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Normal versus half-normal saline in the treatment of children with diabetic ketoacidosis

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Abstract

Objective

This study aims to determine the effect of 0.9% saline (NS) versus 0.45% saline (half NS) on blood pressure and serum electrolytes in children with diabetic ketoacidosis.

Patients and methods

This is a cross-sectional prospective comparative study carried out on 105 patients (1–18 years) from those admitted to the pediatric ICU of Al-Zahraa University Hospital from March 2017 to August 2019. Cases were divided into three groups (35 in each group). Group I patients received a shock, deficit, and maintenance therapy with NS. Group II patients received a shock therapy NS along with deficit and maintenance therapy with half NS. Group III patients received a shock, deficit, and maintenance therapy with half NS.

Results

There were no hypotensive cases among all patients. There was a significant decrease in mean arterial blood pressure in the three groups after treatment. There was a significant increase in serum corrected sodium level in group I after treatment, whereas there was a significant decrease in its level in groups II and III. Serum potassium level showed an insignificant decrease after treatment in all groups. Blood glucose level significantly decreased after treatment in the same group, but in comparison with other groups, the differences were insignificant. Serum osmolality significantly decreased after treatment in all groups. pH significantly increased after treatment in each group, but in a comparison between groups, there were insignificant differences. Group I had the longest pediatric ICU stay.

Conclusions

Our patients continue to maintain normal or even have higher blood pressure levels with no hypotensive cases. The mean arterial blood pressure significantly decreased after treatment with intravenous fluids, especially in the group that received half NS. Rehydration with half NS results in decreased corrected sodium and more decrease in effective serum osmolality.

Keywords: blood pressure, children, diabetic ketoacidosis, normal saline, serum electrolytes

Introduction

A potentially life-threatening complication of diabetes mellitus is diabetic ketoacidosis (DKA). It was first identified in 1886, and it was almost invariably fatal until the advent of insulin therapy in the 1920s [1]. The triads of hyperglycemia, ketosis, and metabolic acidosis describe DKA. This is owing to relative or absolute insulin deficiency and excess counter-regulatory hormones, including glucagon, cortisol, catecholamines, and growth hormones, resulting in hyperglycemia, glycosuria, dehydration, and hyperosmolality of varying intensity [2].

The induction of osmotic diuresis by glycosuria results in major fluid and electrolyte deficits, including sodium, potassium, calcium, magnesium, chloride, and phosphate. Dehydration and hyperglycemia contribute to hypertonicity, causing the

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efflux of water from the intracellular space to the extracellular hypertonic space, as well as the efflux of potassium from the intracellular space, exacerbated by acidosis, lack of successful insulin action, and intracellular protein breakdown [2].

Although DKA mortality is most frequently owing to severe underlying disease and comorbidities, DKA is a hypercoagulable condition itself that leads to potentially fatal complications such as stroke, myocardial infarction, and intravascular coagulation spread. Management includes rehydration; electrolyte derangement correction, especially hypokalemia; insulin administration; metabolic acidosis correction; and treatment of precipitants such as infections, pancreatitis, trauma, and myocardial infarction [3]. DKA is mainly treated with intravenous fluids and insulin [4]. Insulin can be given intravenously or by injection under the skin, depending on the severity [5].

The aim of the present study was to determine the effect of 0.9% saline (NS) versus 0.45% saline (half NS) on blood pressure and serum electrolytes in children with DKA.

Patients and methods

This is a cross-sectional prospective comparative study carried out on 105 patients with DKA (1–18 years) of both sexes [43 (41%) males and 62 (59%) females] from those admitted to the pediatric intensive care unit (PICU) of Al-Zahraa University Hospital from March 2017 to August 2019. Cases were divided into three groups, with 35 patients in each group.

Group I patients received a shock, deficit, and maintenance therapy with NS if random blood sugar (RBS) more than 250 mg/dl and received glucose 5% in NS if RBS less than 250 mg/dl.

Group II patients received a shock therapy with NS) along with deficit and maintenance therapy with half NS if RBS more than 250 mg/dl and received glucose 5% in half NS if RBS less than 250 mg/dl.

Group III patients received a shock, deficit, and maintenance therapy with half NS if RBS more than 250 mg/dl and received glucose 5% in half NS if RBS less than 250 mg/dl.

