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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

Murat Aslan,
Canan Yazıcı Özgür

Which Crystaloid Fluid Should be Used for the Treatment of Diabetic Ketoacidosis: A Retrospective Cohort Study

Diyabetik Ketoasidoz Tedavisinde Hangi Kristaloid Sıvı Kullanılmalıdır: Retrospektif Bir Kohort Çalışması

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Murat Aslan, Canan Yazıcı Özgür
University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Clinic of Anesthesiology and Reanimation, İstanbul, Turkey

Murat Aslan MD (✉),
University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Clinic of Anesthesiology and Reanimation, İstanbul, Turkey

E-mail : aslmurat@hotmail.com
Phone : +90 541 714 10 60
ORCID ID : orcid.org/xxxxxxxxxxxxxxxxxxxxx

ABSTRACT *Objective:* We aimed to compare the advantages and disadvantages of saline (0.9% NACI) and balanced crystalloid (Isolene or Lactated ringer) solutions in patients with DKA (Diabetic ketoacidosis).
Materials and Methods: The study was carried out retrospectively on 80 patients (saline=31, balanced=49) with moderate-to-severe DKA among 129 patients with DKA who were admitted to the adult intensive care unit (ICU) between 2013 and 2023.
Results: DKA resolution time was similar in saline and balance groups [12h(6-16), 9h(7-12), p=0539]. Statistically, the blood chlorine level after DKA resolution was higher in the saline group compared to the balanced group (115±5.5, 110.8±4.4, p<0.001) and the anion gap value was lower [5.9(3.9-10.6), 9.7(7.0-12.0) , p=0.005]. The blood potassium level after DKA solution is lower than normal in the saline group [3.4(3.1-3.6), 3.6(3.2-4.0), p=0.088]. There was no statistically significant difference between saline and balanced groups in terms of 1-month mortality rates [0(0), 2(4.1), p=0.524], need for renal replacement therapy [1(3.2), 2(4.1), p=1.000] and ICU stay hours [46 (32-70), 44 (36-68), p=0.961].
Conclusion: The choice of saline or balanced crystalloid solution as the initial resuscitation fluid has no effect on DKA resolution time, mortality rate and ICU length of stay. However, balanced electrolyte solutions have a lower side effect profile.
Keywords: Diabetic ketoacidosis, saline, balanced crystalloid, resolution, mortality

ÖZ *Amaç:* DKA (Diyabetik ketoasidozis) hastalarında salin (%0.9 NACI) ve dengeli kristaloid (İsolen veya Laktatlı ringer) solüsyonlarının avantaj ve dezavantajlarının karşılaştırılması amaçlandı.
Gereç ve Yöntem: Çalışma 2013 ve 2023 yılları arasında erişkin yoğun bakıma ünitesi (ICU)'ne kabul edilen 129 DKA'lı hasta içerisinden orta-şiddetli DKA mevcut olan 80 hasta (salin=31, dengeli=49) üzerinde retrospektif olarak gerçekleştirildi.
Bulgular: DKA resolusyon süresi salin ve dengeli grubunda benzerdi [12(6-16), 9(7-12), p=0.539]. İstatistiksel olarak salin grubunda dengeli grubuna göre DKA rezolüsyonu sonrası bakılan kan klor düzeyi daha yüksek (115±5.5, 110.8±4.4, p<0.001) ve anion gap değeri ise daha düşüktü [5.9(3.9-10.6), 9.7(7.0-12.0), p=0.005]. Salin grubunda DKA resolusyonu sonrası kan potasyum düzeyleri normalden düşüktü [3.4(3.1-3.6), 3.6(3.2-4.0), p=0.088]. Salin ve dengeli grubu arasında 1 aylık mortalite oranları [0(0), 2(4.1), p=0.524], renal replasman tedavi ihtiyacı [1(3.2), 2(4.1), p=1.000] ve ICU kalış saati [46 (32-70), 44 (36-68), p=0.961] açısından istatistiksel olarak anlamlı bir fark yoktu.
Sonuç: İlk resusitasyon sıvısı olarak salin veya dengeli kristaloid solüsyonun seçiminin DKA resolusyon süresi, mortalite oranı ve ICU kalış süresi üzerine bir etkisi yoktur. Bununla birlikte dengeli elektrolit solusyonları daha az yan etki profiline sahiptir.
Anahtar Kelimeler: Diyabetik ketoasidozis, salin, dengeli elektrolit, rezolüsyon, mortalite

