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Phytotherapy of Male Hypoactive Sexual Desire of Psychogenic Origin: A Preliminary Study

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Abstract

This is a prospective placebo-controlled study to test the efficacy and safety of a dietary supplement (Vigoryx®, FG. -Pharma, Rome-Italy) for men with Psychogenic Hypoactive Sexual Desire (pHSD). The composition of Vigoryx was as follows: selenium 55 mg, L-Carnitine 250 mg, red ginseng 135 mg, aframomum 20 mg and eruca 300 mg.

This is a two-center prospective blind placebo-controlled study. All patients affected by pHSD were considered to be candidates. Sexual desire was assessed in each patient before and after active drug or placebo administration using the International Index of Erectile Function (IIEF15, items 11 and 12) and Patient Global Impression of Improvement (PGI-I, seven grade scale) scores. The patients received Vigoryx® (active drug, Group 1) or a control substance (alimentary starch, Group 2). The differences between the unmatched groups were assessed using the Mann-Whitney Rank test, and the differences between before and after (matched groups) therapy were assessed using the Wilcoxon Signed Rank test. The side effects were compared between the two groups using the chi^2 test.

Eighty-four patients were studied. Forty patients used Vigoryx (Group 1), and 44 used a placebo (Group 2). No significant differences existed between the basal IIEF scores, and between the basal scores and the score achieved after a three-month administration of the control substance; on the other hand, the IIEF score after a three-month administration of Vigoryx was significantly higher than the basal scores and the score achieved after control substance administration. Furthermore, the PGI-I score achieved after active drug administration was significantly higher than the PGI-I score achieved after starch administration. No side effects emerged in either group. Vigoryx is a safe and efficient drug for the treatment of pHSD.

Keywords: Hypoactive Sexual Desire; Medical Therapy; Phytotherapy

Introduction

Hypoactive sexual desire (HSD) is a condition characterized by the absence of or notable decrease in the frequency with which the man experiences desire for sexual activity [1]. A 5% prevalence has been reported [2]. Hypoactive sexual desire can be differentiated from an etiological point of view into hormonal (androgen deficiency, hyperprolactinemia), infective (HIV), secondary to chronic diseases (kidney, liver or heart insufficiency), iatrogenic (antidepressant) or psychogenic [1]. Sexual counselling and/or psychological therapy have been advocated for the treatment of psychogenic HSD (pHSD) [3]. Medical therapy is based on bupropion 150-300 mg/day administration, an antidepressant medication which has an effect on the re-uptake of dopamine and of norepinephrine. Although the efficacy of bupropion was significantly higher than the placebo, the positive response rate was low; therefore, the clinical use of this alternative to psychotherapy was limited [4]. These data compelled the Authors to carry out the following prospective placebo-controlled study to test the efficacy and safety of a dietary supplement (Vigoryx®, FG-Pharma, Rome-Italy) for men with pHSD. The composition of Vigoryx was as follows: selenium 55 mg, L-Carnitine 250 mg, red ginseng 135 mg, aframomum 20 mg and eruca 300 mg.

Materials and Methods

Generalities

This was a two-center (Ferrara [Italy] and Perugia [Italy]) prospective blind placebo-controlled study. The study was authorized by the Institutional Review Boards (IRBs) of Andros - Italia. Written informed consent was obtained from each patient. This study tested the efficacy and safety of Vigoryx® versus a placebo (starch) in improving sexual desire in men affected by pHSD. A power analysis was carried out to estimate the number of observations required to have a reliable chance of detecting the effect sought. There are no formal standards for power (π); the power of our tests was $\pi = 0.90$ as a standard for adequacy [5]. The calculations

were carried out using the G*Power3 program [6]. Enrollment began on 2nd January 2017 and finished on 3rd February 2018.

i. **Inclusion criteria:** All patients presenting with HSD were considered as candidates.

ii. **Exclusion criteria:** The authors decided not to consider patients with non-pHSD or with pHSD associated with other sexual dysfunctions; thus, the exclusion criteria were the following: prostate alterations at digital examination (12 cases), prostate specific antigen > 4 ng/ml (3 cases), hormonal alterations (6 cases), administration of hormonal, antidepressant, antineoplastic, antiparkinson, cimetidine and ranitidine drugs (5 cases), kidney/hepatic insufficiency (2 cases), erectile deficiency (23 cases) and alterations in ejaculation (10 cases).

