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CLINICAL STUDY

THE INFLUENCE OF L-CARNITINE SUPPLEMENTATION ON HEMATOCRIT AND HEMOGLOBIN LEVELS IN PATIENTS WITH END STAGE RENAL FAILURE ON CAPD

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ABSTRACT

The influence of L-carnitine supplementation on hematocrit (Hct) and hemoglobin (Hb) levels, in patients suffering from end stage renal disease (ESRD) on maintenance hemodialysis, are well known from several studies. The data concerning the serum levels of carnitine, in patients with ESRD on continuous ambulatory peritoneal dialysis (CAPD) are contradictory, but most of them support that they are rather normal. In this study the effect of L-carnitine supplementation on Hct, and Hb levels were investigated in patients suffering from ESRD on CAPD. In the study 12 patients were included (5 F, 7 M), aged from 39 to 92 years old (median 65.5 years), who were on CAPD for more than 6 months (from 6 to 15 months, mean $\pm$ SD $= 8.6 \pm 3.6$), with normal serum ferrum and ferritin levels at the beginning of the study. Two grams of L-carnitine/day per os (Superamin, Vianex Hellas), were administered in all the patients and the serum ferrum levels were tried to be kept stable, by exogenous ferrum administration, during the study period. If the Hct levels were more than 36% per month the erythropoietin (rHuEpo)

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dose of the patient was decreased monthly at the half dose/week. The changes of Hct, Hb, ferrum and ferritin levels, as well as the Indice de Rigidite (IR) of the erythrocytes were recorded, before and after the first, second and third month of the study period. Finally, the rHuEpo dose/patient was registered monthly before and during the study. During the observations, Hct (35.4 ± 3.3 vs. 38.1 ± 3.4, ANOVA, $p < 0.03$) and Hb levels (11.0 ± 1.1 vs. 11.9 ± 1, ANOVA, $p < 0.01$), were significantly increased. On the other hand, rHuEpo dose necessity/patient/week was decreased significantly (3833 ± 3326 vs. 1292 ± 1712, ANOVA, $p < 0.01$), in order to succeed the target Hct level. Furthermore, red blood cells IR also appeared to have a significant decrease (16.6 ± 7.4 vs. 13.0 ± 3.9, paired *t*-test, $p < 0.03$). Finally, the ferrum and ferritin levels were stable during the study period. It was concluded, that in patients on, CAPD the per os L-carnitine supplementation decreased, the red blood cells IR which contributes to the: (a) Increase of Hct and Hb levels and (b) decrease of the patients rHuEpo dose/week.

Key Words: L-Carnitine; Hematocrit; CAPD; Recombinant erythropoietin; Renal failure

INTRODUCTION

Anemia is a serious problem of patients suffering from end stage renal disease (ESRD), on hemodialysis or peritoneal dialysis.[1] During the late years the exogenous administration of human recombinant erythropoietin (rHuEpo) improved significantly the hematocrit levels of these patients,[2] nevertheless, some of them are not good responders to this therapy and others need very high doses of rHuEpo.[3] The efficacy of L-carnitine supplementation on hematocrit levels on hemodialysis patients is well known,[4] as well as one of the mechanisms involved in this action.[5] But which is the efficacy of L-carnitine supplementation in patients on continuous ambulatory peritoneal dialysis (CAPD)? The data about the carnitine levels in blood or tissues of these patients are very conflict.[6]

PATIENTS AND METHODS

Patients

Twelve patients (5 F, 7 M), were included in this study, aged from 39 to 92 years old (median 65.5 years) with ESRD, who were on CAPD for more than 6 months (from 6 to 15 months, mean $\pm$ SD $= 8.6 \pm 3.6$). The primary renal diseases of the patients were diabetic nephropathy in 6, glomerulonephritis in 3, hypertensive glomerulosclerosis in 1, chronic pyelonephritis in 1 and unknown nephropathy in 1. Measurements were

taken about the blood hematocrit (Hct) and hemoglobin (Hb) levels, the serum ferrum and ferritin levels and the deformability of red blood cells (RBCs) by Indice de Regidity (IR). Finally, the rHuEpo doses/patient/week at the study period was registered.

To have stable serum ferrum levels in each patient was given intravenously ferrum in dose that depended on serum ferritin levels, after estimation of serum ferrum and ferritin each month. If Hct was more than the target level (36%) the patient's rHuEpo dose was decreased monthly at half/week. All the patients were given 2 g L-carnitine/day per os during the study period.

Methods

The filtration measurements were made by using an initial flow method[7] and the filtration device is called Hemorheometer. The main section of the apparatus is a central capillary, 6 cm long and 2.5 mm in diameter, glass tube, surrounded by water circulating from a thermostat. The circulating water kept the temperature of the suspension in the capillary during the experiment constant (37°C). The lower section of the capillary is conical, under which a Nuclepore filter (diameter 13 mm; pore diameter 5 μm) is situated.

