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OPTIMAL TREATMENT OF HYPOVOLEMIC HYPERTENSIVE CRISES IN CKD NONDIALYZED PATIENTS

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Abstract. Hypovolemia and hypertension are important factors for worsening a previous CKD. The present article highlights the importance of concomitant treatment of both factors in nondialyzed CKD patients with hypertensive crises. Material and methods. The study included 454 patients with chronic kidney disease stage 3 or 4, who were admitted for hypertensive crises and who received treatment in accordance with volemic status and plasma sodium. Results. 96 patients had hypovolemia (21%). Reducing systolic blood pressure ≤ 160mmHg was achieved faster in patients whom hypovolemia was corrected by parenteral route. Patients with hyponatremia received saline solutions via parenteral administration with better clinical benefits than glucose isotonic solutions. Conclusions. Optimal treatment of hypovolemic hypertensive crises requires promptly restoring of plasma volume. In some cases with hyponatremia, infusion of sodium chloride solution will correct, paradoxically, the raise in blood pressure.
Keywords: CKD, hypertensive crises, hypo -/ hypernatremia, hypovolemia

Introduction

Hypertension (HT) represents a major progression factor in chronic kidney disease (CKD) and worsens patient' cardiovascular and cerebrovascular prognosis. Although there is an abundance of researches in this area and numerous therapeutic guides, the adequate control of HT in CKD is difficult to achieve. Furthermore, there is little knowledge regarding the optimal treatment of hypertension crises associated with various hydroelectrolytic disturbances, as often happens in chronic renal failure in predialysis stages, but, as medical data confirmed, the treatment goal is to gradually reduce blood pressure (BP) to establish an adequate long-term follow-up [1-3]. In addition, hydroelectrolytic imbalance should also be slowly corrected to avoid further life-threatening complications [4].

For an adequate therapy approach, the present article highlights the importance of a correct diagnosis of the hemodynamic status and sodium abnormalities identified in nondialyzed CKD patients with hypertensive crises.

Material and methods

Between January 2010 and December 2011, 454 patients with CKD stages 3 or 4 presented at the emergency room of our hospital for hypertensive crises. These patients were admitted in intensive care unit, where permanent monitoring of vital functions (arterial pressure, oxygen saturation and electrocardiogram) was performed. A 10 minute protocol including measuring hemodynamic status and serum sodium was applied before taking any therapy measures.

Diagnosis of hypertensive cries was established by measuring systolic pressure ≥ 200mmHg and simultaneous presence of one of the following symptoms: headache / vertigo,

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tinnitus / phosphenes, dyspnea at rest and / or decubitus, chest tightness, epistaxis.

Calculating GFR using MDRD formula, patients were classified in CKD stage 3 for values between 30 – 59mL/min/1,73m^2 and stage 4 for values between 15 – 29mL/min/1,73m^2.

Hemodynamic status was obtained using Hotman apparatus, Tebco (Integrated Hemodynamic Management System) Hemosapiens, which appreciates patient' volemia by measuring transthoracic vascular bioimpedance.

Exclusion criteria from the study were: age > 65 years; normal levels of nitrogen waste products; acute renal failure; CKD stage 5; acute coronary events (*e.g.*: angina, myocardial infarction); arrhythmia.

T test was applied for statistically analyzing the assessed data and additionally, *parametric* and *nonparametric tests* were performed ($p < 0.05$ was considered statistical significant).

Therapy approach

4 types of water and sodium imbalance were identified [1]:

- Hypervolemia – 319 patients;
- **Hypovolemia associated with hyper- or normonatremia – 57 patients;**
- **Hypovolemia associated with hyponatremia – 38 patients;**
- Normovolemia and normonatremia – 40 patients.

Therapy intervention was applied in the two groups of individuals with hypovolemia. All patients received clonidine 0.15mg or nicardipine 10mg (or both) and volume expansion was performed in two different modalities which were compared and statistically analyzed:

- In the group with **hypovolemia and hyponatremia**, restoring plasma volume with intravenous 5% dextrose solution was compared with intravenous infusion of 0.9% sodium chloride solution. 20 patients received a solution of 0.9% sodium chloride (normal saline) at a rate of 100mL/h (associated with antihypertensive drugs), while the remaining 18 patients received 5% dextrose solution at a rate of 100mL/h. After lowering blood pressure (BP) (systolic less than or equal to 160mmHg), hydration and type of solutions used were influenced by evolution of sodium levels and fluid status, but in this study, we analyzed only the first 24 hours.

