



Fluid Management in Patients with Diabetes Ketoacidosis (DKA): Literature Review

Sandra Pebrianti¹, Bambang Aditya Nugraha², Iwan Shalahuddin^{3*}, Theresia Eriyani⁴

^{1,2,3,4} Fakultas Keperawatan Universitas Padjadjaran

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ABSTRACT

DKA is a state of decompensation of metabolic chaos characterized by triassic hyperglycemia, acidosis, and ketosis which is one of the most serious and life-threatening acute complications of metabolic diabetes mellitus. Diabetic Ketoacidosis (DKA) requires proper treatment and immediate treatment. Management of insulin therapy, intravenous administration of fluids is a key component of DKA management to expand intravascular, interstitial, and intracellular volumes. This Literature Review aims to determine the influence of fluid management in patients with diabetes ketoacidosis. The author uses the method used to conduct a literature review is to search through the internet. Search literature through the internet based on several criteria, namely journals published in the last 10 years. The literature search uses the PubMed, Sage Journals, and Science Direct databases. Keywords used "Fluid Management AND Diabetes Ketoacidosis (DKA)". Then sorted by inclusion criteria, publication year 2017-2022, experimental research design, and written in Indonesian or uk. Based on the results of the study, it can be concluded that there are six fluid administration interventions in Diabetes Ketoacidosis (DKA) patients, namely crystalloid fluid, saline fluid, lyte-148 plasma, potassium, plasma lyte A and the use of two fluids (electrolyte fluid + dextrose). DKA management includes adequate replacement of fluids and electrolytes, especially potassium, as well as continuous administration of insulin. The top priority in the management of DKA is one of them is fluid therapy.

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*) corresponding author

Iwan Shalahuddin, SKM., S.Kep., M.MKes

Departemen Keperawatan Komunitas,
Fakultas Keperawatan, Universitas
Padjadjaran, Jl. Raya Bandung Sumedang
KM.21, Hegarmanah, Jatinangor, Kabupaten
Sumedang, Jawa Barat 45363

Email: shalahuddin@unpad.ac.id

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ABSTRAK

DKA is a state of decompensation of metabolic chaos characterized by triassic hyperglycemia, acidosis, and ketosis which is one of the most serious and life-threatening acute complications of metabolic diabetes mellitus. Diabetic Ketoacidosis (DKA) requires proper treatment and immediate treatment. Management of insulin therapy, intravenous administration of fluids is a key component of DKA management to expand intravascular, interstitial, and intracellular volumes. This Literature Review aims to determine the influence of fluid management in patients with diabetes ketoacidosis. The author uses the method used to conduct a literature review is to search through the internet. Search literature through the internet based on several criteria, namely journals published in the last 10 years. The literature search uses the PubMed, Sage Journals, and Science Direct databases. Keywords used "Fluid Management AND Diabetes Ketoacidosis (DKA)". Then sorted by inclusion criteria, publication year 2017-2022, experimental research design, and written in Indonesian or uk. Based on the results of the study, it can be concluded that there are six fluid administration interventions in Diabetes Ketoacidosis (DKA) patients, namely crystalloid fluid, saline fluid, lyte-148 plasma, potassium, plasma lyte A and the use of two fluids (electrolyte fluid + dextrose). DKA

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INTRODUCTION

Diabetic Ketoacidosis Disease (DKA) is the final state in metabolic disorders due to severe or relative insulin deficiency characterized by triassic hyperglycemia, acidosis and ketosis. Diabetic Ketoacidosis (DKA) is a life-threatening complication of diabetes mellitus (DM) that requires proper treatment and immediate treatment. This condition can occur in patients with or without a previous diagnosis of diabetes mellitus (DM), both type 1 and type 2 DM. DKA is caused by the presence of insulin hormone deficiency and the action of counterregulatory hormones, especially glucagon, which is not inhibited. DKA's biochemical criteria include hyperglycemia, ketosis, and metabolic acidosis. degrees of DKA are divided into mild, moderate, and severe according to the severity of acidosis.

Community data in the United States, Rochester, shows that the incidence of KAD is 8/1000 of DM patients per year for all age groups, while for age groups less than 30 years of age is 13.4/1000 dm patients per year. Other sources mention kad incidence of 4.6 – 8/1000 DM patients per year. KAD is reportedly responsible for more than 100,000 patients treated per year in the United States. Although community data in Indonesia does not yet exist, it seems that the incidence of KAD in Indonesia is not as large as in western countries, given the low prevalence of type 1 DM. Reports of KAD incidents in Indonesia generally come from hospital data and especially in type 2 DM patients (Tarwoto, 2012).