Diagnosis of DKA was based on American Diabetes Association criteria: venous pH less than 7.3 or serum bicarbonate concentration less than 15 mmol/l, serum glucose concentration more than 200 mg/dl (11 mmol/l), and ketonemia, glycosuria, and ketonuria [6].

Patients more than 18 years old were excluded from the study. Patients with a history of renal insufficiency or heart failure, patients with shock, and those with known cases of hypertension or electrolytes abnormalities other than DKA were also excluded.

Methods

All the children included were subjected to the following:

(1) History: it includes any chronic health problems; present infection anywhere; the present condition regarding onset, nature, duration, course, and progression; history of stress exposure; and the dose of insulin taken by the patient.
(2) Clinical examination: clinical evaluation was done for all cases to confirm the diagnosis of DKA and to determine its cause, for example, stress exposure or evidence of infection. Examination includes blood pressure (on admission and discharge), patient's weight (for calculation of insulin and intravenous fluids), the severity of dehydration level (estimated clinically), and level of consciousness, which was assessed according to Glasgow coma scale [7].
(3) Investigation: levels of glucose, urea, creatinine (BT 3500), electrolytes such as Na and K (AVL.988), blood gases, urinary ketones, and sodium levels were determined at admission and on discharge.

Ethical consideration: an informed consent was obtained from the parents of all patients before getting them involved in the study. The steps of the study, the aims, and the potential benefits and hazards were all discussed with the parents. The study was conducted according to the principles expressed in the Declaration of Helsinki.

Statistical analysis of the data

The data were fed to the computer and analyzed using version 20.0.0. of the IBM SPSS software package (IBM). Qualitative data were described using the number and percent. Quantitative data were described using mean and SD. Comparison between different groups regarding categorical variables was tested using χ^2 test. *F* test (analysis of variance) was used for normally distributed quantitative variables, to compare between more than two groups, and post-hoc test (LSD) for pairwise comparisons. Paired t test was used for normally distributed quantitative variables, to compare between two periods, and Mann–Whitney test for abnormally distributed quantitative variables to compare between two studied groups. Kruskal–Wallis test was used for abnormally distributed quantitative variables, to compare between more than two studied groups, and post hoc (Dunn's multiple comparisons test) for pairwise comparisons.

Results

This is a cross-sectional prospective comparative study that was carried out on 105 patients of both sexes [43 (41%) males and 62 (59%) females], with age ranged from 1 to 18 years, from those admitted to PICU Al-Zahraa University Hospital from March 2017 to August 2019.

The results of the study are demonstrated in the following tables and figures.

Table 1 shows no significant changes in demographic data between groups.

Table 2 shows that there were no hypotensive cases (less than fifth percentile) among patients presenting with DKA.

Table 3 shows a significant decrease in the mean arterial blood pressure in the three groups after treatment; especially groups II and III (treated with half NS) showed a more significant decrease in mean arterial blood pressure after treatment than group I (treated with NS).

Table 4 shows that there was a significant increase in serum corrected sodium level in group I after treatment, whereas a significant decrease in its level in groups II and III after treatment, whereas serum potassium level showed an insignificant decrease in its level after treatment in all groups, with no differences among the three groups ($P = 0.415$).

Table 5 shows that blood glucose levels were significantly decreased after treatment in the same group, but in the comparison among three groups, there were insignificant differences among them. Serum osmolality levels were significantly decreased after treatment in all groups, especially group III, which had the lowest serum osmolality level.

Table 1: Comparison among the three studied groups according to demographic data

	Group I ($n=35$) [n (%)]	Group II ($n=35$) [n (%)]	Group III ($n=35$) [n (%)]	P
Sex				
Male	16 (45.7)	13 (37.1)	14 (40.0)	0.731
Female	19 (54.3)	22 (62.9)	21 (60.0)	
Age (years)				
Mean±SD	9.64±3.94	8.73±3.19	9.21±3.98	0.573

Group I: treatment with normal saline. Group II: treatment with normal saline then half-normal saline. Group III: treatment with half-normal saline. Statistically significant at $P \leq 0.05$.

Table 6 shows that pH significantly increased after treatment in each group, but in a comparison among groups, there were insignificant differences among them.

