HYPONATREMIA – RISK FACTOR IN PATIENTS WITH CHRONIC HEART FAILURE – CLINICAL, EVOLUTIVE AND THERAPEUTIC IMPLICATIONS

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HYPONATREMIA – RISK FACTOR IN PATIENTS WITH CHRONIC HEART FAILURE – CLINICAL, EVOLUTIVE AND THERAPEUTIC IMPLICATIONS (Abstract): Patients with heart failure are, by definition, hemodynamically unstable. This condition may be accentuated by medication (digitalis, diuretics, antiarrhythmics), so that they become more sensitive to electrolyte disturbances. Hyponatremia is the most common electrolyte disorder, particularly common in the intensive care unit. **Aim:** the evaluation of the incidence of hyponatremia in patients diagnosed with chronic heart failure in order to establish a correlation with the evolution, prognosis and therapeutic implications. **Material and methods:** We analyzed retrospectively 120 patients diagnosed with chronic heart failure NYHA II-IV classes, admitted in the Cardiology Clinic between 2009 and 2013. We analyzed electrolytic disturbances which occurred during different strategies of therapy. **Results:** 120 patients with heart failure were admitted in the Cardiology Clinic between 2009 and 2013, 92 males and 28 females. Diagnosis was established by classical criteria. Evaluation was very complex and included: complete clinical examination, electrocardiogram, echocardiography, chest ray examination and biochemical analyses especially hepatic, renal function and electrolyte status. **Conclusions:** The data obtained showed that electrolyte disturbances are frequent in patients with chronic heart failure, irrespective of NYHA class. Hyponatremia is usually associated with diuretic therapy and may play a very important role in the subsequent development of life-threating complications. Patients with heart failure who develop hyponatremia during their evolution had a worse prognosis. **Keywords:** ELECTROLYTE DISTURBANCES, HYponatremia, Heart Failure

The patient with heart failure (independent of etiology) is, by definition, a hemodynamically unstable patient in which a therapeutic plan, initially beneficial, may have unexpected side effects, some of them life-threatening (1). This type of patient usually has an electrical and hemodynamic instability related to the underlying disease and potentiated by complications and also by medication (diuretics, digitalis, antiarrhythmics) (1, 2, 3). In these conditions, patients become more sensitive to even minor ele-
trolyte balance disturbances, sometimes reacting violently through serious arrhythmias or conduction disturbances. Despite the advanced therapies of heart failure, the significant associated morbidity or mortality due to complex side effects of therapy was not reduced. The medication of the patient with heart failure involves a complex therapeutic schedule. The diuretic medication is essential and it is pathophysiological addressed to the salt and water retention (3). Although well tolerated by most patients, diuretic medication acting at renal level disrupts the electrolyte balance so that, depending on the type of mechanism, on the patients’ condition at the time, on the associated medication and diet, there may appear other electrolyte and fluid disorders, some of which could be life-threatening (1, 2, 3). Hyponatremia is the most common electrolyte disorder in intensive care units (its frequency is estimated at 30-40% of the hospitalized patients) (4, 5, 6). Hypervolemic hyponatremia, especially, is associated with a bad prognosis in patients with heart failure.

The aim of the study is to evaluate the incidence of hyponatremia encountered in patients with heart failure and to establish a correlation between this disorder and the occurrence of certain complications, and the entailed prognosis and therapeutic implications.

MATERIAL AND METHODS

The study is retrospective and included a group of 120 patients, 92 men (76.66%) and 28 women (23.33%), aged 48-85 years, hospitalized in the 1st Cardiology Clinic between the years 2009-2013 and diagnosed with chronic heart failure of the NYHA II-IV classes.

The classification of patients in the NYHA class of severity of heart failure was as follows:

- NYHA Class II - 19 patients: 10 men, 9 women;
- NYHA class III - 82 patients: 65 men, 17 women
- NYHA Class IV - 19 patients: 14 men, 5 women

The diagnosis of heart failure was based on the known and classical clinical and paraclinical data:

- Symptoms and signs of left ventricular failure (shortness of breath of different degrees, cardiac cough, tachycardia with / without gallop rhythm, presence of organic heart breaths and pulmonary rales stasis);
- Signs of right heart failure: hepatomegaly, peripheral edema (cardiac type), turgid jugular (level I-III), hepatojugular reflux, with or without ascites.

