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Original Article

A STUDY OF NON-HORMONAL AYURVEDIC FORMULATION FOR IMPROVEMENT IN REPRODUCTIVE FUNCTIONS

Sanghi D. K.[2], Joshi S. B[2]., Shamsudin J[2]., Asghar S. [2], Bhatt J. K.[1], Saini V.*[1] and T. Mahandiratha[2].

*1. *B. R. Nahata College of Pharmacy, Mandsaur, M. P.*

2. *Shri Laxmanrao Mankar Institute of Pharmacy (R & D), Amgaon - 441902, Gondia*

Abstract

The problem of stimulation of sexual function and of spermatogenesis and ovogenesis in particular, is both of biological and medical significance, as it is associated with the problem of preservation of the sexual potential of male and female individuals. According to statistical data, 10-20% of all marriages are childless. In about 30-50% of the cases, male sterility is the cause. The diagnostic and treatment of male sterility is still a very difficult task.

Key words: spermatogenesis, ovogenesis, valido, *Tribulus terristris* & *Mucuna pruriens.*

INTRODUCTION

At present, drugs on hormonal basis are predominantly used in the treatment of hypogonadism and genital anomalies. In fact, the substitutive hormonal therapy is sometimes ineffective and quite often it induces a lasting hypofunction of the hypothalamic-pitutary-gonadal axis. Therefore, regardless of the great number of new, highly effective and possibly less harmful drugs. The formulation of a non-hormonal preparation with sufficient activity and without harmful side effects, could contribute to overcoming of the therapeutic problems in the sphere of sexual functional disorders. Why this combination and its pre clinical study? Valido is such preparation containing two indigenous herbs, *Tribulus terristris* and *Mucuna pruriens*. Clinical studies on *Tribulus* have shown improvement in reproductive functions, including increased sperm production and testosterone level in men. When *Tribulus* was given to healthy men in a dose of 750 mg per day for five day, LH and testosterone were elevated 72% and 40% respectively. Estradiol was also elevated by 81%. Women consuming *Tribulus* increase their concentration of hormones including Estradiol, with a very slight effect on testosterone level, thereby improving reproductive function, libido and ovulation. The hormone stimulation by Tribulus has a balanced effect. It doesn't over stimulate the secretion of hormones (Yan W. *et al*, 1996). *Tribulus* has been combined with *Mucuna*. *Mucuna* contains L-dopa, the direct precursor of dopamine in the brain. Tribulus helps the absorption of L-dopa and stops its breakdown. *Tribulus* also contains harmine. Harmine acts on MAOI, leading to higher levels of dopamine in the brain. High dopamine levels in men also stimulate the piturary gland to release LH and in turn inrease in testosterone levels. This of course, enhances libido, increases strength and lean muscle tissue and makes one feel great. Growth hormone (GH) production is also increased in both men and women when dopamine levels are high. *Mucuna pruriens* has shown to increase testosterone level (Amin, K. M. Y., 1996) leading to deposition of protein in the muscles and increased muscle mass and strength (Bhasin, S. *et al*, 1996). *Mucuna pruriens*, in rats had shown to improve the general mating behavior of male rats and significantly augmented all the parameters of mating behavior in rats including ejaculatory latency, increased penile refluxes and mounting frequency (Lubis S. H. A. *et al*, 1981).Thus it can be said that L-dopa, present in *Mucuna Pruriens* (Vaidya, A. B., 1986, Huizing H. 1987, Bell E. A. *et al*, 1971) induces hyper sexuality behavior that supports the relationship of dopamine and Human sexual behavior. As per the indigenous system (Bell E. A. *et al*, 1971) *Mucuna pruriens* stimulates production of semen and delays the time of ejaculation. Mechanism of action of Mucuna pruriens can be explained as above (Suresh Kumar *et al*, 1971).

Each capsule contains extracts from

Tribulus terristris	500 mg
Mucuna pruriens	2.5 gm

Mfg by: Unijules Life Science Pvt. Ltd., Nagpur

CLINICAL STUDIES

MATERIALS AND METHODS

The experimental data from Valido administration have been clinically confirmed. The studies were carried on 212 male individuals, aged between 14 and 60 years. The therapeutic properties of Valido were studied in patients with partial or complete impotence. Both the tolerance and the adverse effects of the product were studied. The studies were carried out by the method of simple blind experiment, using placebo. In nozological terms, the studies covered various types of male impotence: idiopathic oligoasthenozoospermia - 39 patients, resection of the left internal testicular vein in varicocele, with subsequent oligoasthenozoospermia - 50 patients; inflammatory process of the prostate with oligo and azoospermia - 53 patients, primary and secondary male hypogonadism - 20 patients, impotency - 50 patients.

The product was individually administered to all patients who had not received hormonal agents for at least one month prior to the treatment.

