

# NEW THERAPEUTIC STRATEGIES IN PATIENTS WITH METABOLIC SYNDROME AND HEART FAILURE

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**Abstract:** The aim of the study was to investigate the effects of 16-32 mg Candesartan Cilexil (Atacand) in patients with heart failure and metabolic syndrome.

A prospective study with a follow up of 6 months was conducted. Thirty patients with metabolic syndrome and chronic heart failure from The Diagnostic and Treatment Centre, Cluj-Napoca were included into the study.

The homodynamic parameters expressed by ejection fraction, effort tolerance, and clinical symptomatology were improved in the patients treated with Atacand. This treatment efficiently controlled the 24 hour blood pressure, offering an increased cardiovascular protection with no effect on lipid and glucose metabolism.

**Keywords:** candesartan, heart failure, metabolic syndrome

**Rezumat:** S-a efectuat un studiu clinic pe 30 de pacienți cu insuficiență cardiacă cronică și sindrom metabolic, urmăriți în Centrul de Diagnostic și Tratament - Cabinet Cardiologie - Cluj - Napoca-pe o perioadă de 6 luni. Scopul acestui studiu a fost să evalueze efectul benefic al tratamentului cu Candesartan cilexetil (Atacand) în doze 16 mg-32mg, la pacienții cu insuficiență cardiacă cronică. Rezultatele obținute au fost în concordanță cu studiile experimentale și clinice efectuate cu sartani. Atacandul a îmbunătățit simptomele de insuficiență cardiacă, a ameliorat funcția sistolică (FE<sub>s</sub>) și funcția diastolică a ventricolului stâng, la pacienții studiați. El a controlat eficient și susținut tensiunea arterială timp de 24 de ore, oferind o protecție cardio-vasculară superioară. Atacandul nu afectează în sens negativ parametrii plasmei în ceea ce privește metabolismul lipidelor, metabolismul glucidic.

**Cuvinte cheie:** Candesartan, insuficiența cardiacă cronică, sindrom metabolic.

## INTRODUCTION

Heart failure is a clinical and physiopathologic issue directly involved in cardiovascular mortality and morbidity. Heart failure is recognised as a major public health problem in industrialised countries with ageing populations. Treatments for those with CHF depend on the severity of the condition and on many other factors. Because the medical outlook for those with severe CHF remains poor, medical researchers have thought to

develop new and better classes of drugs that address some of the worst effects of CHF.

The aim of the study was to investigate the effects of 16-32 mg Candesartan Cilexil (Atacand) an angiotensin receptor blocker in patients with heart failure.

## MATERIAL AND METHOD

In order to investigate the effects of Candesartan Cilexil (Atacand) therapy on cardiac performance in patients with Congestive Heart Failure, a prospective study has been designed. Thirty patients with an average age of 70 years old, with metabolic syndrome and chronic heart failure from The Diagnostic and Treatment Centre of Cluj-Napoca were included into the study with a follow up of 6 months (January 2006 – June 2007).

A detailed case history and clinical examination findings were recorded along with the baseline symptoms. Laboratory examinations, electrocardiograph monitoring, 2-dimensional echocardiogram, data considering previous medications and the evolution of the patient over the 6 months were all recorded. The diagnosis of congestive heart failure (CHF) was clinical, ethological and echocardiographic. The clinical diagnosis of CHF was made considering the Framingham Criteria for Congestive Heart Failure which requires the simultaneous presence of at least 2 major criteria or 1 major criterion in conjunction with 2 minor criteria. The echocardiographic diagnosis consisted of a decreased ejection fraction and a diastolic dysfunction. The diastolic dysfunction was defined by the following Doppler echographic parameters: E/A <1; TRIV>100ms, DT>240ms, venous pulmonary flow S/D<1.

Patients with congestive heart failure in NYHA functional class II-IV were included in the research.

Patients were divided into 2 different groups, taking into account the left ventricle ejection fraction.

Group A – 18 patients (60%) with CHF and an ejection fraction less than 40% (EF<40%). Group B – 12 patients (40%) with CHF and EF>40%. Patients with collagenosis, haematological and neoplastic disease were excluded from the study.

All patients received Candesartan Cilexil with an initial dose of 4 mg, then 8 mg, once a day with an increase of the dose by personal tolerance to a maximal dose of 32

## CLINICAL ASPECTS

mg/day. All patients gave a full written consent to participate in the study.

