

Fluid management during diabetic ketoacidosis in children: guidelines, consensus, recommendations and clinical judgement

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Two letters in the journal focus on the volume of intravenous fluid to be used during resuscitation and early management of paediatric patients presenting with diabetic ketoacidosis (DKA).^{1,2} The correspondence encapsulates an important debate about intravenous fluids and risk of morbidities, such as cerebral oedema, and provides us with the range in contemporary opinions in the UK.

Lillie *et al*¹ use their insights from the South Thames Retrieval service (STRS) and its 20 referring district general hospitals to highlight a concern about the new British Society for Paediatric Endocrinology and Diabetes (BSPED) guideline³ and integrated care pathway⁴ for the management of DKA. The authors have a network of emergency practice, and they imply that the new emphasis by the BSPED on permissive rather than restrictive (ie, reduced volume rules) intravenous fluids will be disruptive to the measures that they have taken since dealing with three cerebral oedema deaths in their region. Wright and Thomas² have responded on behalf of the BSPED DKA interest group. They emphasise the importance of adequate intravenous fluid resuscitation in limiting morbidity. They also provide an instructive table² showing fluid resuscitation and rehydration volumes used in a number of protocols, including that of STRS and the new BSPED approach. The main differences come down to the estimate of fluid deficit, the use of an intravenous fluid bolus at presentation and the calculation of maintenance fluid requirements.

The STRS approach assumes a 10% fluid deficit in all patients with DKA at presentation, versus the new BSPED guideline's use of three levels in estimated

fluid deficit based on severity of acidosis (ie, pH >7.2, 5%; pH 7.1 to 7.2, 7%; and pH <7.1, 10%). In the STRS approach, an intravenous fluid bolus of 10 mL/kg normal saline (NS) is reserved for patients in shock. In contrast, the new BSPED guideline recommends that all patients with DKA receive an intravenous bolus of 10 mL/kg NS, with an extra 10 mL/kg NS (20 mL/kg in total) for those in shock. Last, in the STRS protocol, the 10% fluid deficit is repaired over 48 hours by adding the volume to restrictive or so-called reduced volume rules for maintenance intravenous requirements and for body weight (ie, up to 10 kg, 2 mL/kg/hour; 10–14 kg, 1 mL/kg/hour and >40 kg, fixed volume 40 mL/hr). The new BSPED guideline also recommends replacing the presumed fluid deficit over 48 hours, but this hourly volume is added to standard (and higher than reduced volume rules) maintenance intravenous fluids.^{4,5}

Now, add to this mixture of opinions, the UK National Institute for Health and Care Excellence (NICE) latest updated pathway for DKA in children and young people.⁶ Like the new BSPED guideline, NICE also estimates fluid deficit based on severity of acidosis. However, severity of fluid deficit is dichotomised to 5% or 10% based on whether pH is above or below 7.1, respectively. Like the STRS approach, there is no routine use of an intravenous NS fluid bolus in severe DKA. Last, like the STRS approach the estimated fluid deficit is repaired over 48 hours by adding the hourly volume to maintenance requirement calculated using reduced volume rules.

How can there be such variance in opinion and recommendations and what should we do? To be fair, the new BSPED guideline³ was only ever '... an interim recommendation pending the publication of the future NICE review.' But, more importantly, the BSPED website acknowledges that the onus for decision-making remains with the clinician; a similar stance on responsibility of guideline users is also taken by NICE.

The new information that seems to have influenced the BSPED and the NICE updates on DKA is the Pediatric Emergency Care Applied Research Network (PECARN) clinical trial of fluid infusion rates for paediatric DKA (FLUID trial).⁷ It is worth re-reading the paper and its protocol and supplementary appendix, in particular have a look at Figure S1 on compliance to assigned fluid rate. The bottom line of the FLUID trial is that neither the rate of administration (*fast* vs *slow* repair) nor the sodium chloride content (NS vs 0.45% saline) of intravenous fluids significantly influenced neurological outcomes. Wright and Thomas² show in their table that the difference between *fast* and *slow* repair in the trial was complex and not only included a difference in timing of fluid-deficit repair (ie, *fast* with 50% repair in first 12 hours followed by 50% repair in next 24 hours vs *slow* repair evenly distributed over 48 hours). It also involved differences in presumed fluid deficit (10% vs 5%) and use of intravenous NS boluses (20 mL/kg vs 10 mL/kg). Close review of the compliance to assigned fluid rate in the FLUID trial (see Supplemental Figure S1⁷) shows that actual fluid received by patients in the *fast* and *slow* repair groups are similar to those suggested by the BSPED and STRS/NICE, respectively. If there is no difference in neurological outcome, does the difference in fluid strategy really matter, as each of our correspondents argue?

To attempt to answer this question we have to look at two key details of the FLUID trial. The first is that of the 1389 patients undergoing randomisation, 1263 (91%) had Glasgow Coma Scale (GCS) score 15, 99 (7%) had GCS score 14 and 28 (2%) had GCS score <14. In essence, the test of *fast* versus *slow* fluid strategy is strongly influenced by patients with DKA who are fully awake at presentation. Both of our correspondents^{1,2} acknowledge that patients with altered mental state raise concern, although their approaches differ—on this matter we have no answer from the FLUID trial. The other detail to consider is that the uniformly used standard insulin infusion rate (0.1 U/kg/hour) differs from the dosing range (0.05 to 0.1 U/kg/hour) used in UK practice.^{3,4,6} One theoretical aim of low-dose insulin (0.05 U/kg/hour)^{8,9} is to avoid too rapid decrease in serum glucose concentration (ie, >5.5 mmol/L/hour), with consequent too rapid change in serum osmolarity, which may increase the risk of cerebral oedema.^{10,11} Does this idea mean that the low-dose insulin strategy enables better tolerance of *fast*-fluid repair rate, with low

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risk of morbidity? Impossible to answer. As we see from the FLUID trial, such a proposition—with an outcome of brain injury in less than 1% of DKA episodes—is likely untestable in a future sufficiently powered clinical trial.

Taking all the above together, there is clearly a need to realign the variance in DKA fluid management reflected in the STRS,¹ BSPED^{2–4} and NICE⁶ approaches. Even though we have gold standard clinical information from the PECARN DKA FLUID trial,⁷ the relevance of that information to all paediatric patients presenting with DKA needs careful consideration. Which means that clinicians still need to exercise judgement in individual situations. Finally, the letter by Lillie *et al*¹ also reminds us of the value of systems of care. Their hub-and-spoke network for emergency DKA care is not just about adopting latest recommendations but is also tasked with bringing about any necessary knowledge-to-action change (see the table and figure 2 as responses to three cerebral oedema DKA deaths),¹ a process called implementation science.¹²

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