Efficacy of myo-inositol in the clinical management of patients with asthenozoospermia

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Abstract. – OBJECTIVE: The aim of this study was to analyze the effect of myo-inositol in combination with minerals and vitamin on sperm motility in patients affected by asthenozoospermia as index of Bulgarian population.

PATIENTS AND METHODS: One-hundred-nine men aged between 18 and 50 years with reduced sperm motility identified by routine semen analysis were enrolled in this study. After excluding any urological problems, three months of treatment with a supplementation based on myo-inositol and other minerals and vitamins (Andrositol, MLD trading, Bulgaria) was prescribed. The sperm motility was evaluated by statistical analysis.

RESULTS: A significant improvement in sperm motility was reported in 85.32% of the patients. Furthermore, the average motility was improved from 20.31% (SD ± 8.5) to 27.98 (SD ± 9.69) after the treatment. In particular, 38 of these patients restored a normal sperm motility (34.86% of the patients) while 14 patients (12.84%) didn't show any beneficial effect and, even if any side effects were reported, 2 patients (1.84%) showed a worsened the motility.

CONCLUSIONS: A treatment with Andrositol significantly improved sperm motility, increasing the likelihood of achieving a spontaneous pregnancy.

Key Words:
Myo-inositol, Asthenozoospermia, Sperm motility.

Introduction

According to the World Health Organization (WHO), the incidence of infertile couples is relatively high with a range from 15% to 20% in developed countries. According to the World Health Organization, the disorders in spermatogenesis in male infertility occur in almost 50% of all the cases[1]. In recent decades there has been an unexplained reduction, not only in sperm quality and quantity, but also in the volume of the ejaculate. This evidence allows to speculate that the number of male infertility factors will keep increasing in the future and this issue will become more significant[2].

An important impact of male infertility caused by environmental factors such as bad habits (alcohol and smoking), body overload and mainly the reluctance of men to conduct prevention is widely reported[3].

A reduced fertility is often related to a lower sperm motility. Over the recent years, the percentage of motile sperms in the ejaculate is constantly reducing; indeed, the latest edition of WHO indicated a percentage of sperms progressive motility less than 32% as a parameter of reduced chance of getting pregnant spontaneously[1].

The etiopathogenesis of male infertility is extremely complex, and the factors and processes causing these disorders in the reproduction are different. A common cause of reduced sperms motility seems to be related to the toxic action of reactive oxygen species (ROS)[4]. This is the reason why modern biology has been highly focused on studying the molecular mechanisms related to stress response in fertility.

The presence of ROS in the semen is an etiological factor of male infertility[5]. Pathological effects of free radicals in male reproductive tract are associated with DNA fragmentation, lipid peroxidation, and apoptosis, and these lead to reduced fertility and miscarriages[6]. Due to this evidence, antioxidant species were introduced in the management of male infertility. Between these molecules, Selenium and L-Arginine had shown a strong impact in contrasting ROS generation and restoring the oxidative status of the seminal environment[7-10].

Myo-inositol (MI) is an isomer of the inositol family. In nature are present 9 isomers of this sugar-like and MI represents the most abundant one. It plays a key role in more than one cellular pathways as FSH, insulin and TSH second intracellular messenger[11]. It has been also dem-

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onstrated an important effect of MI in improving semen parameters such as motility, morphology, and quality, both *in vitro* and *in vivo*[11-16]. From the reported studies, the effect of this isomer seems to be related to an improvement in the membrane potential of spermatozoa's mitochondria and in the reduction of the semen amorphous material that frequently impairs the male fertility.

Based on this evidence, recent scientific researches have been focused on the clinical use of MI in the management of male infertility caused by semen alterations.

The aim of this study was to investigate the effect of MI and other nutrients on sperm parameters in patients affected by asthenozoospermia.

Patients and Methods

In this prospective longitudinal study, 109 patients with asthenozoospermia were enrolled. All the participants signed an informed consent form. A routine semen analysis was used to establish a reduced sperm motility, which was the inclusion criteria of the trial in object. Semen samples were collected via masturbation after 48 hours and up to 72 hours of sexual abstinence. Samples were subjected to complete liquefaction at 37°C for 20 minutes. The sperms number, motility, and morphology were then assessed. Patients with established asthenozoospermia were directed to an urologist in order to exclude the presence of any urological problems. Other exclusion criteria were the presence of acute and chronic infections and alcohol intake.

Assessment of Motility

The sperm motility rate was carried out in two replications via a wet preparation according to the latest WHO recommendations, 2010.

To prepare the wet preparation - 10-µl semen were spotted and covered with 22 × 22 mm coverslips, and all spermatozoa visible in the field were then assessed.

Semen parameters were evaluated before (T0) and after a 3 months-treatment (T1) with a dietary supplement based on: 1 g of myo-inositol, 30 mg of L-carnitine, L-arginine and Vitamin E, 55 µg of selenium, and 200 µg of folic acid (Andrositol, MLD Trading, Bulgaria), taken twice a day.

The average from the counting was calculated and the results reported. When the difference between the two counting was very large, a new preparation was prepared and recounted.

The control medical examinations of the sperm were made through the routine semen analysis described above.

