

Meglumine Sodium Succinate in Diabetic Ketoacidosis

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Summary

The most common agent used for infusion therapy in patients with diabetic ketoacidosis (DKA) is isotonic 0.9% sodium chloride solution. However, infusion of required volumes can result in development of iatrogenic complications — i. e., worsening of metabolic hyperchloremic acidosis in DKA patients with already altered acid-base balance. Balanced crystalloid solutions can be used as alternative to saline.

Objective. To evaluate the feasibility of using meglumine sodium succinate (MSS) balanced crystalloid solution in DKA.

Material and methods. We examined 2 groups of patients, 30 subjects each, with moderate and severe diabetic ketoacidosis admitted to anesthesiology and intensive care unit. Patients from both groups were administered with insulin and an infusion therapy was employed according to current clinical guidelines for the management of patients with complications of diabetes mellitus. In the comparison group, infusion therapy included 0.9% sodium chloride, 4% potassium chloride, and 5% dextrose. In the study group MSS intravenous drip infusions 10 ml/kg/daily were added to the infusion protocol. Volumes and infusion rates were comparable in both groups. The following indicators were evaluated: time to resolution and DKA resolution rates during thorough monitoring (first 48 hours of therapy), the time (in hours) before discontinuation of insulin infusion; the time to complete consciousness recovery (15 items on the Glasgow Coma scale); the duration (in hours) of stay in the intensive care unit (ICU), dynamics of blood electrolytes; parameters of acid-base balance; levels of glycemia and lactatemia.

Results. All patients improved and were transferred from ICU, the mortality rate was 0%. Infusion of MSS shortened the time to DKA resolution (30.0 h [24.0 h; 36.0 h] in the study group, vs 44.5 h [36.5 h; 51.5 h] in the comparison group ($P=0.001$)); DKA resolution rates during 48 hours from initiation of therapy achieved 90.0% (27) in the study group, vs 66.7% (20) in the comparison group ($P=0.060$)); duration of intravenous insulin infusion was 32.0 h [24.5 h; 40.0 h] in the study group vs 48.0 h [40.0 h; 55.5 h] in the comparison group ($P=0.001$)); duration of ICU stay was 41.0 h [30.0 h; 48.0 h] in the study group, vs 56.0 h [50.0 h; 66.3 h] in the comparison group ($P=0.001$).

Conclusion. Infusion of a balanced succinate-containing crystalloid solution improves the results of DKA treatment, as compared to traditional infusion of 0.9% sodium chloride.

Keywords: meglumine sodium succinate; diabetic ketoacidosis; diabetes mellitus; infusion therapy; acidosis; crystalloid solution; Reamberin

Conflict of interest. The authors declare that there is no conflict of interest. LLC «NTFF «POLISAN» was not the initiator of the study and had no influence on study design, analysis of obtained data, interpretation of the results and writing of this paper.

Introduction

Diabetic ketoacidosis (DKA) is a serious complication of uncontrolled diabetes mellitus (DM) that requires urgent medical intervention.

The total number of patients with diabetes mellitus in the Russian Federation as of January 1, 2019 was 4,584,575 (3.12% of the Russian population), including 5.6% (256,200) of type 1 diabetes, 92.4% (4.24 million) of type 2 diabetes, and 2% of other types of diabetes. Worldwide, 3–4% of the adult population has diabetes mellitus, 95% of them type 2 DM. It is predicted that its prevalence could reach 552 million people by 2030. The preva-

lence of DKA is 46 cases per year per 10,000 people with diabetes. The predominant age of onset is less than 30 years [1]. The differences in the risk of DKA in different types of diabetes can be seen in the prevalence of ketoacidotic coma in Russia, which is 1.25% in type 1 DM, while in type 2 diabetes it is 0.05% [2].

DKA is characterized by a clinical and laboratory triad of hyperglycemia, ketonemia, and metabolic acidosis with increased anion gap [3]. Ketones are formed from β -hydroxylated fatty acids during fasting or insulin deficiency. They include acetate, acetoacetic acid, and beta-hydroxybutyrate, which

act as strong ions. In patients with DKA, acidosis is caused by increased ketones and lactate due to tissue hypoperfusion. Due to hyperglycemia-induced increased urine output, dehydration is common in DKA patients [4].

In this context, the primary therapeutic intervention, which precedes the correction of insulin deficiency, is fluid therapy. Its strategy is still under discussion. The use of isotonic crystalloid solutions for the treatment of DKA is a generally accepted principle. Current recommendations for fluid therapy in DKA include isotonic 0.9% sodium chloride with possible addition of potassium chloride [1, 5–7].

