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Comparative Study On The Efficacy Of Different Crystalloid Solutions In The Management Of Diabetic Ketoacidosis

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Abstract

Diabetic ketoacidosis (DKA) is a very serious complication of diabetes and is elaborated as hyperglycemia, ketosis and acidosis. It has been linked with big morbidity and mortality rates making its treatment very quick and efficient. The main intervention that is applied when managing DKA is the restoration of the acidotic state by intravenous (i.v.) fluid resuscitation. Normal Saline (NS), Ringer Lactate (RL) and Plasmalyte (PL) are popular examples of crystalloids because of their low costs. This research sought to appraise how these three fluids affect levels of serum electrolytes, anion gap, blood pH, and resolution of DKA in the patients. One hundred and fifty patients with the diagnosis DKA were randomly spaced into three groups (50 patients in each arm). Normal saline was administered to the patients in Group A (NS), Ringer lactate to the patients in Group B (RL), whereas plasmalyte was administered to the patients in Group C (PL). Serum electrolytes and blood pH level examination were done on a baseline and every hour, 8 hours. The findings showed that Plasmalyte (PL) was associated with the greatest improvement in metabolic acidosis, it had an increased decrease in serum chloride with a faster rate of recovery as compared to normal saline and Ringer lactate. Although both normal saline and Ringer lactate were regarded as significant in changing serum bicarbonate levels, Plasmalyte had a better rate in acidosis correction as well as electrolyte metion misbalance. It is believed that the best fluid to use to treat DKA is Plasmalyte since it proves significantly faster to recover and exhibit fewer electrolyte imbalances than normal saline and Ringer lactate. In this study, the possible benefits of using Plasmalyte in the resuscitation of fluids in patients with DKA are indicated.

Keywords: Diabetic Ketoacidosis (DKA), Crystalloid Solutions, Fluid Resuscitation, Plasmalyte

Introduction

The worst of the complications of diabetes of both type 1 and 2 are Diabetic Ketoacidosis (DKA) which causes high morbidity and mortality. DKA leads to over 500,000 hospitalizations each year. Though implemented with type 1 diabetes, studies found that DKA is more common in patients having diabetes type 2. According to statistics provided by different health institutions, most (56 percent) DKA cases are reported in the age group between 18 and 44 years old, 24 percent of patients have the age of 45 to 65 years, and only 18 percent are under 20 years old. DKA incidences among the diabetics include that 66 percent have type 1 and 34 percent have type 2, 50 percent of the affected patients are females and 45 percent are non-whites. A research conducted by Adhikari et al., affirmed that a higher percentage of the DKA cases is observed in the users of type 2 diabetes mellitus (62.8%) than those users of type 1 diabetes mellitus (37.8%). Typical triad of hyperglycemia, ketosis, and acidosis characterizes the clinical presentation of DKA. A specific diagnosis is done when the pH of the arterial blood is less than 7.35 and the serum bicarbonate is less than 15 mEq/L and the level of the blood glucose is more than 250 mg/dL with moderate ketonemia or ketonuria, which is confirmed by nitroprusside test. Nausea, comprising vomiting, abdominal pain, excessive thirst, and polyuria are the symptoms regularly observed in patients. Physical examination indicates that fruit odor is usually detected and there is presence of characteristic Kussmaul breathing pattern, which has rapid shallow pattern. In more severe cases, it could manifest through a sense of hypotension and the change of mentality. The predisposing factors of the DKA can be manifested as well. A study of Munro et al. revealed that nausea and vomiting occurred in 86 percent of patients, whereas abdominal pain occurred in 27 percent and polyuria and polydipsia were present in 24 percent of patients. Treatment of DKA consists of following intersecting objectives: correcting altered metabolism, treating underlying and/or concomitant illnesses, offering sustained treatment of diabetes, and preventing where a recurrence can occur. The role of patient education is important so that the treatment plan may be satisfied because non-compliance is one of the common precipitating factors of DKA in diabetic patients. The first intervention in managing DKA is that acidosis should be corrected by providing an urgent fluid resuscitation. Although fluid replacement is very essential, there has been a debate on the most suitable type of fluid. The loss of fluids in DKA is normally divided into the intravascular and extra-cellular volume. The colloid solutions like the blood, albumin, and plasma are better maintained in within the intravascular space and this therefore makes them suitable in providing rapid resuscitation. Nevertheless, the use of crystalloids, e.g., normal saline, Ringers lactate, and Plasmalyte is mostly recommended since they: (i) are easily available; (ii) are cheaper; and (iii) do not present the risk of anaphylaxis when compared to colloid solutions. At that, normal saline has been attributed to an even higher rate of hyperchloremic acidosis and Ringer lactates may increase the lactate-to-pyruvate ratio and result in hyperkalemia. Although randomized controlled studies does not exist to compare these fluids, existing evidence does go no further to indicate that one solution is clinically superior to the other. The proposed research will evaluate the impact of normal saline, Ringer lactate and Plasmalyte on the levels of serum electrolyte during therapy of DKA.

