Fluid resuscitation in diabetic ketoacidosis and the BPSED guidelines: what we still don’t know

Mark J Peters

The 2020 British Society for Paediatric Endocrinology and Diabetes (BPSED) guideline differs from the previous iteration and the more conservative National Institute of Health and Care Excellence 2016 guideline for diabetic ketoacidosis in children and young people (2015). It recommends a more liberal approach to initial fluid resuscitation and a reduced enthusiasm for using inotropes. This contrasts with shock resuscitation guidance elsewhere. In septic shock acute fluid resuscitation is now recommended to be more selective and conservative, and the early use of vasoactive drugs is supported.1

So why did BPSED make a new recommendation for diabetic ketoacidosis (DKA)? Recent correspondence2 suggests that it arose from: (A) expert interpretation of physiological data suggesting hypoperfusion as the precursor to cerebral oedema; (B) the Pediatric Emergency Care Applied Research Network (PECARN) fluid in DKA randomised controlled trial3 and (C) regional audit data. Such evidence is not compelling.

Physiological and imaging data suggest cerebral hypoperfusion may not be present at baseline. In 1948, Kety et al4 measured cerebral blood flow (CBF) in adults with DKA: none had CBF below the normal range and several were hyperaemic. Glaser et al5 interpreted MRI scans of patients in DKA as suggesting increased CBF. Some of this excess may have resulted from treatment. If concern about hypoperfusion is key, it is not clear why increasing perfusion with inotropes rather than fluid is discounted. Inotropes have the advantage of not reducing osmolarity, and rapid falls in osmolarity probably contribute to cerebral oedema. The PECARN study3 was prompted by concerns about this mechanism. It compared high and lower volume and tonicity fluid regimens in children with DKA. There was no difference in the primary outcome of significant neurological deterioration. Children at high risk of cerebral oedema at baseline were excluded, and clinically evident brain injury was so rare: 12 episodes (0.9%) that the study was not powered to inform on relative risk. Last, use of unpublished audit data in the development of guidelines is unconventional. Most guidelines state the methodologies in advance and specifically avoid the use of non-peer-reviewed data as a potential source of bias.

Perhaps something more fundamental needs to be considered when discussing intravenous fluid resuscitation. This is a very difficult area to study. There is no high-performing, or universally accepted, definition of shock in children; hypotension definitions are problematic, and the severity of shock does not always relate to the probability of a poor outcome; positive acute physiological responses (improvements in heart rate and perfusion) correlate poorly with outcomes, the risks and benefits of fluid resuscitation are highly sensitive to the cause of shock (eg, myocarditis less benefit than hypoxaemia), the timing (early resuscitation more benefit than late resuscitation) and the healthcare system in which the resuscitation is being provided (greater risk when no access to positive pressure ventilation, lower risk on an intensive care unit).1

Defining shock is especially problematic in DKA. Acidosis and hypocarbia cause a range of clinical features independent of tissue oxygen delivery, for example, tachycardia, tachypnoea and reduced skin perfusion,6,7 and adaptive metabolism (eg, raised serum lactate8) that can easily be misinterpreted as signs of shock.

The degree of physiological disturbance with severe acidosis, tachypnoea and poor perfusion would be associated with very...
Aim for future guidelines might be a more approach stratified for the specific risks of cerebral oedema versus shock in an individual case.

What we don’t yet know about the BSPED guidelines is: why they choose to recommend more aggressive resuscitation in a low-risk situation? Fluids carry a potentially important risk of harm even in the absence of the predominant additional risk of cerebral oedema.

The general principle should be that we do not intervene without evidence. We don’t yet know where the balance of risks and benefits sits for early volume expansion in DKA. But any change requires a justification than can be considered by the potential users of the guideline.

Twitter Mark J Peters @pus27
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ORCID iD Mark J Peters http://orcid.org/0000-0003-3653-4808

REFERENCES


