Pharmacological Reports 70 (2018) 227–232

Contents lists available at ScienceDirect

Pharmacological Reports

journal homepage: www.elsevier.com/locate/pharep

Original article

The effect of bromocriptine treatment on sexual functioning and depressive symptoms in women with mild hyperprolactinemia

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ARTICLE INFO

Article history:
Received 16 September 2017
Accepted 17 October 2017
Available online xxx

Keywords:
Depressive symptoms
Dopamine agonists
Hyperprolactinemia
Sexual functioning

ABSTRACT

Background: Elevated prolactin levels are associated with sexual dysfunction in women. No previous study has investigated the effect of dopamine agonists on sexual functioning in women.
Methods: The study enrolled 30 young women with mild hyperprolactinemia (serum prolactin levels in the range between 25 and 50 ng/mL), 15 of whom were later treated with bromocriptine (5–10 mg daily), as well as 14 age- and weight-matched healthy women. All women completed a questionnaire evaluating female sexual function (Female Sexual Function Index – FSFI) and a questionnaire evaluating the presence and severity of depressive symptoms (Beck Depression Inventory Second Edition – BDI-II)
Results: Women with mild hyperprolactinemia had a lower total FSFI score, lower scores in all domains of sexual functioning (desire, arousal, lubrication, and dyspareunia), as well as a lower total BDI-II score than control women. Bromocriptine increased the FSFI score and tended to reduce BDI-II score. Moreover, the drug normalized desire, arousal, lubrication and dyspareunia, as well as improved orgasm and sexual satisfaction and this action correlated with changes in prolactin levels and an improvement in insulin sensitivity. No changes in sexual functioning and depressive symptoms were observed in untreated women with mild hyperprolactinemia and healthy controls.
Conclusions: Bromocriptine treatment improves female sexual functioning and slightly affects depressive symptoms in women with elevated prolactin levels and this effect is related to its prolactin-lowering and metabolic effects.

Introduction

The results of recent studies suggest that prolactin is implicated in the regulation of sexual functioning. Masturbation- or coitus-induced orgasm elevates serum prolactin levels, an effect not observed if sexual arousal is not accompanied by orgasm [1,2]. The degree of this surge depends on orgasm quality as well as on sexual satisfaction [3]. An increase in prolactin levels is more pronounced if orgasm is caused by penile-vaginal intercourse in comparison with orgasm induced by masturbation [4]. Based on these findings it may be assumed that an increase in prolactin secretion may be a neurohormonal index of sexual satiety, an objective index of orgasm and orgasm quality, as well as that changes in prolactin secretion may play a role in a negative feedback loop aiming at reducing sexual arousal [1,3,4].

Unlike acute changes in prolactin levels, chronically elevated serum prolactin seem to exert a negative impact on sexual functioning in both sexes. Male patients with prolactinoma were more frequently diagnosed with hypoactive sexual desire than control subjects [5]. However, the risk of relevant hypoactive sexual desire was lower in patients with severe hyperprolactinemia than in men with low testosterone levels [6]. In women, elevated prolactin levels were found to be associated with a lower total score of the female sexual functioning index, as well as lower scores for all domains: sexual desire, sexual arousal, lubrication, orgasm, sexual satisfaction and dyspareunia [7,8].

Cabergoline and bromocriptine, considered the first line treatment option for hyperprolactinemia [9], lead to an increase in the number of erections in men with elevated prolactin levels [10,11]. Very little is known about the effect of dopamine agonists or other agents affecting prolactin levels on other aspects of sexual functioning, and these data are available only for men. Cabergoline

Abbreviations: BDI-II, Beck Depression Inventory-Second Edition; FSFI, female sexual function index; HDL, high-density lipoprotein; HOMA1-IR, the homeostatic model 1 for insulin resistance index; LDL, low-density lipoprotein; SD, standard deviation.

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https://doi.org/10.1016/j.pharep.2017.10.008
1734-1140/

enhanced all parameters of sexual drive and function, as well as positive perception of the refractory period [12]. In turn, protirelin, a stimulator of prolactin secretion, produced significantly longer ejaculation latency during the first sequence of sexual activity, but only a small reduction in sexual drive and function [12]. Therefore, the aim of this study was to assess the effect of bromocriptine on female sexual functioning and depressive symptoms in men with mild hyperprolactinemia.

Materials and methods

Patients

The study population consisted of 32 women (20–40 years old) with recently diagnosed and previously untreated mild hyperprolactinemia who were recruited among women with a history of infertility. All participants gave written, informed consent, and the local ethics committee approved the study protocol. Mild hyperprolactinemia was diagnosed if serum prolactin levels were more than 25 ng/mL but less than 50 ng/mL on two different days. The subjects were excluded if they met at least one of the following criteria: prolactinoma, mixed pituitary tumors (secreting prolactin and other pituitary hormones), other hormonally active and non-functioning pituitary adenomas, macroprolactinemia, any other chronic disorders, any treatment, pregnancy or lactation, and poor patient compliance. We also excluded women with a history of urogynecological operations that might affect sexual function, sexually inactive women, as well as women receiving any treatment. The control group (group C) included 14 age-, weight- and blood pressure-matched healthy women. The study was approved by the local institutional review board.