KAD is one of the most serious and life-threatening acute complications of metabolic diabetes mellitus. The mortality rate of patients with KAD in developed countries is less than 5% and many flashlights, some other sources mention 5-10% 2.2 – 10% 5, or 9-10%. While in clinics with simple facilities and elderly patients the mortality rate can reach 25-50%. The mortality rate becomes higher in some of the conditions that accompany KAD, such as sepsis, severe shock, extensive acute myocardial infarction, elderly patients, high initial blood glucose levels, uremia and low blood acidity levels. Death in kad patients of young age can generally be avoided by a quick diagnosis, appropriate and rational treatment according to his pathophysiology. In patients of the elderly age group, the cause of death is more often triggered by the underlying disease factor.

Successful management of KAD requires correction of dehydration, hyperglycemia, acidosis and electrolyte abnormalities, identification of comorbid precipitation factors, and most importantly continuous monitoring of the patient. KAD management includes adequate fluid therapy, adequate insulin administration, potassium therapy, bicarbonate, phosphate, magnesium, therapy against hyperchloremic conditions and the administration of antibiotics according to indications. A very important factor to pay attention to is the introduction of complications due to therapy so that the therapy given does not actually worsen the patient's condition.

DKA emergency can cause fatal complications for sufferers with a mortality rate of 0.5 to 7% (Faisal, F.,

Adelaine, A. T., & Nurhayati, T., 2020). DKA risk factors include patients who have just been diagnosed with DM, non-compliance with insulin, infections, myocardial infarction, acute abdomen, trauma, thyrotoxicosis, cocaine, and antipsychotics. while the clinical picture in DKA patients includes symptoms of hyperglycemia, respiratory kumaul, acetone-scented breath, loss of extracellular fluid volume, nausea, vomiting, abdominal pain, and loss of consciousness.

Insulin deficiency that occurs in DKA causes hyperglycemia, and further triggers the body to lose fluids and electrolytes (sodium, potassium, and chlorides) through urine, and as a result there is a loss of extracellular fluid (Febrianto, D., & Avoidati, E., 2021). Due to the loss of a large enough volume of fluid through urine due to hyperglycemia, DKA sufferers generally experience very severe dehydration. So the management of DKA includes adequate replacement of fluids and electrolytes, especially potassium, as well as continuous administration of insulin. The top priority in the management of DKA is fluid therapy. Insulin therapy will only be effective if fluid is administered in the early stages of therapy and only fluid therapy will make blood sugar levels lower.

The purpose of preparing this Refiew Literature report is to identify how fluid management in patients with DKA is accompanied by the effectiveness of its management.

METHOD

The type of review used in writing this article is narrative review. Narrative review aims to identify and summarize previously published articles, avoid duplication of research, and look for new areas of study that have not yet been studied (Ferrari, 2015). This paper focuses on topics related to fluid management in patients with diabetes ketoacidosis (DKA). Literature search conducted during March-May 2022. Before conducting a search to include relevant literature, we followed a search strategy using the population, intervention, comparison, outcome method for literature review. The search for articles was carried out using the following keywords: Population: DKA patients, Intervention: Fluid management, Comparison: Differences in fluid types, Outcome: Comparison of clinical results of fluid administration in DKA patients Literature search was carried out using several databases, namely PubMed, SAGE Journal, and ScienceDirect. At this stage the researcher conducted a search for reference sources using a combination of keywords in English: fluid management, diabetic ketoacidosis. The inclusion criteria in this study are articles that discuss fluid management in DKA patients, articles in English and Indonesian, limitations of articles published in the last 5 years (2017-2022), and full text articles. Articles of the type of review, only abstract, and preliminary studies are excluded.

Literature search using several sources, namely PubMed, SAGE Journal, and ScienceDirect. The purpose of the article search is to get articles from Indonesia or abroad that discuss

the management of fluid therapy in DKA patients accompanied by the effectiveness of its management

The method used to perform a literature review is by searching through the internet. Literature searches through the internet are based on several criteria, namely articles discussing fluid management in DKA patients, articles with English and Indonesian, limitations of articles published in the last 5 years (2017-2022), and full text articles. The article is of the review type, only abstract, and preliminary studies are excluded. The keywords used are using a combination of keywords in English: fluid management AND diabetic ketoacidosis.

