

L-carnitine fumarate, L-acetyl-carnitine and other components in male infertility: a pilot study of nutraceuticals on sperm motility

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Summary

The aim of this study was to evaluate any possible effect a combination of L-carnitine, fumarate, acetyl-L-carnitine, fructose, citric acid, selenium, co-enzyme Q10, vitamin C, zinc, folic acid and vitamin B12 (Proxceed[®]) on sperm motility in a group of patients with unexplained asthenozoospermia.

Thirty two patients received 1 sachet/day of Proxceed[®] for three months. Sperm parameters were studied before, during and after this treatment. Motility was also studied by the means of a computerized analysis (CASA system).

The results of this study indicate that Proxceed[®] is able to increase sperm motility, both in a quantitative and qualitative manner. We conclude that oral administration of Proxceed[®] may improve sperm quality, at least in patients with idiopathic asthenozoospermia.

Key words

L-carnitine • Male infertility • Sperm motility

Introduction

In spite of the progress in knowledge of the physiological mechanisms of spermatogenesis, of its endocrine stimulation and of intratesticular paracrine control, the possible therapies and applications resulting from this knowledge are still scarce. In fact, to date a therapeutic approach of oligoasthenozoospermia (OAT) based on an etiopathogenetic diagnosis is possible only in a small percentage of cases. This type of approach, which is obviously the most correct, has limitations partly due to not understanding fully the mechanisms at stake in determining infertility, especially as far as damage to sperm maturation is concerned, and partly due to the fact that often at the moment of diagnosis the *noxa patogena* is no longer evident nor identifiable and thus not resolvable. The OAT therapy is often based on attempts to correct the symptomatology of the seminal fluid.

Symptomatic treatment of idiopathic dyspermia is used both in cases where an etiological diagnosis is impossible and also in cases of permanent dyspermia after resolving the basic *noxa patogena*. The following are among the substances that have been used: L-carnitine

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and acetyl-carnitine, co-enzyme Q10, L-arginine, callicreine, pentoxifilline, phosphatidylcholine, vitamins (above all A., C and E) ¹ and glutathione ^{2 3}.

L-carnitine (LC) is a water-soluble molecule, present both in plasma and in the tissue where it can be found free-moving or bound to fatty acids in the membranes in the form of acylic derivatives.

Carnitine is an essential cofactor in the transfer of lipids into the mitochondrion where they are metabolized for energy in the beta-oxidation process. The role of carnitine in cellular metabolism is as such better known in the mitochondrions where the interaction between the metabolism of the fatty acids and the glucose is fundamental for the production of cellular energy. Moreover, the activity of carnitine has been proposed also for the antioxidising systems. Male germ cells have low levels of molecules and enzymes with antioxidising functions and present a particular structure of polyunsaturated fatty acids in the membrane. These fats are particularly susceptible to the lipoperoxidative phenomena associated with forms of OAT ⁴.

In the last few years, preparations based on dietary supplements, vitaminic complexes and nutritional principles have come to be used also in the treatment of infertility, following the latest indications of nutraceutics. By this term we mean the use of nutritional substances added to a normal diet in order to promote a healthy and active way of life. Nutraceutics research, of French origin, is based on the principle of nutritional synergy: "the wider the range of nutrients taken, the greater will be the assimilation and efficacy of these, while at the same time, lesser quantities will be needed of each specific nutrient". Recently in Italy a product called Proxeed NF® (Sigma Tau) has been commercialized, which is made up of the following: L-carnitine fumarate: 250 mg, acetyl-L-carnitine hydrochloride: 75 mg, fructose: 250 mg, citric acid: 50 mg, selenium: 50 µg, coenzyme Q10: 20 mg, vitamin C: 90 mg, zinc: 10 mg, folic acid: 200 µg and vitamin B12: 1.5 µg. The L-carnitine and the acetyl-L-carnitine participate in important metabolic processes involved in the production of energy and the upkeep of normal cellular functioning. Fructose and citric acid are essential for energetic metabolism. The coenzyme Q10 is a natural fat-soluble antioxidant which protects against lipidic peroxidation and oxidative damage to the DNA. Selenium is an essential component for cellular protection and for defence against the free radicals of oxygen. Zinc is a micro-element that is essential for cellular division and protection, as well as being a scavenger of the free radicals of oxygen. Vitamin C

has an antioxidising action and promotes the use of microelements such as zinc. Folic acid and vitamin B12 are essential elements for energetic metabolism and cellular division. The various components of this product taken singly show a positive action on the sperm parameters, particularly on the total and forward motility.

The aim of our work was to assess the efficacy of this important combination of components on the kinetic parameters of the spermatozoa in an open study.

Materials and Methods

We studied a group of 32 infertile patients, aged between 20-40 years with the following seminal characteristics: sperm concentration 10-60x10⁶/ml, total motility 5-40%, forward motility.

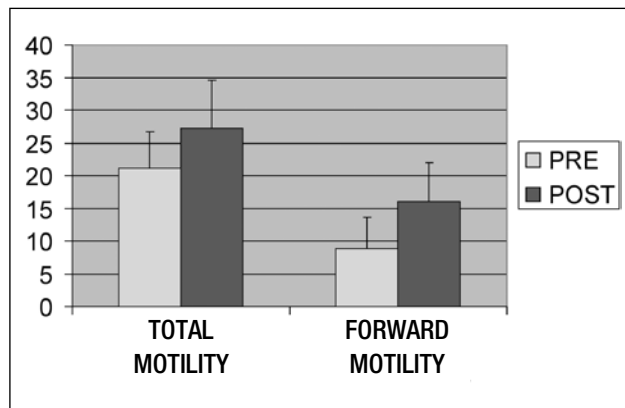
≤ 15% and atypical forms ≤ 90%. None of the patients presented antispermatozoa antibodies, systemic or endocrine illnesses, infections of the genital tract, mono or bilateral testicular hypotrophy, varicocele with testicular hypotrophy, cryptorchidism and mump orchitis in the pubescent phase, and none had undergone surgical operations in the genital area.

