Original Article

Hypertonic Saline Solution for Renal Failure Prevention in Patients with Decompensated Heart Failure

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Summary

Background: Hyponatremia and congestive phenomena indicate a bad prognosis in decompensated heart failure. The occurrence of renal failure is associated to an increased death risk.

Objective: To evaluate the safety and efficacy of the hypertonic saline solution in patients with decompensated heart failure for renal failure prevention.

Methods: Patients with decompensated heart failure, congestion and hyponatremia participated in the study. In addition to the standard treatment, the patients received hypertonic saline solution and were submitted to clinical as well as laboratory assessment.

Results: Nine patients were enrolled in the study. Mean age was 55 + 14.2 years, being 5 male (55.5%) and 4 (44.5%) female patients. All of them presented functional class III-IV of the New York Heart Association (NYHA), and 5 (55.5%) received dobutamine. All of them presented initial creatinine > 1.4 mg/dl. The mean tonicity of the solution was 4.39% + 0.018% (2.5% to 7.5%) and the duration of treatment was 4.9 days + 4.1 days (1-15 days). There were no severe adverse effects; none of the patients presented clinical worsening or neurologic disorders; hypokalemia occurred in 4 cases (44.5%). The comparison of the variables before and after treatment showed a decrease in urea (105 mg/dl + 74.8 mg/dl vs. 88 mg/dl + 79.4 mg/dl; p = 0.03) and increase in the urinary volume (1,183 ml/day vs. 1,778 ml/day; p = 0.03); there was no tendency to creatinine decrease (2.0 mg/dl + 0.8 mg/dl vs. 1.7 mg/dl + 1.0 mg/dl; p = 0.08). Despite the elevation in sodium levels (131 mEq/l + 2.8 mEq/l vs. 134 mEq/l + 4.9 mEq/l) and weight decrease (69.5 kg + 18.6 kg vs. 68.2 kg + 17.1 kg), there was no statistically significant difference.

Conclusion: The use of hypertonic saline solution in patients with decompensated heart failure can be a safe therapeutic method and potentially related to clinical improvement and renal failure prevention. (Arq Bras Cardiol 2007;88(6):624-628)

Key words: Hypertonic solutions; heart failure; renal insufficiency; hyponatremia.

Introduction

Patients with decompensated heart failure have distinct characteristics and some aspects of its presentation have received special attention due to its association with a worse prognosis[1,2]. Advanced age, the presence of hypotension and shock and hyponatremia are known markers of a worse prognosis, among others[3,4]. In this situation, the presence of renal failure has shown to be an important risk factor; even a creatinine increase of 0.3 mg/dL in patients with decompensated heart failure is a marker of a higher risk of death[5].

The congestive phenomena can be present in up to 70% of the patients admitted at the hospital due to decompensated heart failure[2], with a high rate of diuretic resistance being observed among these patients[6]. In these conditions, the occurrence of renal failure becomes even more important and it can be related to the abrupt decrease in the effective plasma volume, the use of angiotensin-converting enzyme inhibitors (ACEI) and angiotensin II receptor blockers, the presence of low cardiac output and the neurohormonal adaptations.

The currently available treatment strategies include hydric restriction, use of intravenous diuretics, association of diuretics, and administration of inotropics[7], artificial methods of ultrafiltration[8], vasopressin antagonists[9] and natriuretic peptides[10]. However, these treatment modalities have not been associated to a better prognosis and they are limited by conditions such as availability, high cost, poor patient compliance to the dietary restrictions, diuretic resistance and worsening of renal function.

Hypertonic saline solutions have been tested in different clinical situations of cardiovascular system failure, such as hemorrhagic and septic shock[11]. Recently, some authors have proposed the use of hypertonic saline solution for the control of congestive phenomena in patients with decompensated heart failure, congestive phenomena and hyponatremia[12-14].

Thus, the safety of the hypertonic saline solution use was evaluated in a series of patients with decompensated heart

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Manuscript received December 12, 2006; revised manuscript received March 15, 2007; accepted April 16, 2007.

failure, as a strategy for the control of congestive symptoms, correction of hyponatremia and renal failure prevention.