The presentation of the results of the study of each literature used, the information of which will be presented in the form of a narrative. The narrative that is made will contain the management of fluid therapy in DKA patients accompanied by the effectiveness of its management that has been obtained from previous literature searches. The presentation of the results of data extraction is presented in the form of a table consisting of the title of the article, the author of the article along with the year of publication of the

article, the type of research, research methods and research results.

RESULTS AND DISCUSSION

The articles obtained are sorted to get articles according to the topic of the literature study carried out. Article sorting is carried out by adjusting to the established inclusion and exclusion criteria.

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) The findings obtained 6 articles that met the criteria with the characteristics of research publications conducted in the United States (n=4), Poland (n=1), and Australia (n=1). There are 6 types of fluid management in Diabetes Ketoacidosis (DKA) patients given in the six articles, namely crystalloid fluid, saline fluid, lyte-148 plasma, potassium, plasma lyte A and the use of two fluid bags (electrolyte fluid + dextrose).

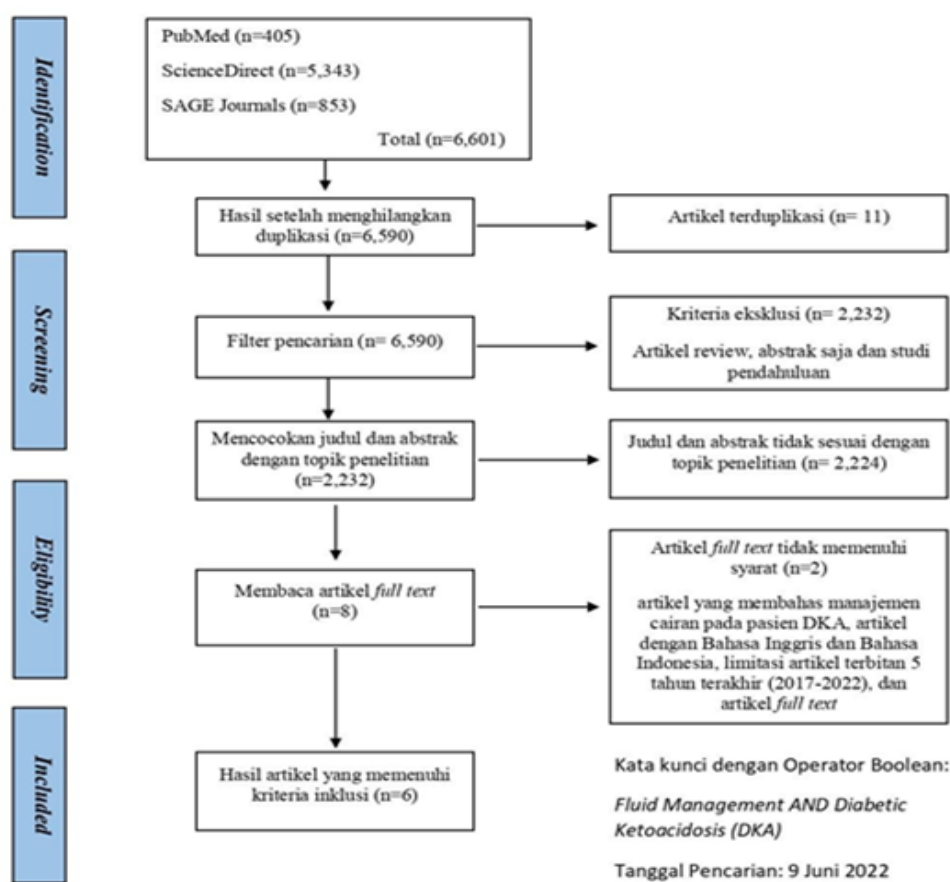


Figure 1. PRISMA Flow Diagram

Table 1. Literature Analysis Results

Title, Author of the Year	Purpose	Research Design	Sample	Conclusion
Clinical effects of balanced crystalloids vs saline in adults with diabetic ketoacidosis: a	To compare the clinical effect of balanced crystalloids with the clinical effect of saline for the	Subgroup analysis in adults with DKA in 2 companion trials, namely Saline Against Lactated Ringer's or Plasma-Lyte in the	271 patients treated in the ER received icd-10-CM codes for DKA; 172 of these patients met the feasibility criteria of the study and were included	Subgroup analysis in adults with DKA in 2 large pragmatic experiments, administration of liquids with balanced crystalloids was associated with a faster resolution of