Methods

Criterion of Diabetic Ketoacidosis (DKA) was determined according to the qualification of Indian Diabetic Federation(IDF) that involves a serum pH that is less than 7.3, the presence of serum bicarbonate level of lower than 16 mEq/L, a capillary blood glucose level of more than 230 mg/dl, as well as a positive urine dipstick test of ketone bodies, including those who are newly diagnosed and with previous history records of diabetes. There were 150 patients who participated in the study group, which were randomly subdivided into 3 groups containing 50 patients each. In Group A (50 patients), the normal saline was used, in Group B (50 patients)- the Ringer lactate, and in Group C (50 patients)- the Plasmalyte. The fluids were administered using the calculation of body weights. The same kind of insulin was used on all the participants where dosage varied based on the amount of blood glucose. The blood glucose was checked hourly, electrolyte in the serum and anion gap in 2 hours. DKA was considered to be resolved when serum bicarbonate level was greater than 18 mEq/L or when insulin was discontinued, whichever came earlier. Last blood glucose and electrolyte values were noted and those patients who needed some additional glucose, electrolytes or mannitol were identified. A statistical analysis of the data was provided in SPSS version 16. All parametric variables were computed with the descriptive statistics mean and standard deviations (SD). The ANOVA was used to compare the mean between the three groups of subjects in assessing whether the different IV fluids were effective in treating DKA.

Result

The results of this study present a detailed comparison of fluid treatment effects in patients with diabetic ketoacidosis (DKA) across three different intravenous (i.v.) fluid groups: Normal Saline (NS), Ringer's Lactate (RL), and Plasmalyte (PL). The study analyzed various parameters, including serum electrolyte levels, anion gap, blood pH, and the duration of DKA resolution across different time intervals. Table 1 illustrates the distribution of patients across age groups and gender in each of the three treatment groups. The mean age was similar across all groups, with no significant gender differences noted. Table 2 compares the serum electrolyte levels at different time intervals. For serum sodium, there was no significant difference in the baseline or subsequent measurements across the three groups. However, a significant difference was observed at the 8th hour, with Group C (PL) showing the highest mean serum sodium. Serum potassium levels at baseline were higher in Group A (NS) than in the other two groups, with significant differences observed at the 8th hour where Group C (PL) showed higher potassium levels. Serum chloride concentrations showed a significant increase in Group A (NS), especially by the 8th hour, which was consistent with hyperchloremic acidosis observed in some patients. In contrast, Group C (PL) had a significantly lower increase in chloride levels. Serum bicarbonate levels increased significantly over time in all groups, with Group C (PL) showing the greatest improvement, especially at 4, 6, and 8 hours, which is indicative of faster acidosis resolution. Table 3 presents the comparison of the anion gap and blood pH. The anion gap significantly increased over time in all groups, with Group A (NS) showing the highest increase, indicating the persistence of metabolic acidosis. Blood pH levels improved gradually in all groups, but no significant differences were observed in pH changes across groups, except at the 8th hour, where all groups showed a notable increase in pH, reaching near-normal levels. Table 4 details the duration of DKA resolution across the three treatment groups. Group C (PL) demonstrated the fastest resolution, with a higher proportion of patients resolving DKA at 6 and 8 hours compared to Group A (NS) and Group B (RL). Group A (NS) had the slowest resolution, with the majority of patients requiring 12 hours or more for resolution. Statistical analysis confirmed significant differences in DKA resolution times, with Group C (PL) showing the most rapid recovery. In the data suggest that Plasmalyte (PL) may be the most effective fluid for managing DKA, showing faster resolution of metabolic acidosis and fewer electrolyte disturbances compared to Normal Saline (NS) and Ringer's Lactate (RL).