Introduction

Diabetic ketacidosis (DKA) is a metabolic disorder characterized by hyperglycemia, ketosis, and severe dehydration (due to osmotic diuresis) caused by the absence or deficiency of insulin (1). The frequency of diabetic ketoacidosis varies between 2.8-6.3% and is increasing gradually (2,3). Although DKA can be seen in all age groups, 80% of it consists of people over the age of 18

(3). Although DKA is mostly seen in patients with Type-1 diabetes (2/3), it can also be seen in patients with Type-2 diabetes (4). Although infection is the most common cause of DKA triggering in patients with diabetes mellitus, it can also occur due to events such as not using insulin therapy, trauma, myocardial infarction, cerebrovascular accident, and pancreatitis (3,5).

Due to the deep metabolic acidosis present, DKA treatment is usually performed in intensive care units (ICU) (6). The mainstay of treatment in DKA is intravenous (IV) replacement of existing insulin deficiency and fluid loss. Crystalloids are thought to be superior to colloids in IV fluid replacement (7-9). However, the debate continues as to whether saline (0.9% NaCl) or balanced crystalloid solutions are superior (9-10).

The aim of this study was to investigate the clinical advantages and disadvantages of saline and balanced crystalloid solutions as initial resuscitation fluids in patients admitted to the ICU (Intensive Care Unit) for moderate to severe DKA.

Materials and Methods

Design and Study Population

Patients admitted to the adult ICU for DKA between 2013 and 2023 were evaluated retrospectively. Among 129 patients admitted to the ICU, those with mild DKA, recurrent ICU hospitalizations due to DKA, those who had mixed fluid replacement (>1 L intake from the other fluid group), those whose blood gas and electrolyte (Na, K, Cl) were not checked every 2-4 hours, those who were not given crystalloid solutions. Patients with end-stage renal failure, multiple organ failure (MOF), pregnant women, patients under the age of 18 and over the age of 90 were excluded from the study (Figure 1).

These patients were divided into 2 groups, who received saline (0.9% NaCl; pH 5.5) or balanced crystalloid solutions [(Izolen; pH 7.4, Na 140-141 mEq/L, Cl 98-103 mEq/L, K 5-10 mEq/L, Acetate 27-47 mEq/L and others) or (Lactated Ringer; pH 6.5, Na 130 mEq/L, Cl 98-109 mEq/L, K 4-5 mEq/L, Lactate 27-28 mEq/L and others)] as the first resuscitation fluid during ICU follow-up until DKA resolution.

The study was conducted in full accordance with local Good Clinical Practice Guideline and current legislations. Ethical approval was obtained from the local ethics committee (Decision number: 2023/10, Date:22.05.2023).

Protocol

The diagnosis of DKA was made if the following 3 criteria were met:

Having a blood glucose level of >250 mg/dL on admission to the hospital or having known diabetes mellitus,

Having ≥ 2+ ketonuria in the urine,

Serum HCO3 concentration <15 mmol/L and/or venous Ph<7.3

Patients with DKA were categorized as mild (serum bicarbonate, 15-18 mEq/L; AG >10; plasma glucose concentration, >250 mg/dL), moderate (serum bicarbonate, 10-15 mEq/L; AG >12; plasma glucose concentration, >250 mg/dL), or severe (serum bicarbonate, <10 mEq/L; AG >12; plasma glucose concentration, >250 mg/dL). AG (Anion GAP) was calculated as follows.

$$AG = (Na+K)-(Cl+HCO3)$$

After the diagnosis of DKA, IV insulin and fluid loadings were performed in the first hour before coming to the ICU in all patients. On admission to the ICU, empirical antibiotic therapy was initiated for the patients whose clinical and laboratory parameters were compatible with infection (WBC>20,000 X109/L, CRP>5 mg/L or Procalcitonin>0.5 ng/ml).

The follow-up and treatment algorithm of patients diagnosed with DKA and admitted to the ICU is summarized below (Figure 2).

