

Sodium chloride 0.9% versus Lactated Ringer in the management of severely dehydrated patients with choleraform diarrhoea

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Abstract

Introduction: Although experience within Peru suggests clinical and physiological benefits of treating dehydration caused by diarrhoea with Lactated Ringer's solution (LR) over sodium chloride 0.9%, (NaCl) there is little documented scientific evidence supporting this view. It is important to clarify this issue and determine the best solution for use during epidemics.

Methodology: Forty patients suffering from dehydration due to choleraform diarrhoea were enrolled in the study. Twenty patients were treated using NaCl (Group A) and the other twenty with LR (Group B). After diuresis recovery was achieved, the patients were continued on a course of oral rehydration salts. Serum electrolytes, arterial pH, HCO₃⁻, and pCO₂ were measured at three stages: at admission, after diuresis recovery, and after 12 hours.

Results: Acidosis was corrected more quickly with LR than NaCl. The hyperosmolality and hypernatremic states were corrected with both solutions.

Conclusion: LR use resulted in a better clinical response than NaCl, illustrated by more rapid physiological correction, showing that mixed metabolic acidosis was corrected more quickly and more appropriately with this treatment.

Key words: cholera; diarrhoea; isotonic solutions; Lactated Ringer's solution; rehydration; sodium chloride 0.9%

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Introduction

According to the World Health Organization (WHO), cholera is one of the principal indicators of a lack of social development, and remains a threat to public health worldwide, affecting almost all developing countries in a dramatic way, especially areas with unsanitary conditions [1]. The number of cases reported by the WHO in 2006 showed an increase of 79% during 2005, reaching the level seen at the end of the 1990s. Fifty-two countries reported cases, some of them for the first time, with 6,311 deaths occurring in 236,896 cases. It is suspected that this data vastly underrepresents the true number of global cases; therefore, the true burden of this disease is thought to be much greater [1].

Among people developing symptoms, 80% of episodes are of mild or moderate severity. Among the remaining cases, 10%-20% develop severe watery diarrhoea with signs of dehydration [1,2]. Thus treatment with intravenous solutions such as sodium chloride 0.9% (NaCl) or Lactated Ringer's solution (LR) is the principal treatment [2]. While LR is the

treatment recommended by the WHO in cases of severe dehydration [1,3], we have not found support for this view in other literature.

In Peru, a widely used scheme during the cholera epidemic of 1991 was based on rehydration in two phases [4]. This scheme reduced mortality rates and acute renal failure produced by cholera to very low levels [4-11]. Today the general consensus is that LR is more effective than NaCl [1,12]. However, scientific evidence is not fully documented on this point as few articles that compare these solutions are available in the literature. Such studies would be very useful in epidemic situations such as the ongoing cholera epidemic in Haiti [13].

A study by Hinostraza *et al.*, documenting their experience in Peru, suggested that LR is more effective for the treatment of cholera than NaCl [6]. Their study followed 13 patients until the recovery of diuresis [6], but the small sample size limits the interpretation of the results. Hence the aim of the current study is to verify physiological differences between the vigorous expansion with NaCl or LR

using a properly comparable sample population followed by a longer period of time.

Methodology

We conducted a longitudinal and observational study involving patients who came to the Emergency Department of Cayetano Heredia Hospital (Lima, Peru) with severe dehydration due to choleric diarrhoea (watery stools in severely dehydrated patients with suspected cholera) who agreed to participate in the study between 1997 and 2007. Severe dehydration was defined as the presence of oliguria (urinary flow less than 40 ml/h at admission) and hypotension (systolic blood pressure below 90 mmHg). Pregnant women, those under 18 years old, patients with previous renal disease, and those with prior diagnosis of acute renal insufficiency were excluded from the study at the time of admission. The remaining 40 patients, consisting of 19 males and 21 females, were randomly allocated to either Group A or Group B on admission to the Emergency Department. All patients followed the rehydration scheme used in the hospital, which has two phases of rehydration: the first consisted of rapid expansion of 50 ml/kg/h of an intravenous solution NaCl (Laboratorios Unidos SA, Lima, Peru) (Group A) or LR (Laboratorios Unidos SA, Lima, Peru) (Group B) and finished when urinary flow was greater than 40ml/h. In the second phase, we administered 800 ml/h of oral rehydration salts [(ORS); Laboratorios Unidos] SA, Lima, Peru) to all the patients, considering also their oral tolerance. Finally, the end cut-off point of the study was 12 hours after the recovery of diuresis.