Paraclinical exploration of the patients included:

- Chest radiography - objectified cardiomegaly (ICT over 0.55) with or without signs of pulmonary stasis or pleural effusions.
- Echocardiography (2D, M mode, Doppler) objectified cardiac cavities dilation with decreased contractile function parameters (ejection fraction, shortening fraction), and other aspects: valvular regurgitation, intracardiac thrombus, and presence of spontaneous contrast and signs of hypertension pulmonary artery. Echocardiography was essential for identifying the etiology of heart failure.
- Peripheral venous pressure was elevated in most patients with right heart failure component.
- 12 leads surface ECG, in which these were sought: rhythm or management disturbances, ischemo-lesional changes, over-stress of certain cavities, changes due to
electrolyte disturbances.
- Biochemical balance included: hepatic function (transaminases, bilirubin, GGT), renal function (urea, creatinine, uric acid, creatinine clearance, RA), serum electrolytes (Na⁺, K⁺, Ca²⁺, Mg²⁺);
- Paraclinical investigation was complemented with complete blood count, spirogram and determination of blood gases and pH.

Patient evaluation was performed first at the time of admission and subsequently, depending on each particular case, was performed daily during hospitalization.

The etiology of heart failure was as follows:
- Ischemic dilated cardiomyopathy - in 30% of cases;
- Ethanolic dilated cardiomyopathy - in 35% of cases;
- Mixed dilated cardiomyopathy (ischemic, toxic, diabetic) - 20% of cases.
- Valvular heart disease - 15% of cases.

Etiology was based on personal history, physical examination and echocardiographic data resulted from examination. In some cases, the presence of the biochemical markers that supported chronic alcoholism was added to these.

Patients’ treatment was strictly individualized according to the hemodynamic status at the time of hospitalization, the etiological features, the presence or absence of arrhythmias and/or conduction disturbances and included, besides the appropriate hygienic-dietary measures, the following:
- Diuretic: loop – 15% of patients, spironolactone + loop diuretic combination - 85% of patients;
- Nitrate type vasodilator - 75% of patients;
- Converting enzyme inhibitor (ACEI) - adjusted doses of TA- was administered to 85% of patients (65% received perindopril, 20% received ramipril);
- Beta blocker - 90% of patients (55% carvedilol, bisoprolol 35%);
- Digoxin - 45% of patients;
- Amiodarone - 30% of patients;
- Anticoagulant - 65% of patients;
- Antiplatelet - 75% of patients received aspirin (in 50% of the cases it was associated with an anticoagulant), 28% of patients receiving clopidogrel.
- Dopamine (vasodilator dose) was necessary in 35% of cases because of signs of low cardiac output or renal failure.

Patients received therapeutic regimens that included combinations tailored to each individual case, as follows:
- Loop diuretic + vasodilator (nitrate) + beta blocker + ACE inhibitor - 15% of cases;
- Loop diuretic + spironolactone + ACE inhibitor + beta blocker + vasodilator (nitrate) - 40% of cases;
- Loop diuretic + spironolactone + ACE inhibitor + beta blocker + digoxin + vasodilator - 20% of cases;
- Loop diuretic + ACE inhibitor + amiodarone + vasodilator - 25% of cases.

All patients received an antiplatelet regimen and in 65% of the cases an anticoagulant administration was necessary.

Introducing the anticoagulant regimen was imposed by the presence of echocardiographic intracavitary thrombus or spontaneous contrast, by the presence of dilated right cavities and other clinical signs suggestive of thromboembolism associated phenomena. Throughout the immobilization in bed prophylactic doses of low molecular weight heparinwere also injected.

The nitrate type vasodilator (small doses) was used with preference in patients...
with signs of left ventricular failure considered to be due to ischemia and in patients with evident pulmonary stasis with normal values of arterial blood pressure.

RESULTS AND DISCUSSION

120 patients, 92 men and 28 women, aged between 48-85 years and diagnosed with chronic heart failure of the NYHA II-IV classes were hospitalized in the 1st Cardiology Clinic between 2009 and 2013.

Most of the patients were male and were included in NYHA class III - 82 patients (68.33%), (65 men and 17 women). 19 patients (15.83%) were included in NYHA Class IV (14 men, 5 women).