Data Collection

Study data were obtained retrospectively from the 'ImdSoft-Metavision/QlinICU Clinical Decision Support Software' system. Age, gender, BMI (Body mass index),

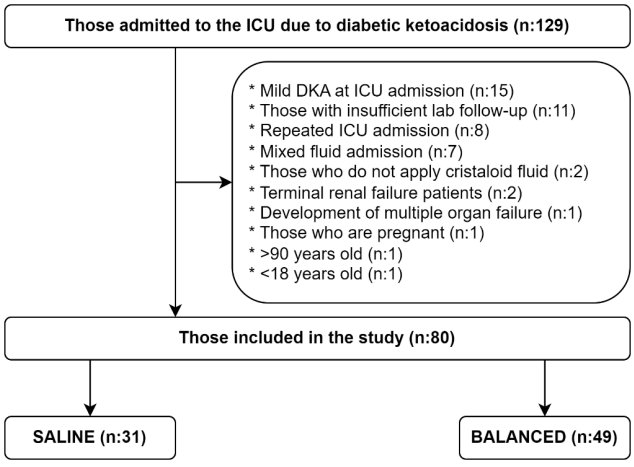

Figure 1. The study flowcharts

comorbidities, WBC (White blood cell), Hemoglobin, platelet, blood gas (pH, PCO2, HCO3, Base excess, Lactate), glucose, urea, creatinine, total bilirubin, Na, Cl, K, CRP (C-reactive protein) and procalcitonin data were collected for all patients at ICU admission. Again, using these data, CCI (Charlson Comorbidity Index), SOFA (Sequential Organ Failure Assessment) ve AKI (Acute Kidney Injury) scores were calculated (Appendix). Afterwards, DKA resolution time (Ph≥7.3 and HCO3 ≥15) was determined in all patients. Data on total insulin used, crystalloid solutions (normal saline, balanced crystalloid), 5-10% dextrose solution, amount of KCl replacement used during this period were collected. Finally, data on the total LOS (length of stay) in the ICU, the need for RRT (Renal replacement therapy) and in-hospital 1-month mortality were collected for all patients.

Statistical Analysis

Statistical analysis was made using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA).

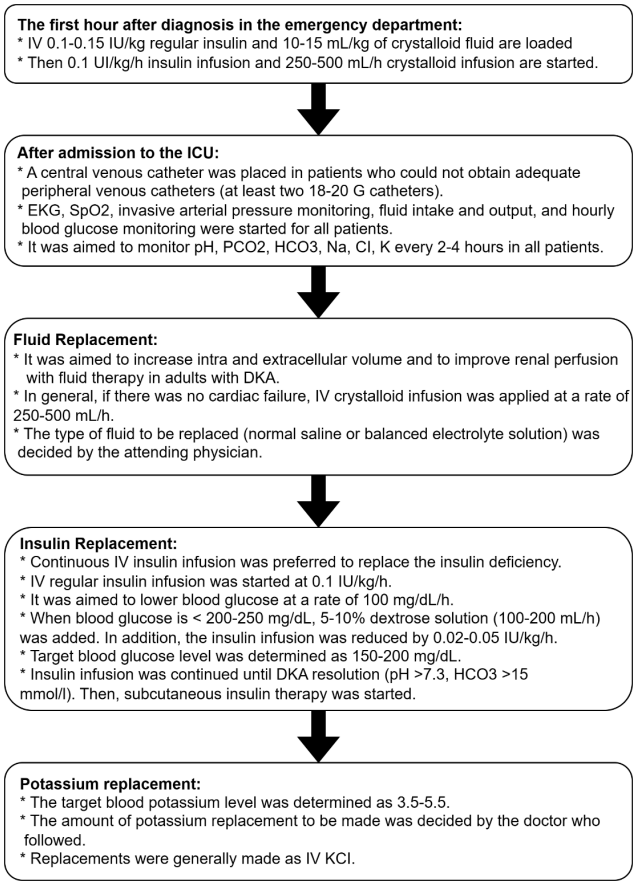

Figure 2. Diabetic ketoacidosis follow-up and treatment algorithm
DKA: Diabetic ketoacidosis, IV: Intravenous

The Shapiro-Wilk test was used to determine if the data were normally distributed. Categorical variables are given as frequency (n) and percentage (%), numerical variables mean ± standard deviation or median with interquartile range (IQR) Independent-Samples T test was used to compare the quantitative variables with normal distribution between the two groups. Mann-Whitney U test was used for comparisons between two groups of quantitative variables that did not show normal distribution. Pearson Ki-kare, Continuity correction or Fisher's exact test were used to compare categorical variables. Statistical significance was accepted as $p<0.05$.