However, the use of unbalanced solutions can lead to hyperchloremia and aggravate the pre-existing acidosis, promoting disorders of coagulation, cardiac, immune and renal function (due to renal arteriolar narrowing), provoking oliguria and delayed control of acidosis [4, 7–9, 11]. Preference should be given to balanced polyionic solutions [12].

Since meglumine sodium succinate (Reamberin®) has an electrolyte composition close to plasma electrolyte composition and contains succinate as an alkaline reserve, the inclusion of Reamberin® in the treatment is thought to lead to a more rapid resolution of DKA due to the correction of hypoxia associated with most urgent conditions [7, 9, 13]. However, the use of balanced crystalloids in the treatment of DKA is associated with the risk of alkalosis and hyperkalemia, which requires a detailed study of this problem.

The aim of our study was to provide a rationale for the use of a balanced crystalloid solution containing meglumine sodium succinate (Reamberin®) in DKA.

Materials and Methods

A noninterventional prospective study was performed. A total of 60 patients (32 male, 28 female), aged 18 to 75 years, admitted to the emergency department of the Russian Railway Clinical Hospital (Barnaul, Russia) with DM complicated by DKA were enrolled. Diabetes mellitus type 1 was diagnosed in 34 patients and diabetes mellitus type 2 in 26 patients. On admission, 32 patients had moderate DKA, while 28 patients were diagnosed with severe DKA according to the classification of Dedov et al. (2021) [5].

Depending on the type of fluid therapy, patients were divided into 2 groups of 30 patients each. Randomization was performed using the envelope method. Subdivision of patients into subgroups according to the type of DM was considered inappropriate because of the small number of patients. Patients in group 1 received fluid therapy according to the algorithm described in the clinical guidelines [5]. Sodium chloride 0.9% with potassium chloride added if necessary was used. In the second group, the basic fluid therapy was partially replaced by Reamberin® balanced solution 10 ml/kg per day until the ketoacidosis was resolved. When the plasma glucose concentration reached 14 mmol/l (usually by the end of the second day), rehydration was continued with oral fluids and 150–200 ml of 5% dextrose, depending on the actual need [1, 5, 6].

The time of initiation of fluid therapy, its rate and daily volume were comparable in both groups (Table 1).

Fluid therapy was started immediately after the patient was admitted to the ICU. After 2 hours, insulin was administered as follows: an initial dose of rapid-acting insulin 0.1 IU/kg real body weight by bolus injection through an infusion device after the initial infusion load. The rate of intravenous insulin administration was adjusted according to the rate of reduction of hyperglycemia and averaged 3 mmol/l/h (no more than 4 mmol/l/h) [1, 5].

Inclusion criteria were age 18 to 75 years inclusive; documented diabetes mellitus; diagnostic criteria for ketoacidosis such as plasma glucose level >13 mmol/L, hyperketonemia (>5 mmol/L), ketonuria (≥++), metabolic acidosis (pH <7.3); clinical, functional and laboratory signs of dehydration.

Exclusion criteria were hypersensitivity to components of Reamberin; conditions requiring administration of sodium bicarbonate solution; absence of clinical and laboratory criteria for DKA; urgent diseases of other organs and systems requiring specific drug therapy or surgical intervention.

The clinical assessment of the patient's status and the need for rehydration was based on the volume status according to the results of the PLR test. A 15% increase in the cardiac index (CI) when the patient's legs were elevated, registered by hemodynamic monitoring, and its return to the baseline level when the legs were lowered, indicated «re-

Table 1. The characteristics of the fluid therapy ($M \pm SE$).

Stages	Total volume (composition) of infusion in groups. mL		P
	Control	Reamberin	
During the first 2 hours	1413.78±179.18 (KCl 4%; NaCl 0.9%)	1500.8±191.4 (Reamberin; KCl 4%; NaCl 0.9%)	0.094
Day 1	4523.7±313.64 (KCl 4%; NaCl 0.9%)	4802.56±321.31 (Reamberin; KCl 4%; NaCl 0.9%)	0.056
Day 2	2544.48±199.96 (KCl 4%; NaCl 0.9%; Dextrose 5%)	2701.44±213.88 (Reamberin; KCl 4%; NaCl 0.9%; Декстроза 5%)	0.062

sponder» status (all participants were found to have this), which provided a rationale for planned rehydration therapy.