Hyponatremia (serum sodium values between 128-110 mmol/l) was present in all patients with NYHA IV class heart failure receiving diuretic therapy.

From the NYHA III class of heart failure only 35 patients (42.68%) developed hyponatremia after diuretic therapy. Clinically, these patients presented generalized oedema upon admission.

The etiology of heart failure was: dilated cardiomyopathy (ethanolic or ischemic) and valvular heart disease.

All the patients were previously treated with diuretics (loop diuretics alone or in combination with spironolactone). In 5% of cases, hyponatremia persisted after stopping the administration of the diuretic, so it was considered dilution hyponatremia and significantly correlated with increased mortality in this group.

The correction of hyponatremia was difficult, with partial response, limited to fluid restriction and administration of sodium chloride, while continuing the diuretic. In 10% of cases, the patients developed symptoms and signs of brain oedema (disorientation, seizures, confusion, lethargy). Neurological symptoms were correlated with serum sodium values under 120 mmol/l. Gastrointestinal symptoms were present in all the patients: anorexia, nausea, vomiting. In 20% of case signs of neuromuscular damage were present: muscle cramps, generalised weakness. Persistent and refractory hyponatremia was associated in our study with a great incidence of malignant ventricular arrhythmias (ventricular tachycardia and fibrillation). These arrhythmic complications determined the revaluation of the therapeutic plan.

The occurrence of hyponatremia was followed by the impossibility of continuing the administration of diuretic therapy that still remained necessary in the presence of generalized oedema.

In 15% of cases, these electrolyte disturbances have been associated with inflection of the renal function, that is, increased urea and creatinine values understood as renal functional failure and whose main cause was the diuretic abuse with subsequent reduction in pressure renal perfusion. In 7% of cases, renal failure was corrected by temporary withdrawal of the diuretic and proper hydration. In 35% of cases, the administration of vasodilator dose dopamine was necessary (2-3 mcg/kg/min). The final prognosis was worse, 25% of patients died during hospitalization. The main causes of death were: asystole and ventricular malignant arrhythmias.

CONCLUSIONS

Electrolyte disturbances are common in patients with heart failure, regardless of NYHA functional class. In most cases this is due to medication, especially to the diuretic therapy. Hyponatremia is an independent negative prognostic factor especially in patients enrolled in the NYHA IV
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functional class and it is often associated with increased mortality. The correction of hyponatremia is very difficult, with partial response, limited to fluid restriction and administration of sodium chloride. The treatment of hyponatremia can lead to potentially dangerous complications. It is essential to monitor the serum sodium level daily in patients with heart failure and a high risk to develop hyponatremia.

REFERENCES


NEW TREATMENT FOR MULTIDRUG-RESISTANT TUBERCULOSIS

Tuberculosis (TB) is an infectious disease with high morbidity and mortality. Difficulties related to the diagnosis and treatment of TB have increased incidence of multidrug-resistant tuberculosis (MDR-TB). Management of MDR-TB cases is more difficult because the treatment is longer, less potent, more toxic and more expensive, and determines a cure rate very low and a relapse rate very high. In this situation, the development of novel anti-tubercular drugs has become a necessity. Bedaquiline known as TM207 or R207910 is a diarylquinoline that inhibit synthesis of adenosine triphosphate (ATP) by specific binding to bacterial ATP synthetase. This new compound is active against sensitive and resistant strain of Mycobacterium, replicating or dormant bacteria. Clinical trials in MDR-TB patients conducted in South Africa revealed that bedaquiline (400 mg daily for 2 weeks and then 200 mg three times a week, in oral administration) has an early bactericidal activity similar to rifampicin and isoniazid, increased the rate of sputum conversion and also decreased the time for sputum conversion. The same study showed that the most common side effects caused by bedaquiline were: nausea, increase QT interval and the level of transaminases. United States Food and Drug Administration approved bedaquiline for treatment of MDR-TB, when no other drug is available. World Health Organization recommends bedaquiline for adult patients with pulmonary MDR-TB, but also argues the need for the studies about long-term safety (Goel D. Bedaquiline: A novel drug to combat multiple drug-resistant tuberculosis. J Pharmacol Pharmacother. 2014 Jan;5(1):76-8. doi: 10.4103/0976-500X.124435).

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