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Original Article

A Comparative Study between Ringer Lactate, Normal Saline and Plasmalyte on the Serum Electrolytes of Patients with Diabetic Ketoacidosis

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Abstract

Background: The triad of DKA includes hyperglycaemia, ketosis, and acidemia. The management of diabetic ketoacidosis is complex and involves many aspects. It includes identification and correction of all the metabolic abnormalities and treating all the co-morbid and precipitating conditions. In DKA the most important and the initial step of management is correction of acidosis by rapid fluid replacement using a crystalloid and among them the most commonly used were 0.9% normal saline or ringer lactate.

Aim: 1. To compare individually, the effects of Ringer lactate, Normal saline and plasmalyte on the serum electrolytes during the recovery period of diabetic ketoacidotic patients.

2. To determine the IV fluid most suitable for fluid resuscitation in the management of diabetic ketoacidosis.

Materials and Methods: A prospective comparative study was done on 120 patients with diabetic ketoacidosis reported to our hospital over a period of one year from June 2015 –Nov 2016. The patients were divided into three groups of 40 in each group. Group A (40) were administered normal saline, Group B (40) were given ringer lactate and Group C (40) were given plasmalyte. Patient's blood glucose was measured on an hourly basis and their serum electrolytes and anion gap were measured for every 2 hours. *Results:* Among the intra-group comparison the serum sodium and chloride levels showed a statistically significant increase among the patients treated with normal saline (Group A) and plasmalyte (Group C). Serum potassium levels had shown a statistically significant increase among the patients treated with ringer lactate (Group B) and plasmalyte (Group C) and the serum bicarbonate levels had shown a statistically significant increase among all the three groups. Among the inter-group comparison serum potassium and bicarbonates level showed a more significant increase in plasmalyte group than that of the patients who received normal saline and ringer lactate. Among the three groups DKA status had resolved more early in the patients who had received plasmalyte, six patients in this group had got the DKA status resolved in 6 hrs and another eleven patients had got DKA resolved in 8 hrs and for the remaining 23 patients it got resolved in 10 hrs. *Conclusion:* In patients with diabetic ketoacidosis which is considered as a life-saving emergency condition should be treated promptly with a better I.V. fluid which would resolve the condition at the earliest. In our study it was proven that the plasmalyte was a better crystalloid than 0.9% NS and RL in resolving DKA at a faster rate.

Keywords: Diabetic Ketoacidosis; Normal Saline; Ringer Lactate; Plasmalyte; Serum Electrolytes.

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Introduction

Diabetic Ketoacidosis (DKA) being the most serious complication of type 1 and type 2 diabetes is more

commonly associated with significant morbidity and mortality [1]. DKA is responsible for more than 500,000 hospital days per year [2,3]. It was once considered that DKA was most commonly occurredin type 1 diabetes but many studies had shown that DKA was also common in type 2 diabetes [4-6]. National Centre for health statistics showed that most patients with DKA were between the ages of 18 and 44 years (56%) and 45 and 65 years (24%), with only 18% of patients <20 years of age. Two-thirds of DKA patients were considered to have type 1 diabetes and 34% to have type 2 diabetes; 50% were female and 45% were non-white.[2]Another previous study by Adhikari et al., also showed predominance of type 2 diabetes mellitus (62.8%) as compared to type 1 diabetes mellitus (37.8%) who presented with DKA [7].

The triad of DKA includes hyperglycaemia, ketosis, and acidemia. An arterial pH of less than 7.35, a Serum Bicarbonate (HCO_3^{-}) value of less than 15 mEq/L, and a blood glucose level of greater than 250 mg/dl with a moderate degree of ketonaemia and/or ketonuria (as determined by nitroprusside method) are necessary for the diagnosis of DKA [8]. DKA usually presents with symptoms like nausea, vomitingandpain abdomen. They may also have increased thirst and polyuria. On examination usually a fruity odour can be smelt and the breathingpatternis typical of DKA, rapid shallow kussmaul breathing. Severe cases may present with hypotensionandaltered sensorium. Features of the precipitating cause may also be present. A study was done by Munro et al., who noticed the frequency of nausea and vomiting (86%), pain abdomen (27%) and polyuria/polydipsia in 24% of patients [9]. The management of diabetic ketoacidosis is complex and involves many aspects [10]. It includes: a. identification and correction of all the metabolic abnormalities b. treating all the co-morbid and precipitating conditions c. long term treatment of diabetes and prevention of recurrence. Another most important aspect of management is patient education so as to ensure compliance to treatment as non-compliance may lead to DKA in patients with DM .