Fig. 1 shows that group I (treated with NS) had the longest period of PICU stay (time to resolution of DKA).

Discussion

DKA is characterized by the triad of hyperglycemia, ketosis, and metabolic acidosis [2]. More frequently, DKA complicates type 1 diabetes mellitus rather than type 2 and carries the risk of severe morbidity and mortality [3]. DKA management involves rehydration, correction of electrolytes particularly hypokalemia, administration of insulin, correction of metabolic acidosis, and treatment of precipitants such as trauma and infections [3].

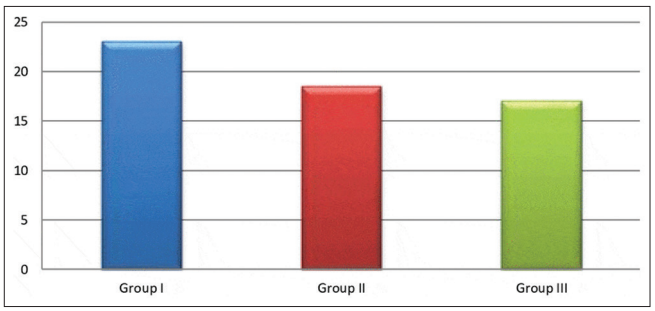

Figure 1: Comparison among the three studied groups according to the duration of PICU stays (time to resolution of DKA) ($P1 = 0.007$*, $P2 < 0.001$*, $P3 = 0.376$). $P1$: P value for comparing between group I and group II. $P2$: P value for comparing between group I and group III. $P3$: P value for comparing between group II and group III. DKA, diabetic ketoacidosis; PICU, pediatric intensive care unit.

Table 2: Comparison among the three studied groups according to blood pressure percentile at presentation of diabetic ketoacidosis

	Group I ($n=35$)		Group II ($n=35$)		Group III ($n=35$)	
	Systolic BP	Diastolic BP	Systolic BP	Diastolic BP	Systolic BP	Diastolic BP
BP percentile	N	N	N	N	N	N
More than 95 percentile	19	10	15	5	15	3
From 90 to 95 percentile	4	3	4	3	4	4
From 5 to 90 percentile	12	22	16	27	16	28
Less than 5% percentile	0	0	0	0	0	0
Sum	35	35	35	35	35	35

BP, blood pressure.

Table 3: Comparison among the three studied groups according to mean arterial blood pressure level

ABP	Group I ($n=35$) (mmHg) (mean±SD)	Group II ($n=35$) (mmHg) (mean±SD)	Group III ($n=35$) (mmHg) (mean±SD)	P
Before treatment	92.23±18.79	86.74±6.91	86.98±7.86	0.087
After treatment	88.11±7.24	81.94±7.11	79.74±7.22	<0.001*
Significance between groups	P_1=0.019*	P_2<0.001*	P_3=0.215	
P_4	0.039*	0.032*	<0.001*	

ABP, arterial blood pressure. P_1: P value for comparing between group I and group II. P_2: P value for comparing between group I and group III. P_3: P value for comparing between group II and group III. P_4: P value for paired t-test for comparing between before and after results in each group. *Statistically significant at $P \leq 0.05$.

Table 4: Comparison among the three studied groups according to electrolytes (corrected sodium and serum potassium)

	Electrolytes	Group I ($n=35$) (mean±SD)	Group II ($n=35$) (mean±SD)	Group III ($n=35$) (mean±SD)	*P*
Corrected Na (mEq/l)	Before treatment	141.2±4.98	142.1±3.74	142.1±4.13	0.392
	After treatment	141.94±6.11	140.02±3.11	139.44±3.3	0.021*
	Significance between groups	P_1=0.039*	P_2=0.022*	P_3=0.742	
	P_4	0.001*	0.001*	<0.001*	
Serum potassium (K+) (mEq/l)	Before treatment	4.51±0.64	4.74±0.95	4.42±0.68	0.034*
	After treatment.	4.24±074	4.35±0.49	4.11±0.57	0.524
	Significance between groups	P_1=0.005*	P_2=0.211	P_3=0.194	
	P_4	0.452	<0.001*	0.024*	

P_1: *P* value for comparing between group I and group II. P_2: *P* value for comparing between group I and group III P_3: *P* value for comparing between group II and group III P_4: *P* value for paired *t*-test for comparing between before and after results in each group. *Statistically significant at $P \leq 0.05$.