Using this method, 40 patients, who were allocated randomly, were enrolled for the study. We stopped the recruitment because when we analyzed both groups at that point, we found statistically significant results; thus it was not ethical to continue with the patient enrollment.

Blood gases, serum lactate, plasma-urine electrolytes, serum creatinine, and plasma-urine osmolality were measured in blood and urine, respectively, in order to assess the physiological changes throughout the follow up of the patients at three stages: 1) at admission of the patient to the emergency room ("baseline"); 2) at two hours after the treatment started (the approximate time of diuresis recovery); and 3) at the end of the observation period (12 hours after diuresis recovery, *i.e.* approximately 14 hours after admission approximately).

We calculated the anion gap (AG) as the difference between plasma concentrations of sodium

(Na⁺) and the amount of chlorine (Cl⁻) and bicarbonate (HCO₃⁻). The urinary anion gap (AGU) was calculated by subtracting the concentration of chlorine from the urinary concentrations of sodium plus potassium. Carbon dioxide partial pressure in blood (pCO₂) was measured by the blood gases analysis.

For the data analysis, we used the statistical program Epi-Info v.5 (Center for Diseases Control Atlanta, GA, United States of America). The values are reported as arithmetic mean ± 1 standard deviation (± 1SD) for those with normal distribution and Kruskal Wallis for values with modal distribution. A p value of < 0.01 was accepted as statistically significant.

The study protocol followed the standard norms of the Helsinki Declaration and was approved by the local ethics committee. All patients entering the study signed a written informed consent, agreeing to participate in this investigation.

Results

A total of 40 patients participated in the study; 20 patients were in group A, and 20 in group B. Our results showed that the required time to achieve diuresis, the infused volume during the rapid expansion phase, the total oral volume, the endovenous infused volume during the 12 hours, and the oral tolerance for 12 hours post-urination were similar in patients treated with NaCl or LR (Table 1). There was no statistical significance between the two groups when comparing their general characteristics (Table 1).

Table 2 shows the values of arterial pH, pCO₂, bicarbonate, anion gap, serum creatinine and serum lactate at the time of admission ("baseline") and after treatment (2 and 14 hours post-admission). The values of serum osmolality and electrolytes in both groups at the time of admission to the hospital ("baseline") and during evolution (2 and 14 hours post-admission) are also summarized in Table 2, as well as the urinary osmolality and electrolyte concentration. Acidosis was corrected quicker with LR (pH A: 7.19 ± 0.06 and 7.27 ± 0.08 and B: 7.33 ± 0.06 and 7.33 ± 0.05 when diuresis was recovered and after 12 hours, respectively; HCO₃⁻ A: 12.4 ± 2.75 and 14.6 ± 3.41mEq/l and B 16.6 ± 2.34 and 17.6 ± 3.1mEq/l; Chloremia: A: 120 ± 7.8 and 113 ± 3.8mEq/l and B: 107 ± 3.3 and 109 ± 4.6mEq/l.) The hyperosmolality and hypernatremic states were corrected with both solutions (Natremia: A: 146 ± 3.3 mEq/l, and B: 141 ±

Table 1. Characteristics of patients at baseline and in the rehydration phase

	Group A NaCl 0.9% (n = 20)	Group B Lactated Ringer's (n = 20)
Baseline characteristics		
Age (years)	38.75±16.41	38.75±16.76
Sex (m/f)	8/12	11/9
Weight (Kg)	62.97±8.32	64.81±12.97
Time of disease before arriving to the Emergency Room (hours)	10.75±9.73	6.65±2.97
Rehydration phase		
Time to recover diuresis (hours)	1.53±0.67	1.66±0.53
Infused volume during the rapid expansion phase (liters)	6.51±2.47	6.25±1.39
Total infused volume during the maintenance phase (liters)	24.94±14.42	27.77±25.66
Endovenous infused volume 12 hours post-urination (liters)	5.72±2.45	7.41±3.56
Post-urination oral tolerance (ml/hour)	519.5±233.9	674.7±342.1

p < 0.05

43.2; *Serum osmolality*: A 301 ± 10 mOsm/Kg and B: 289 ± 7 mOsm/Kg when diuresis was recovered).