- In the group with **hypovolemia associated with hyper - or normonatremia**, free oral liquid intake was compared with intravenous hydration with isotonic 5% dextrose solution. 28 patients were treated with intravenous hydration with 5% dextrose solution at a rate of 100mL/h concomitant with antihypertensive medication (clonidine/nicardipine, or both); the other 29 patients received only oral antihypertensive treatment (clonidine/nicardipine, or both), and patients were free to oral fluid intake according to thirst.

The following variables were measured and compared: duration until TAs decreases ≤ 160mmHg, duration until volemia was restored and duration until natremia was corrected. The study was conducted for the first 24 ore after hospital admittance and, during the treatment intervention, the patients were carefully evaluated (permanent monitoring of BP, ECG, volemic status, natremia measured every 2 h).

Results

1. Group with hypovolemia and hyponatremia (Figure 1, 2)

In the **subgroup treated with 0.9% sodium chloride solution**:

- restoring volemic status was achieved on average after 7.8 hours;
- lowering of systolic blood pressure ≤ 160mmHg was noted after an average of 6.7 hours;
- correction of natremia was obtained in all patients (during the 24h of the study) on average after 12.3 hours after starting the treatment.

In the **subgroup treated with 5% dextrose solution**:

- restoring volume status was achieved on average after 11.8 hours;
- systolic blood pressure reached target values set by an average of 14.2 hours;
- sodium levels normalized only in 4 patients after a mean treatment duration of 14 hours, but in the remaining patients, hyponatremia persisted even after 24 hours.

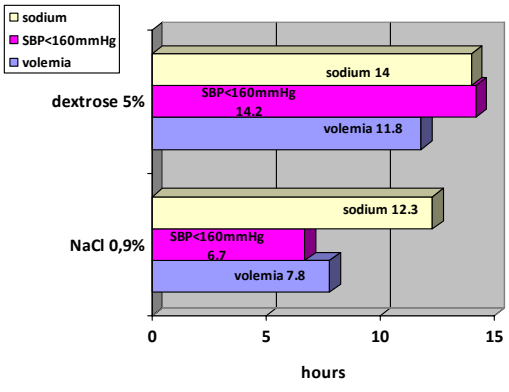

Figure 1. Mean duration of achieving study targets (normalization of sodium and volemia, SBP ≤ 160mmHg) in the group with hypovolemia and hyponatremia according to the treatment applied.

2. Group with hypovolemia associated with hyper- or normonatremia (Figure 3, 4)

- In the subgroup treated with the intravenous

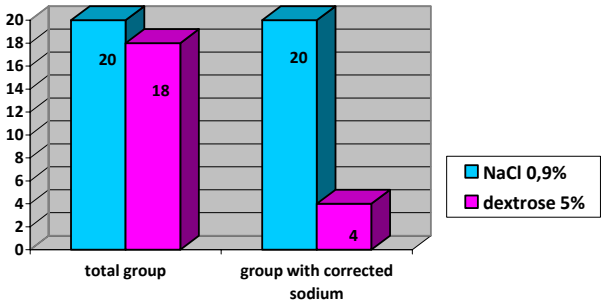

Figure 2. Plasmatic sodium was corrected only in 4 patients in the subgroup treated with dextrose 5%

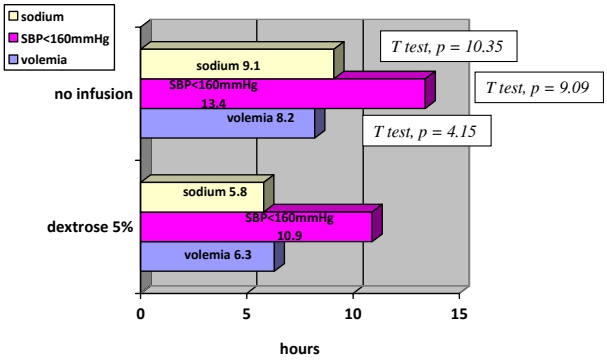

Figure 3. Mean duration of achieving study targets (normalization of sodium and volemia, SBP ≤ 160mmHg) in the group with hypovolemia and hyper- or normonatremia according to the treatment applied

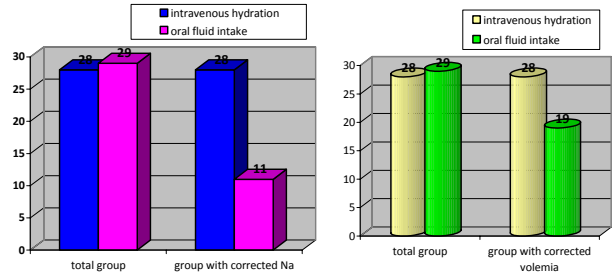

Figure 4. Plasmatic sodium was corrected only in 11 patients and volemic status was normalized only in 19 patients in subgroup without intravenous dextrose

glucose solution and antihypertensive agents:

- SBP was reduced to ≤ 160mmHg after a median of 10.9 hours;
- volemia was corrected after an average of 6.3 hours;
- serum sodium normalized or remained normal in all patients after a mean of 5.8 hours.