Statistical Analysis

The results are presented as mean ± standard deviation (SD). The difference in sperm motility between before and after treatment were statistically analyzed through the Student's paired *t*-test. The statistical data was performed by software package IBM SPSS Statistics 20. A *p*-value of less than 0.05 was considered as significant.

Results

The semen of 109 men, aged between 18 and 50 years, affected by asthenozoospermia was analyzed. Sperm motility was traced before and after 3 months of treatment with Andrositol (MLD trading, Bulgaria). The distribution of both samples was normal, and a statistical dependence between the two groups was found.

The percentage of average motility before the treatment with Andrositol was 20.31% (SD ± 8.5) while after a percentage of 27.98 (SD ± 9.69) was recognized after the treatment (*p*-value < 0.05) (Table I).

This improvement confirmed the following results where the 50.46% (55 patients) of the cohort showed an improvement in motility after the treatment and, in particular, the 34.86% (38 patients) reported semen motility parameters comparable with the normal ones. On the other hand, 14 patients didn't show a response to the treatment (12.84%), while 2 patients showed reduced motility after treatment, making 1.84% of the sample (Table II). No side effects were reported during the treatment.

Discussion

Some authors reported an improvement of semen quality after 3 months of supplementation with MI in associations with antioxidant

Table I. Average sperm motility rate before and after the treatment.

T0	T1	*p*-value
20.31 SD ± 8.5	27.98 SD ± 9.69	< 0.05

Table II. Patients segmentation based on the semen motility outcome.

	No. patient	%
No. of patients with restored normozoospermia	38	34.86
No. of patients with improved motility	55	50.46
No. of patients with no response to the treatment	14	12.84
No. of patients with worsened motility	2	1.84
Tot patients	**109**	**100**

and other nutrients, in patients affected by oligoasthenozoospermia[17]. MI seems to play an important role in the maturation of sperms during the migration from the epididymis. In fact, MI shows a gradient of concentration, most abundant in the seminal plasma increasing along epididymis and deferent ducts[18]. Furthermore, a low concentration of MI in this district was associated with a reduced sperms production. Recent studies showed MI playing a crucial role in spermatogenesis and spermatozoa migration through the testis compartments. In particular, Baht and Eisenbach reported the involvement of MI in spermatozoa chemotaxis and thermotaxis due to the activation of phospholipase C (PLC). In particular, this process seems to induce a higher production of inositol 3 phosphates (IP3) at sperm mitochondrial level improving calcium uptake and consequently sperm motility[14].

Furthermore, MI improves properly the quality of the semen. Indeed, it improves the spermatozoa motility ameliorating the mitochondrial potential membrane and improving the morphology of the mitochondrial membrane and their volume. This is easily observable in a better morphology of spermatozoa sheath.

A low quality semen seems to be strictly related to the presence of amorphous material in the semen and, on this regards, MI is able to remove it, reducing semen viscosity and consequently improving the chances to obtain a spontaneous pregnancy[19].

The advantages of MI are also in the metabolic and hormonal balance of the patients regulating the action of several hormones such as FSH, insulin, and TSH[15].

A relevant number of authors agree that L-carnitine can increase the likelihood of spontaneous pregnancy increasing idiopathic oligoasthenozoospermia[20,21]. Furthermore, L-carnitine plays an important antioxidant role in the cellular energy metabolism, including at the testis and epididymis level, improving the quality and motility of sperm.

Some authors demonstrated an involvement of folic acid and zinc in the characteristics of seminal fluid[22]. According to them, a dosage of 5 mg/day of folic acid and 66 mg/day of zinc sulfate show an improvement in number and motility of sperm. The relationship between genetically determined defects in folate metabolism and conditions of subfertility in men were well established. Elevated levels of homocysteine were retrieved in patients with oligozoospermia and/or asthenozoospermia, which directly worsen spermatogenesis.

The effect of antioxidants on sperm was widely reported in the literature[22,23].

Selenium antioxidant activity, mediated by several selenoproteins, is involved in crucial physiological pathways. In particular, the phospholipid hydroperoxide glutathione peroxidase (PHGx) is crucial for male fertility preserving from the strong oxidative stress due to the numerous and rapid divisions that characterize the germ cells.

On the other hand, selenium is a necessary component of the structural integrity of the sperms. In fact, natural levels of selenium are related to normal motility and sperm count[7].

The combination of selenium (225 mg/day) and vitamin E (400 mg/day) results in a reduction of oxidative stress reflected by spectrophotometric assessment of malondialdehyde after 3 months of treatment. Vitamin E is localized in the cell membrane, forming a protective layer against free radicals and reducing the levels of malondialdehyde, it improves sperms motility. Also, the addition of selenium increases the efficacy of vitamin E[23].

In this study was confirmed that a dietary supplementation of MI, L-carnitine, L-arginine, vitamin E, selenium and folic acid can improve the sperm motility with the absence of side effect and that 34.86% of the treated patients restore a motility comparable with normosperm parameters.

Conclusions

The results show an improvement of sperm motility in patients affected by asthenozoospermia, and it could be considered a safety approach to manage male idiopatic infertility. Anyway, further analyses are needed to elucidate the effects and roles exerted by the Andrositol components.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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