LETTER

Response to: Management of fluids in paediatric diabetic ketoacidosis: concerns over new guidance

Despite the introduction of more restrictive fluid in the management of diabetic ketoacidosis (DKA) such as that advocated by Lillie *et al*,[1] there is little epidemiological evidence to suggest that more restrictive regimens have reduced the incidence of cerebral oedema. Cerebral oedema occurs prior to the administration of fluid in up to 19% of cases, and subclinical oedema has been demonstrated on MRI in up to 50% of cases.[2 3] Why some patients evolve cerebral oedema and others do not and the role of fluids remain unclear and contentious. Experts suggest that it results from initial hypoperfusion followed by vasogenic/reperfusion injury rather than the traditional view of osmotic changes.

In 2019, a multidisciplinary expert working group (including paediatric intensivists) was convened by the British Society of Paediatric Endocrinology and Diabetes to review the previous guideline published in 2015 following the National Institute for Clinical Excellence (NICE) review.[4] Firstly to consider the clinical implications of the recently published Pediatric Emergency Care Applied Research Network (PECARN) DKA FLUID study and secondly to address clinician's concerns as to whether the more restrictive fluid regime introduced in 2015 may be overly restrictive, potentially delaying recovery and increasing morbidity particularly acute kidney injury. Several regional audits were shared within the group and a number of deaths were noted.

The PECARN study randomised 1389 cases of DKA and examined both a rapid versus slow fluid regimen and also 0.45% vs 0.9% saline[5] (see table 1). There was no difference in the incidence of cerebral oedema or adverse neurological outcomes of more rapid fluid administration. The majority of patients in the study had modest ketoacidosis (mean pH=7.16), but examination of the lowest pH quartile (pH<7.1) demonstrated that in the rapid fluid group only 11/131 (8.4%) had a decline in Glasgow Coma Score compared with 18/151 (11.9%) in the slow group. The 2015 NICE guideline cited six small predominantly case–control studies as evidence that higher volumes of fluid administration may exacerbate cerebral oedema (four studies suggested that fluids were not a factor).[4] The most influential study, with the highest evidence weighting, was a case–control study. While analysis adjusted for baseline differences, the mean pH of those who evolved cerebral oedema was pH=7.0 compared with the controls pH=7.2.[6]

While we would be the first to acknowledge that many of the recommendations of the guideline are based on expert consensus, the new evidence from the FLUID study was strong, physiological data suggest hypoperfusion is a factor, audit data were reviewed and the group supported adopting a more liberal fluid regimen similar to that used in the most widely implemented international guideline, that of the International Society for Pediatric and Adolescent Diabetes (ISPAD).[7]

While the point Lillie *et al* make about peripheral vasoconstriction is a valid one, the guideline does not advocate assessing shock purely based on capillary refill. The Advanced Paediatric Life Support (APLS) criteria to assess shock which de-emphasise reliance on capillary refill and stress the importance of other markers for shock are advocated. A 20 mL/kg bolus for 'reduced conscious level/coma' is not advocated. A child with both shock and a reduced conscious level would receive a fluid bolus; however, cerebral blood flow is dependent on cerebral perfusion pressure and intracranial pressure. Rising intracranial pressure due to incipient cerebral oedema combined with reduced cerebral perfusion consequent to undertreated shock would have deleterious effects on cerebral blood flow.

The guideline continues to advocate the judicious use of fluids in DKA ketoacidosis but emphasises the importance of adequate resuscitation.

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Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Commissioned; internally peer reviewed.

Table 1 Fluid regimens for the Pediatric Emergency Care Applied Reserach Network study (PECARN) DKA FLUID trial (fast and slow fluid treatment arms) compared with the new BSPED guideline, International Society for Pediatric and Adolescent Diabetes (ISPAD) guideline and the 2015 National Institute for Clinical Excellence/BSPED guideline

	PECARN study—fast fluid	PECARN FLUIstudy—slow fluid	New BSPED guideline	ISPAD guideline	Old 2018 BSPED guideline	South Thames retrieval service guideline
Assumed fluid deficit	10% deficit All patients irrespective of pH	5% deficit All patients irrespective of pH	pH>7.2%–5% deficit pH 7.1–7.2%–7% deficit pH <7.1%–10% deficit	Moderate 5%–7% Severe 7%–10%	pH 7.1–7.3%–5% dehydrated pH<7.1%–10% dehydrated	10% deficit All patients irrespective of pH (incorporated in maintenance rate)
Bolus advised	20 mL/kg, all patients	10 mL/kg, all patients	10 mL/kg, all patients 20 mL/kg, if shocked	10 mL/kg, all patients 20 mL/kg, if shocked	10 mL/kg, only if shocked	10 mL/kg, only if shocked
Deficit replacement timing	½ over first 12 hours Remainder over next 24 hours Plus maintenance fluids	Evenly over 48 hours Plus maintenance fluids	Evenly over 48 hours Plus maintenance fluids	Evenly over 48 hours Plus maintenance fluids	Evenly over 48 hours Plus maintenance: <10 kg 2 mL/kg/hour 10–40 kg 1 mL/kg/hour >40 kg 40 mL/hour	Fluid rate incorporates deficit: <10 kg 4 mL/kg/hour 10–40 kg 3 mL/kg/hour 40–60 kg 2 mL/kg/hour >60 kg 120 mL/hour

BSPED, British Society of Paediatric Endocrinology and Diabetes; DKA, diabetic ketoacidosis.

To cite Wright N, Thomas R. *Arch Dis Child* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/archdischild-2020-319746

Accepted 6 July 2020

► http://dx.doi.org/10.1136/archdischild-2020-319117

Arch Dis Child 2020;**0**:1–2. doi:10.1136/archdischild-2020-319746

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