Patient Assessment

Clinical history, physical examination, bilateral scrotal doppler scans, blood hormonal levels (Follicle Stimulating Hormone [FSH], Luteinizing Hormone [LH], Estradiol [E2], Testosterone [T], Prolactin [PRL], Aspartate Transaminase (AST), Alanine Aminotransferase (ALAT), Prostate Specific Antigen (PSA) creatininemia and azotemia were collected from each patient. Before and after active drug or placebo administration, the patients were evaluated using the following scales: International Index of Erectile Function (IIEF15), items 11 and 12 regarding sexual desire, and Patient Global Impression of Improvement (PGI-I). The items used from the IIEF15 were: item 11: "How often did you felt sexual desire in the past 4 weeks?" and item 12: "How would you rate your sexual desire in the past 4 weeks?" [7]. The PGI-I score is a seven grade scale: 1: very much better, 2: much better; 3: slightly better, 4: no change, 5: slightly worse; 6: much worse, 7: very much worse [8].

The patients were randomly assigned to one of the two groups to receive either Vigoryx® or a control substance (alimentary starch) for 3 months. Randomization was carried out using an online randomizer http://www.blia.it/utili/casuali/. The IRB reviewed the unblinded data for patient safety; there were no interim analyses for efficacy. The patients were randomly assigned to one of the two groups to receive the active drug (Vigoryx®) one tablet/day (Group 1) or a control substance (Group 2) (one tablet containing 100 mg of alimentary starch once a day) for three months.

The dosage of the active drug was assessed on the basis of previous preparation tests, carried out by collecting and assessing the scores of the scales before and after Vigoryx® administration. One group of ten pHSD patients received one tablet a day and one group of ten pHSD patients received one tablet twice a day, both for a period of 3 months; the scores of the IIEF-15 and he PGI-1 were collected and compared. Since all patients in both groups identically improved their scores either by assuming 1 tablet/day or 2 tablets/day of Vigoryx®, the beneficial effects of 1 or 2 tablets were considered identical. As a result, a one-tablet sachet once a day dosage was adopted.

Endpoints & Statistical Analysis

With respect to the efficacy of Vigoryx®, the primary endpoint was an improvement in the scores of the IIEF 15 and the PGI-I scales. The differences between the unmatched groups were assessed using the Mann-Whitney Rank test, and the differences between before and after (matched groups) treatment were assessed using the Wilcoxon Signed Rank test. The side effects were compared between the two groups using the chi^2 test [7].

Procedures to Ensure Blindness

Blindness of drug delivery was ensured with the use of color-coded sachets. Nurses delivered the active drug and the control substance in anonymous color-coded sachets; the nurses were blinded to the delivery of the color code of the bags, and the Authors were blinded to the color code. All study personnel and participants were blinded to the treatment assignment for the duration of the study. Only the Andros IRB saw the unblinded data in order to alert physicians in the case of major side effects, but this was never necessary, and no one from the IRB had any contact with the study participants. The color and number codes were disclosed at the end of the study [9].

Results

In total, 97 patients were studied. Three patients abandoned the study owing to the insufficient therapeutic effect of the active drug, and ten patients violated the protocol; thus, 84 patients were studied. Their clinical and demographic characteristics are presented in (Table 1). Forty patients received the active drug (Group 1), and 44 received a placebo (Group 2).

	Group 1: Vigoryx (n. 40)	Group 2 Control substance (alimentary starch) (n. 44)
Age (years)	37 (30-52)	36 (30-55)
Duration of symptoms (months)	18 (12-23)	17 (12-22)
Blood level of total testosterone (normal range 240-950 ng/dl)	450 (255-860)	460 (260-880)
Blood level of prolactin (normal range: 2-18 ng/ml)	10.0 (2-17)	11.0 (3-18)
Blood level of follicle-stimulating hormone (normal range: 1.5-12.4 mIU/ml)	4.7 (2-11)	5.8 (2.5-11.7)
Blood level of luteinizing hormone (normal range: 1.8-12.0 mUI/ml).	5.0 (2.7-11)	5.3 (2.9-11)
Blood level of prostatic specific antigen (normal range < 4 ng/ml)	1.6 (0.3-3.6)	1.7 (0.2-3.7)

Table 1: Baseline demographic and clinical characteristics of each group. Data are shown as median values, and the ranges are in parentheses. No differences between the comparisons were significant when examined using the Mann-Whitney Rank test.

The results of active drug or placebo administration are presented in (Table 2). No significant differences existed between the basal IIEF scores, and between the basal scores and the score achieved after the three-month administration of control substance, on the other hand IIEF 15 score after a three-month administration of Vigoryx was significantly higher than the basal scores and the score achieved after control substance administration. Furthermore, the PGI-I score achieved after active drug administration was significantly higher than the PGI-I score achieved after starch administration. No side effects emerged in either group ($chi^2 < 1$, p not significant).