In DKA the most important and the initial step of management is correction of acidosis by rapid fluid replacement. While it is accepted that fluid resuscitation is a crucial factor, the exact type of fluid to be used remains controversial. Half of the fluid loss in DKA is from the intravascular compartment and the other half is from the extracellular compartment. Colloid solutions are more effectively retained in the intravascular compartment than crystalloid solutions, and are most efficient for rapid resuscitation [11]. Blood, albumin, plasma are colloids and normal saline, ringer-lactate, plasmalyte are crystalloids. Crystalloids are preferred as they are readily available and inexpensive compared to colloid solutions. Unlike colloid solutions, they also don't carry the risk of anaphylaxis. Certain disadvantages in normal saline like increased incidence of hyperchloremic acidosis [12] and the usage of ringer lactate would exacerbate lactate to pyruvate ratio and hyperkalemia [13]. No randomised controlled trials are currently available to support the superiority of one fluid over another. Yet, there is no evidence in the literature that this is clinically significant or dangerous to patients. So the present study was undertaken to assess the effectiveness of normal saline, ringer lactate and plasmalyte on serum electrolytes in the management of diabetic ketoacidosis.

Aim

To assess the effectiveness of ringer lactate, normal saline and plasmalyte on the serum electrolytes among the patients with diabetic ketoacidosis.

Methodology

A prospective comparative study was done on 120 patients with diabetic ketoacidosis reported to our hospital over a period of one year from June 2015 – Nov 2016. The study was conducted after getting the clearance from the institutional ethical committee and the informed consent from the patients. The patients were diagnosed as DKA based on the ADA criteria which statesserum pH <7.3, serum bicarbonate <16 mEq/l, capillary blood glucose > 230 mg/dl and the urine dipstick test show positive for ketone bodies with newly diagnosed or previous history of diabetes. The patients were divided into three groups of 40 in each group. Group A (40) was administered normal saline, Group B (40) was given ringer lactate and Group C (40) was given plasmalyte. The fluids were administered as per the body weight calculation. All the 120 patients were given similar type of insulin with the dose variation according to the blood sugar levels. Patient's blood glucose was measured on an hourly basis and their serum electrolytes and anion gap were measured for every 2 hours. In this study we considered DKA to be resolved when serum bicarbonate > 18 mEq/l or when Insulin is discontinued, whichever had occurred first. The end readings of blood sugar and electrolytes were assessed. Patients who had needed glucose

supplementation, electrolytes and mannitol were noted.

All the data were entered in SPSS version 16. Mean and SD were derived for all the parametric variables and ANOVA analysis was done for comparing the means between the three groups in assessing the effectiveness among the three intravenous fluids.

Results

Table 1 shows the age and sex wise distribution of the study population. The male and female study subjects were almost equal in number in all the three groups. The minimum age among the study subjects was 26 years and the maximum age was 58 and the mean age was 33 years. There is no statistical significant difference in the age group between the three groups.

The serum electrolytes level at the time of admission (baseline) and their levels after the initiation of treatment once every two hours for eight hours were shown in Table 2. The levels were actually measured for 14 hours but for majority of the patients the DKA had resolved in eight hours and so for analysis purpose we had taken the levels only for the eight hours. Among the intra-group comparison the serum sodium and chloride levels had shown a statistically significant increase among the patients treated with normal saline (Group A) and plasmalyte (Group C). The mean chloride level among the normal saline group at the end of 8th hr was 115meq/l which was higher than the other two groups but it was not found to be statistically significant ($p>.05$). Serum potassium levels had shown a statistically significant increase among the patients treated with ringer lactate (Group B) and plasmalyte (Group C) and the serum bicarbonate levels had shown a statistically significant increase among all the three groups. Among the inter-group comparison serum potassium and bicarbonates level showed a more significant increase in plasmalyte group than that of the patients who had received normal saline and ringer lactate. The blood sugar levels had shown a steady decline among all three groups over a period of time. Patients who had received plasmalyte had shown a statistically decrease of blood sugar when compared the blood sugar levels among the patients who had received normal saline and ringer lactate (Figure 1).