To assess central hemodynamics, including the PLR test, tetrapolar rheovasography was performed with the KM-AR-01 DIAMANT cardio-respiratory and tissue hydration monitor. The following parameters were measured:

- heart rate (HR)
- cardiac index (CI)
- peripheral vascular resistance index (PVRI)
- stroke index (SI)
- extracellular fluid volume (EFV)
- intracellular fluid volume (IFV).

20 healthy subjects were studied as a control group while central hemodynamic parameters were assessed.

Non-invasive blood pressure (NIBP), electrocardiogram, SpO₂, respiratory rate (RR), body temperature, urine output rate were monitored in the intensive care unit, fluid balance was controlled by assessment of administered and excreted fluid.

DKA severity, acid-base status, plasma ion levels, and laboratory criteria for organ and system function were determined at the following intervals

Rapid glycemic test: hourly until plasma glucose (PG) dropped to 13 mmol/L, then, if stable, every 3 hours. Material was capillary blood tested on Biosen C-Line Clinic/GP+.

Urine or plasma analysis for ketone bodies: twice daily for the first 2 days, then once daily on the URILIT-150 device.

Plasma Na⁺ and K⁺: baseline, then at least twice daily. Venous blood was tested on the EasyLite Calcium Na/K/Ka/pH meter.

Clinical chemistry (urea, creatinine, lactate): baseline, then once daily. Venous blood was tested on Thermo Scientific Indiko Plus.

Blood gases and pH (venous blood): once every 6 hours until resolution of DKA, then once or twice daily until ABB normalized. Mixed venous blood was collected from the central venous catheter near the right atrium and tested using the Abbott i-Stat CG4+Cartridge test system.

The following efficacy endpoints were assessed:

A. Primary efficacy endpoints included:

- 1) Rate of resolution of DKA during follow-up (within the first 48 hours of therapy).
- 2) Time (in hours) from initiation of therapy to resolution of DKA. DKA resolution criteria included plasma glucose <11.1 mmol/L and two of the following: plasma bicarbonate ≥18 mmol/L, venous blood pH >7.3, or strong ion gap ≤12 mmol/L.
- 3) Time (in hours) to discontinuation of insulin infusion.
- 4) Time to full recovery of consciousness (15 points on the GCS).
- 5) Length of stay in the ICU (in hours).
- 6) Mortality in the ICU.

B. Secondary efficacy endpoints were:

- 1) Changes in blood electrolytes
- 2) Changes in acid-base parameters
- 3) Changes in blood glucose and lactate.

Various statistical methods were employed depending on the distribution type of variables and the aim of the study [14, 15].

We used skewness and kurtosis parameters, which characterized the shape of the distribution curve, to estimate the distribution type of variables. Continuous variables with normal distribution were reported as $M \pm SE$, where M is the sample mean and SE is the standard error of the mean. For variables with non-normal distribution, medians with first and third quartiles were reported. The qualitative variables were reported as observed frequencies and percentages.

In cases of normal distribution and equality of variance, Student's t -test was used to compare means. Equality of variance was assessed using Fisher's F criterion. In the case of non-normal distribution and inequality of dispersion, the Mann-Whitney non-parametric U -criterion was used.

Pearson's χ^2 criterion for four-way contingency tables was used to compare qualitative variables. For small frequencies (5 to 10), Yates' correction for continuity was used. For frequencies less than 5, Fisher's exact method for four-way contingency tables was used.

Differences were considered significant at $P < 0.05$, where p is the probability of first-order error in testing the null hypothesis. In all cases, two-tailed versions of the criteria were used.

Data were processed and visualized using Statistica 12.0 (StatSoft) and Microsoft Office Excel 2017.

Results

The baseline characteristics of the patients in the study groups are shown in Table 2.

The baseline status of the patients in the two groups was not comparable in several parameters (age, body mass index (BMI)), baseline glycated hemoglobin, glucose and urea levels, which was related to the variability of the clinical course of DM and a relatively small sample of patients. However, it is noteworthy that blood glucose, glycated hemoglobin, and urea levels were higher in patients in the Reamberin group than in the control group.

Central hemodynamic and fluid compartment parameters were identical between participants and healthy controls. CBV and extracellular fluid compartment were significantly lower by 18.9% ($P=0.001$) in the patients than in the control group on admission. Intracellular fluid compartment was also lower by 1.9% ($P=0.001$) and SI was lower by 40.5% ($P=0.001$). CI values in the patient and healthy control samples did not differ (Table 3), and their maintenance within normal limits in the presence

Table 2. Baseline patient characteristics ($M \pm SE$, Me [Q1; Q3] or % (N)).