Results

A total of 80 patients (saline=31, balanced=49) were included in the study. The majority of ICU admissions in both saline and balanced groups were patients admitted from the emergency department [n:29(93.5%), n:44(89.8%), p=0.700, respectively,]. Others were admitted from external centers, post-op or normal in-patient services. There was no statistically significant difference between saline group and balanced crystalloid group in terms of length of stay (hours) in the emergency department [3.5(2.0-5.0), 4.0(2.6-5.8), p>0.077, respectively] (Table 1).

There was no statistically significant difference between saline group and balanced crystalloid group in terms of age, gender and BMI (p=0.335, p=0.940, p=0.090, respectively,). There was no statistically significant difference between saline group and balanced crystalloid group in terms of CCI score and SOFA mortality score (p= 0.568, p=0.381, respectively). DKA was most common in Type-1 diabetes in both saline and balanced crystalloid groups [22 (71.0), 38 (77.6), p=0.691, respectively]. The most common cause of DKA in both saline and balance crystalloid group was infection [22 (71.0), 33 (67.3), p=0.926, respectively]. There was no statistically significant difference between saline group and balanced crystalloid group in terms of DKA severity (p=0.093). There was no statistically significant difference between the saline and balanced crystalloid groups in terms of the rate of development of AKI due to DKA [14(45.2%), 20(40.7%), p=0.637, respectively]. There was no statistically significant difference between saline group and balanced crystalloid group in terms of ICU admission laboratory parameters (p>0.05) (Table 1).

Although DKA resolution time was higher in the saline group, there was no statistical difference with balanced crystalloid solution [12 (6-16), 9 (7-12), p=0.539, respectively].

The amounts of total insulin, fluids and 5-10% dextrose solutions used in IV therapy were similar in both groups (p= 0.921, p=0.693, p= 0.932, respectively). There was no statistically significant difference between saline group and balanced crystalloid group in terms of the number of patients given KCl and amount of KCl replacement (p=1.000, p=0.331, respectively) (Table 2).

There was statistically significant difference between saline group and balanced crystalloid group in terms of the blood chlorine level after DKA resolution (115±5.5, 110.8±4.4, p<0.001, respectively).There was statistically significant difference between saline group and balanced crystalloid group in terms of the anion gap value after DKA resolution [5.9 (3.9-10.6), 9.7(7.0-12.0), p=0.005,

Table 1. Demographic and clinical characteristics

	Salıne (n=31)	**Balanced (n=49)**	**p-value**
ICU admission type (ED), n(%)	29(93.5)	44(89.8)	0.700
ED duration (h), median(IQR)	3.5 (2.0-5.0)	4 (2.6-5.8)	0.077
Age, median(IQR)	35 (21-53)	27 (20-48)	0.335
Female, n(%)	16 (51.6)	27 (55.1)	0.940
Body Mass Index, mean±SD	23.0 ± 3.1	24.6 ± 4.6	0.090
CCI Score, median(IQR)	2 (1-3)	1 (1-2)	0.568
SOFA Score, median(IQR)	1 (0-2)	1 (0-2)	0.381
Type-1 Diabetes Mellitus, n(%)	22 (71.0)	38 (77.6)	0.691
Cause of DKA (Infection), n(%)	22 (71.0)	33 (67.3)	0.926
Severe DKA, n(%)	17 (54.8)	37 (75.5)	0.093
Admission Lab, median(IQR)			
Ph, median(IQR)	7.15 (7.03-7.25)	7.13 (7.07-7.20)	0.607
PCO2 (mmHg), median(IQR)	18 (10-22)	16.9 (11.7-21.4)	0.953
HCO3 (mmol/L), median(IQR)	9 (6.5-11.2)	8.2 (7.1-9.8)	0.499
Base excess (mmol/L), mean±SD	-21.6 ± 5.6	-22.7 ± 4.4	0.336
NA (mmol/L), median(IQR)	134 (132-137)	134 (131-137)	0.886
K (mmol/L), median(IQR)	4.6 (4.2-5.3)	4.5 (3.9-5.0)	0.254
CI (mmol/L), mean±SD	102.5 ± 8.4	102.0 ± 6.7	0.757
Anion gap, median(IQR)	24.8 (21.6-30.1)	26.8 (23.0-30.3)	0.412
Lactate (mmol/L), median(IQR)	1.6 (1.2-2.8)	1.4 (1.2-2.3)	0.583
Glukoz (mg/dL), median(IQR)	360 (268-466)	281 (240-351)	0.082
Urea (mg/dL), median(IQR)	38 (31-54)	30.3 (19.3-50.0)	0.091
Creatınıne (mg/dL), median(IQR)	0.95 (0.79-1.18)	0.89 (0.73-1.13)	0.716
Total Bilirubin (mg/dL), median(IQR)	0.32 (0.2-0.5)	0.25 (0.18-0.44)	0.534
CRP(mg/L), median(IQR)	10.5 (1.95-43.75)	13.5 (5.2-56.0)	0.474
Procalcitonin (ng/ml), median(IQR)	0.5 (0.2-2.5)	0.75 (0.27-3.74)	0.537
Hemoglobin (g/dL), median(IQR)	12.4 (10.9-13.3)	12.7 (11.0-13.7)	0.448
Platelet ($X10^9$/L), mean±SD	300 ± 133	297 ± 120	0.904
WBC ($X10^9$/L), mean±SD	17.6 ± 5.8	18 ± 7.9	0.824
AKI, n(%)	14 (45.2)	20 (40.7)	0.637
AKI-1	12 (38.7)	18 (36.7)	
AKI-2	2 (6.5)	1 (2.0)	
AKI-3	0 (0)	1 (2.0)	

