the trial we found that rapid fluid resuscitation had no benefit- our only conclusion is that boluses are harmful when used for shock in the illnesses we studied."

Professor Sarah Kiguli, Chief Principal Investigator in Uganda said: "The results have surprised me, particularly as I had seen some children getting better after being given large volumes of fluids. But more importantly the results went against the recommendations of the WHO and the normal practice in wealthy countries, and this surprised me greatly. Finding this out before we started to encourage the use of fluid resuscitation children with severe infections and shock across Africa was incredibly important. It will save many lives in

future."

The study authors agree that further research is needed in countries where fluid resuscitation is already standard practice, although the results in Africa may not be directly applicable to wealthy countries. One reason for this is that sophisticated life support equipment is available in wealthier countries and is available along with fluid resuscitation as part of a 'package of care'.

Professor Diana Gibb from the Medical Research Council Clinical Trials Unit said: "The treatment may not carry the same risks in wealthy countries because children are healthier, and in particular have few problems of underlying long-standing malnutrition or anaemia. However, the clear findings from the FEAST trial do question the use of boluses for severe infections even in wealthy countries and more research is needed."

The researchers have stressed the need to continue to use fluid resuscitation to treat diarrhoea and other conditions like burns and trauma, where children lose fluids. For these conditions, where fluid resuscitation will continue to be a vital life-saving treatment, they advise that current WHO recommendations should stay the same. Children with severe malnutrition were not included in the trial as fluids are not recommended as part of their treatment.

More information: The paper 'Mortality after Fluid Bolus in African Children with Severe Infections' will be published online by the New England Journal of Medicine on 2000 BST 26 May 2011.

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