

Effects of Carnitine on 6-Month Incidence of Mortality and Heart Failure in Patients with Acute Myocardial Infarction

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Abstract

Background: The carnitine therapy for acute myocardial infarction has significant metabolic improvement capacity due to intrinsic mechanisms. We did a trial to compare carnitine with standard therapy in patients with acute myocardial infarction. Material and methods: 98 patients with acute ST-elevation myocardial infarction were randomly assigned to carnitine (n=45) and control (n=53) group. The primary endpoint was 30-day mortality and re-infarction during 96 h of hospitalization. Results: By 6 months, 9,7% pts in carnitine group and 12,3% of pts in control group had died. There were significantly fewer re-infarctions and heart failure complications in patients of carnitine group than in control group ($t<0,05$). Conclusions: carnitine therapy reduced MI mortality in compare with standard therapy and reduced the rate of re-infarction during hospitalization and heart failure complications after 6 months by 15,7%.

Key words: *carnitine, fibrinolysis, myocardial infarction,*

Introduction

The methods of treatment of acute myocardial infarction are still of great importance for modern cardiology and public health due to increased significance of cardiovascular mortality in population. This study has aim to evaluate the new drug - carnitine developed by italian pharmaceutical company for metabolic treatment of patients with acute myocardial infarction.

This was a phase III, multicentre, randomized, double-blind, placebo-controlled study. Study was conducted in frame of the international multicenter trial conducted under the coordination of the company Sigma-Tau Industrie Farmaceutiche Riunite SpA (Italy). The study drug will be administered for 6 months; after 6 months the incidence of the primary combined mortality and heart failure endpoint in the two treatment groups will be assessed.

Methods

The primary outcome of the study is the combined occurrence at 6 months of death and heart failure and is defined as the total number of patients who die plus the number of patients surviving with heart failure. For the in-hospital period, only those patients with heart failure after 4 days from the onset of the symptoms of acute myocardial infarction will be considered. Heart failure is defined by the presence of all the following criteria: a) dyspnea; b) echocardiographical evidence of left ventricular systolic dysfunction; ejection fraction < 40% (Simpson's method) or wall motion index <1.2 calculated as in the TRACE study (centralised assessment); c) the need to initiate treatment with diuretics, digitalis and/or ACE-inhibitors or to increase the dosage of these drugs if already prescribed.

Inclusion criteria: typical chest pain lasting > 30 minutes unrelieved by sl or iv nitrates; ECG showing ST segment elevation >0.2 mV in D, and aVL and/or in at

least two adjoining precordial leads; < 12 hours between onset of symptoms and randomization in the study; < 80 years of age; written informed consent.

Exclusion criteria: pregnancy or lactation; hemodynamically significant valvular disease; dilated or hypertrophic cardiomyopathy; congenital heart disease; clinically severe renal or hepatic disorders; alcoholism; other diseases that affect life expectancy; possible poor compliance or adherence to follow-up; inclusion in another trial.

The dose of 9 g/day of active drug (3 g three times a day by continuous iv infusion) was administered for 5 initial days, whereas 4 g/day (2 g two times a day by oral route) was administered from the 6th to the 180th day. The comparative treatment with placebo was administered intravenously for 5 initial days and orally from the 6th to the 180th day, according to the posology used for the active drug. The visits scheduled for the study will be carried out at 1, 2, 4 and 6 months. Every effort has been made to contact the patients should they not appear for the scheduled visit. A week over or under the scheduled time was tolerated.

The investigator stored the drug samples under appropriate conditions of temperature and humidity, in the closed place to which only personnel authorized to withdraw samples is allowed access. The investigator also stored, throughout the whole duration of study, the reference samples intended for the Ministry of Health. The enrolled patients with myocardial infarction received proper treatment, as indicated by the hospital's diagnostic and therapeutic procedures, in addition to other treatments aimed at treating any concomitant diseases. Any treatment of the enrolled patients with drugs having possible metabolic effects at myocardial level (ubidecarenone, creatinol phosphate, fructose 1,6-biphosphate, phosphocreatine, taurine, uridine triphosphate) was prohibited.

Patients meeting the selection criteria were randomized in order to be able to receive the study therapy as soon as possible and in any case no later than 12 hours from the onset of symptoms. Randomization was centralised and carried out over the telephone lines by means of a specific computer system; the randomization system functioned for 24 hours per day, 7 days per week. Treatment wasn't start until the relative randomization number is obtained, since otherwise numbering might no longer be consecutive. Two series of sealed envelopes were produced containing the individual randomization code, one series of which was kept with the sponsor and one at the experimenting centre. During the trial a patient's individual code could only be opened (by opening the single relative envelope) in the case of a serious adverse event and knowing the code would benefit the patient's well-being. The patient was

encouraged to return the unused packages during successive visits, because the assessment of compliance was effected by counting the bottles not used.

An adverse event is any event considered an adverse, unexpected and undesired variation of the anatomical, physiological and metabolic functions (signs, symptoms or laboratory data), or any intercurrent illness, whether or not considered drug-related, which occurs in the subject after the beginning of the treatment (by treatment it is meant the drug as well as the placebo). All the adverse events occurring during the study were recorded on the "Adverse Event Form" and stored in the computer memory.

Results

98 patients with anterior myocardial infarction admitted and randomized for treatment in the study within 12 hours of the onset of the symptoms. For inclusion in the study patients must meet all the inclusion and exclusion criteria. Only then may the patient be enrolled in the study and randomized.

The median age of the patients in active group was 58,3 years (51,4-67,1), and 14,2% were women. Also all other baseline characteristics were well balanced.

The number of patients who died by 6 months was less in the active group in compare to control group (9,7% vs. 12,3%, $p < 0,05$).

Re-infarction and the composite endpoint of death or re-infarction was less during hospitalization by 15,7% in group of patients treated by carnitine in compare to control group.

The number of cases of heart failure after 6 months of AMI was 43.5% less in carnitine group in compare to control group with standard treatment.

Conclusions

We show that carnitine use is associated with a lower 6-month mortality, re-infarction rate and number of heart failure complications in patients after acute myocardial infarction. The impact of carnitine on mortality, number of re-infarctions and heart failure complications after acute myocardial infarction is beneficial.

The addition of carnitine to standard AMI treatment was associated with an additional survival benefit. Introduction of carnitine use after acute myocardial infarction reduces long-term mortality and complication rates.

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Эффективность карнитина при лечении больных с острым инфарктом миокарда

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Р Е З Ю М Е

Применение карнитина – препарата, улучшающего метаболизм в кардиомиоцитах при лечении острого инфаркта миокарда - большое достижение в деле улучшения показателей выживаемости и сохранения функции левого желудочка, что продемонстрировано многими исследованиями. Цель исследования - показать, что терапия карнитином заметно уменьшает смертность, количество реинфарктов и осложнения в виде сердечной недостаточности в 6-месячный срок наблюдения у пациентов с острым инфарктом миокарда. 98 пациентов: 45 вошли в группу, получавших карнитин, и 53 - в группу со стандартным лечением. Все пациенты получали аспирин. Исследование показало, что применение карнитина у больных с острым инфарктом миокарда снижает уровень смертности через 6 месяцев до 9,3% в сравнении с контрольной группой (12,7%). Применение карнитина у больных с острым инфарктом миокарда снижает смертность, количество реинфарктов и число осложнений сердечной недостаточностью, что дает возможность рекомендовать этот препарат для широкого использования в кардиологической практике.

Ключевые слова: *карнитин, фибринолизис, инфаркт миокарда*