ORIGINAL RESEARCH PAPER
Volume - 13 | Issue - 12 | December - 2024 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

EVALUATING FLUID MANAGEMENT IN DIABETIC KETOACIDOSIS

Emergency Medicine
Tyre, JA
Podesta, T.
Tyre, NM.
Silvestri, V.

ABSTRACT

Diabetic Ketoacidosis is a critical illness that requires aggressive fluid resuscitation, electrolyte correction, and glucose control. The specific intravenous fluid used is a debatable topic among healthcare providers and hospitals. The controversy is due to the vastly different characteristics of 0.9% normal saline and lactated ringers. Normal saline, the standard of care, is more acidic and less physiologic when compared to lactated ringers. Review articles and clinical trials were reviewed to gather information regarding the topic. One clinical trial compiled from numerous sub-group studies shows promising results for lactated ringers being the superior fluid of choice. However, two smaller studies reviewed revealed insignificant data. Due to the limited subjects studied in the clinical trials, this study cannot support or reject the idea that lactated ringers are superior to normal saline in treating diabetic ketoacidosis.

KEYWORDS

INTRODUCTION AND BACKGROUND

Diabetic Ketoacidosis (DKA) is a common reason for a person with type one diabetes mellitus to be admitted to the intensive care unit. It occasionally occurs in patients with type two diabetes [1]. DKA is associated with increased healthcare costs and mortality (1-5%) compared to other hospital admissions [1,2]. Diabetic ketoacidosis has shown to be detrimental to children and adolescents with it being the number one cause of morbidity and mortality in those groups [3,4]. 50% of the pediatric diabetes-related deaths were found to have cerebral edema. The cerebral edema in those patients correlated with the severity of acidosis and dehydration [3]. Other factors that were believed to result in cerebral edema were rapid fluid infusion time, hypotonicity of fluids, and hyponatremia. Hypokalemia is a common complication of DKA management from insulin therapy requiring potassium infusions to prevent muscle weakness and cardiac arrhythmia.

The pathophysiology of diabetic ketoacidosis stems from the body's inability to utilize glucose to produce adenosine triphosphate (ATP) because of reduced insulin/insulin receptor interaction. Fat is then broken down into ketone bodies to provide energy, resulting in decreased serum pH [5]. Since the cells cannot absorb glucose from the serum, the glucose levels in the serum are elevated. Hyperglycemia leads to increased glucose loss in the urine due to oversaturation of the sodium/glucose transporters in the proximal convoluted tubule. Higher levels of glucosuria lead to increased water loss in the urine because water follows glucose in a process called osmotic diuresis. The urinary depletion of water makes the serum hyperosmolar, therefore, fluid resuscitation is crucial in managing DKA.

The current guideline for fluid replacement for DKA patients recommends using Normal Saline (NS). However, this therapy is not perfect. Many physicians and hospitals now prefer to begin fluid resuscitation therapy with Lactated Rings (LR) based on its composition and potentially quicker resolution of acidosis in patients with DKA.

REVIEW

Pathophysiology of Diabetic Ketoacidosis

Insulin is secreted by the beta cells of the pancreas to maintain blood glucose levels. Insulin stimulates the insulin receptors authorizing intracellular glucose uptake so that the cell can metabolize the carbohydrate for ATP production. However, when a patient is in DKA, glucose utilization is minimal. This results in three main problems: volume depletion, electrolyte abnormalities, and an acidic serum pH. Volume depletion occurs when the accumulation of glucose results in the serum becoming hyperosmolar. Hyperosmolarity leads to osmotic diuresis, which is polyuria and polydipsia. This results in a deficit of ~6L in total body water [6].

Decreased insulin interaction with the Insulin receptor causes inhibition of the Na+/K+ ATPase pump with accumulation of potassium outside of the cell and reduced potassium concentration in the cell [7]. However, the K+/H+ pump is not dependent on insulin. The K+/H+ pump allows more Hydrogen ions into the cell to try to compensate for the acidic serum in exchange for pumping potassium ions out of the cell. Therefore, potassium serum values will likely be increased even though the body will be at a potassium deficit. Elevated glucose levels alter the sodium concentration which leads to pseudohyponatremia.