ED: Emergency Department, CCI: Charlson Comorbidity Index, SOFA: Sequential Organ Failure Assessment, DKA: Diabetic Ketoacidosis, CRP: C-reactive protein, WBC: White blood cells, AKI: Acute Kidney Injury

respectively]. There was no statistically significant difference between saline group and balanced crystalloid group in terms of blood potassium level after DKA resolution [3.4(3.1-3.6), 3.6(3.2-4.0), p=0.088, respectively]. There was no statistically significant difference between saline group and balanced crystalloid group in terms of blood pH, PCO2, HCO3, Base excess and sodium levels after DKA resolution (p>0.05) (Table 2).

There was no statistically significant difference between saline and balanced group as the first resuscitation fluid in terms of mortality, LOS in the ICU and RRT (p=0.524, p=0.961 p=1.000, respectively) (Table 2).

The range of increase in blood Cl level and decrease in the amount of anion gap were more pronounced in the saline group than in the balanced group. On the other hand, the ranges of improvement in blood PCO2, HCO3 and base excess values were lower in the saline group. The range of change in other laboratory parameters (pH, Na, K) was similar in both groups (Figure 3).

Discussion

We conducted this study to determine the advantages and disadvantages of saline and balanced crystalloid solutions used as the initial resuscitation fluid in patients developing DKA. We did not detect any difference between saline and balanced crystalloid solutions in terms of DKA resolution times, 1-month mortality rate and ICU length of stay. At the

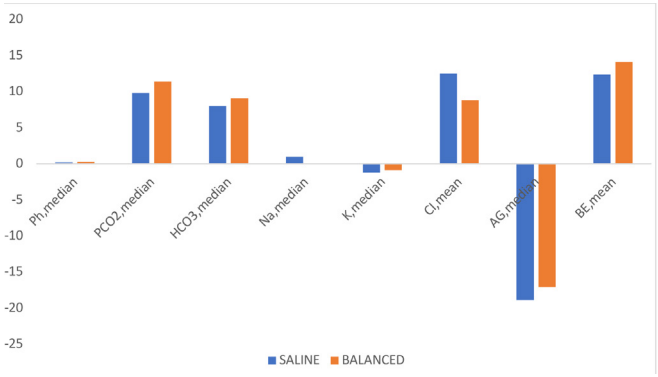

Figure 3. Comparison of the range of change in laboratory values in patients treated with saline and balanced fluid
AG: Anion gap, BE: Base excess

Table 2. Treatment outcomes of patients receiving saline and balanced crystalloid fluids