The patients were administered Proxeed NF® at a dose of 1 sachet/day for three months. The study included analysis of seminal fluid and sperm kinetics with the CASA system at baseline and after three months of therapy. Analysis of the seminal fluid was carried out according to WHO criteria (1999). By means of the CASA system the following kinetic parameters were assessed: mean curvilinear velocity, linearity, maximum width of lateral beats of the head (ALH – amplitude of lateral head) and frequency of beats (BCF – beat cross frequency). The mean and the standard deviation was calculated for all the seminal variables.

Results

The results of the analysis of the semen showed a statistically significant increase in total and forward motility after three months of treatment; in fact the average total motility before and after treatment was 21.2 ± 5.6 % and 27.2 ± 7.4% respectively, while the forward motility was 8.9 ± 4.7% before and 16.1 ± 5.9% after therapy (Fig. 1). As far as the computerized study of sperm kinetics is concerned, the data show a statistically significant increase in mean velocity and linearity of the spermatozoa; also the ALH and BCF values showed an increase, although these last did not reach statistical significance.

Figure 1. Means and SD of total and forward motility pre and post treatment.



Discussion

Nutraceuticals is a new term which derives from the combination of the words 'nutrition' and 'pharmaceuticals'; its principal aim is to study the combined nutrient and pharmaceutical properties of foods that have beneficial effects on human health. It has been developing over the last years as a complementary sector to the field of pharmaceuticals, as an adjuvant in the maintenance of physiological homeostasis and as prevention of cellular stress from free radicals. It is worthy of note that nutraceutical supplements must be based on actual necessity, just as pharmacological ones, in order to not risk causing damage rather than benefits to the patient. As such, it is fundamental to increase clinical studies and trials in order to identify the actual needs of each single individual and consequently formulate the most appropriate nutraceutical response. Among the substances in this group of nutraceuticals are included the following: L-carnitine, Acetyl-L-carnitine, Fructose, Citric acid, Selenium, Coenzyme Q10, Vitamin C, Zinc, Folic acid, Vitamin B12. These have been used in various clinical trials, either singly or in combination, in the therapy of alteration of seminal parameters, especially that of sperm motility. Our group carried out two controlled studies on the use of carnitine and its metabolites in the treatment of selected forms of male infertility. The first was a double-blind crossover trial, using carnitine and placebo. One hundred infertile patients were selected aged between 20-40 years with the following seminal characteristics: sperm concentration 10-20x10⁶/ml, total motility 10-30%, forward motility <15% and atypical forms <70%. The patients were administered L-carnitine at doses of 2 gr/die or placebo. The study was organized in phases of two months of run-in, two months of therapy/placebo, a further two months of wash-out and two months of

therapy/placebo. A statistically significant increase in concentration values and in total and forward motility was found in patients who were administered therapy compared to those treated with placebo. Improvement of sperm motility was more marked in those patients who presented a lower concentration of normo-kinetic spermatozoa before therapy (number of spermatozoa with total motility <10x10⁶ and forward motility <5x10⁶ / ejaculate) ⁵.

The second was a double-blind randomized study the aim of which was to determine the efficacy of combined therapy of L-carnitine and L-acetyl carnitine. Sixty infertile patients aged between 20-40 years were selected according to the following criteria: sperm concentration 10-40 x 10⁶/ml, forward motility <15%, total motility 10-40%, atypical forms < 80%. The patients were administered a combined therapy of L-carnitine (2g/die) and L-acetyl carnitine (1g/die) or placebo. The study was organized in phases of 2 months of run-in, 6 months of therapy or placebo followed by 2 months of follow-up. Also in this study the most significant increase of forward motility was observed in patients with initially lower kinetic values (number of spermatozoa with total motility < 5x10⁶ and forwards motility < 4x10⁶/ejaculate) ⁶.

Other studies have demonstrated the efficacy of this therapy in patients with OAT associated with varicocele ⁷ and in patients with prostate-vesicular-epididymitis ⁸.

The data published with reference to controlled studies of efficacy show that treatment with carnitine and its derivatives is able to improve sperm motility, especially in groups of patients with more marked asthenozoospermia.

The current study has confirmed the positive effect of these substances on sperm motility; despite the limited number of patients, a statistically significant increase in sperm motility (both total and forward) was found after therapy with Proxeed NF[®], associated with a statistically significant increase in the kinetic parameters, velocity and linearity, assessed with the CASA system. These results appear particularly significant and interesting in the light of the fact that our group of patients was characterised by an idiopathic asthenozoospermia.

In conclusion, this study has demonstrated a clear positive effect of the oral administration of Proxeed NF[®] on the kinetics of the spermatozoon in a selected group of subjects affected with asthenozoospermia *sine causa*. Thus, we propose this type of therapeutic approach as a possible technique for treating selected forms of male infertility, also

in view of the serious lack of treatments that are efficacious on the mechanisms of activation and maintenance of sperm kinetic parameters. This therapy could also be indicated in the preparation of the male partner in couples following intrauterine insemination programmes or other assisted fertilization techniques.

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