Parameter	Values in groups		P
	Control, N=30	Reamberin, N=30	
Age, years	36.67 $\pm$ 3.29	49.37 $\pm$ 3.09	0.007
BMI, kg/m ²	24.27 $\pm$ 0.90	28.30 $\pm$ 1.25	0.011
Diabetes mellitus (percentage of type 1 DM)	70.0% (21)	43.3% (13)	0.068
HbA1c, %	9.70 [8.27; 10.70]	11.18 [10.16; 12.24]	0.025
DM manifestation as the cause of DKA	6.7% (2)	10.0% (3)	0.999
Disease/surgery/trauma as the cause of DKA	43.3% (13)	46.7% (14)	0.795
Patient non-compliance as the cause of DKA	50.0% (15)	43.3% (13)	0.605
DKA severity			
Glucose, mmol/L	21.74 [19.11; 26.90]	28.82 [21.36; 32.69]	0.028
pH	7.21 $\pm$ 0.02	7.22 $\pm$ 0.02	0.755
Bicarbonate, mmol/L	11.99 $\pm$ 1.37	12.88 $\pm$ 1.19	0.623
Anion gap, mEq/L	21.70 $\pm$ 1.41	21.84 $\pm$ 1.33	0.945
Glasgow scale, points	15.00 [15.00; 15.00]	15.00 [13.25; 15.00]	0.844
Severe DKA (percentage)	53.3% (16)	40.0% (12)	0.301
Other parameters prior to treatment initiation			
Na, mmol/L	132.61 $\pm$ 0.95	132.56 $\pm$ 1.36	0.976
Cl, mmol/L	98.96 $\pm$ 0.92	97.83 $\pm$ 0.98	0.406
K, mmol/L	4.17 $\pm$ 0.17	3.98 $\pm$ 0.22	0.489
Lactate, mmol/L	2.86 [2.00; 3.94]	3.01 [2.06; 4.56]	0.291
Urea, mmol/L	9.93 $\pm$ 0.89	13.95 $\pm$ 1.47	0.024
Creatinine, μ mol/L	112.5 [95.4; 128.5]	116.7 [86.4; 138.3]	0.247

Table 3. Baseline hemodynamic parameters in the studied patients and healthy controls, $M \pm SE$.

Parameter	Values in samples		P
	Patients, N=60	Healthy controls, N=20	
Heart rate, bpm	113.9 $\pm$ 1.9	67 $\pm$ 4.1	0.001
Stroke index, mL/m ²	22.5 $\pm$ 1.5	37.8 $\pm$ 3.3	0.001
Cardiac index, L/min/m ²	2.6 $\pm$ 0.2	2.5 $\pm$ 0.3	0.07
Systemic vascular resistance index, dyn $\times$ s $\times$ cm ⁻⁵ /m ²	2332.6 $\pm$ 196.8	3000.2 $\pm$ 403.4	0.001
Urine output rate, mL/kg/h	0.32 $\pm$ 0.09	1.04 $\pm$ 0.13	0.04
Extracellular fluid, %	81.1 $\pm$ 2.6	100.2 $\pm$ 0.6	0.001
Intracellular fluid, %	98.1 $\pm$ 1.0	100 $\pm$ 0.1	0.001
Circulating blood volume, %	81.1 $\pm$ 2.6	100.2 $\pm$ 0.6	0.001

Table 4. Changes in central hemodynamic parameters in the general patient population during treatment (N=60, $M \pm SE$).

Parameter	Values during fluid therapy		P
	Prior to initiation	Two hours after initiation	
Heart rate, bpm	113.9 $\pm$ 1.9	91.4 $\pm$ 8.3	0.001
Stroke index, mL/m ²	22.5 $\pm$ 1.5	31.7 $\pm$ 3.6	0.001
Cardiac index, L/min/m ²	2.6 $\pm$ 0.2	2.8 $\pm$ 0.3	0.22
Systemic vascular resistance index, dyn $\times$ s $\times$ cm ⁻⁵ /m ²	2332.6 $\pm$ 196.8	2539.6 $\pm$ 473.1	0.491
Urine output rate, mL/kg/h	0.32 $\pm$ 0.09	0.71 $\pm$ 0.18	0.05

Table 5. Treatment outcomes by study group (Me [Q1; Q3] or % (N)).