Methods

The patients were selected for the study from December 2005 to November 2006, in a tertiary university hospital specialized in Cardiology. The inclusion criteria were: age older than 18 years, presence of decompensated heart failure[15], serum sodium < 135 mEq/L and presence of signs of pulmonary congestion (defined as the presence of pulmonary rales or radiological signs indicative of pulmonary venous congestion) or systemic congestion (indicated by the presence of lower limb edema, ascites, hepatomegaly and jugular stasis > 4 cm from the manubrium-sternal angle), despite treated by standard therapy for at least 48 hrs. The exclusion criteria included the presence of specific causes for cardiac decompensation (pulmonary embolism, myocardial ischemia, arrhythmias, infection, anemia) and the presence of several primary valvulopathies.

Intervention - The treatment considered to be standard includes rest, restriction of salt (2 g/day) and water intake, intravenous furosemide, oral vasodilator (angiotensin converting enzyme inhibitor, angiotensin II receptor blockers or the association of hydralazine and nitrate), spironolactone and maintenance of the betablocker dose used chronically by the patient; in the presence of signs of low cardiac output, dobutamine was used. In addition to the standard treatment of the decompensated heart failure, the patients received an infusion of hypertonic saline solution administrated to peripheral vein for one hour, twice a day, associated to furosemide. The tonicity of the solution was based on previous protocols[10-12], with modifications being carried out according to the intensity of the congestive phenomena, such as the degree of hyponatremia as well as the presumed risk of renal failure.

The initial dose of diuretics was determined by the physician in charge of the case and was modified according to the initially obtained response.

Variables studied - The patients were submitted to daily clinical evaluations and weight and urinary volume were also measured on a daily basis. Sodium, potassium, urea, creatinine and hemoglobin were measured in peripheral blood throughout the intervention.

Statistical analysis - The values of continuous variables are expressed as mean ± SD. For the comparison of the continuous variables, we used the paired Student's *t* test and p values < 0.05 were considered statistically significant.

Table 1 – Clinical characteristics of the patients studied

Variable	n (%)/mean + SD
Number of patients	9
Age (years)	55 ± 14.2
Sex	
Female	4 (44.4%)
Male	5 (55.6%)
Atrial Fibrillation	3 (33.3%)
Diabetes mellitus	3 (33.3%)
Arterial hypertension	3 (33.3%)
Signs of hypoperfusion	3 (33.3%)
Signs of congestion*	9 (100%)
Functional Class (NYHA)	
III	1 (11.1%)
IV	8 (89.9%)
Etiology	
Chagasic	1 (11.1%)
Ischemic	3 (33.3%)
Others	5 (55.6%)
LVDD (mm)	61.5 ± 9.2
LVEF	32.3 ± 15.9
Creatinine (mg/dl)	2 ± 0.8
Sodium (mEq/l)	131 + 2.8
Hemoglobin (g/dl)	10.8 + 2.5
Intravenous Inotropic Drugs	5 (55.6%)
ACEI/ARB	4 (44.4%)
Hydralazine	6 (66.7%)
Betablocker	4 (44.4%)
Spironolactone	3 (33.3%)
Intravenous Furosemide	9 (100%)
Thiazide Diuretics	4 (44.4%)

** Lower-limb edema, pulmonary rales; ascites; hepatomegaly; jugular stasis > 4 cm. n - number of patients; SD - standard deviation; NYHA - New York Heart Association; LVDD - left ventricle diastolic diameter; LVEF - left ventricle ejection fraction; ACEI - angiotensin-converting enzyme inhibitor; ARB - angiotensin-II receptor blockers.*

Results

In total, 9 patients were included in the study (Table 1). All of the patients presented creatinine values above normal ranges; only 2 patients had urinary volume > 1 ml/kg/min on the day before the start of the intervention and four patients had urinary volume < 0.5 ml/kg/min. One of the patients was undergoing peritoneal dialysis for congestion control.

The mean tonicity of the solution used was 4.39% ± 0.018% (2.5 to 7.5%) and the duration of the treatment was 4.9 days ± 4.1 days (1 day to 15 days). All patients received at least one day of treatment, 8 patients received at least 2 days of treatment and 7 patients received at least three days of treatment. All of the patients tolerated the medication infusion. No severe adverse events were observed and no pulmonary or systemic congestion was observed in any case. No neurological disorders were observed. The mean dose of intravenous furosemide used was 177.5 mg ± 177.7 mg (60 mg to 600 mg). Hypokalemia with the need for potassium replacement was the most frequent complication, occurring in 4 cases (44.6%).