Study design

Women planning pregnancy (group A) were then treated with bromocriptine, while women who did not want to become pregnant in the following six months (group B) were left untreated. The starting dose of bromocriptine was 1.25 mg once daily in the evening. This dose was gradually titrated to achieve normal prolactin levels, but no more than to 10 mg daily (in two or three divided doses) and the final dose (on average, 8.0 mg daily) was administered for the following 3 months. Compliance with bromocriptine treatment was regarded as satisfactory if the number of tablets returned ranged from 0% to 10%.

Laboratory assays

Laboratory investigations were performed at baseline and at the end of the treatment. Venous blood samples were obtained between 8 and 9 a.m. (to avoid possible circadian fluctuations in the parameters studied) following at least a 12-h overnight fasting. Plasma glucose, plasma lipids (total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides) were measured by routine laboratory techniques using commercially available kits (Roche Diagnostics, Basel, Switzerland). Serum levels of insulin and prolactin were assayed by direct chemiluminescence using acridinium ester technology (ADVIA Centaur XP Immunoassay System, Siemens Healthcare Diagnostics, Munich, Germany). The homeostasis model assessment 1 of insulin resistance (HOMA1-IR) was calculated by dividing the product of insulin (mIU/L) and glucose (mg/dL) by 405.

Questionnaires

After venipuncture, all participants were asked to complete a questionnaire assessing their demographic characteristics, smoking, physical activity, education, occupation, stress exposure, general health, the number and duration of marriages, the number of sexual partners, deliveries and abortions. They were also asked to fill in questionnaires evaluating their sexual function (the female sexual function index – FSFI) and depressive symptoms (the Beck Depression Inventory Second Edition – BDI-II).

FSFI consists of 19 questions, divided into 6 domains: desire (items 1 and 2), arousal (items 3–6), lubrication (items 7–10), orgasm (items 11–13), satisfaction (items 14–16), and pain (items 17–19). Each answer is rated on a scale ranging from 0 to 5 or 1 to 5 (0 means no sexual activity in the four weeks) [13,14]. The total FSFI score, obtained from the sum of the items in each domain multiplied by the domain factor (0.6 for desire, 0.3 for arousal and lubrication, and 0.4 for orgasm, satisfaction, and pain), may range from 2.0 to 36.0. The total FSFI score less than 26.55 is indicative of sexual dysfunction [13,14].

BDI-II is adjusted to measure depressive symptoms corresponding with the diagnostic criteria for depressive disorders outlined in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [15,16]. BDI-II consists of 21 items rated on a scale from 0 (not present) to 3 (severe). The total score, being a sum of the item scores, may range from 0 to 63. The BDI-II score of 0–13 was categorized 'minimal', 14–19 'mild', 20–28 'moderate severe', and 29–63 'severe' depression [15].

Statistical analysis

Quantitative data without a normal distribution were natural log-transformed to yield normal distributions prior to statistical analysis. The study groups were compared using analysis of covariance followed by Bonferroni post hoc tests after consideration of age, smoking, body mass index, waist circumference, marital status, education, occupational activity, type of work, profession, physical activity, stress exposure as well as well as blood pressure as potential confounders. Group differences of nominal data were calculated by the χ^2 test. The differences between the means of variables within the same treatment group were analyzed with Student's paired *t*-test. Correlations were calculated using Pearson's *r*-tests. Statistical significance was defined as p less than 0.05.

Results

General characteristics of the study groups (Table 1)

There were no significant differences in age, smoking, physical activity, body mass index, waist circumference, education, occupational activity, a type of work, stress exposure, the number and duration of marriages, the number of deliveries, the number of sexual partners and blood pressure between the study groups.

Bromocriptine treatment was well tolerated. Two patients terminated the study before its end: one because of orthostatic hypotension and the other because of hallucinations. The remaining bromocriptine-treated women and all bromocriptine-naïve women reported no significant adverse effects and completed the study.

Biomarkers (Table 2)

With the exception of a marked reduction of prolactin levels, a decrease in HOMA1-IR as well as an insignificant reduction in plasma triglycerides (−10%), $p = 0.078$, bromocriptine treatment of hyperprolactinemic women remained without any effect on the plasma levels of the remaining biomarkers. In bromocriptine-naïve women with hyperprolactinemia and in the control group, prolactin, glucose, HOMA1-IR and lipids remained at a similar