Glaser 2013

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Bibliographic Reference	Glaser NS; Wootton-Gorges SL; Buonocore MH; Tancredi DJ; Marcin JP; Caltagirone R; Lee Y; Murphy C; Kuppermann N; Subclinical cerebral edema in children with diabetic ketoacidosis randomized to 2 different rehydration protocols.; Pediatrics; 2013; vol. 131 (no. 1)

Study details

Study type	**Randomised controlled trial (RCT)**
Study location	USA
Study setting	Emergency department
Study dates	2008 and 2011
Duration of follow-up	Vital signs were evaluated hourly. Neurologic status was assessed hourly by using an age-appropriate Glasgow Coma Scale (GCS)14 for all patients, and every 30 minutes for patients with altered mental status.

Study type	Randomised controlled trial (RCT)
	Serum electrolyte concentrations, venous pH, and PCO2 were measured at presentation and every 3 hours, and blood glucose concentrations were measured hourly until the intravenous insulin infusion was discontinued. Patients underwent DWI at 3 time points: (1) 3 to 6 hours after the initiation of DKA treatment (defined by the administration of the first fluid bolus), (2) 9 to 12 hours after the initiation of DKA treatment, and (3) after recovery from DKA (≥72 hours after initiation of treatment)
Sources of funding	Supported by the National Institutes of Health (grant R01 NS048610 to Dr Glaser). Funded by the National Institutes of Health (NIH).
Inclusion criteria	Children aged 8 to 18 years old, were diagnosed with type 1 diabetes and had DKA
Exclusion criteria	Children were excluded if they had dental hardware that could interfere with MRI or cognitive deficits that would limit ability to cooperate with imaging. Children transferred to the study center after beginning DKA treatment were also excluded.
Sample size	18 patients
Condition specific characteristics	DKA defined as serum glucose >300 mg/ dL, venous pH <7.25, or serum bicarbonate <15 mEq/L, and a positive test for urine ketones
Interventions	**Rapid rate** **Intravenous fluid bolus**: 20 mL/Kg **Assumed fluid deficit:** 10% of body weight **Rate of deficit replacement:** Two-thirds over first 24 h; One-third over next 24 h **Urine output replacement:** Half of urine vol replaced while serum glucose level is >250 mg/dL **Fluid type:** 0.9% saline while serum glucose is >250 mg/dL, followed by 0.45% saline. For both protocols, insulin was initiated after the first fluid bolus as a continuous infusion of 0.1 U/Kg/hour. Potassium was administered as an equal mixture of potassium chloride and potassium phosphate. To optimize patient safety, regardless of protocol assignment, additional fluid boluses could be administered if these were thought necessary based on circulatory status. Similarly, treating physicians were able to adjust fluid infusion rates if it was felt that the rate prescribed by the study protocol might compromise patient safety. **Slower rate** **Intravenous fluid bolus:** 10 mL/Kg **Assumed fluid deficit:** 7% of body weight **Rate of deficit replacement:** Evenly over 48 h **Urine output replacement:** None

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	Fluid type: 0.9% saline while serum glucose is >250 mg/dL, followed by 0.45% saline. For both protocols, insulin was initiated after the first fluid bolus as a continuous infusion of 0.1 U/Kg/hour. Potassium was administered as an equal mixture of potassium chloride and potassium phosphate. To optimize patient safety, regardless of protocol assignment, additional fluid boluses could be administered if these were thought necessary based on circulatory status. Similarly, treating physicians were able to adjust fluid infusion rates if it was felt that the rate prescribed by the study protocol might compromise patient safety
Outcome measures	**Treated for suspected cerebral oedema** **Risk of cerebral oedema** High risk defined as SUN in the upper quartile (≥27 mg/dL) and/ or pH in the lower quartile (≤6.97)

Study arms

Rapid rate (N = 8)
Slower rate (N = 10)

Characteristics

Arm-level characteristics

	Rapid rate (N = 8)	Slower rate (N = 10)
Age (years) MedianIQR	11.5 (9 to 14)	15 (9 to 18)
% Female Percentage (%)	62	40
New onset diabetes (%) No of events	n = 1 ; % = 12	n = 1; % = 10

Cochrane risk of bias tool 2.0 (RoB 2.0)		
Section	Question	Answer
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns (Significant difference in age of children in the two arms. Slower rate group had older children.)
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Low
Overall bias and Directness	Risk of bias judgement	Some concerns (Randomisation- Significant difference in age of children in the two arms. Slower rate group had older children.)
	Overall Directness	Indirectly applicable (Intravenous bolus volume was different in the two arms. Outcomes not specified in review protocol.)