The evolution of the variables studied during the first three days of treatment is shown in Figure 1. The comparison between the pre- and post-treatment values of the variables is shown in Table 2. After the administration of the hypertonic saline solution, there was a decrease in the urea levels, increase in 24-h urinary volume and a tendency to decrease in creatinine levels. Despite the increase in sodium levels and the decrease in the weight of the patients, these variables did not reach a statistically significant difference.

Discussion

In the present study, the administration of a hypertonic saline solution to a series of 9 patients with decompensated heart failure was related to an increase in urinary volume, tendency to increase in serum sodium as well as the improvement in renal function parameters, without the occurrence of cardiovascular or neurological adverse events.

Hypertonic saline solutions have been tested in clinical situations of cardiovascular failure, such as hemorrhagic and septic shock, being important the contributions of national authors in this area[10]. In animal models of hypovolemia, the infusion of a hypertonic saline solution promotes increase in arterial blood pressure and cardiac output. These effects are attributed to the increase in plasma volume, peripheral vasodilation[16] and the direct cardiac inotropic effect[17].

The existence of vasodilation, not only mesenteric, but

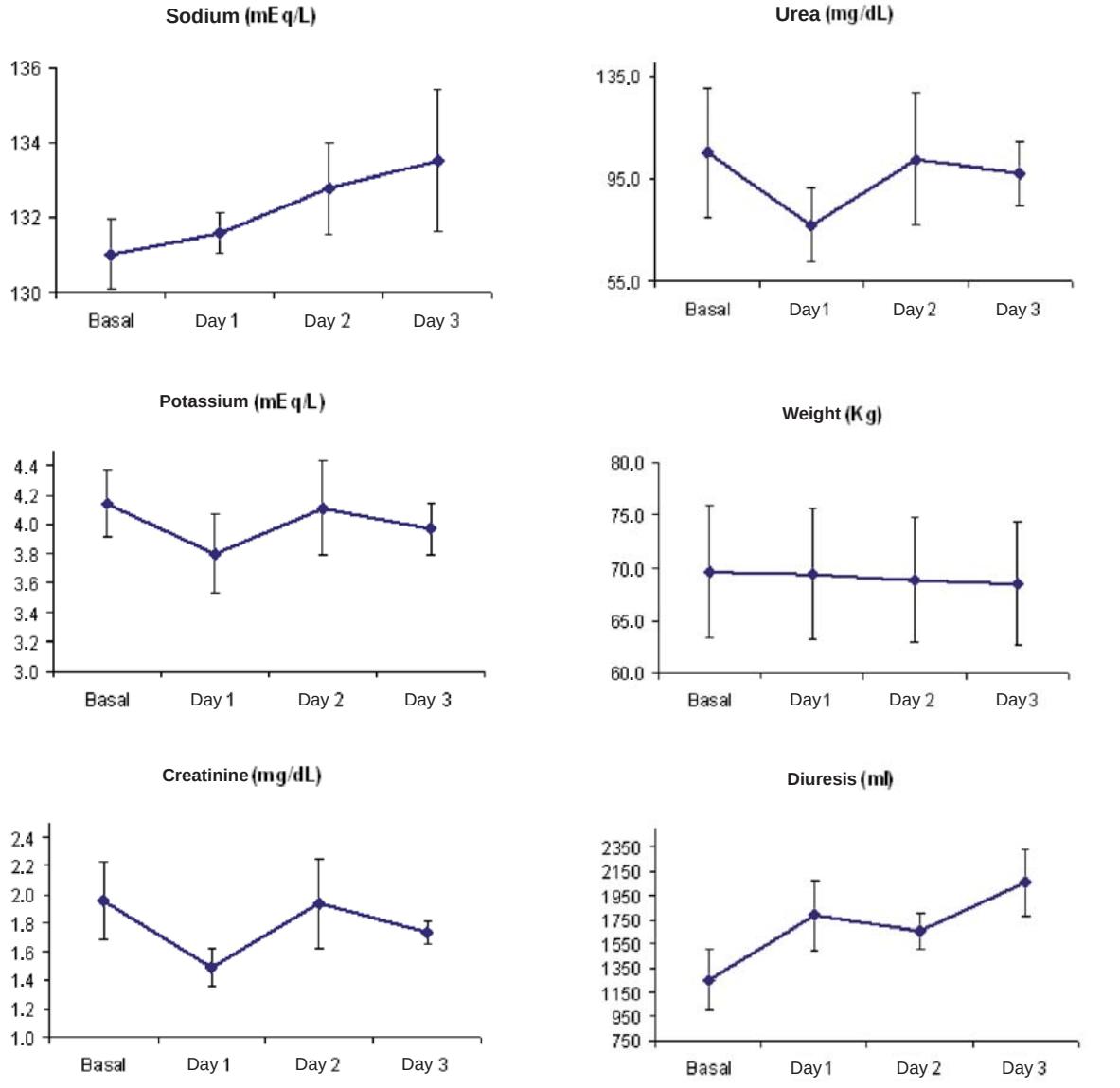

Fig. 1 – Evolution of the clinical and laboratory variables during the first three days of administration of the hypertonic saline solution protocol.