The metabolic status of the patients was evaluated by symptoms and by clinical examination for detecting the possible comorbidities and complications, laboratory examinations for glucides, lipids, hydroelectrolitic and vitamin balance

Regarding this study we evaluated the effects of Candesartan Cilexil on

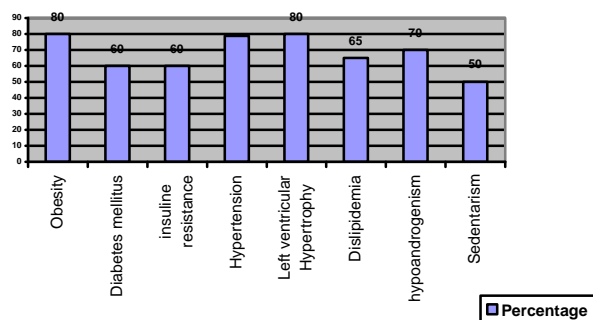
- clinical symptoms of congestive heart failure (CHF)
- in controlling the blood pressure
- the systolic and diastolic left ventricle function in patients with CHF
- lipids and glucides metabolism
- the hospitalization rates of the patients with CHF

### RESULTS

A comparative study of the risk factors was made in the study population.

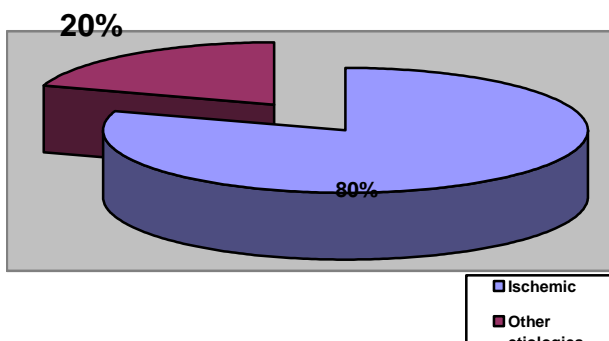
We found an increase prevalence of hypertension, obesity, hypoandrogenism diabetes mellitus, dyslipidemia, sedentarism as seen in fig. 1.

**Fig.1 Prevalence of risk factors in the study population**

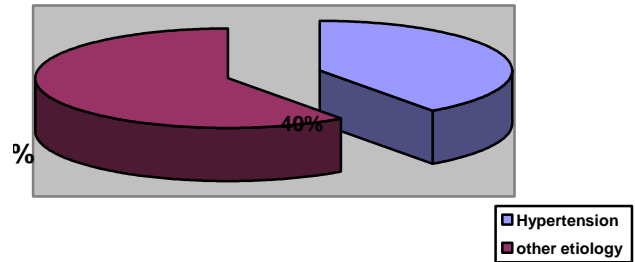


The prevalence of diabetes mellitus was increased in patients from group A (50%) compared to group B (30%). The association of diabetes mellitus represented an increased risk factor for both groups. In the study population, the ischemic etiology was increased in group A and hypertension was found to be increased in group B as seen in fig. 2 and fig. 3.

**Fig.2. Group A - CHF etiology**

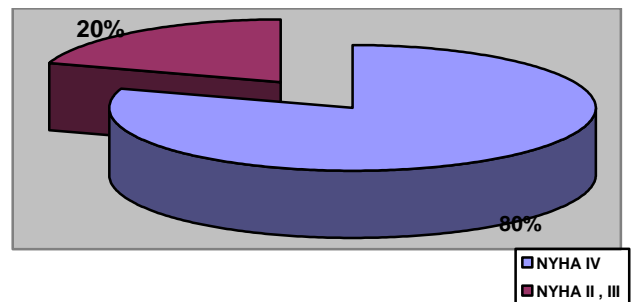


**Fig.3. Group B – congestive heart failure etiology.**

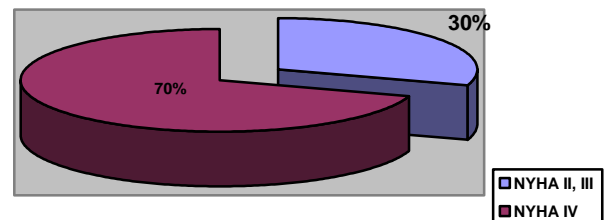


The severity of NYHA functional class was significantly influenced by the ischemic etiology and by the association of diabetes mellitus, an increased number of patients being in NYHA functional class IV from group A than from group B as seen in fig.4 and fig.5