subgroup analysis of cluster randomized clinical trials	treatment of acute in adults with DKA (Diabetic Ketoacidosis).	Emergency Department (SALT-ED) and the Isotonic Solutions and Major Adverse Renal Events Trial (SMART). Randomized clinical trials compared balanced crystalloids vs saline in patients in the Emergency Department (ER) and Intensive Care Unit (ICU).	in this analysis	DKA than saline. These results suggest that balanced crystalloids may be preferred over saline for acute management in adults with DKA
Self, W. H., Evans, C. S., Jenkins, C. A., Brown, R. M., Casey, J. D., Collins, S. P., (2020).				
Balanced Crystalloid Versus Normal Saline as Resuscitative Fluid in Diabetic Ketoacidosis	To assess the clinical results associated with the use of Ringer Lactate (RL) compared to Normal Saline (NS) as a resuscitation fluid in diabetic ketoacidosis (DKA)	Single-center retrospective cohort study in adult patients treated at the University of New Mexico Hospital.	A total of 541 admissions for DKA were identified during the study period and 215 that did not meet the study feasibility criteria were excluded from the analysis.	In this study, a statistically significant decrease was obtained in the incidence of iatrogenic hyperchloremia with the use of LR compared to NS as fluid resuscitation in DKA. Serum creatinine was more elevated in the LR group than in the NS group at 48 hours. Preferential use of balanced crystalloids for fluid resuscitation in DKA may reduce the incidence of hyperchloremia and support kidney recovery.
Carrillo, A. R., Elwood, K., Werth, C., Mitchell, J., & Sarangarm, P. (2022).				
Sodium chloride or Plasmalyte - 148 evaluation in severe diabetic ketoacidosis	To determine whether treatment with Plasma Lyte-148 (PL) compared to sodium chloride 0.9% (NaCl) resulted in a faster resolution of diabetic ketoacidosis (DKA) and whether acetate in PL potentiates ketosis.	This study used the SCOPEDKA trial design which included clusters, crossovers, open label, randomized, controlled trials	The samples in this study were all patients aged 16 years and over who came to the emergency department (ER) and ICU at participating locations during the intervention period with severe DKA. Patients were collected from September 2019 to September 2020 and enrolled 90 patients in 7 locations	In this study, patients with severe DKA who were given plasma Lyte-148 fluid with which was given sodium chloride liquid could produce a faster resolution of metabolic acidosis, accompanied by lower serum chloride concentrations and without increased ketone formation. there is one thing that is significantly considered, namely the use of Plasma Lyte-148 (PL) in DKA patients is the potential for acetate anions contained in PL to be converted into acetoacetate and potentiate ketosis. DKA resolution tends to occur more quickly in the PL group which means that PL acetate does not contribute to excessive ketone formation in DKA patients. the frequency of side effects such as hypoglycemia and hypophosphateemia was also lower in the OT group.
Ramanan, M., Attokaran, A., Murray, L., Bhadange, N., Stewart, D., Rajendran, G., ... & Venkatesh, B (2021)				
Potassium-Containing Fluids for Diabetic Ketoacidosis	To determine the concentration of potassium for IV fluids used in the treatment of diabetic ketoacidosis (DKA)	Retrospective chart review	The samples in this study were 113 patients aged <21 years with laboratory-confirmed diabetes ketoacidosis at Children's Hospital of The King' s Daughters (CHKD) Emergency Department.	The use of iv potassium fluid is most abundant in the treatment of diabetes ketoacidosis. It was proven that while following the DKA treatment protocol, the use of potassium 40 mEq/L IV fluid did not show an increased risk of hyperkalemia because most patients maintained the goal of serum potassium concentration.
Guise, R., Ausherman, K., & Vazifedan, T. (2021).				
Comparison of Plasma-Lyte A and	The purpose of this study was to	Retrospective analysis	84 patients treated for DKA were mild,	The average key time results for DKA resolution were