	Saline (n=31)	**Balanced (n=49)**	**p-value**
DKA resolution time(Hour), median(IQR)	12 (6-16)	9 (7-12)	0.539
IV replacements therapies, median(IQR)			
Total insulin, IU	40 (26-64)	42 (28-56)	0.921
Total dextrose (5-10%), L	1 (1-2)	1 (1-2)	0.932
Total fluid, L	4 (2.0-7.0)	3.5 (3.0-5.3)	0.693
KCl, mEq	40 (40-90)	50 (50-100)	0.331
Number of patients given KCl, n(%)	4 (12.9)	7 (14.3)	1.000
After resolution lab			
Ph, median(IQR)	7.35 (7.33-7.38)	7.34 (7.31-7.38)	0.232
PCO2 (mmHg), median(IQR)	27.8 (25.5-31.0)	28.3 (26.0-33.5)	0.390
HCO3 (mmol/L), median(IQR)	17.0 (16-18)	17.3 (16-19)	0.317
Base excess (mmol/L), mean±SD	-9.22±2.2	-8.58±2.8	0.283
Anion gap, median(IQR)	5.9 (3.9-10.6)	9.7 (7.0-12.0)	0.005*
Na (mmol/L), median(IQR)	135 (132-139)	134 (131-137)	0.454
K (mmol/L), median(IQR)	3.4 (3.1-3.6)	3.6 (3.2-4.0)	0.088
Cl (mmol/L), mean±SD	115.0±5.506	110.8±4.4	<0.001*
RRT need, n(%)	1 (3.2)	2 (4.1)	1.000
LOS in ICU (Hour), median(IQR)	46 (32-70)	44 (36-68)	0.961
Mortality, n(%)	0 (0)	2 (4.1)	0.524

DKA: Diabetic Ketoacidosis, IV: Intravenous, Lab: Laboratory, RRT: Renal Replacement Therapy, LOS: Length of Stay, ICU: Intensive Care Unit, *p<0.05

same time, the choice of saline and balanced electrolyte solution did not change the total amount of insulin used. In two prospective randomized controlled trials in 2011 and 2012 comparing the use of saline and balanced crystalloid solutions in the treatment of DKA, no superiority of either crystalloid solution was found (11-12). In a retrospective study of 85 patients in the emergency department in 2018, no difference was found in the time to resolution of DKA with the choice of crystalloid solution (13). Subsequently, in a post hoc secondary subgroup analysis of 172 patients that included 2 randomized controlled trials on emergency room and ICU patients in 2020, balanced crystalloid solution therapy was associated with faster resolution of DKA (14). Finally, in a meta-analysis of 8 randomized controlled trials involving a total of 482 patients comparing saline and balanced crystalloid solutions in 2022, it was found that the use of saline caused a slight increase in the risk of DKA resolution time and hospital stay compared to balanced crystalloid solutions (1). In our study, the DKA resolution time was longer in those receiving saline therapy, but this was not statistically significant. When all these studies are evaluated together, there is no evidence that saline solutions are superior to balanced crystalloid solutions. On the contrary, a significant number of these studies show that the use of saline can lead to hyperchloremic acidosis and prolongation of DKA resolution time.

In our study, when DKA resolution was achieved, an increase in blood chlorine level was observed in both groups. However, the increase in blood Cl level range was much more pronounced in the saline group compared to the balanced group. At the same time, the range of decrease in the amount of anion gap was much more pronounced in the saline replacement group. On the other hand, the range of recovery of blood PCO2, HCO3 and base deficit was lower in the saline group. Studies have shown that hyperchloremic acidosis, low anion gap and renal HCO3 loss may develop due to rapid and high volume iv infusion of high volume acidic saline solution (1,15). Therefore, while DKA regresses with insulin replacement in the saline replacement group, metabolic acidosis due to hyperchloremia may develop. In addition, although the duration of DKA resolution was longer in the saline group, the amount of HCO3 increase and the range of base excess recovery amount may have been lower. It is observed that hyperchloremia developed in the balanced group, although not as much as in the saline group. This may be due to the use of saline solution to replace insulin, potassium and other IV drugs.

The number and amount of patients receiving potassium replacement were similar in both groups. The potassium level measured after resolution of DKA was lower in the saline group, but within the lower limits in both groups. When DKA develops due to insulin deficiency, potassium levels tend to decrease intracellularly and increase extracellularly (3). Later, with the initiation of insulin therapy, hypokalemia may develop due to the shift of potassium into the cell (4). Therefore, potassium replacement is required. The low potassium levels measured after resolution of DKA in our patient population, especially in the saline group, suggest that potassium replacement was inadequate.