However, the correction occurred more quickly with LR, which had the additional advantage that it did not produce hyperlactatemia, Urinary sodium concentration was statistically significant (95 ± 42 mEq/l in group B compared to 138 ± 42 mEq/l in group A) at the time of urination (2 hours post admission).

Discussion

Our study involved two groups of patients with similar demographic characteristics, suffering from severe dehydration due to choleraform diarrhoea. One group was treated with NaCl and the other with LR. Our results showed some statistical significance between the two groups regarding the physiological response to the initial rehydration. At hospital admission, the acid-base status of each patient was primarily characterized by acidemia, which was caused by metabolic acidosis with high anion gap and respiratory acidosis. We emphasize that the fall of the anion gap, from the time of admission to the time of urination, did not correlate with an equivalent increase of bicarbonate. Thus a different and additional component, apart from the tissue hypoperfusion, could be responsible for the initial metabolic acidosis of these patients [14,15]. Hence the hypothesis described in a previous publication, *i.e.* that patients developed metabolic acidosis with high anion gap mainly due to lactic acidosis, is not sustainable in our study [16], because only one patient of the 11 patients who were evaluated at admission had serum lactic acid greater

than 5 mEq/l. The most likely hypothesis is that metabolic acidosis depends on bicarbonate loss and, in this case, the increased anion gap appeared due to the accumulation of other anions.

We found that patients in group B had increased values of lactic acid when compared to their basal status because they received an extra contribution of lactate in the solution. However, this increase was not enough to generate a severe hyperlactatemia. There was no statistical significance when compared with the results of group A, probably because the number of observations was small.

The results of this investigation confirmed that both solutions were effective in solving high anion gap acidosis [12]. However, the correction of the acidemia was delayed with NaCl, whereas the patients who were treated with LR had significant improvement of acidemia by the correction of the two components of the metabolic acidosis, which has been seen in the clinical state of the patients.

Compensatory mechanisms of metabolic acidosis include buffering with bases in both the intra and extracellular space, as well as pulmonary hyperventilation. The latter mechanism avoids extreme drop in blood pH by eliminating CO₂. Several physiological investigations have studied it, showing how to predict the level to which the pCO₂ should decrease in certain situations of metabolic acidosis (12 to 36 hours of its occurrence) [17]. Our patients arrived with a level of pCO₂ above the predicted value; therefore, there was an additional contributing factor for their acidemia. Moreover, the lack of a complete respiratory response could be explained because the patients came to the hospital within 11 hours from the

