Williams 2020

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Bibliographic Reference	Williams, V.; Jayashree, M.; Nallasamy, K.; Dayal, D.; Rawat, A.; 0.9% saline versus Plasma-Lyte as initial fluid in children with diabetic ketoacidosis (SPinK trial): A double-blind randomized controlled trial; Critical Care; 2020; vol. 24 (no. 1); 1

Study details

Study type	**Randomised controlled trial (RCT)**
Study location	India
Study setting	Pediatric Emergency and Intensive care units of a large tertiary, teaching and referral hospital
Study dates	August 2017 to December 2018
Duration of follow-up	Patients were followed up till discharge from PICU or ward or death, whichever was earlier. Post discharge, the children were assessed in the PICU and diabetic followup clinics.
Sources of funding	This study was supported by the Indian council of Medical Research (ICMR), as a part of DM dissertation
Inclusion criteria	All consecutive children > 1 month to < 12 years who presented to the pediatric emergency room with DKA as defined by the International Society of Pediatric and Adolescent Diabetes (ISPAD-2014) were enrolled into the study

Study type	Randomised controlled trial (RCT)
Exclusion criteria	Children with symptomatic cerebral edema (GCS < 8 at presentation) or known chronic kidney disease or liver disease or who had received pre-referral fluids and/or insulin at the time of hospital presentation were excluded.
Sample size	66
Loss to follow-up	2 patients lost at follow up
Condition specific characteristics	The severity of DKA was classified as mild if pH was between 7.2 and 7.3, moderate if pH was between 7.1 and 7.2, and severe if pH was < 7.1. DKA defined as blood glucose > 200 mg/dl and blood ketones >3 mmol/L and venous pH <7.3 or bicarbonate <15.mEg/L
Interventions	**0.9% normal saline** **DKA protocol:** volume calculated based on deficit (6.5-10%) and maintenance fluid as per Holliday Segar. Fluids given over 48 hours as hourly infusion. Eligible children who presented in shock [perfusion abnormalities with or without hypotension (blood pressure < 5th centile for age)], received trial fluid bolus of 20 ml/kg over an hour. Insulin was started at 0.05 U/kg/h in all after initial hour of fluid therapy. Fluids were changed to 0.45% saline and 5% dextrose once blood glucose fell below 250 mg/dl. In case of persistently high blood glucose, the clinician went through a checklist that included patency of intravenous cannula, insulin preparation and its shelf life, and appropriateness of dilution before increasing insulin to 0.1 U/kg/h. **Plasma-Lyte-A** **DKA protocol:** volume calculated based on deficit (6.5-10%) and maintenance fluid as per Holliday Segar. Fluids given over 48 hours as hourly infusion. Eligible children who presented in shock [perfusion abnormalities with or without hypotension (blood pressure < 5th centile for age)], received trial fluid bolus of 20 ml/kg over an hour. Insulin was started at 0.05 U/kg/h in all after initial hour of fluid therapy. Fluids were changed to 0.45% saline and 5% dextrose once blood glucose fell below 250 mg/dl. In case of persistently high blood glucose, the clinician went through a checklist that included patency of intravenous cannula, insulin preparation and its shelf life, and appropriateness of dilution before increasing insulin to 0.1 U/kg/h.
Outcome measures	**Incidence of acute kidney injury (AKI)** defined with either KDIGO or pRIFLE criteria **Healthcare utilisation - Need for renal replacement therapy (RRT)** Till discharge from PICU or ward or death, whichever was earlier **Healthcare utilisation- Need for ventilation** Till discharge from PICU or ward or death, whichever was earlier **Mortality in hospital** **Cerebral oedema** Till discharge from PICU or ward or death, whichever was earlier **Healthcare utilisation- Length of intensive care unit (ICU) stay**

Study type	**Randomised controlled trial (RCT)**
	Healthcare utilisation - length of hospital stay days

Study arms

Plasma-Lyte- A (N = 34)
0.9% Saline (N = 32)

Characteristics

Arm-level characteristics

	Plasma-Lyte- A (N = 34)	**0.9% Saline (N = 32)**
Age (years) Median IQR	7.8 (4 to 11.6)	6.6 (2.9 to 10.1)
% Female Sample Size	n = 16 ; % = 47	n = 17 ; % = 53
New onset of diabetes No of events	n = 17 ; % = 50	n = 24 ; % = 75
Duration of diabetes in known type 1 diabetes months MedianIQR	26.7 (7.2 to 47.8)	15.4 (6.1 to 32.2)
Severity of DKA		
Severe		
Number (%)	n = 20 ; % = 58.8	n = 20 ; % = 62.5
Moderate		
Number (%)	n = 11 ; % = 32.4	n = 11 ; % = 34.4
Mild		
Number (%)	n = 3 ; % = 8.8	n = 1 ; % = 3.1

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 between the number of children with new onset DKA)

Cochrane risk of bias tool 2.0 (RoB 2.0)		
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 (Significant difference between the number of children with new onset DKA)
	Overall Directness	Directly applicable