	Group 1: Vigoryx (40 patients)		Group 2: alimentary starch (44 patients)		P			
	Before adminis tration (a)	After adminis tration (b)	Before adminis tration (c)	After adminis tration (d)	Wilcoxon Signed Rank test		Mann-Whitney Rank test	
					(a) v/s (b) = 0.003	(c) v/s (d) = 0.5	(a) v/s (c) = 0.5	(b) v/s (d) = 0.003
IIEF 15 score.	4 (2-6)	8 (4-10)	4 (2-6)	4 (2-6)				
PGI-1 score.	n.t.	2 (1-3)	n.t.	4 (3-5)			(b) vs (d) = 0.009	

Table 2: Comparisons between the scores of the International Index of Sexual Dysfunction (IIEF15) (items 11 and 12) and of the score of the Patient Global Impression of Improvement (PGI-I).

- The scores were assessed before and after a 3-month administration of the active drug (Vigoryx, 1 tablet/day for three months) or of the control substance (alimentary starch, 100 mg/day for three months). Forty patients used the active drug (Group 1) and 44 used the control substance (Group 2).
- The IIEF15 items used were: item 11: "how often did you feel sexual desire in the past 4 weeks?" and item 12:" How would you rate the level of your sexual desire in the past four weeks?". The lowest total score was 2, and the highest total score was 10 [7].
- The PGI-I grades are: 1: very much better, 2: much better; 3: slightly better, 4: no change, 5: slightly worse; 6: much worse, 7: very much worse [8]. The composition of Vigoryx was as follows: selenium 55 mg, L-Carnitine 250 mg, red ginseng 135 mg, aframomum 20 mg and eruca 300 mg.
- The differences between the unmatched groups were assessed using the Mann-Whitney Rank test, and the differences between before and after (matched groups) treatment were assessed using the Wilcoxon Signed Rank test. V/s = versus; n.t. = not testable. The data are presented as a median and as a range (min-max)

Discussion and Conclusions

Our data showed that Vigoryx was an active and safe drug for improving HSD. The authors cannot indicate the exact mechanism of action of Vigoryx since it is a multicomponent drug, the pharmacological composition of which legitimates its efficacy. As indicated above, Vigoryx contains selenium 55 mg, L-Carnitine 250 mg, red ginseng 135 mg, aframomum 20 mg and eruca 300 mg.

In fact, according to the US National Academy of Sciences, for adults, 55 mg is the recommended daily selenium intake. The functions of selenium in the body are mainly linked to its antioxidant properties as it is an essential part of important antioxidant enzymes [10]. Selenium is one of the potentially beneficial nutrients for the central nervous system the deficiency of which provokes recurrent mood disorders and/or anxiety [11].

L-Carnitine is an endogenous substance which acts as a carrier for fatty acids across the inner mitochondrial membrane, necessary for subsequent beta-oxidation and ATP production. In addition to its important role in the metabolism of lipids, L-Carnitine is also a potent antioxidant which protects tissues from oxidative damage. L-Carnitine supplementation may be useful not only in preventing tissue deficiency of this element, but also in avoiding oxidative damage secondary to the increased production of reactive species in these diseases. Considering the ability of l-carnitine to easily cross the blood-brain barrier, l-carnitine supplementation may also be beneficial for the central nervous system metabolism [12]. L-Carnitine (ALC) has neuromodulator effects on both synaptic morphology and synaptic transmission, resulting in euphoric activity [13].

Ginseng has significant effects on neurological and psychiatric symptoms in older men, and on the psychomotor functions of healthy humans via the interaction of some components of ginseng (ginsenosides) with the ascendant reticular system of the encephalic trunk [14].

Aframomum melegeta is a species in the ginger family, Zingiberaceae, whose active principle is gingerol. Gingerol prevents testicular toxicity via the inhibition of oxidative stress and endocrine disruption in rats exposed to organochloride pesticides; gingerol enhances the key functional enzymes involved in spermatogenesis, and in testicular steroidogenesis and maintains the histoarchitecture of the testes and epididymis in rats exposed to organochloride pesticides [15].

Eruca sativa is known as a garden plant used in folk medicine to enhance sexual desire in males. In reality, Eruca preserves the testosterone secretion of rat testicles exposed to organochloride pesticides [16], and possesses a strong scavenging activity of free oxygen radicals [17].

As a conclusion, Vigoryx is a safe and efficient drug for improving pHSD, which might also improve the efficacy of phosphodiesterase-5 inhibiters (PDE5 is) for the treatment of erectile dysfunction when associated with pLHD, but this will be the subject of a future paper.

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