The duration of the treatment depended on acuteness of the disease - 30-60 days on the average and 90 days. The mean daily dose was 3-6 capsules. Some of the patients were favorably affected by 3 capsules daily whereas the other administered 6

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capsules (3 x 2). The andrological state was used as the basis for the adequate evaluation of the re-productivity of the patients. The basic parameters of sperm were observed, i.e. volume and pH of the ejaculate, concentration of spermatozoa (number/1 ml), percentage of motile spermatozoa, mean rate of population motility and percentage of pathological forms of the spermatozoa. Detailed case history on the sexual behavior of the patients was recorded prior to and after the therapeutic Valido course. The effect of the product on hair growth was observed in some patients.

The changes observed in the serum levels of gonadotropins, progesterone, testosterone, estradiol and cholesterol. The changes also observed in testosterone serum levels in the Valido treated patients. The hormonal levels were radioimmunologically determined using kits and reagents. The results from these studies were statistically assessed by variation analysis.

RESULTS

Significant changes in spermatozoan motility were found after Valido intake for 60 days (with a daily dose of 3 capsules) by males with idiopathic oligoasthenozoospermia. The numbers of spermatozoa with normal motility, as well as the mean motility rate, were increased. The percentage of the motile spermatozoa was 29, on the average, prior to the treatment and reached up to 36.66 after the treatment ($p<0.005$). The mean motility rate of spermatozoa prior to the treatment was 1.95 mm/sec., after the treatment - 3.63 respectively ($p<0.001$). No changes were observed in the ejaculate volume. In both cases (before and after treatment) the ejaculate volume was within the limits of the norm, about 4 ml on the average. The number of spermatozoa in the treated patients was higher by 3 ml/ml ejaculate on the average. In some cases, normalization of the spermogram occurred during repeated treatment with a daily dose of 6 capsules. In these cases, the improvement of the sperm gram (normalization of the increased viscosity, increased ejaculate volume, increased concentration and accelerated motility of the spermatozoa) was accompanied by elevation of the serum levels of the lutenizing hormone and testosterone and reduction of the estradiol level.

The patients with idiopathic azoospermia after 90 day treatment with a daily dose of 1.5 gm are of particular interest. The results were significant in three of all 7 patients treated. No spermatozoa were detected prior to the treatment. After the treatment, 3.5-million/1 ml ejaculate were recorded in one of the patients, 15 million/ml in the second and 28 million/ml in the third. The percentage of motile spermatozoa in the first patient was 10 and in the other two - between 25 and 30. The motility rate of the spermatozoa was about 5 mm/sec. In two of the patients, 30 - 40 spermatozoa per field were observed and in the third - about 5 spermatozoa per field after the treatment, compared with the absence of any prior to the treatment. One of the patients failed to be affected by the product.

The studies on the patients from that nozological group continued with the administration of maintenance dose. The clinical comparison of the results from the treatment with provirone of patients with idiopathic azoospermia and after Valido administration revealed a favorable effect on three of the patients (out of 6), unsuccessfully treated with provirone for a long period of time. The results in the patients with varicocele and oligoasthenozoospermia as regards the motility of the spermatozoa were identical in the reports of all research teams, regardless of the differences in the doses and duration of the treatment. It was found an average of 26.88% motile spermatozoa prior to the treatment and after 60-day course with a dose of 1 capsule, three times daily - 39% ($p<0.02$) with a mean motility rate of spermatozoa 2.06 mm/sec prior to the treatment and 4.44 mm/sec. post treatment respectively. No change in the ejaculate volume was found. It is been observed more pronounced changes in the ejaculate volume after 90-day treatment with a daily dose of 1.5 gm (4.5 ml compared to 1-2 ml prior to the treatment, i.e. an average of 1.55 ml of ejaculate volume in all patients). The number of spermatozoa in 1 ml reached the values in 100% of the patients treated. The mean percentage of motile spermatozoa prior to the treatment was 2.06 and was increased to 33.09 (Tables 1, 2, 3).

Table 1: Results of Valido treatment (1 capsule 3 times daily for 60 days) of 38 males with idiopathic oligoasthenozoospermia (represented in mean values)

Indices	Before treatment	After treatment
a. Concentration of spermatozoa, million/ml	22.97	26.66
b. Motility, %	29.00	35.66*
c. Motility rate, mm/sec.	1.95	3.76*

Table 2: Results of Valido treatment (1 capsule 3 times daily for 60 days) of 16 males after varicocele operation with existing oligoasthenozoospermia

Indices	Before treatment	After treatment
a. Concentration of spermatozoa, million/ml	21.31	26.75
b. Motility, %	11.53	39.06*
c. Motility rate, mm/sec.	2.00	4.44*

Table 3: Results of Valido treatment (2 capsules 3 times daily for 90 days) of 36 males after varicocele operation and existing oligoasthenozoospermia

Indices	Before treatment	After treatment
a. Concentration of spermatozoa, million/ml	40.60	76.00*
b. Motility, %	3.05	33.09*
c. Motility rate, mm/sec.	2.06	4.44*

*The data are statistically significant.

The results of Valido administration to patients with unilateral or bilateral hypothrophy of the testes and azoospermia deserve particular attention. The patients complained of a sense of heaviness and distention, as well as of a slight pain in the testes between 40th and 60th day after the start of the treatment with a daily dose of 6 capsules. Upon examination, a slight pain in the testes occurred upon palpation, as well as a slight swelling, with no other evidence of pathological changes. Improvement both as regards the ejaculate volume and the concentration and motility of the spermatozoa was observed towards the end of the treatment. The testosterone serum level was elevated from 1.75 mg/ml to 3.75 mg/ml.

