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Concise Review: Efficacy and Safety of Verona in Patients with Oligospermia_ Meta Analytical Insight and Management

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ABSTRACT

Different studies have been conducted to evaluate the efficacy of Verona, a polyherbal formulation for in the treatment of oligospermia at the different Centers of Medical Sciences, hospitals and Clinics. Patients at the different centers diagnosed with idiopathic oligospermia were recruited and administered Verona at a dose of 2 capsules bid for varying periods of time scale in months. In meta-analytical approach, the values for semen measurements were determined such as low sperm count, poor sperm motility and abnormal shape that best discriminate between fertile and infertile men and to evaluate the relative value of standard semen measurements values.

Keywords: Review, Efficacy, Safety ,Verona.

INTRODUCTION

In general, couples experiencing infertility where in male factor is associated may lead to infertility. The primarily infertile is expressed as the couple who has been unable to conceive even after one year of unprotected coitus. However, the WHO guidelines report that a man with a sperm count of <20 millions/ml is considered having oligospermia. It is reported that nearly 100 million people around the world are living with erectile dysfunction [1] . The present study was carried out to evaluate the efficacy and safety of Verona, herbal formulation manufactured by Herbion Pakistan (Pvt) Limited. The formula of Verona consists of active components such as Tribulus teristeris, Withania somnifera, Mucuna pruriens, and Argirea speciosa designed to improve number and morphology of sperms. The effect of Verona was evaluated by the changes in the following basic spermatic parameters to ejaculate volume, concentration of the spermatozoids, percent of sperms motility and percent of abnormal forms. Different authors have executed different studies on Verona and their work is summarized as concise metaanalysis.

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REPORTED STUDIES

A study on the herbal preparation of Verona has been carried out by Alyavi AL [2] , in which Verona active components exhibited beneficial effects on improvement of mental and physical activity, increases

vitality and potency (sexual drive). It restored and stimulated Leydig's cell as well as the growth of seminal cells, increases amount of Sertoli's cells; neutralizes effects of ageing, provides cellular energy supply and raises resistibility in condition of stress and strain. Total patients with erectile dysfunction selected were 20 and Verona was administered accordingly. Ages of the patients recorded from 25 to 64 years and duration of disease noted as lasting from one to five years from sign and symptoms point of view. Exclusion criteria set indicate, patients with spermogram abnormalities were not included into the study, as the course of treatment at specified pathology according to the instruction should last not less than 18 weeks. Dosage of Verona prescribed is 2 capsules 2 times a day i.e. in the morning and in the evening. Duration of treatment course was 16 days. Verona was administered on the background of physiological treatment describing the efficiency of preparation before the treatment patients complained of general fatigue, decrease of mental and physical efficiency, increased irritability, irascibility, muscular and articulate pains, reduction of sexual drive and potency. After treatment patients have been noted for improvement of general condition, reduction of irritability, increase of physical, mental and impellent activity, and also increase of sexual drive and potency. No adverse reactions were observed during the treatments with the Verona preparation. It was concluded that the Verona preparation can be recommended for usage as stated. This was rather a preliminary study that exhibited the performance on male sexual health.

A study on the Verona to assess on the patients suffering from the properties range in impaired spermatogenesis and male infertility was conducted by Gaybullaev AA [3] are described herewith.

Background:

Verona is a natural potency stimulator and its oral preparation is recommended for erectile dysfunction where as treatment increases libido and sexual reflexes as well as treats male infertility and associated complaints. The study procedure were as follows general clinical patient's condition, complaints, disorder medical history, personal history, general examination such as body weight, height, chest circumference, arms swing, lower thochanteric size, intertrochanteric size, interachromial size. Male genital system test were investigated as Lab tests; Spermatogramm before treatment and after 12 weeks treatment (on 85th day of observation); Endocrinal status and sexual glands, LH; FSH; testosterone; prolactin before treatment and after 12 weeks treatment (on 85th day of observation).

The following basic common male infertility reasons leading to impaired spermatogenesis were excluded in group selection that is varicocele. Infection and inflammatory genital conditions. The pathospermia of unknown etiology e.g. oligo-, terato-, asthenozoospermia and related medical condition were also checked and excluded from the study.