Anion gap and blood PH values had shown a statistically significant increase over a period of time among the patients in all three groups. Whereas the inter-group comparison had not shown statistical significant difference between the three groups (Table 3).

The mean duration of stay in ICU among the patients who had received NS was 13.57 hrs, for RL it was 11.0 hrs and in plasmalyte group it was 9.5 hrs. The patients who had received plasmalyte required less hours of stay in ICU when compared to the patients who had received NS and RL and the difference was found to be statistically significant and similarly the quantity of fluids required by plasmalyte group was less than that of NS and RL group (Table 4).

Among the three groups DKA status had resolved more early in the patients who had received plasmalyte, six patients in this group had got the DKA status resolved in 6 hrs and another eleven patients had got DKA resolved in 8 hrs and for the remaining 23 patients it got resolved in 10 hrs, whereas in the other two groups (NS and RL) none of the patients had got DKA resolved in the first 8 hrs and in these groups only from 10 hrs the DKA had started resolving and the difference had shown a statistically significant difference ($p<.0001$) (Table 5).

Table 1: Age and sex wise distribution of the study population

Age Group	Gender	Group A (NS) (n=40)	Group B (RL) (n=40)	Group C (PL) (n=40)
25 – 30	Male	2	0	6
	Female	4	8	3
31 – 35	Male	3	8	3
	Female	5	0	1
36 – 40	Male	2	0	0
	Female	6	0	2
41 – 45	Male	1	8	6
	Female	0	0	2
46 – 50	Male	2	0	0
	Female	5	0	10
51 – 55	Male	8	8	0
	Female	0	0	0
56 – 60	Male	1	0	5
	Female	0	8	2
Mean ± SD		33.65±4.26	33.66±5.36	32.11±3.96

Table 2: Comparison of serum electrolytes among the study population over the period of time

Sr. Sodium	Time	Group A (NS) (n=40)	Group B (RL) (n=40)	Group C (PL) (n=40)	P value (ANOVA)
	Baseline	134.22±2.06	137.6±2.21	135.75±3.21	0.828
	2ndHr	136.25±1.98	139.2±3.2	136.4±2.86	0.721
	4thHr	137.05±1.82	138.2±2.89	137.17±3.1	0.817
	6thHr	138.7±2.10	139.2±1.98	139.58±2.62	0.879
	8thHr	139±2.16	137.8±2.25	140.2±1.12	0.542
P value (ANOVA)		**0.0241**	0.0821	**<.0001**	
Sr.Potassium	Baseline	5.26±0.78	4.52±0.82	4.72±0.75	0.719
	2ndHr	5.15±0.91	4.68±0.74	4.69±0.82	0.648
	4thHr	5.09±0.82	4.88±0.81	4.64±1.01	0.438
	6thHr	4.85±1.01	4.92±1.21	5.1±0.52	0.828
	8thHr	4.67±0.94	5.01±0.71	5.3±0.37	**0.037**
P value (ANOVA)		0.731	**0.0317**	**0.0001**	
Sr.Chloride	Baseline	102.9±2.5	104.4±3.24	103.7±3.21	0.873
	2ndHr	104.3±1.98	105.4±3.15	105.1±2.87	0.912
	4thHr	106±2.24	105±2.89	104.72±3.02	0.729
	6thHr	109.25±2.72	106.6±1.72	105.72±2.18	0.718
	8thHr	115.7±3.04	106.4±2.10	108.25±1.92	0.821
P value (ANOVA)		**0.0181**	0.0718	**<.0001**	
Sr.bicarbonates	Baseline	10.45±1.25	11±1.01	10±1.52	0.917
	2ndHr	11.6±1.72	12.6±0.92	12.6±1.01	0.382
	4thHr	11.96±0.85	12.4±0.98	15±0.91	**<.0001**
	6thHr	14.35±0.92	15.2±0.82	17.25±0.72	**0.001**
	8thHr	15.72±1.28	17±1.16	19.83±0.98	**<.0001**
P value (ANOVA)		**0.001**	**0.0001**	**<.0001**	