Sodium Chloride 0.9% for Fluid Resuscitation of Patients With Diabetic Ketoacidosis Oliver, W. D., Willis, G. C., Hines, M. C., & Hayes, B. D. (2018).	compare Plasma-Lyte A (PL) and 0.9% sodium chloride (NS) in terms of diabetic ketoacidosis resolution time (DKA).		moderate and severe.	similar between the PL (19.74 hours) and NS (18.05 hours) groups. Patients treated with OT experienced a significantly greater increase in pH in the period from 4 to 6 hours to 12 hours. Chloride levels were significantly higher and the anion gap was significantly lower for the NS group in the period from 6 to 12 hours.
Potential clinical benefits of a two-bag system for fluid management in pediatric intensive care unit patients with diabetic ketoacidosis Velasco, J., Fogel, J., Levine, R., Ciminera, P., Fagan, D., & Bargman, R (2017)	To compare the fluid management system of one bag and two bags in relation to the incidence of hypoglycemia, correction of serum bicarbonate, correction of pH and return from the pediatric intensive care unit (PICU).	<i>Retrospective cohort study</i>	61 patients aged less than 21 were treated at the PICU with a diagnosis of DKA. Of the 61 patients, 38 were treated with a one-bag system and 23 were treated with a two-bag system	The two-bag system has a significantly lower incidence of hypoglycemia compared to the single-bag system. The two-bag system is significantly less hours of stay on the PICU than the single-bag system. However, there is no significant difference between bag systems for hours for pH and bicarbonate correction

Diabetes Ketoacidosis (DKA) patients are severely dehydrated so fluid replacement is needed. But under these conditions it is not allowed to make too quick corrections. This can lead to cerebral edema, hypoglycemia, and hypokalemia. Based on the search of the literature, it can be known that there are several types of fluids that can be administered to patients. The following are some types of fluids that can be given to patients with DKA (Ismail, M. T., & Elbaih, A. H, 2020).

Balanced crystalloids

Based on the research of Self et al. (2020), balanced crystalloid fluids contain physiological concentrations of chlorides and additional anions that are metabolized into bicarbonates that cause a neutral or slightly alkaline effect when infused. DKA's current clinical practice guidelines recommend saline as the fluid of choice for volume expansion, evidence comparing saline to balanced crystalloids in this population is undervalued. Thus the study of Self et al. (2020) is expected to add to the accumulation of evidence suggesting that balanced crystalloids are better resuscitation fluids than saline for many patients and may have specific benefits for patients with DKA.

In addition, the research of Carrillo et al. (2022) says that Lactated Ringer's (LR) is a balanced crystalloid that is more similar to physiological electrolyte concentrations and is beneficial in maintaining electrolyte levels within the normal range when used as a large volume resuscitation fluid. LR has a chloride content of 109 mEq/L and is less likely to trigger hyperchloremia, acid-base disorders, and MMR. Iatrogenic hyperchloremia was significantly lower in patients treated with LR-based fluids when compared to saline resuscitation in the management of DKA (Carrillo, A. R, at al, 2022).

Saline

Administration of saline fluid in DKA patients can result in iatrogenic acidosis which aggravates metabolic acidosis caused by DKA itself (Self et al., 2020). It was also reported that one patient died in the group given saline fluid. In line with research (Carrillo et al., 2022) the administration of NS

(Normal Saline) fluid can significantly lead to higher iatrogenic hyperchloremia. Some data suggest that administration of ns in large quantities has been associated with the incidence of hyperchloremia, hypernatremia, acute kidney injury (MMR), and non-anion gap metabolic acidosis (Allen, C. H, at al, 2016). In addition, the prevalence of the incidence of hypertension in patients given NS has an influence on renal function, both at the beginning and in additional disorders (Becherucci, F, at al, 2016).