Insulin deficiency causes the body to undergo ketogenesis, where fatty acids and amino acids are broken down to produce energy. During this process, ketone bodies are formed. Alkaline bicarbonate ions can buffer the acidic ketones, but when all of the bicarbonate ions are consumed, there is no longer a sufficient buffer for all the ketones produced. The consumption of bicarbonate ultimately leads to an increased anion gap metabolic acidosis [5].

Current Fluid Resuscitation Recommendations For DKA

Current guidelines suggest starting 0.9% normal saline for DKA [5,8,9]. The normal saline rate should be given around 1L/hour initially and then decreased gradually over the next few hours [1]. Current guidelines also state that whenever the sodium levels normalize, 0.9% normal saline can be changed to 0.45% saline [1].

	Na+	K+	Cl-	Lactate	Osmolar	Acetate	Gluconate
Normal plasma	135-145	3.5-5.0	94-111	<2	275-290	0.2	-
0.9% NS	154	-	154	-	308	-	-
LR	130	4	109	28	273	-	-
Plasma Lyte	140	5.0	98	-	294	27	23

Figure 1 [11] [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6467313/]
0.9% Normal Saline

The primary advantages of 0.9% Normal Saline (NS) begin with its inexpensiveness and vast availability in hospitals across the United States. The disadvantages of NS in DKA include reducing the number of electrolytes available [table], acidic pH (5.5) compared to normal plasma, and no buffer for the acids in the serum [10]. The electrolytes available include sodium and chloride at 154 mEq/L each, both above physiologic levels [11]. DKA management aims to reduce the acidic state. NS is questionable in correcting the acidic environment since it is acidic and known to cause non-anion gap hyperchloremic metabolic acidosis from the infusion alone [5,12]. Also, the acidic solution will increase the amount of hydrogen ions in the serum. The cells will take up these hydrogen ions in exchange by placing potassium ions outside of the cell, potentially worsening the hyperkalemia.

Lactated Ringers

Like NS, Lactated Ringers (LR) is a balanced colloid that is vastly available and is comparable to NS in cost [5]. LR is closer to physiologic electrolyte levels than NS [11] [figure]. Fluid resuscitation with LR ensures that the potassium level is less likely to be low [5]. LR is also closer to physiologic pH at 6.5 and has less risk of developing metabolic acidosis[11]. Some studies found that patients treated with LR resolved ketoacidosis faster than those treated with NS and less time spent on the insulin drip [5,8].

Plasma Lyte (PL) is another balanced colloid similar to LR. PL has a more physiologic pH than LR and a higher buffering capacity. Studies are minimal regarding PL's effects on DKA patients. Also, it is unlikely to be incorporated into hospital protocol since it is more expensive than LR and NS.

Patient Studies

Self WH et. al compiled a group of sub-studies to provide data on 172 individuals with diabetic ketoacidosis who received fluid in the form of normal saline (controls) or balanced crystalloids [5]. In the emergency department and intensive care unit, the sub-studies included the following study designs: pragmatic, multiple crossover, cluster, and randomized controlled trials. The control group contained 78 individuals. 94 individuals in the treatment group received balanced crystalloids. The balanced crystalloids group included those receiving lactated ringers(96.7%) or plasma-lyte (3.1%). The results revealed a statistically significant decrease in time to DKA resolution and duration of insulin infusion. Balanced crystalloids also significantly decreased the risk of new-onset hypokalemia (potassium <3 mmol/L) compared to normal saline. There was no increased risk of hyperkalemia associated with using balanced crystalloids.

Yan JW et al. conducted a triple-blind randomized controlled trial observing 52 individuals [9]. 25 patients were given LR, and 27 were in the control group (NS). Unfortunately, this study did not have any statistically significant results, and the results were inconsistent with those of the trial conducted by Self WH et al. Another study observing 58 patients (29 controls, 28 LR) produced similar, nonsignificant results [13].