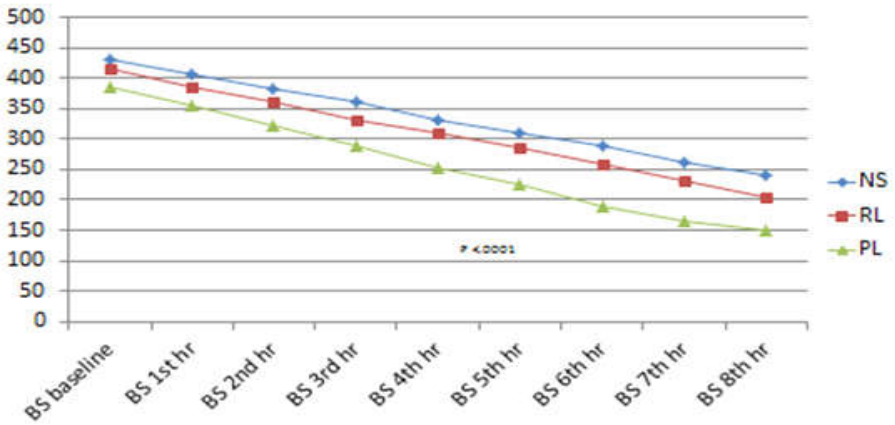

Fig. 1: Line diagram showing the blood sugar levels among the three groups over a period of time

Table 3: Anion gap and the blood PH values among the study population during the course of treatment

Anion gap	Time	Group A (NS) (n=40)	Group B (RL) (n=40)	Group C (PL) (n=40)	P value (ANOVA)
	Baseline	9.77±0.78	10	9.25	0.892
	2ndHr	10.57±0.84	11.4	10.61	0.742
	4thHr	12.57±0.88	11.6	10.94	0.0751
	6thHr	12.72±0.64	12	12.24	0.925
	8thHr	12.72±0.52	12.8	11.88	0.816
	P value (ANOVA)	**<.0001**	**<.0001**	**<.0001**	
Blood PH	Baseline	7.18±0.04	7.18	7.19	0.915
	2ndHr	7.21±0.08	7.21	7.23	0.815
	4thHr	7.24±0.12	7.24	7.27	0.732
	6thHr	7.26±0.05	7.26	7.26	1.000
	8thHr	7.29±0.08	7.30	7.31	0.921
	P value (ANOVA)	**<.0001**	**<.0001**	**<.0001**	

Table 4: Duration of ICU stay and the amount of fluids required among the study population

Variables	Group A (NS) (n=40)	Group B (RL) (n=40)	Group C (PL) (n=40)	P value (ANOVA)
ICU stay in Hrs	13.57	11.0	9.5	<.0001
Fluids required in Ltrs.	4.60	4.12	3.41	<.0001

Table 5: Distribution of study population based on their duration of DKA status resolved

Duration of DKA resolved	Group A (NS) (n=40)	Group B (RL) (n=40)	Group C (PL) (n=40)	P value (ANOVA)
6 hrs	0	0	6	<.0001
8 hrs	0	0	17	<.0001
10 hrs	7	16	40	<.0001
12 hrs	24	32	40	<.0001
14 hrs	40	40	40	1.000

Discussions

The first and foremost step in the management of diabetic ketoacidosis is the correction of acidotic state by administering i.v. fluids. Among the intravenous fluids crystalloids are more preferred than the colloids because of the cost effectiveness. Various available crystalloids have their own advantages and disadvantages.

Normal saline when infused it gets rapidly distributed between the compartments of the extracellular space and it remains in the body for a very long time. In normovolaemic patients, expansion of the intravascular volume persists for as long as 6 h after infusion of normal saline, even though most of the infused volume is found in the interstitial compartment [14,15]. As normal saline contains a higher concentration of chloride, its infusion increases the plasma chloride concentrations, which is associated with renal vasoconstriction and decreased glomerular filtration rate (GFR) [16]. In our patients also out of the 40 patients who had received normal saline four patients had developed hyperchloremic acidosis which was latter corrected.