Plasma Lyte-148

Based on the research of Ramanan et al. (2021), Plasma Lyte-148 (PL) is a buffer salt solution containing a chloride concentration lower than SC (sodium chloride 0.9%) and acetate and gluconate as additional anions. It has been evaluated in two randomized trials, namely with pediatric patients and adult patients with DKA. Experiments of pediatric patients showed no difference between the OT and SC groups in the development of acute renal injury (main outcome) or other clinical outcomes (Makris, K., & Spanou, L, 2016). Meanwhile, adult patient trials showed faster acidosis resolution in the PL group (Plasma Lyte-148). Secondary analysis of two other cluster randomized trials showed faster DKA resolution with the use of balanced crystalloids (including PL and sodium lactate compounds) compared to SC (sodium chloride 0.9%) (Wolfsdorf, J. I, at al, 2018). Plasma Lyte-148 can produce a faster resolution of metabolic acidosis in adult patients with severe diabetic ketoacidosis compared to 0.9% sodium chloride. Plasma Lyte-148, when used as an intravenous fluid therapy for patients with diabetic ketoacidosis, does not cause an increase in ketosis. Thus, for patients with severe DKA, treatment with PL can result in a faster resolution of metabolic acidosis compared to SC (Besen, B. A. M. P., Boer, W., & Honore, P. M, 2021).

Kalium

During DKA, potassium is lost from intracellular tissues due to hypertonicity and is then excreted from the body through emesis and osmotic diuresis. In addition, the loss of potassium in the body can go through the excretion of urine

due to secondary hyperaldosteronism. Administration of fluids with a potassium concentration of 40 mEq / L can cause potassium to shift intracellularly, so as to reduce the risk of hyperkalemia (Guise et al, 2021; Veltri, K. T., & Mason, C, 2015).

Plasma-Lyte A

Based on research conducted by Oliver et al. (2018), the average time for DKA resolution is similar between the OT and NS groups (19.74 vs. 18.05 hours). Although they found no time difference in DKA resolution, researchers observed changes in serum biochemistry that could show a faster resolution (Von Oettingen, J. E, at al, 2018). Patients in the PL group experienced a significantly greater increase in pH over a period of 4 to 6 hours and 6 to 12 hours when compared to the initial pH measurement of patients. In addition, based on secondary studies conducted by Chua et al., (2012) detected a tendency to faster DKA resolution in their patients treated with PL than those treated with NS.

Use of 2 bags (Electrolyte liquid + dextrose)

The one-bag and two-bag system has been widely used for fluid management in DKA patients. There are two different approaches to fluid management on DKA. Traditionally, that is, one IV liquid bag with electrolyte is used. Then when blood glucose levels drop, a new bag with the appropriate glucose content is used to replace the previous bag even though it has not been completely discharged. Whereas in the use of a two-bag system, it consists of two bags with identical electrolyte content but with different dextrose concentrations and then given simultaneously into one IV line. So that the two-bag system can allow a faster response time for IV fluid replacement and constant administration of dextrose fluid.

Based on research conducted by Velasco et al. (2017) stated that DKA patients who received IV fluids using a two-bag system had a significantly lower incidence of hypoglycemia in the first 24 hours after starting treatment compared to the one-bag system. This decrease in hypoglycemia occurs because the two-bag system allows for a faster adjustment of IV fluid changes in response to a decrease in blood glucose due to the ongoing work of insulin (Haas, N. L, at al, 2018). The study also found that patients who used the two-bag system spent less time on the PICU than patients with the single-bag system. However there is no significant difference for pH or bicarbonate correction between single-bag systems or two-bag systems.

CONCLUSIONS AND SUGGESTIONS

Based on the data and research results in the reviewed article, it can be concluded that there are six fluid administration interventions in patients with diabetes ketoacidosis (DKA), namely the administration of crystalloid fluid, saline, plasma lyte-148, potassium, plasma lyte A and the use of two fluid bags (electrolyte fluid + dextrose). Each fluid has special benefits for patients with DKA as in Plasma Lyte-148 does not cause ketosis, Plasma-Lyte A can increase the pH value significantly, potassium with a concentration of 40 mEq / L is able to shift intracellularly so as to reduce the risk of hyperkalemia, Balanced crystalloids are better than saline. Saline interventions in the reviewed results stated that it could result in iatrogenic acidosis which aggravated metabolic acidosis. The administration of 2 bags of

electrolyte fluid + dextrose directly through the IV allows for faster adjustment of iv fluid changes in response to a decrease in blood glucose.

Recommendations for subsequent researchers are expected to conduct further literature reviews by paying attention to other variables that have not been touched by this review.

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Conflict of Interest Statement

The authors state that there is no potential conflict of interest with respect to the writing and publication of this article.

Reviewer's Advice

The authors leave it entirely up to the maintainers to review our articles, and the reviewer results are relayed back to us if they need to be corrected according to the input of the reviewer team.

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