Table 2 – Clinical and laboratory variables before and after hypertonic saline solution protocol

Variable	Before (mean + SD)	After (mean + SD)	p value
Sodium (mEq/l)	131 ± 2.8	134 ± 4.9	ns
Potassium (mEq/l)	4.1 ± 0.7	4.0 ± 0.7	ns
Urea (mg/dl)	105 ± 74.8	88 ± 79.4	0.03
Creatinine (mg/dl)	2.0 ± 0.8	1.7 ± 1.0	0.08
Hemoglobin (g/dl)	10.8 ± 2.5	10.6 ± 2.2	ns
Weight (kg)	69.5 ± 18.6	68.2 ± 17.1	ns
Diuresis*	1.183	1.778	0.03

** Comparison between the 24 hrs before starting the protocol and 24 hrs after the end of the protocol. SD - standard deviation; ns - non-significant.*

also renal, is particularly important, as these are the more intensely hypoperfused zones in cases of hypovolemia[16]. This hemodynamic effect, associated to the decrease in blood viscosity and the immunomodulatory effect[18], makes the hypertonic saline solution potentially beneficial to patients with heart failure and signs of congestion. In this situation, the regular use of diuretics and vasodilators can lead to the reduction in plasma volume and tissue hypoperfusion, phenomena related to clinical signs of hypovolemia, such as arterial hypotension and increase in urea and creatinine, both markers of worse prognosis.

In the present study, the use of the hypertonic saline solution was safe, with no worsening signs of pulmonary as well as systemic congestion. Historically, the use of the hypertonic saline solution in patients with cardiopathies has been restricted. Such limitation is due to animal models of shock, in which the occurrence of hypotension and arrhythmia was observed after a fast infusion of hypertonic saline solution[19]. However, no significant adverse effects have been reported in physiological studies in humans[20,21], or in clinical studies (cardiogenic shock due to right ventricular dysfunction after pulmonary embolism[22] and heart failure[10-12]).

The results of the present study indicated clinical improvement of the patients with the use of the hypertonic saline solution, characterized by increase in the urinary volume and weight decrease in the patients. The weight decrease did not reach statistical difference, probably limited by the sample size. These data are in accordance with the results obtained by other authors, who reported improvement in the congestive phenomena, assessed by clinical parameters as well as by the decrease in B-type natriuretic peptide levels[10].

Although serum sodium increase was observed in the present study with the use of the hypertonic saline solution, the difference was not statistically significant, probably limited by the sample size. This finding is in accordance with other authors[10-12]. Neither previously reported studies nor our experience showed an association between serum sodium increase and the onset of neurological symptoms. A decrease in urea and a tendency to decrease in serum creatinine levels were observed with the use of the hypertonic saline solution. Previous studies, carried out in patients with decompensated heart failure, with no vasoactive drugs and normal renal function, also indicated the protective value of the hypertonic saline solution in renal function[11]. The findings in the present study, however, are noteworthy due the fact that this sample consisted of patients at high risk for renal failure development. The value of the hypertonic saline solution in a high-risk population for the occurrence or worsening of renal failure had not been previously reported.

Limitations - The results obtained are in accordance with the experimental and clinical evidence reported by other authors; however, it is a non-controlled study, with a limited number of patients, which did not evaluate the long-term effects of the intervention. Additionally, the protocol used allowed the use of the saline solution with different tonicities and different doses of furosemide. The variability in the doses used was intentional and is part of the group's experience gain with this new treatment modality. These two aspects related to the medication doses make the intervention heterogeneous, which might have influenced the results obtained. It is also possible that existing differences might have been underestimated, considering the limited sample size.

Conclusion

The hypertonic saline solution has the potential to become a safe and effective method for the clinical improvement and sodium increase in patients with decompensated heart failure with signs of congestion and hyponatremia, with a protective effect against the occurrence of renal failure in these circumstances.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any graduation program.

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