In both patient groups, the rate of patients who developed AKI at admission to the hospital was similarly high. AKI may develop due to renal perfusion impairment, as well as deterioration in all tissue perfusion due to severe volume deficit due to osmotic diuresis. High- volume replacement is needed for the treatment of AKI (16). However, there are concerns that renal vasoconstriction and decreased glomerular filtration rate may occur due to hyperchloremia associated with saline infusion (15,17). In our study, although AKI rates were high in both groups on admission, the need for RRT was similarly low. In a study evaluating 15,802 critically ill patients hospitalized in multicentric ICU in 2018, no statistically significant difference was found between the use of saline or balanced crystalloid solutions and the need for new RRT and the rate of development of permanent renal dysfunction (18).

Both patient groups consisted mostly of young patients who did not have any additional comorbidities other than diabetes mellitus. Therefore, CCI score values were low in both groups. Again, SOFA score values used to predict mortality were low in both patient groups. Low SOFA score values were consistent with our low overall mortality rate. Although SOFA score values were low, the majority of the patients included in the study in both patient groups consisted of patients with severe DKA.

Patients with Type 1 diabetes mellitus constituted the majority of both patient groups. Although DKA can be seen in Type-2 diabetes mellitus due to insulin resistance, it is most likely to occur in Type-1 diabetes mellitus, which mainly develops due to insulin insufficiency (4,6). In our study, as in the literature, the most common cause of DKA in both patient groups was infection (3,5). Correspondingly, both patient groups had higher WBC, CRP, or procalcitonin values.

The current study has several limitations: Firstly, the study was retrospective. Due to the retrospective nature of the

study, some patients who were not followed up frequently and in accordance with the study protocol had to be excluded from the study. However, considering the original studies on DKA, it was important to ensure that a significant number of DKA patients were examined. Secondly, the study was single-centered. Thirdly, although the amount of intravenous insulin and crystalloid loading administered within the first hour after the diagnosis of DKA is standardized, the lack of recorded data on the exact amount of treatments administered during the period until ICU admission is an important limitation. Mean length of stay in the emergency room was similar in both groups. Although the mean length of stay in the emergency department before ICU admission was similar in both groups, we did not include the treatment administered in the emergency department in our evaluation of both patient groups. We planned to compare the treatment after ICU admission.

Conclusion

There was no superiority of saline compared to balanced crystalloid solution as the initial resuscitation fluid in patients with DKA. On the contrary, it was found that rapid and high volume saline solution use can lead to the development of hyperchloremic metabolic acidosis. Greater attention should be paid to adequate potassium replacement, whether saline solution or balanced solution is used. In addition, potassium replacement with potassium phosphate would be more appropriate to prevent hyperchloremia.

However, no effect of saline or balanced crystalloid solutions selection on mortality and ICU stay was found. The advantages of saline solution such as cost and ease of supply may make it a reason of choice for centers with limited resources. However, in the treatment of DKA, we recommend the use of balanced crystalloid solutions as the first choice, as they have a lower side effect profile.

Ethics

Ethics Committee Approval: The study was conducted in full accordance with local Good Clinical Practice Guideline and current legislations. Ethical approval was obtained from the University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Committee (Decision number: 2023-10-, date: 22.05.2023).

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: M.A., C.Y.Ö., Concept: M.A., C.Y.Ö., Design: M.A., C.Y.Ö., Data Collection and Process: M.A., C.Y.Ö., Analysis or Interpretation: M.A., Literature Search: M.A., Writing: M.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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Appendix.
1- Charlson comorbidity indexes of the patients; It was calculated by entering patient data from the https://www.mdcalc.com/calc/3917/charlson-comorbidity-index-cci website.
2- SOFA scores of the patients; It was calculated by entering patient data from the https://www.mdcalc.com/calc/691/sequential-organ-failure-assessment-sofa-score website.
3- 2012 KDIGO AKI scores of the patiens: It was calculated by entering patient data from the https://kdigo.org/wp-content/uploads/2016/10/KDIGO-2012-AKI-Guideline-English.pdf