Parameters of severity and outcome	Values in groups		P
	Control, N=30	Reamberin, N=30	
Duration of DKA, hours	44.5 [36.5; 51.5]	30.0 [24.0; 36.0]	0.001
Resolution of DKA within 48 hours, percentage	66.7% (20)	90.0% (27)	0.060
Duration of insulin infusion, h	48.0 [40.0; 55.5]	32.0 [24.5; 40.0]	0.001
Time to complete recovery of consciousness, h	0.0 [0.0; 0.0]	0.0 [0.0; 4.0]	0.627
ICU treatment time, h	56.0 [50.0; 66.3]	41.0 [30.0; 48.0]	0.001
Mortality rate in the ICU, %	0	0	—

of reduced stroke volume was achieved by significant tachycardia.

The above results (Table 4) demonstrate the reversal of hemodynamic disturbances caused by fluid therapy.

The treatment efficiency outcomes are shown in Table 5. The data show that the duration of DKA, insulin infusion and ICU treatment was significantly shorter in the Reamberin group than in the control group ($P=0.001$).

Table 6. Changes in acid-base status in the study groups ($M \pm SE$ or $Me [Q1; Q3]$).

Parameter and time point	Values in the groups				P
	N	Control	N	Reamberin	
Venous blood pH					
Within the first 24 hours					
1–6 h	30	7.21±0.02	30	7.22±0.02	0.703
7–12 h	29	7.27±0.02	30	7.30±0.02	0.187
13–18 h	25	7.30±0.01	30	7.34±0.01	0.037
19–24 h	27	7.33±0.01	30	7.38±0.01	0.003
25–48 hours later					
25–30 h	15	7.32±0.01	18	7.38±0.01	0.003
31–36 h	25	7.36±0.01	14	7.40±0.01	0.029
37–42 h	11	7.35±0.01	6	7.42±0.01	0.010
43–48 h	20	7.38±0.01	7	7.43±0.01	0.010
Bicarbonate, mmol/L					
Within the first 24 hours					
1–6 h	30	11.99±1.37	30	12.88±1.19	0.623
7–12 h	29	14.05±1.12	30	16.88±0.90	0.053
13–18 h	25	16.83±1.23	30	19.81±0.75	0.045
19–24 h	27	17.79±0.99	30	22.38±0.62	<0.001
25–48 hours later					
25–30 h	15	17.60±1.34	18	23.04±0.84	0.001
31–36 h	25	20.42±0.80	14	24.05±0.71	0.004
37–42 h	11	19.39±1.07	6	24.60±0.81	0.005
43–48 h	20	22.65±0.55	7	24.61±0.91	0.078
Anion gap, mEq/L					
Within the first 24 hours					
1–6 h	30	21.60±1.40	30	21.67±1.36	0.970
7–12 h	29	21.06±1.18	30	17.91±1.09	0.054
13–18 h	25	18.04±1.27	30	15.37±0.94	0.092
19–24 h	27	16.40 [13.00; 18.95]	30	12.24 [10.43; 15.44]	0.038
25–48 hours later					
25–30 h	15	17.36±1.74	18	13.24±0.94	0.049
31–36 h	25	14.20 [9.90; 17.79]	14	10.30 [9.53; 11.54]	0.107
37–42 h	11	15.32±1.26	6	11.92±1.11	0.093
43–48 h	20	11.86±1.01	7	9.65±1.26	0.250

Note. N — number of measurements.

The changes in blood acid-base status in the groups of patients studied are shown in Table 6.

The addition of Reamberin to the infusion therapy protocol improved the basic parameters of acid-base balance intrinsic to ketoacidosis.

The changes in plasma electrolytes in two groups of patients are summarized in Table 7.

The urea level on day 1 and 2 was higher in the Reamberin group than in the controls. No significant differences between the two groups of patients in plasma electrolytes were found.

Discussion

According to current critical care guidelines for diabetic acidosis, the primary goal is to correct water and electrolyte disturbances. Dehydration is controlled by increasing the volume of extracellular fluid through intravenous infusion of crystalloid solutions. CBV replenishment helps stabilize the cardiovascular system, increases tissue sensitivity to insulin by reducing plasma osmolality, improving tissue perfusion, as well as decreasing the production of insulin antagonists [6, 16], which explains the feasibility of administering crystalloid solutions first, followed by insulin. This is accompanied by a more manageable fall in a blood glucose level in

response to insulin administration compared to its use in severe dehydration.