The pain in the testicular region upon palpation abated within 2-3 months after treatment. Valido administration to patients with chronic inflammatory process of the prostate and disorders in the spermogram led to insignificant changes in these cases when the inflammatory process had been treated previously.

No changes were found in patients with chronic inflammation of the prostate (not treated previously). Out of 14 patients with reduced libido and absence of pathology in the male genital organs, treated for 30 days (daily dose - 2 capsules, three times), 12 manifested obvious improvement of the libido, one patient - a slight improvement (after a 60 day treatment cycle) and no effect was observed in another one. Out of a total of 36 patients with chronic prostatitis and reduced libido, 15 were very favorably affected by the end of the treatment cycle (a total dose of 90-100 g), 12 favorably and in 9 of the cases with a duration of the inflammatory process over 5 years, no effect occurred. The patients with hypotrophy of the testes and idiopathic azoospermia had no complaints as regards the libido, but in the course of the treatment aimed at improving the spermogram an apparent libido enhancement was recorded. Out of 9 patients treated for one of the gravest forms of male hypogonadism (Klinefelter's syndrome, due to chromosomal anomalies), the libido was enhanced in three of the patients, erection was reported in two and sexual intercourse and masturbation were reported in another two patients. Elevated levels of lutenizing hormone after the treatment were found in these patients. The levels of the remaining sexual hormones and cholesterol were reduced.

Two of the patients with secondary insufficiency of sexual glands (Noonan's syndrome) attained improvement of the libido and erections during the treatment. The self-confidence was improved in one of them and in the second - hair grew in the male genital region.

The results of the treatment of three patients with cryptorchidism (one of them with uncorrected malformation) comprised improvement of the libido and often masturbation. The duration of the erection was prolonged in one patient from that group, aged 37. The spermogram of the same patient was significantly better compared to the initial status one month after treatment, i.e. on day 90 hr after the beginning. One patient with secondary hypogonadism reported hair growing in the axillary and genital region, parallel with enhanced libido and frequent masturbation.

The serum testosterone levels were elevated in 20 patients from various nozological groups, the initial and final values being within the norm. In seven patients with testosterone serum level below the lower limit of the norm, the physiological levels were reached after the treatment, whereas in the rest of the patients with normal initial levels, the testosterone was not significantly changed after treatment.

Tolerance and side effects

All clinicians engaged in the studies reported a very good tolerance and no drug-related side effects. The clinical laboratory data on Valido treated males showed no deviations in the blood count, ESR, flocculation tests and urine.

DISCUSSION OF THE RESULTS

The clinical studies on a total of 212 patients (males with disorders in the sexual function) confirmed the experimental data on a pronounced stimulating effect of the Valido on the sexual functions. It restored and improved the libido in all forms of impotency after the administration of a mean daily dose of 1.5 gm for 30-40 days. This suggests that not only the diminished libido was stimulated, but also that a therapeutic effect on both primary and secondary male hypogonadism was present. The assumption that the product was a favorable effect on spermatozoa motility after 60 day administration corresponds to the experimental data, according to which it stimulates both the mitosis and maturation of the germinal cells.

It is well known that at least 80 days elapse from the time of the division of the spermatogonia till the formation of a mature spermatozoon in males, hence the concentrations of the spermatozoa in the semen are different within that period. The team that used a therapeutic course of 90 days observed very good results in terms of both the motility and the concentration of the spermatozoa in the ejaculate. The studies of ejaculate from patients receiving the product for 60 days proved its apparent effect on the motility of the spermatozoa and an insignificant effect on their concentration on the basis of identical initial spermatozoal levels, as well as the presence of identity in the nozological groups prior to the treatment.

This confirms the fact that the minimum therapeutic cycle should last at least as long as one complete germinal cycle (i.e. 80-90 days in males). Both idiopathic oligo and azoospermia are diseases with so far undistinguished etiology. The serum levels of sex steroids are not changed in the majority of the patients with

such deviations and good therapeutic levels of the product are observed.

No data are available from testes biopsy that can throw light as to which of the phases of this complicated process of spermatogenesis has been affected pathologically and hence favorably affected by the product. Kumanov *et al* advanced the hypothesis of diminished central effect of the product, associated with its mechanism of action, based on the elevated level of the luteinizing hormone. On the other hand, they admitted the existence of a peripheral effect, which could be responsible for the effect of the product on hair growth.

The reduced level of serum cholesterol under the effect of the product provided grounds for the same authors to assume that it also had an effect of cholesterol metabolism. The mechanism of action of Valido has not been elucidated so far. It can be concluded, on the basis of the clinical studies carried out so far, that it has a very good stimulating and therapeutic effect in all forms of impotency, as well as a very good therapeutic effect in patients with oligoasthenospermia. The product has a very good tolerance and no undesired side effects. Based on the data presented so far, we recommend Valido for the treatment of impotency and debility, due to oligospermia and diminished motility of spermatozoa.

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