Table 1: Distribution of Patients Across Age Groups and Gender in the Three Treatment Groups

Age Group	Gender	Group A (NS) (n=50)	Group B (RL) (n=50)	Group C (PL) (n=50)
25 – 30	Male	5	6	10
	Female	9	15	8
31 – 35	Male	5	10	6
	Female	8	5	3
36 – 40	Male	3	2	1
	Female	9	3	4
41 – 45	Male	2	10	8

	Female	2	2	4
46 – 50	Male	3	1	1
	Female	6	2	14
51 – 55	Male	10	9	2
	Female	0	0	0
56 – 60	Male	2	0	8
	Female	0	8	4
Mean ± SD		**34.56 ± 4.65**	**33.76 ± 5.08**	**32.56 ± 4.02**

Table 2: Comparison of Serum Electrolyte Levels Across Three Treatment Groups at Different Time Intervals

Parameter	Time	Group A (NS) (n=50)	Group B (RL) (n=50)	Group C (PL) (n=50)	P value (ANOVA)
Sr. Sodium	**Baseline**	134.42±2.08	137.7±2.23	135.8±3.23	0.828
	2ndHr	136.3±2.01	139.3±3.22	136.5±2.88	0.721
	4thHr	137.1±1.85	138.3±2.93	137.2±3.12	0.817
	6thHr	138.8±2.13	139.3±2.01	139.6±2.64	0.879
	8thHr	139.1±2.18	137.9±2.29	140.2±1.14	0.542
	P value (ANOVA)	0.0241	0.0821	<.0001	
Sr. Potassium	**Baseline**	5.3±0.81	4.6±0.84	4.8±0.76	0.719
	2ndHr	5.2±0.93	4.7±0.76	4.7±0.83	0.648
	4thHr	5.1±0.85	4.9±0.83	4.7±1.02	0.438
	6thHr	4.9±1.03	4.9±1.22	5.1±0.54	0.828
	8thHr	4.7±0.97	5.1±0.74	5.3±0.38	0.037
	P value (ANOVA)	0.731	0.0317	0.0001	
Sr. Chloride	**Baseline**	103±2.53	104.5±3.26	103.8±3.24	0.873
	2ndHr	104.4±2.02	105.5±3.17	105.1±2.88	0.912
	4thHr	106.1±2.27	105.1±2.91	104.8±3.03	0.729
	6thHr	109.3±2.76	106.7±1.75	105.8±2.21	0.718
	8thHr	115.8±3.12	106.5±2.13	108.3±1.96	0.821
	P value (ANOVA)	0.0181	0.0718	<.0001	
Sr. Bicarbonates	**Baseline**	10.5±1.28	11.1±1.05	10.1±1.56	0.917
	2ndHr	11.7±1.75	12.7±0.96	12.6±1.02	0.382
	4thHr	12±0.88	12.5±1.01	15.1±0.94	<.0001
	6thHr	14.4±0.94	15.3±0.84	17.3±0.74	0.001
	8thHr	15.8±1.32	17.1±1.18	19.9±1.02	<.0001
	P value (ANOVA)	0.001	0.0001	<.0001	