When the drug was included in treatment complex the following reliable ($p < 0.05$) values changes from initial were observed: sperm quantity increased by 52.3%; sperm viscosity reduced by 64.2%; spermatozoa count per ml of sperm increased by 118.2%; mobile spermatozoa count increased by 153.9%; immobile spermatozoa count reduced by 84.9%; live spermatozoa count increased by 72%; dead ones reduces by 58%; abnormalities in head reduced by 62.8%, cervix reduced by 63.4%, tail reduced by 48.4%. Leucetine grains contents increased by 64.3%. Boettcher's crystals disappeared in all 6 patients; Agglutination was absent in 86.7%; Fructose contents increased by 42.3%. Laboratory investigation done are a) General blood test: the drug did not change blood formula; b) Urine sediment microscopy: no changes were observed; c) Hormonal status of patients before the drug administration after course completion all 4 parameters were within limits for healthy individuals.

Data comparison with main group similar parameters of 10 patients administered complex therapy without Verona was carried out the mean age noted are 28.5±0.968. In comparison of basic parameters after

treatment reliable differences of the following criteria were noted: Sperm quantity is higher in the main group by 23%. The percentage of actively mobile spermatozoa is higher in the main group by 9.5%. Leucetine grains count is higher. The percentage in the main group (by 34.8%). Fructose content in semen is higher in the main group by 19.3. The percentage spermatogenesis cells are higher in the main group by 42.9%. Hormonal levels in all 10 patients of the main group after treatment are within limits; 3 deviations were seen in control group; testosterone level was low in 2 patients, LH was low in 1 patient.

In another study executed by Kukes VG [4] on the Verona was conducted in order to assess the efficacy and safety in functional sexual disorders in males originating in development of chronic asthenizing diseases. Study of the drug impact on to specific clinical symptoms depending on age, duration of treatment, somatical difficulty and other factors as well as side effects and possible effect of the medicine with elaboration of recommendations for their elimination and prevention. The determination of indications and contraindications for use of the drug as well as evaluation of the impact of Verona capsules on the condition of spermatogenesis by studying basic characteristics to ejaculate.

The study characteristics were analysed for clinical efficacy of Verona compared with placebo. Verona was approved on 50 males (ages from 39 to 53 years) with sexual disorders of functional genesis. Complaints of reduced libido, erection as appeared during escalation of chronic asthenia diseases were noted. Verona is administered orally 2 capsules twice a day and duration of treatment is 8 weeks.

Inclusion criteria:

Fifty males with sexual disorders of functional genesis developed on the background of chronic asthenia diseases were observed. Patients were divided into 2 groups: basic (test) and comparison (control) group. Both groups were similar in age and suffering from seriousness of disease. The basic group consisted of 30 males with took Verona. The comparison group consists of 20 males took placebo. The inclusion criteria whereas follows male patients with sexual disorders of functional genesis; Age from 25 to 52 years and patient's written agreement consent was obtained. Exclusion criteria are with drawl by the patient's or his relatives' request, patients hypersensitive to the drug's components and completely excluded from this research were patients unable to understand researcher's explanations related to the study process and associated and accompanying disease affecting the sexual disorders, also patients refused to sign the written agreement for participating in the study.

Evaluation of efficacy was conducted by the way of dynamic investigational and clinical observation. Sexual activity characteristics of the patients were ranged from 1 to 4 points. These indices were correlated with psychological test results (method HAM – health-activity-mood) and analysis of blood circulation in hypogastric and dorsal penile arteries (Toshiba Doppler machine, Japan). "Improvement" meant combination of positive dynamics of subjective and objective indices, "insignificant improvement" indicated as positive changes of only subjective indices. There were "lack of effect" and "deterioration" variants as well. Evaluation of the drug safety was based on the data of unwanted actions of the drug observed during the treatment.

The results compiled on the fifty males aged 36 to 53 years with sexual disorders formed during development of chronic asthenia diseases i.e. neuro-vertebrogenic and psycho-vegetative syndromes were observed during the study. All the patients besides complaints of asthenia nature (easy fatigue, irritation, general weakness) noted sexual dysfunctions appeared or intensified during the basic disease. Patients' complaints had stereotype nature and came to decreased libido, weak erection and in most cases fast ejaculation. At the checkup time sexual activity, erection level, intercourse duration, evaluation of sexual activity success was limited to 1.5 – 1.9 points averaging 1.6 point (with maximal 4.0 points). There were no fundamental changes in groups' (neuro-vertebrogenic or psycho-vegetative) sexopathological

picture. Various phases of asthenia with clear emotional (anxious or depressive) component were followed up in psychological study. Level of linear speed of blood circulation in penile arteries (averaging 18 cm/s varies insignificantly from the norm of 20 cm/s) showed absence of significant vascular disturbances. Ejaculate changes were displayed in 14 out of 30 (46%) patients and in 9 out of 20 (45%) in the comparison group.

