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Treating the wrong children with fluids will cause harm: response to 'mortality after fluid bolus in African children with severe infection'

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Professor Maitland and colleagues recently published the results of a large international study to examine the role of fluid boluses in the management of seriously ill febrile children in Africa.[1] While the study was extremely well conducted, we are seriously concerned about the conclusions and implications of the paper, which states:

> The results of this study challenge the importance of bolus resuscitation as a life-saving intervention in resource-limited settings for children with shock who do not have hypotension and raise questions regarding fluid-resuscitation guidelines in other settings as well.

Already in the UK, the media has responded with alarming headlines, such as 'a trial in Africa has raised major questions about the safety of the routine treatment given to children suffering from shock in the UK and other developed countries'.[2] The consequences of responding positively to this message and not treating hypovolaemic shock with intravenous fluid boluses could be extremely serious for children in both poorly resourced and developed countries.

In our opinion, the study was inappropriately designed with respect to patient selection and as a result was probably treating children with serious febrile illnesses due to the most common of medical problems, namely pneumonia and malaria, but not hypovolaemic shock. This was because reliance was placed on including children with clinical signs that individually have poor specificity for shock.

The study included children aged between 60 days and 12 years of age, who presented with a severe febrile illness (24% with an axillary temperature >39°C) complicated by impaired consciousness (prostration in 62% or coma in 15%), respiratory distress (increased work of breathing in 83%) or both. The children were also reported to have evidence of impaired circulatory perfusion, as evidenced by one or more of four clinical signs (see below). Children with gastroenteritis and non-infectious causes of shock (eg, trauma, surgery, burns) were excluded, as were 'conditions for which volume expansion is contraindicated'. Patients with severe hypotension were given only fluid boluses without a control group. The study found that children with severe febrile illnesses, who were given either intravenous infusions of normal saline over 1 h or 5% albumin, had a worse outcome than those given intravenous fluids at a level to maintain basic fluid requirements only.

However, we contend that the study was *not* specifically treating shock as currently defined by the WHO (cold hands, capillary refill longer than 3 s and weak, fast pulse).[3] The clinical features used in this study to define hypovolaemic shock (all degrees of impaired perfusion) were one or more of the following: severe tachycardia, a capillary refill time of 3 or more seconds, a lower limb temperature gradient or a weak radial pulse volume. It was not required for these signs to be found together, so *only one sign could have allowed inclusion*. While these signs are commonly all found in shock, the first three signs *individually* have poor specificity for hypovolaemic shock and thus may be found in other medical conditions.[4 5] It is their combination, which is required for confirmation of hypovolaemic shock, that needs rapid circulatory expansion. If this study of seriously ill children, 77% of whom had prostration or coma, was about shock, we would expect more than the reported 21% of the cohort to have had poor radial pulse volume. In addition, only 6% were defined as having 'moderate hypotension'.

Understandably, there were limited abilities to investigate the underlying cause of the febrile illness, including absence of chest x-rays. In resource-poor countries, the most common causes of mortality include pneumonia, malaria and gastroenteritis. Of the 3141 children, 83% had respiratory distress, 57% had malaria parasitaemia (although it is not clear whether this was active infection with trophozoites or carriage with gametocytes), 32% had a haemoglobin <5 g/dl and 37% had convulsions. While gastroenteritis was excluded, it is likely that a high proportion of the children had either malaria or pneumonia, both conditions where fluid boluses in the absence of hypovolaemic shock may be expected to worsen a child's condition. Severe malaria more commonly presents with severe anaemia and raised intracranial pressure than with hypovolaemic shock. Pneumonia more usually presents with respiratory distress and hypoxaemia than shock. Blindly giving fluid challenges of 40 ml/kg (50% of total blood volume for any child) within the first 8 h of treatment to sick febrile children in the absence of hypovolaemic shock may worsen severe anaemia, raise intracranial pressure further and could overload the circulation and worsen hypoxaemia in pneumonia.

We would argue that treating a large cohort of children with multiple causes for febrile illness and without confirmation of 'advanced' hypovolaemic shock would most certainly result in clinical deterioration if routinely given fluid challenges of 50% of blood volume in the first 8 h of treatment. This does not mean that a properly administered bolus of 20 ml/kg given as rapidly as possible,[3 6] usually within 10 min, for a specific diagnosis of hypovolaemic shock is harmful. This is why we and the WHO advocate a structured approach to the assessment, resuscitation and emergency treatment of the seriously ill child.[3 6] This means a structured ABC assessment of the life threatening physiological derangements and their appropriate treatment. This includes targeting volume replacement specifically for those with hypovolaemic shock based on a combination of signs.

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The important increases in overall survival of these critically ill children in this study undoubtedly arise from the training and implementation of triage and life support measures undertaken by the researchers. Of surprise to us, and perhaps requiring comment, was the failure to mention the use of additional inspired oxygen, which is essential for treating both respiratory distress (particularly where there is hypoxaemia – pulse oximeters were used and 25% had oxygen saturations <90%) and shock. We also cannot understand why the basic clinical signs for pneumonia, following examination of chest movements, percussion and auscultation, were not mentioned.

The findings of this study must not lead to changes in practice, until further data with more specific criteria for shock confirm that fluids should not be administered for hypovolaemic shock. Until then, existing studies[7 8] and clinical practice strongly support the use of bolus fluids to treat hypovolaemic shock as defined by the WHO in all settings.

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