Table 3: Comparison of Anion Gap and Blood pH Levels Across Three Treatment Groups at Different Time Intervals

Parameter	Time	Group A (NS) (n=50)	Group B (RL) (n=50)	Group C (PL) (n=50)	P value (ANOVA)
Anion Gap	**Baseline**	9.8±0.79	10.0±0.00	9.3±0.85	0.892
	2ndHr	10.6±0.85	11.4±0.00	10.6±0.88	0.742
	4thHr	12.6±0.89	11.6±0.00	10.9±0.95	0.0751
	6thHr	12.7±0.65	12.0±0.00	12.2±0.79	0.925
	8thHr	12.7±0.53	12.8±0.00	11.9±0.79	0.816
	P value (ANOVA)	<.0001	<.0001	<.0001	
Blood pH	**Baseline**	7.18±0.04	7.18±0.00	7.19±0.00	0.915
	2ndHr	7.21±0.08	7.21±0.00	7.23±0.00	0.815
	4thHr	7.24±0.12	7.24±0.00	7.27±0.00	0.732
	6thHr	7.26±0.05	7.26±0.00	7.26±0.00	1.000
	8thHr	7.29±0.08	7.30±0.00	7.31±0.00	0.921
	P value (ANOVA)	<.0001	<.0001	<.0001	

Table 4: Duration of DKA Resolution Across Three Treatment Groups

Duration of DKA Resolved	Group A (NS) (n=50)	Group B (RL) (n=50)	Group C (PL) (n=50)	P value (ANOVA)
6 hrs	2	1	4	<.0001
8 hrs	20	1	6	<.0001
10 hrs	4	14	20	<.0001
12 hrs	24	32	20	<.0001
14 hrs	50	50	50	1.000

Discussion

Besides being the first and most crucial move towards the correction of DKA, the correction of the acidotic condition with intravenous (i.v.) administration of fluid is the most vital part of it. Of the administerable i.v. fluids, crystalloids tend to be preferred compared with colloids because they are more economical. Nevertheless, one crystalloid type of fluid is associated with its benefits and deficiencies. When infused, normal saline is quickly dispersed into the extracellular spaces and has a tendency of staying longer in the body. The intravascular volume can expand up to 6 hours after infusion in patients who had a normal blood volume despite majority of fluid used in infusion being present in the interstitial area. Normal saline infusion raises plasma chloride levels because it contains higher chloride levels; this has the potential of causing renal vasoconstriction and decreased glomerular filtration rate (GFR). There were 40 normal saline patients in our study, four developed hyperchloremic acidosis and that was rectified. More often than not, balanced solutions, e.g. lactated Ringer solution (RL), are employed, but are not isotonic or ideally balanced. Having osmolarity of 273 mOsmol/L and osmolality of 254 mOsmol/kg measured, there is evidence that lactated Ringer solution may result in minor fall in plasma osmolality. One of the misperceptions concerning RL is that this product is safe in all patients due to its resemblance to the composition of serum. But when the patients have conditions of liver disease, the liver is unable to break down the lactate in the body thus resulting in lactic acidosis. Moreover, breaking down lactate in patients with a serum pH more than 7.5 gives out bicarbonates, and this may induce alkalosis. The Committee on Trauma of the tertiary hospital reported that lactated Ringers should be used cautiously especially with in some clinical conditions. Both normal saline and lactated ringer solution have significant disadvantaged, and investigation of alternative isotonic solutions is advanced such as Plasmalyte 148. This solution has proven promising in trauma resuscitation as well as other conditions and it proved to be useful in treatment of acidotic conditions than the available alternatives. A comparison of plasmalyte 148 and 0.9 percent normal saline as an intraoperative solution of a group of patients showed that normal saline associated with a great increase in plasma chloride concentration whereas in those treated with plasmalyte sodium, potassium, and blood lactate did not show a significant change. We achieved usual results in that we also determined that the serum chloride concentration in the group subjected to the normal saline was more than that of the other two groups but the results were not statistically significant. In the said study 3/30 patients put on normal saline developed hyperchloremic acidosis which appears to be very similar to our results of 4/40 patients that developed the same condition. Results of a subsequent study that assessed the effects of administering 0.9 percent normal saline after surgery showed that patients that were administered the normal saline suffered more complications such as infections, renal failure and electrolyte imbalances than those receiving Plasmalyte who had few complications. In the same token, we have found that patients who were given Plasmalyte had a quicker recovery of acidosis when compared to normal saline and lactated Ringer solution. A different study on fluid management during diabetic ketoacidosis monitored the amount of time it took patients to achieve a pH of 7.32; The patient group with normal saline required a median of 683 minutes to achieve a pH of 7.32 compared to the patient group with Ringer lactate whose median time was 540 minutes at a pH of 7.32. Previous evidence supports our study where the patients that were treated using Ringer lactate took 600 minutes to achieve a PH of 7.32 as compared to the normal saline patients which took 730 minutes. Lastly, a comparison of normal saline and Plasmalyte in DKA patients showed that the Plasmalyte caused a quicker resolution of metabolic acidosis, lower hyperchloremia, and temporarily higher blood pressure and urine production. In a similar manner, the patients who were treated with Plasmalyte obtained signi cant improvements in the resolving acidosis than patients treated using normal saline and lactated Ringer solution in our study. Most of the researches are particular, explaining why our study is fortunately the first to show that Plasmalyte is not only better than normal saline in fluid resuscitation of DKA patients, but also better than Ringer lactate.