Table 5: Comparison among the three studied groups according to blood glucose levels and serum osmolality levels

Blood glucose level	Group I ($n=35$) (mg/dl) (mean±SD)	Group II ($n=35$) (mg/dl) (mean±SD)	Group III ($n=35$) (mg/dl) (mean±SD)	*P*
Before treatment	473.72±84.17	422.34±114.21	439.3±120.77	0.893
After treatment	143.98±24.88	15214±22.13	143.94±34.11	0.612
Significance between groups	P_1=0.481	P_2=0.541*	P_3=0.628*	
ᵗ*P*	<0.001*	<0.001*	<0.001*	
Serum osmolality (mmol/l) (mean±SD)				
Before treatment	302.93±12.17	306.1±12.21	311.9±9.97	0.594
After treatment	315.39±98.25	284.57±7.11	279.89±18.94	0.031*
Significance between groups	P_1=0.541	P_2=0.039*	P_3=0.037*	
P_4	<0.001*	<0.001*	<0.001*	

P_1: *P* value for comparing between group I and group II. P_2: *P* value for comparing between group I and group III. P_3: *P* value for comparing between group II and group III. P_4: *P* value for paired t test for comparing between before and after results in each group. *Statistically significant at $P \leq 0.05$.

Table 6: Comparison among the three studied groups according to arterial blood gas (pH)

	Group I ($n=35$)	Group II ($n=35$)	Group III ($n=35$)	*P*
Before treatment				
Mean±SD	7.06±0.11	7.14±0.10	7.13±0.10	0.009*
Significance between groups	P_1=0.004*	P_2=0.014*	P_3=0.674	
After treatment				
Mean±SD	7.38±0.03	7.38±0.02	7.38±0.03	0.842
P_4	<0.001*	<0.001*	<0.001*	

P_1: *P* value for comparing between group I and group II. P_2: *P* value for comparing between group I and group III. P_3: *P* value for comparing between group II and group III. P_4: *P* value for paired *t*-test for comparing between before and after results in each group. *Statistically significant at $P \leq 0.05$.

The present study aims to evaluate the effect of NS versus half NS on blood pressure and serum electrolytes in children with DKA.

In our study, we found that there were no hypotensive cases (less than the fifth percentile) among patients presenting with DKA. In agreement with our study, Deeter *et al*. [8] found that despite their dehydration, patients generally continue to maintain normal or even high blood pressure, possibly owing to elevated plasma catecholamine concentrations, increased release of antidiuretic hormone in response to hyperosmolality, which increases blood pressure via V2 receptors, or other factors [8].

Our study showed a significant decrease in mean arterial blood pressure in the three groups after treatment; especially groups II and III (treated with half NS) showed a more significant decrease in mean arterial blood pressure after treatment than group I (treated with NS). A study by Deeter *et al*. [8] found that 58% of patients had admission systolic hypertension (≥95th %). None of the patients had hypotension on admission. During the first few hours after initiation of insulin and intravenous fluid therapy, 82% exhibited hypertension on at least one blood pressure reading. Over time, and at discharge, the number of patients with hypertension decreased [8].

In the present study, we found that regarding serum electrolytes after treatment, there was a significant increase in serum corrected sodium level in group I after treatment with NS, whereas a significant decrease in its level in groups II and III after treatment with half NS. However, serum potassium level

showed an insignificant decrease in its level after treatment in all groups, with no differences among the three groups ($P = 0.415$). In agreement with our result, the study by Basnet *et al*. [9] found that there were insignificant differences among the three groups regarding corrected sodium pretreatment, but after treatment, there were significant differences among the three groups, as the group with half NS had a lower level of corrected sodium. Van Zyl *et al*. [10] found that regarding serum sodium, there was an increase in its level after treatments and hydration, with insignificant differences between different methods of hydration ($P = 0.504$); moreover, the level of serum potassium decreased after treatment and hydration, with insignificant differences between different methods of hydration ($P = 0.722$).