- In the group treated only with antihypertensive agents:

- SBP decreased ≤ 160mmHg after a mean of 13.4 hours;
- volemia was corrected within 24 hours of the study only in 11 patients after a mean of 8.2 hours (probably by oral intake of liquids that the patients have consumed); in the remaining patients, hypovolemia persisted more than 24 hours;
- serum sodium remained normal or normalized in 19 patients after an average of 9.1 hours. In the remaining patients, there was no significant change in sodium levels (changes occurred within the normal range or less than 2mEq/L in those with pretreated hypernatremia).

Discussion. Statistic relevance of data

As we have already stated in a previous article [5], in the total group of patients with hypertensive crisis and CKD, there is a significant proportion of patients with hypovolemia (21%).

Statistical analysis of the results (Figure 1) showed that *in group with hypovolemia and hyponatremia*, **correction of the volume status** was achieved significantly faster in patients receiving parenteral sodium chloride solution in comparison with those receiving parenteral hydration with dextrose isotonic solution (*T test, p = 13.96*). Also, the time until **systolic blood pressure achieved target values** was significantly lower in the patients group treated with saline *versus* patients hydrated with isotonic glucose (*T test, p = 27.44*). ***Serum sodium correction*** was achieved significantly faster in the group treated with saline in comparison with isotonic glucose-treated group in which, in a large part of the patients, serum sodium levels remained below normal (*T test, p = 2.60*).

In the *group with hypovolemia and hyper- or normonatremia*, statistical analysis of the results (Figure 3) showed that the time in which **systolic blood pressure reached target level** was significantly lower in patients who received infusion of 5% glucose solution than in patients who did not receive parenteral hydration with glucose solution and were allowed to hydrate orally by thirst (*T test, p = 9.09*). In the same time, the period in which **volemia has returned to normal** values was significantly lower in patients receiving parenteral hydration with isotonic glucose versus those that were hydrated orally (*T test, p = 4.15*). **Serum sodium correction** was achieved significantly faster in the group treated with parenteral glucose 5% (*T test, p = 10.35*). In subgroup without parenteral treatment, an important proportion of patients did not reach target values for volemia and natremia.

Both statistics highlight the importance of plasma volume correction in hypovolemic hypertensive crises, simultaneously with the administration of the antihypertensive drugs. In the group not receiving parenteral hydration, correction of volume expansion was achieved more slowly and

in fewer patients, along with slower normalization of systolic blood pressure values. This observation is in concordance with literature data [6,7] which stipulate that there is a decreased thirst in patients with CKD and acute hypertension, as a result of dysfunction of baroreceptors and altered sympato-vagal response; reduced orally fluid intake may induce hypovolemia.

The concept of correcting hypovolemia with saline solutions is not new, but logically as etiologic treatment in patients with concomitant hyponatremia [7-9]. By correcting plasma sodium and increasing volemia, the stimulation of renin-angiotensin and peripheral resistance are decreased and the blood pressure is lowered. Although it increased volemia, administration of glucose solutions in patients with hyponatremia did not correct sodium levels; in patients with oliguria, especially if they are in an advanced stage of chronic kidney disease, there is a high risk of dilutional hyponatremia which can be corrected only by urgent hemodialysis. Although administration of saline solution in hypovolemic hypertension is stipulated in several studies [7-9], in clinical practice it may be noted a restraint regarding this attitude, especially when there is an acute and severe increase of blood pressure. In our study, careful monitoring of patient's state (*e.g.*: signs of hypervolemia, blood pressure monitoring) was performed in order to prevent any harmful events. It would useful if future guidelines of hypertension treatment would cover this area of complications of HT, but we consider that objective assessment of volemic status would be mandatory. Appreciation of volemic status only by clinical signs may be subjective and may lead to misinterpretations and dangerous treatment, especially in CKD patients.

Conclusions

Systemic hypertension and hypovolemia are important factors for worsening of a previous CKD. The presence of hypovolemia is registered with significant frequency in hypertensive crises of patients with nondialyzed CKD. Management of concomitant hypertension and hypovolemia requires, beside antihypertensive drugs, promptly restoring of volume status, preferable by parenteral route. In cases with hyponatremic hypovolemia, infusion with sodium chloride solution will correct, paradoxically, the raise in blood pressure.

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