CBV is replenished in patients who respond to infusion therapy, as determined by the PLR test. A good response, indicated by a 15% increase in cardiac index after leg elevation and its return to baseline after leg lowering, suggests dehydration and a likely positive response to fluid therapy.

The fluid deficit in patients with diabetic ketoacidosis is 50–100 ml/kg real body weight and depends on the severity of DKA. In this case, a large volume of fluid must be replenished within 24–48 hours. The recommended solution for infusion therapy is 0.9% sodium chloride or 0.45% sodium chloride for sodium levels above 145 mmol/L [5, 17].

Currently, more clinicians are inclined to a restrictive strategy of fluid therapy, including control of hemodynamic parameters and body fluid compartments. Restrictive fluid therapy in our study implied replenishment of circulating blood volume in case of actual hypovolemia, as well as its continuation in volumes not involving dangerous excessive fluid infusion.

The rate of replenishment of hypovolemia in the first 2 hours was about 10 ml/kg/h and did not depend on the type of fluid. The rate of further

Table 7. Changes in electrolytes and clinical chemistry parameters in the study groups ($M \pm SE$, $Me [Q1; Q3]$).

Parameter. mmol/L	Values in groups				<i>P</i>
	<i>N</i>	Control	<i>N</i>	Reamberin	
Na ⁺					
12 h	30	134.73±0.97	30	135.16±1.15	0.777
24 h	30	135.60 [133.20; 138.13]	30	136.00 [133.63; 138.65]	0.761
36 h	27	136.63±0.70	20	137.83±1.04	0.324
48 h	25	137.43±0.69	14	137.69±1.03	0.829
Cl ⁻					
12 h	30	99.73±0.85	30	100.17±0.76	0.705
24 h	30	102.17±0.79	30	100.63±0.69	0.147
36 h	27	102.11±0.79	20	102.15±0.71	0.972
48 h	25	103.00 [102.00; 105.00]	15	102.00 [99.00; 105.00]	0.275
K ⁺					
12 h	30	3.92±0.12	30	3.87±0.12	0.764
24 h	30	3.91±0.10	30	4.01±0.08	0.402
36 h	27	3.90±0.11	20	3.94±0.10	0.818
48 h	25	3.87±0.11	15	3.82±0.09	0.785
Lactate					
24 h	29	1.93 [1.21; 2.31]	30	1.29 [0.86; 2.01]	0.576
48 h	24	1.28±0.12	14	1.31±0.19	0.914
Urea					
24 h	30	6.86±0.52	30	9.82±1.00	0.012
48 h	25	6.03±0.54	14	9.56±1.35	0.026
Creatinine					
24 h	30	86.57 [76.75; 95.79]	30	86.87 [72.83; 105.26]	0.186
48 h	25	79.33±3.38	14	91.42±10.37	0.284

Note. *N* — number of measurements.

rehydration was determined by central hemodynamic parameters and urine output rate. It averaged 2–3 ml/kg/hour during the first day. With positive clinical trends, improved ABB, stabilization of glucose levels, the rate of fluid therapy did not exceed 1–3 ml/kg/hour during the second day. This approach helped to avoid iatrogenic complications such as cerebral or pulmonary edema.

Despite the paramount importance of normal saline in DKA, recent clinical guidelines [1,5] emphasize the risk of hyperchloremic metabolic acidosis due to its high chloride content (154 mmol/L). Increasing the plasma chloride level decreases the bicarbonate concentration, while diluting the blood with a large volume of buffer-free fluid results in dilutional acidosis. Therefore, the use of normal saline in DKA may actually worsen its course [18].

This, together with the antioxidant, antihypoxic, and energy-protective properties of sodium meglumine succinate [19–21], suggests that its use may improve the outcome of intensive care in patients with diabetic ketoacidosis.

In our study, the addition of Reamberin to fluid therapy protocol resulted in a more rapid resolution of ketoacidosis than the use of normal saline alone. Increased bicarbonate buffering capacity due to succinate metabolism resulted in earlier pH normalization. The anion gap in the Reamberin group decreased over time, in contrast to the control group. This explained the faster resolution of DKA, allowing patients to be switched to subcutaneous insulin administration.

Conclusion

The addition of Reamberin (sodium meglumine succinate), a balanced crystalloid solution containing succinate, to fluid therapy protocol for DKA resulted in faster resolution of ketoacidosis, discontinuation of intravenous insulin, and transfer from the intensive care unit. These effects were achieved by increasing blood buffering capacity and earlier normalization of blood pH.

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