Table 2. Acid base status and electrolytes during rehydration

	Group A NaCl 0.9%			Group B Lactated Ringer's		
	Baseline	2 hours	14 Hours	Baseline	2 hours	14 Hours
pH	7.20±0.09	7.19±0.06	7.27±0.08	7.25±0.10	7.33±0.06*	7.33±0.05*
PCO ₂ (mmHg)	31.7±4.34	32.2±4.95	30.9±3.99	31.1±1.23	31.3±5.48	32.3±3.55
HCO ₃ ⁻ (mEq/l)	12.7±3.18	12.4±2.75	14.6±3.41	13.2±3.37	16.6±2.34*	17.6±3.1*
Anion gap (mEq/l)	27.2±5.58	13.9±6.32	12.45±4.13	26.7±7.16	17.32±4.86	11.59±6.37
Serum creatinine (mg/dl)	2.74±1.08	1.25 ± 0.46	0.78±0.20	2.49±1.41	1.49±0.71	0.91±0.42
Serum lactate(mEq/l)	2.95±2.9	2.01±1.25	1.42±0.64	1.61±0.27	2.41±1.43	1.15±0.51
Serum Na ⁺ (mEq/l)	145±4.2	146±3.3	140±43.9	145±4.6	141±43.2*	140±2.9
Serum K ⁺ (mEq/l)	3.8±0.3	4.1±0.9	4.5±1.3	4.3±40.7*	4.6±0.9	5.1±1.4
Serum Cl ⁻ (mEq/l)	105±5.0	120±7.8	113±3.8	105±3.3	107±3.3*	109±4.6*
Serum osmolality (mOsm/Kg)	304±9	301±10	290±9	301±18	289±7*	287±11
Urinary Na ⁺ (mEq/l)	12±38	138±43	71±53	0**	95±42*	75±54
Urinary K ⁺ (mEq/l)	9±22	23±12	42±36	0**	39±2	34±22
Urinary Cl ⁻ (mEq/l)	12±47	121±49	98±63	0**	93±51	100±77
Urinary osmolality (mOsm/Kg)	720±175	371±493	362±194	0**	351±88	310±140

*p < 0.01 when compared to NaCl 0.9%

**Urinary electrolytes were not comparable at baseline, as in group A there were only three samples, whereas in group B samples were not obtained despite the patients were catheterized.

onset of symptoms, as it has been suggested in a previous study [18]. The pCO₂ of patients in both groups evolved similarly. However, the early increase in serum bicarbonate in the group treated with LR allowed them to reach compatible values with adequate pulmonary compensation at the time of urination (2 hours post-admission), whereas the group treated with NaCl merely reached the expected levels of pCO₂ in the final control (14 hours post-admission).

The levels of sodium and plasma osmolality were slightly above the normal range at admission, which is consistent with the slight hiposmolality that has been described for patients with choleraform diarrhoea. Nonetheless, the highest concentration of sodium in NaCl was reflected in the increased serum sodium concentration at the end time of the intravenous expansion.

Our patients came to the hospital with normal serum potassium levels even though the total body potassium deficit usually occurs in diarrhoeas. The explanation of this is based on the necessity of losing between 200 and 350 mEq of potassium to diminish its plasma concentration in 1 mEq/l, and in the fact that this diarrhoea just provokes a minimum loss of potassium [19]. Furthermore, adult patients with cholera lose between 6 and 10 liters of diarrhoea

before hypovolemic shock appears; thus it is very unlikely to reach a level that produces hypokalemia.

Patients in the group treated with LR had higher levels of serum potassium at admission, in spite of the randomization, than those treated with NaCl. However, no statistical significance was found throughout the treatment (values were within the normal range after treatment). This result shows that LR contains an adequate concentration of potassium which does not increase the risk of hyperkalemia in intravenous rehydration.

Even though the chlorine blood concentration was above the upper limit of the normal range, it was similar in both groups at admission. Then, at the end of the first phase of rehydration, there was a significant increase of chloremia in the NaCl group, probably for the highest concentration of chlorine in that solution. This difference was still evident in the final control. Serum creatinine was elevated at admission but it decreased to near normal limits after the first phase of rehydration and in the third control. Nonetheless, there was no statistical significance between the two groups in the three points of the study. This shows that the initial azoemia was pre-renal [14].

Although no statistical difference was found when comparing the tolerated volume between groups, we

observed that patients treated with LR suffered less from vomiting, and ingested greater volumes of ORS in the maintenance phase compared to patients treated with NaCl; thus LR could improve oral fluid intake. On the other hand, no difference was seen in the intravenous volume used by the two groups.

Conclusion

Our study confirmed our prior clinical appraisal, showing that LR has a better clinical correction than NaCl, illustrated by more rapid physiological correction, showing that mixed metabolic acidosis was corrected quicker and more appropriately with this treatment. Hyperosmolality and hypernatremic states were also corrected with both solutions, but more quickly with LR. We wish to emphasize that expansion with LR did not produce hyperlactatemia; therefore, we can recommend it as the best solution to treat in severely dehydrated patients with choleraform diarrhoea as it offers better clinical response and more physiologic correction.

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