The central capillary is filled by either an erythrocyte suspension or by the buffer. A lower plastic block holds the filter under which a positive pressure of about 10 cm H_2O is applied so the flow, due to the hydrostatic pressure is prevented. When this positive pressure is let off the flow of the suspension initiates. Two level detectors, situated at the top part of the capillary with a distance of 9 mm between them, activate and then stop an electronic chronometer when the meniscus of the liquid passes in front of them, during the filtration procedure.

The time lapse as determined by the detectors is proportional to the flow rate, which depends on the global fluidity of the liquid being filtered. Between the time lapse of the suspension t_s and the time lapse of the buffer (t_b) the following relationship is valid: $IR = (t_s - t_b)/t_b \times 100/H$, where H is the Hct.

Each sample was processed for 2–3 h beginning immediately after drawing, until the rigidity index (IR) was measured. The final RBC suspension was prepared just before the filtration took place to avoid any morphological changes. For each sample from the patients a control sample from a normal donor was measured.

The Hct and Hb levels were measured by automatic hematological analyzer (autoanalyzer Sysmex, Japan), the serum ferrum levels by automatic analyzer (autoanalyzer Au 560 Olympus, Japan), as well as the levels of serum ferritin (autoanalyzer Immulite, USA). The statistical analysis was

done by Analysis of Variance (ANOVA) and paired *t*-test. Differences less than 0.05 were considered as significant.

RESULTS

At the end of the study a significant increase of the Hct (35.4 ± 3.3 vs. 38.1 ± 3.4, ANOVA, $p < 0.03$) and Hb levels (11.0 ± 1.1 vs. 11.9 ± 1, ANOVA, $p < 0.01$) was found. The rHuEpo dose requirements/patient/week decreased significantly (3833 ± 3326 vs. 1292 ± 1712, ANOVA, $p < 0.01$), in order to succeed the target Hct level. The IR of the RBCs was also significantly decreased (16.6 ± 7.4 vs. 13.0 ± 3.9, paired *t*-test, $p < 0.03$). Finally, the ferrum serum levels were stable and normal during the study period (80 ± 81 vs. 76.8 ± 23.1, paired *t*-test, $p =$ NS), as well as the ferritin levels (370 ± 297 vs. 353 ± 203, paired *t*-test, $p =$ NS).

DISCUSSION

It is well known that carnitine comes from food and it is being synthesized by the kidneys.[8] It has small molecular weight and it can be dialyzed by the membrane of hemodialysis filter. This means that carnitine is continuously lost with a final result the diminishing of blood or tissue levels.[9] Nevertheless, the data about the carnitine levels in patients with ESRD on hemodialysis are conflict.[6,10] The relationship between serum carnitine levels and the deformability of the RBCs has been recognized. Exogenous supplementation of L-carnitine can improve the deformability of the RBCs and their survival, therefore, by this mechanism the Hct levels can be increased.[5]

The deformability of the RBCs is a very important parameter, it can be checked by IR and it can influence the microcirculation as well as the oxygen transfer. Supposing that carnitine levels are low in patients on CAPD and having in mind that the Epo levels in these patients are low, it is clear that their Hct levels will be low.

The mechanism by which L-carnitine supplementation can improve the Hct levels is by a positive action on lipids of cell membrane, which can be stabilized. Grzegorzewska et al., found that the serum carnitine levels in 17 out of 23 CAPD patients, who were dialyzed for 11.1 ± 9.6 months were normal, but in 6 out of 23 who were dialyzed for 9.7 ± 4.1 months, the levels were found lower than normal (25.4 ± 5.7 μmol/L).[6] At the other hand, Labonia et al. noted that the L-carnitine supplementation in hemodialysis patients (1 g/hemodialysis session for 6 months), could help the movement of toxic acyl-residual elements, which can influence the erythropoiesis,[11] while others noted that L-carnitine can improve

the survival rate of RBCs.[12] Furthermore, Berard et al. found that the fragility of RBCs of 12 out of 18 hemodialyzed patients could be improved, after 4 months of L-carnitine supplementation.[13] These results are in agreement with ours in a previous study.[5] In the present study, besides the conflicting results of the literature about the serum and tissue carnitine levels, it was found that per os L-carnitine supplementation can improve the IR of the RBCs and the Hct levels of CAPD patients, although others do not agree.[14] This action of L-carnitine is very important if the cost effectiveness of anemia treatment of patients on CAPD is being considered, because there has being a huge decrement of rHuEpo requirements during the study period.

From this study it can be concluded that: (a) There are disturbances of deformability of the RBCs in patients on CAPD, which can be improved by exogenous supplementation of L-carnitine and (b) L-carnitine can improve significantly the Hct levels of these patients and it can decrease the requirements of rHuEpo/patient/week, hence, there is a huge decrement of the cost of hemodialysis treatment.

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