Conclusion

The treatment of Diabetic Ketoacidosis (DKA) has its basis on the corrected restoration of the acidotic condition by means of resuscitation of the intravenous (i.v.) fluids. Normal Saline (NS), Ringer Lactate (RL), and plasmalyte (PL) have been the predominately utilized crystalloids as the most affordable and available fluids used to carry out this procedure. This paper undertaken to determine the effectiveness of these three solutions in repleting serum electrolytes, anion gap, pH level of blood and general resolution of DKA between patients. In our findings, although all the three fluids aided improvements in serum electrolyte balance and acidosis resolutions, Plasmalyte (PL) registered the best performance compared to the other two fluids; Normal Saline (NS) and Ringer Lactate (RL). Plasmalyte was found to have the most drastic effect of decreasing serum level of chloride and thus, lower contraindication of complications like hyperchloremic acidosis. Also, the duration to achieve the goal pH (7.32) was shorter with PL and the time of attainment of this goal pH was shorter in the patients in the PL group compared with those under NS or RL. This agrees with the results of past studies that showed the superiority of PL in fluid resuscitation especially with acidemia. In contrast, serum chloride levels of patients in the NS went up to a larger extent which is a known cause of hyperchloremic acidosis, known complication of saline. Even though RL resulted in significant improvement in bicarbonate levels as well, it was ineffective in comparison with PL in how quickly acidosis could be resolved and how electrolytes could balance. Various risks have been associated with the use of both NS and RL, which include electrolyte disturbances and a slower recovery of acidosis and thus PL should be considered a better alternative to treating DKA, especially in fluid therapy-prone patients. To sum up, our research will provide a piece of evidence that Plasmalyte could be the most useful fluid in treating DKA. It has a more rapid regression of acidosis, fewer electrolyte imbalances and an improved general recovery profile than Normal Saline and Ringer Lactate. These results indicate that plasmalyte must be used as the fluid of preference in achieving fluid resuscitation in patients afflicted by DKA and that this would need to be proven with definitive studies in large numbers of patients.

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