Shafi 2018

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Bibliographic Reference	Shafi, Obeid; Kumar, Virendra; Initial Fluid Therapy in Pediatric Diabetic Ketoacidosis: A comparison of Hypertonic Saline Solution and Normal Saline Solution.; Pediatric endocrinology, diabetes, and metabolism; 2018; vol. 24 (no. 2); 56-64

Study details

Study type	**Randomised controlled trial (RCT)**
Study location	India
Study setting	Emergency and Pediatric Intensive Care Unit (PICU) of a tertiary care children's hospital
Study dates	November 2011 to April 2013
Duration of follow-up	The two groups were compared for: • Changes in heart rate, blood pressure (Systolic [SBP], Diastolic [DBP] and Mean [MBP]), respiratory rate, sodium levels, chloride levels, lactate, pH and blood sugar at 1, 2, 4, 6, 12, 24 and 48 hours. • Time needed for the correction of hyperglycemia (< 250 mg/dL). • Time needed for the resolution of ketoacidosis: defined as bicarbonate >18 mEq/L, venous pH ≥7.3, anion gap <14 mEq/L [any two]. • Cerebral edema: occurrence of an abnormal Glasgow Coma Scale (GCS<14) during the treatment.
Sources of funding	Not reported
Inclusion criteria	Subjects with age ≤18 years with a diagnosis of DKA were screened for the inclusion in the study and were included if they met the criteria for having moderate-severe DKA

Study type	Randomised controlled trial (RCT)
Exclusion criteria	Patients with a history suggestive of chronic systemic illnesses, Patients with underlying neurological abnormalities or concomitant head trauma, meningitis or other conditions which would affect mental status evaluation and monitoring, Patients who have already received intravenous fluid (≥ 5 mL/kg) prior to the enrolment into the study, refusal of consent
Sample size	20
Loss to follow-up	Not reported
Condition specific characteristics	Moderate -severe DKA defined as blood glucose >11 mmol/L (200 mg/dl) and pH<7.25 or bicarbonate <10 mmol/L and ketonemia and/or ketonuria
Interventions	**0.9% normal saline** Children randomised to the 0.9% saline received 20 ml/kg of solution during the initial 1 hour of fluid therapy. The rest of the fluid and management was per the written DKA management protocol followed by the treating unit, which is based on the ISPAD clinical practice consensus guidelines. After the initial fluid, all the patients received isotonic fluid (0.9% saline) solution for a duration of 4 hours followed by a solution consisting of 0.45% saline, with an aim to correct the dehydration over 48 hours. Insulin infusion was started after 1 hour, upon the completion of initial fluid therapy. The starting dose of insulin infusion for all patients was 0.1 unit/kg/hr and the solution was prepared by diluting 50 units of regular (soluble) insulin in 50 mL of normal saline. **Hypertonic Saline (3% NaCl)** Children randomised to the hypertonic saline (3% NaCl) received 20 ml/kg of solution during the initial 1 hour of fluid therapy. The rest of the fluid and management was per the written DKA management protocol followed by the treating unit, which is based on the ISPAD clinical practice consensus guidelines. After the initial fluid, all the patients received isotonic fluid (0.9% saline) solution for a duration of 4 hours followed by a solution consisting of 0.45% saline, with an aim to correct the dehydration over 48 hours. Insulin infusion was started after 1 hour, upon the completion of initial fluid therapy. The starting dose of insulin infusion for all patients was 0.1 unit/kg/hr and the solution was prepared by diluting 50 units of regular (soluble) insulin in 50 mL of normal saline.
Outcome measures	**Cerebral oedema** occurrence of an abnormal Glasgow Coma Scale (GCS < 14) during the treatment **Chloride concentration (mEq/L)** **Time needed for the correction of hyperglycaemia** hours. blood sugar <250 mg/dL **Time needed for the resolution of acidosis** hours. Defined as bicarbonate > 18 mEq/L, venous pH ≥ 7.3, anion gap < 14 mEq/L (any two)

Study arms

0.9% saline (N = 20)
hypertonic saline (3% NaCl) (N = 20)

Characteristics

Study-level characteristics

	Study (N = 40)
Age group (2-5 years) Percentage (%)	25
Age group (6-10 years) Percentage (%)	32.5
Age group (11-18 years) Percentage (%)	42.5
% Female Percentage (%)	57.5

Arm-level characteristics

	0.9% saline (N = 20)	**hypertonic saline (3% NaCl) (N = 20)**
Severity of DKA		
Severe		
No of events	n = 16 ; % = 80	n = 15 ; % = 75
Moderate		
No of events	n = 4 ; % = 20	n = 5 ; % = 25

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 (Baseline differences not specified for important factors such as age, sex, type of diabetes)
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

Cochrane risk of bias tool 2.0 (RoB 2.0)		
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 (Baseline differences of some characteristics not reported)
	Overall Directness	Directly applicable