Six males in the basic group had the volume of ejaculate about 2.0 – 2.3 ml that is a lower limit of the norm. In others, 8 cases it was about 3.2 – 4.4 ml. Concentration of spermatozoa in 8 cases was close to the lower norm limit (20-30 million/ml) that is 21-29 million/ml. In 6 cases with spermatozoa concentration around 14-18 million/ml 1 stage of oligospermia was diagnosed. Spermatozoa motility (conditional norm is over 40% of progressive activity) was 37-39% in 3 cases, 34-36% in 5 cases (mild asthenospermia). Six males had a more distinct asthenospermia as up to 27-32% of mobile forms. Increased amount of pathological spermatozoa forms (over 40%) was found in 8 cases; in 5 cases it was 41-42%, in 3 cases as 43-45%. Generally changes in all analyzed indices were found in 6 patients. These changes may be consequences of former specific infections transferred into chronic form. Similar changes were found in the comparison group. First stage oligospermia was noted in 5 cases, and asthenospermia as in 7 cases. Increased content of pathological forms with over 40% and was found in 4 cases. According to the study plan patients were divided in to 2 groups. Basic group included 30 patients taking Verona; the comparison group included 20 patients who took placebo. After the treatment with Verona 21 out of 30 (70%) patients noted improved quality of sexual intercourse mostly in form of intensified libido and erection averaging 1.2 point in comparison with the initial level limited in 2.5-2.8 points. In the basic group improved condition with subjective and objective characteristics dynamics was found in 11 males, insignificant improvement was found in another 10 males. Lack of effect was noted in 8 cases, deterioration (further libido decreasing) was found in 1 case. Efficacy level of the therapy having a general toning up nature did not depend on the type of disorders such as vertebrogenic or psycho-vegetative. In the comparison group positive changes at the sexual activity level were noticed in reliably lesser part of cases by 35% (7 out of 20 patients).

In the comparison group similar dynamics of HAM indices were noted in lesser number of observations in 9 out of 20 (45%) patients. Positive changes of quantitative and qualitative ejaculate characteristics were noted during Verona treatment. Thus in 6 cases with ejaculate volume 2.0-2.3 ml increase of 0.2-0.4 (13%) was noted and that indirectly proves positive influence of the drug on excretion function level. During Verona treatment increase in spermatozoa concentration found clear with slight changes was noted as well. In 6 out of 8 patients with 21-29 million cells/ml this index was increased by 2-6 million averaging 12%. In case of 1st stage of oligospermia (less than 20 million/ml) 3 patients had an increase of 1-2 million cells; other 3 patients had no changes. Similar mild regulating action of Verona was noted in evaluation of spermatozoa motility. Positive changes were noted in 5 cases of unclear asthenospermia with initial 34-36% of mobile forms. Increase of 4% was observed in this situation. In other cases (3 males with normal indices and 6 patients with indices below 32%) motility was either increased by 1-2% (6 patients) or did not change at all. Similar picture was observed in percent change of pathological forms. In case of conditional norm – up to 40% of changed cells (6 males) or index increase up to 43-45% (4 patients) changes didn't exceed 1-2%. However 4 patients with 41-42% had normalized index. There were no significant changes in spermatograms in the comparison group. It was concluded that this study confirmed by clear reduction of complaints and additional checkup data in 70% of observations reliably exceeding therapy results in the comparison group.

In continuation further study on clinical efficacy and safety of Verona was carried out by Agasarov LG. [5]. The objective of this study was to determine the efficacy and safety of the drug "Verona" in functional

sexual disorders in males originating and/or intensified during development of vertebrogenic syndromes. Analysis of clinical efficacy of Verona is made in comparison with placebo-controlled method using a pharmaceutical product without active ingredients but having the same shape, color, taste, administration method. Method of the study was simple blind. The study includes consecutively executed phases: Evaluation of initial parameters excluding patients within study limits, comparative analysis of therapy results in the singling aspects of efficacy and safety.

