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ORIGINAL ARTICLE

Clinical Trial of Fluid Infusion Rates for Pediatric Diabetic Ketoacidosis

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RobotReviewer report

Risk of bias table

trial	design	n	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment
Fluidi e chetoacidosi (Pediatria).pdf	RCT	?? ?	+	+	+	+

Characteristics of studies

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Population	1. Patients Children were eligible for enrollment in the trial if they were between 0 and 18 years of age and had received a diagnosis of diabetic ketoacidosis (defined as a blood glucose level of >300 mg per deciliter [Fluid Infusion for Pediatric Diabetic Ketoacidosis or other conditions that could affect neurologic function; diabetic ketoacidosis for which the patient had already received substantial treatment; known pregnancy; or factors for which treating physicians determined that a specific fluid and electrolyte therapy was necessary. 2. Children who presented with a Glasgow Coma Scale score of 11 or lower (on a scale ranging from 3 to 15, with lower scores indicating worse mental status) were excluded after year 2 because many participating clinicians believed that fluid regimens for such children should not be determined on the basis of randomization.
Interventio	1. Patients Children were eligible for enrollment in the trial if they were between 0 and

n	18 years of age and had received a diagnosis of diabetic ketoacidosis (defined as a blood glucose level of >300 mg per deciliter [Fluid Infusion for Pediatric Diabetic Ketoacidosis or other conditions that could affect neurologic function; diabetic ketoacidosis for which the patient had already received substantial treatment; known pregnancy; or factors for which treating physicians determined that a specific fluid and electrolyte therapy was necessary.
Outcomes	1. Secondary outcomes included short-term memory during treatment for diabetic ketoacidosis (forward and backward digit-span recall; scores range from 0 to 16, with higher scores indicating better short-term memory) 18 ; clinically apparent brain injury (defined as a deterioration in neurologic status leading to initiation of hyperosmolar therapy or endotracheal intubation or resulting in death) during treatment for diabetic ketoacidosis; and shortterm memory, contextual memory, and IQ 2 to 6 months after the episode of diabetic ketoacidosis . 2. Glasgow Coma Scale and digit-span assessments continued for 24 hours or until resolution of diabetic ketoacidosis (as defined by the transition to subcutaneous insulin) if diabetic ketoacidosis resolved before the 24-hour time point. 3. Subgroup Analyses of Mental Status Analyses of the relative risk of a decline to below 14 in the Glasgow Coma Scale score in subgroups defined according to age and history of diabetic ketoacidosis among patients who had Glasgow Coma Scale scores of 14 or 15 at baseline did not show differential treatment effects (Fig.

Bias	Judgement	Support for judgement
Random sequence generation	low	1. Randomization was stratified according to baseline Glasgow Coma Scale score (14 or 15 vs. <14) and center (if the Glasgow Coma Scale score was <14). 2. Children were then randomly assigned to one of four treatment regimens: fast rate of rehydration with fluid that had 0.45% sodium chloride content, fast rate of rehydration with fluid that had 0.9% sodium chloride content, slow rate of rehydration with fluid that had 0.45% sodium chloride content, and slow rate of rehydration with fluid that had 0.9% sodium chloride content. 3. Patients and their parents or guardians were unaware of the treatment-group assignments .
Allocation concealment	low	1. Patients and their parents or guardians were unaware of the treatment-group assignments . 2. Randomization was stratified according to baseline Glasgow Coma Scale score (14 or 15 vs. <14) and center (if the Glasgow Coma Scale score was <14). 3. Given that patients who underwent randomization a second time could have been randomly assigned to a treatment regimen that was different from the first regimen they had been assigned to, a single patient could be represented in more than one treatment group in the analyses.
Blinding of participants and personnel	low	1. Patients and their parents or guardians were unaware of the treatment-group assignments . 2. It was not possible for clinicians to be unaware of the treatment-group assignments because of the need to know the fluid protocol for clinical decision making. 3. To address variations in the diagnosis of clinically apparent brain injury, records of encounters with patients in which hyperosmolar therapy, endotracheal intubation, or death were documented were reviewed by an adjudication committee that included two pediatric critical care physicians and one pediatric emergency medicine physician, all of whom were unaware of the treatment-group

		assignments.
Blinding of outcome assessment	low	1. To address variations in the diagnosis of clinically apparent brain injury, records of encounters with patients in which hyperosmolar therapy, endotracheal intubation, or death were documented were reviewed by an adjudication committee that included two pediatric critical care physicians and one pediatric emergency medicine physician, all of whom were unaware of the treatment-group assignments. 2. Data were analyzed for 855 episodes (66.4%), for which follow-up occurred within 6 months after the patient's discharge from the hospital (756 within 4 months and 99 between 5 and 6 months). 3. Me thods Overview of the Trial We conducted this randomized, controlled trial at 13 emergency departments in the Pediatric Emergency Care Applied Research Network (PECARN), all of which were located in urban centers in the United States.