Some of the most commonly used 'balanced' solutions (like lactated Ringer's solution) are neither isotonic nor they are precisely balanced. With an osmolarity of 273 mOsmol/L and a measured osmolality of 254 mOsmol/kg some of the studies had shown that the infused lactated Ringer's solution had led to a small decrease in plasma osmolality [17,18]. A common myth exists stating RL is safe for all patients, it is very close to serum but if a patient has liver disease, lactic acidosis can develop when the liver fails to break down the lactate. Also, if the patient have a serum pH greater than 7.5, bicarbonate will form as the lactate breaks down causing alkalosis. The American College of Surgeons' Committee on Trauma (ATLS, 1997) recommends lactated Ringers because large volumes of saline can induce hyperchloremic acidosis. The same cited studies indicated large volumes of RL contributing to cerebral edema. These two fluids each having their negative attributes almost lead to use of a different isotonic fluid known as Plasmalyte 148 for trauma patient resuscitation, which had now even shown some better results in patients with acidotic state [19].

A study done by McFranle etal [20] on comparison between plasmalyte 148 and 0.9% normal saline for intra-operative patients and had shown that the chlrodies had shown a statistical significant increase among the patients who had received 0.9% NS than that of plasmalyte and also shown that no significant changes in plasma sodium or potassium or blood lactate concentrations in either group, whereas in our study though the serum chloride levels among the normal saline group was higher than the other two groups it had not shown a statistical significant difference. In the above mentioned study out of 30 patients 3 patients had developed hyperchloremic acidosis which is almost in par with our study where out of 40 patients 4 had developed this condition. In another study done by Shaw et al [21] had shown that the patients who had received 0.9% NS during postoperative period after abdominal surgery had reported with increased complications like postoperative infections, renal failure, electrolyte disturbances and acidosis requiring investigations whereas patients treated with plasmalyte these complications were minimal.

A study done by Van Zyl D G et al [22] on the fluid management in diabetic ketoacidosis had shown that the median time to reach a pH of 7.32 for the 0.9% sodium chloride solution group was 683 min (95% CI 378-988) and for Ringer's lactate solution 540 min (95% CI 184-896), whereas in our study to reach the pH of 7.32 it took 600 minutes patients who received RL and 730 minutes for patients who had 0.9% NS, so the results were almost similar to the studies done

earlier.

In another study done by Chua HR etal [23] on comparison between 0.9% NS and plasmalyte among the DKA patients concluded that patients with DKA who were resuscitated with PL instead of NS had faster initial resolution of metabolic acidosis and less hyperchloremia, with a transiently improved blood pressure profile and urine output and similarly in our study also patients treated with plasmalyte had shown a statistically significant resolution of acidosis at a much faster rate than that of the normal saline and ringer lactate group. As most of the studies had compared either 0.9% NS and plasmalyte or RL and 0.9% NS in our review we were not able to find out any comparison done between 0.9% NS and plasmalyte in treating diabetic ketoacidosis. So this study would be a first of its kind proving that plasmalyte as a better intravenous fluid than that of 0.9% NS and RL to be considered for fluid management among patients with diabetic ketoacidosis.

Conclusions

Physicians should always be in watch when prescribing fluid as any fluid can be harmful if dosed incorrectly. Differences in immediate efficacy between crystalloid and colloid solutions are modest at best, but the differences in longer-term safety appear more significant. But considering the cost factor today crystalloids play a major role in the fluid management. In patients like diabetic ketoacidosis which is considered as a lifesaving emergency condition should be treated promptly with a better i.v. fluid which would resolve the condition at the earliest. In our study it was proven that the plasmalyte was a better crystalloid than 0.9% NS and RL in resolving DKA at a faster rate. But more randomized controlled trials should be conducted to further extrapolate and emphasise on which crystalloid has a better efficacy in treating DKA, as most of the earlier studies was done in different conditions and nor particular to DKA.

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