CONCLUSION

After reviewing the studies, only one study provided statistically significant data on a relatively small number of patients. Given the composition and pH of LR, it seems that LR would be the better choice for DKA physiologically. The benefits of potassium concentration, osmolarity, and pH of LR should be studied further in managing DKA.

Given the limited clinical trials and varying results, this study cannot support or reject the idea that LR is superior to NS in managing DKA. To get the most accurate data, we recommend more research with a blinded, randomized controlled trial with more individuals.

REFERENCES

1. Westerberg DP. Diabetic ketoacidosis: evaluation and treatment. *Am Fam Physician*. 2013;87(5):337-346.
2. Fayfman M, Pasquel FJ, Umpierrez GE. Management of Hyperglycemic Crises: Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar State. *Med Clin North Am*. 2017;101(3):587-606. doi:10.1016/j.mcna.2016.12.011
3. Hsia DS, Tarai SG, Alimi A, Coss-Bu JA, Haymond MW. Fluid management in pediatric patients with DKA and rates of suspected clinical cerebral edema. *Pediatr Diabetes*. 2015;16(5):338-344. doi:10.1111/pedi.12268
4. Dunger DB, Sperling MA, Acerini CL, et al. European Society for Paediatric Endocrinology/Lawson Wilkins Pediatric Endocrine Society consensus statement on diabetic ketoacidosis in children and adolescents. *Pediatrics*. 2004;113(2):e133-e140. doi:10.1542/peds.113.2.e133
5. Self WH, Evans CS, Jenkins CA, et al. Clinical Effects of Balanced Crystalloids vs Saline in Adults With Diabetic Ketoacidosis: A Subgroup Analysis of Cluster Randomized Clinical Trials. *JAMA Netw Open*. 2020;3(11):e2024596. Published 2020 Nov 2. doi:10.1001/jamanetworkopen.2020.24596
6. Gosmanov AR, Gosmanova EO, Kitabchi AE. Hyperglycemic Crises: Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar State. In: Feingold KR, Anawalt B, Blackman MR, et al., eds. *Endotext*. South Dartmouth (MA): MDText.com, Inc.; May 9, 2021.
7. De Meyts P. The Insulin Receptor and Its Signal Transduction Network. In: Feingold KR, Anawalt B, Blackman MR, et al., eds. *Endotext*. South Dartmouth (MA): MDText.com, Inc.; April 27, 2016.
8. Johnson J, Drincic A, Buddenhagen E, Nein K, Samson K, Langenhan T. Evaluation of a Protocol Change Promoting Lactated Ringers Over Normal Saline in the Treatment of Diabetic Ketoacidosis. *J Diabetes Sci Technol*. Published online March 7, 2024. doi:10.1177/19322968241235941
9. Yan JW, Slim A, Van Aarsen K, et al. Balanced crystalloids (Ringer's lactate) versus normal Saline in adults with diabetic Ketoacidosis in the Emergency Department (BRISK-ED): a protocol for a pilot randomized controlled trial. *Pilot Feasibility Stud*. 2023;9(1):121. Published 2023 Jul 13. doi:10.1186/s40814-023-01356-5
10. Reddi BA. Why is saline so acidic (and does it really matter?). *Int J Med Sci*. 2013;10(6):747-750. Published 2013 Apr 17. doi:10.7150/ijms.5868
11. Semler MW, Kellum JA. Balanced Crystalloid Solutions. *Am J Respir Crit Care Med*. 2019;199(8):952-960. doi:10.1164/rccm.201809-1677CI
12. Panchal V, Sivasubramanian BP, Samala Venkata V. Crystalloid Solutions in Hospital: A Review of Existing Literature. *Cureus*. 2023;15(5):e39411. Published 2023 May 23. doi:10.7759/cureus.39411
13. Van Zyl DG, Rheeder P, Delport E. Fluid management in diabetic-acidosis--Ringer's lactate versus normal saline: a randomized controlled trial. *QJM*. 2012;105(4):337-343. doi:10.1093/qjmed/hcr226