In contrast to our results, Savas-Erdeve *et al*. [11] compared the efficiency of fluid therapy with different sodium concentration between two groups of children with type 1 DKA. The first group received an IV solution with a Na concentration of 75 mEq/l, and the second group received a solution with a Na concentration of 100 mEq/l. They found that the course of serum sodium at follow-up was not found to show any difference between patients of the two groups [11]. However, there are no randomized controlled trials supporting the use of one fluid over another in DKA. The varied recommendations over the last 50 years for fluid therapy in DKA stand as a testament to the uncertainty in this area [12]. Therefore, from a physiological perspective, the ideal fluid for accurate replacement of losses from all compartments would be half NS. However, because of its large volume of distribution, the rate of restoration of the circulating volume may be protracted. If the corrected serum sodium is normal or exceeds 155 mmol/l, the American Diabetes Association recommends that half NS is commenced at a rate of 4–14 ml/kg/h [13]. Potential advantages include the correction of dehydration with the avoidance of sodium overload and hyperchloremia. Though, the evidence for this recommendation is limited. It has been suggested that very hypotonic solutions (<75 mmol/l of sodium) have been suggested to contribute to a decrease in plasma osmolality and hyponatremia, predisposing to cerebral edema [13].

Regarding the serum potassium level in adults with DKA, they have total body potassium deficits in the range of 3–6 mmol/kg; data in children are sparse. As a result of hypertonicity, insulin deficiency, and buffering of hydrogen ions within the cell, the main potassium loss is from the intracellular pool. At the time of presentation, serum levels of potassium may be normal, elevated, or decreased. Hypokalemia can be associated with a prolonged disease period, whereas hyperkalemia is mainly owing to decreased renal function. Insulin administration and acidosis correction will push potassium back into cells, reducing serum levels [14].

In the present study, we found that the blood glucose level significantly decreased after treatment in the same group, but in the comparison among the three groups, there were insignificant differences between them. In the study by Taylor *et al*. [15], they showed that level of blood glucose decreased after treatment as they measured it at 0, 4, 8, 12, 16, and 20 h. Although rehydration alone induces a certain decrease in the concentration of blood glucose, insulin therapy is necessary for normalizing the blood glucose concentration and suppressing lipolysis and ketogenesis. Although various routes and doses have been used, substantial evidence suggests that the standard treatment should be 'low dose' intravenous insulin administration [2]. In agreement with our result, Basnet *et al*. [9] found that baseline variables, except initial serum glucose, were similar in the three groups, and the rate of change in glucose was similar in all the three groups.

In the present study, we found that serum osmolality was significantly decreased after treatment in all groups, especially in group III, which had the lowest osmolality level. Basnet *et al*. [9] found that the fall in effective serum osmolality from admission to the resolution of DKA was greater in the half NS group C when compared with the NS group A.

In the present study, we found that pH was significantly increased after treatment in each group, but in the comparison among the three groups, there were insignificant differences between them. It is proposed that rehydration with NS may contribute to hyperchloremia and a hyperchloremic metabolic acidosis, with a persisting base deficit and may cause renal vasoconstriction and decreased glomerular filtration rate [16,17]. Alternatively, this acidosis may represent a physiological response to resolving DKA rather than a result of the hydration fluid itself [18]. In DKA, there is an increase in chloride reabsorption in the proximal renal tubule in response to decreased bicarbonate generation secondary to the loss of ketone substrates in the urine. NS has a strong ion difference of zero, which on administration in large quantities will tend to produce a dilutional acidosis [19].

In the present study, we found that group I (treated with NS) had the longest period PICU stay, with P value of 0.001. This is consistent with the finding of Basnet *et al*. [9], who concluded that the PICU stay was longer in the NS group.

Conclusion

Our patients continue to maintain normal or even have higher blood pressure levels with no hypotensive cases among patients. The mean arterial blood pressure was significantly decreased after treatment with intravenous fluids especially in the group that received half NS in comparison with the other groups. Rehydration with NS resulted in an increase in duration and PICU stay. Rehydration with half NS resulted in a decrease in corrected sodium and more decrease in effective serum osmolality. Further studies comparing the balanced electrolytes solutions to saline solutions should be done. Moreover, a larger prospective randomized trial of NS versus half NS in the treatment of DKA of children is needed.

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Conflicts of interest

There are no conflicts of interest.

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