Inclusion criteria include patients who were administered to thirty males aged 26 to 53 with sexual complaints appeared or intensified on the background of chronic lumbosacral neurovertebrogenic syndromes escalation were observed. Special attention was paid to possible changes of spermogram during the study. The comparison group of 20 males who were placed in placebo. Clinical diagnosis was confirmed by pathopsychological and electrophysiological checkup results. Exclusion criteria: Patients were excluded due to: By the patient's or his relatives' request, Patients hypersensitive to the drug's components completely excluded were patients unable to understand researcher's explanations related to the study process due to unwanted occurrences and accompanying disease and because of proved organic genesis of the sexual disorders and patients refused to sign the written consent for participating in the study. Verona was administered orally 2 capsules twice a day – in the morning and in the evening preferably with milk. Duration of treatment was 8 weeks (2 months). Dopplerography results reflected a drop (unreliable regarding control) in volumetric blood flow level in hypogastric arteries in 22% of patients. Insignificancy of changes in linear velocity in dorsal penile arteries combined with "normal" indices of electro stimulating myography Atahanov Sh.E., 2006 [6] proved functional nature of observed disorders.

Values of a separate task on ejaculate analysis showed changes in 21 (42%) patients. In 9 cases volume of obtained sperm varied from 2.0 to 2.3 conforming to the lower norm limit. Oligospermia of 1 degree with spermatozoa concentration limited to 14-18 million/ml (the lower "norm" limit is equal to 20-30 million/ml) was diagnosed in 9 patients. Spermatozoa concentration was close to that limit in 8 patients fluctuating between 21 and 29 million/ml. unclear asthenospermia was noted in 8 observations with 34-39% of mobile spermatozoa (conditional norm over 40%). Five males had clear asthenospermia with 27-32% of active forms. Increased content of pathological forms of spermatozoa (over 40%) was found in 10 males, in 6 observations by 41-42% and in 4 cases by 43-45%. These changes may be consequences of specific chronic infections.

Results were deduced according to the study scheme and patients were divided into 2 clinically comparable groups. Basic group consisted of 30 patients using Verona; comparison group consisted of 20 people and received a variation of placebo therapy. It was demonstrated that during Verona treatment 22 out of 30 patients had increased libido, frequency of spontaneous morning erections grew. Fourteen patients noted clearly intensified erection sufficient for introjection and prolonged sexual intercourse limited to 2-3 minutes. Ranged indices of sexual activity increased with reliably lower rate – no more then 0.2-0.4 points in the comparison group.

Improved condition with objective and subjective characteristics dynamics was established in 15 males (mostly in patients with strong sexual constitution, i.e. with high reserve capabilities), insignificant improvement in 7 males. Lack of effect was noted in 7 cases, deterioration at in 1 case. Positive changes in sexual activity in the comparison group were noted in 7 cases (35%). Positive changes in ejaculate characteristics were noted during Verona treatment as well. Thus in 6 cases with ejaculate volume 2.0-2.2 ml increase of 0.2-0.3 (12%) was established. The mean time increase in spermatozoa concentration was observed especially in initially unclear expressed changes. In 4 out of 5 patients with 21-29 million cells/ml the index grew 2-6 million averaging 12%, in case of oligospermia of 1 degree only in 1 male

out of 5. Similar mild regulating action of the drug was noted in spermatozoa motility evaluation. Positive changes with 5% index increase were established in 5 cases of mild asthenospermia with initial 34-36 of mobile forms. In other cases (of "normal" value or indices below 35%) there were no significant changes. Similar dynamics were noted in pathological forms content. In case of 41-42% initial values (4 patients) normalized indices were observed but in 43-45% of modified forms changes did not exceed 1%. There were no significant changes in any of analyzed spermograms indices in the comparison group. Thus positive influence of Verona was proved during the study and that confirms its prospective use in sexopathological practice. Verona endurance is estimated as good and no unwanted effects and allergic reactions were revealed during the treatment. Deterioration of 1 patient's condition in shape of increasing asthenia cannot be connected with the drug use.

CONCLUSIONS

Administration of Verona in sexual dysfunctions in males is a safe way of treatment providing positive results. This is proved by reduction level of basic subjective and objective indices exceeding placebo therapy results. The noted changes in the level of psycho-vegetative response during Verona treatment should be defined as predictably significant in stability of obtained results. Over all the drug Verona is well tolerated, no side effects were seen. It is a safe method of male infertility treatment with sufficiently good results which is confirmed by reliable changes of objective world-wide accepted patient's status evaluation criteria. Administration of Verona in sexual disturbances of functional genesis in males is a safe way of treatment providing stable positive results due to its general toning and increased action. This is confirmed by clear reduction of complaints and additional checkup data in 70% of observations reliably exceeding therapy results in the comparison group. Verona has mild spermatogenesis regulating action leading to normalization of basic indices of the process.

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