**Fig.4 The NYHA functional class in group A at the beginning of the treatment**

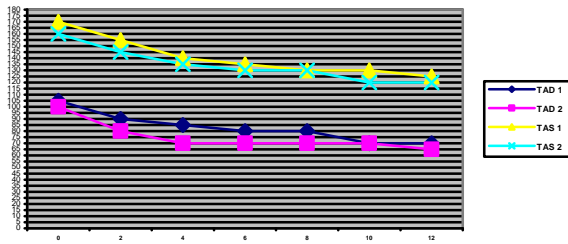


**Fig.5 The NYHA functional class in group B at the beginning of the treatment**



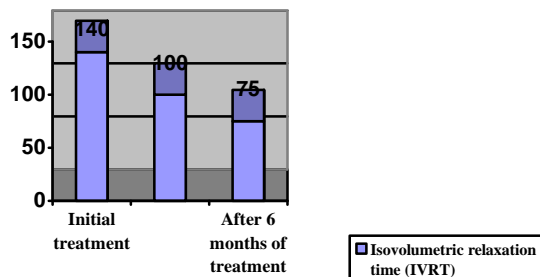
We followed the clinical parameters evolution during the treatment at 3 and 6 months. The CHF symptoms ameliorated first after 3 months of treatment and all the symptoms disappeared after 6 months of treatment. The heart rate and blood pressure were efficiently controlled after 3 months of Atacand treatment as seen in fig.6

**Fig.6 The blood pressure control after Atacand treatment**



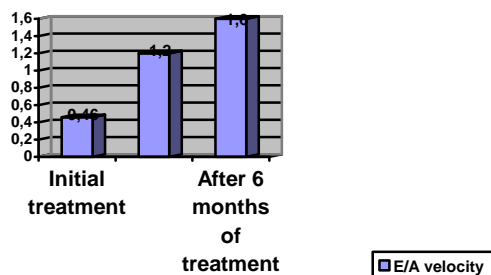
By Angiotensin receptor blockers treatment of the heart performance was improved by the increased ejection fraction. After 3 months of Atacand treatment an significant increase in ejection fraction was seen in patients from group B (40%) as against those from group A (30%). After 6 months of Atacand treatment the ejection fraction increased more in patients from group B (in 60%) than in the patients from group A (40%). Atacand treatment significantly decreased the isovolumetric relaxation time (IVRT) from 140ms to 75 ms after 6 months of treatment in the treated patients as seen in fig.7.

**Fig.7 . Evolution of isovolumetric relaxation time after Atacand treatment**



After 6 months of Atacand treatment, there was an increase of the E/A rate, with better diastolic filling patterns of the left ventricle in the study population as seen in fig.8.

**Fig.8. E/A velocities rate evolution after Atacand treatment**



This study showed that diastolic dysfunction represented by altered left ventricular relaxation ameliorated after 6 months of treatment with Atacand. After 6 months of Atacand treatment, the rate of hospitalization decreased at

5%. The Atacand treatment was initiated at a low dose with a progressive increase of the dose, with a maximum dose of 32 mg/day. The most common side effect was transitory headache.

## DISCUSSIONS

The results of the present study, as those found in other studies, like (Charm Alternative, Charm Added, Charm Preserved) (6,7) and these results demonstrated that Candeasartan administration in congestive heart failure ameliorated clinical symptoms, increased the effort tolerance, ameliorated the hemodynamic parameters (EF, left ventricle telediastolic volume).

The identification of the risk factors represents the main therapeutical target in the prevention of cardiovascular disease.

The data about the evidence of diabetes mellitus in patients with CHF, especially by ischemic etiology, were the same as those from literature (8). The presence of diabetes mellitus represents a severity element during the evolution of CHF. The glucose metabolism abnormalities were associated with systolic and diastolic dysfunction of the left ventricle and with ventricular remodelling.

The diabetes mellitus and obesity are the risk factors for CHF, associated with insulin resistance. Insulin resistance and hypertension as its consequence are included into the metabolic syndrome, a pathological entity with an increased cardiovascular risk.

The association of Atacand treatment to the conventional therapy for CHF significantly decreased the rate of hospitalization for patients with CHF (1).

The positive impact of the treatment with Atacand on patients already on medication for CHF suggested a special protection over cardiovascular events, by blocking the rennin angiotensine system.

## CONCLUSIONS

- Sartans realise a supplementary benefice in the treatment and prognosis of congestive heart failure
- The treatment with Sartans in congestive heart failure has to be done under close surveillance for haemodynamic status of the patients.
- The main effect of Atacand treatment in Congestive heart failure and metabolic syndrome is the improvement in the quality of patients' life.

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