ORIGINAL RESEARCH—INTERSEX AND GENDER IDENTITY DISORDERS

Side Effects of Pharmacotherapy on Bone with Long-Acting Gonadorelin Agonist Triptorelin for Paraphilia

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ABSTRACT

Introduction. There have been limited research studies concerning the use of libido inhibitors for the treatment of patients with a paraphilia. Observational studies suggest that agents that lower testosterone are an effective treatment for paraphilia.

Aim. We report a case of hormonal treatment of paraphilia that was associated with side effects.

Method. A 35-year-old man with a paraphilia was treated with long-acting gonadorelin.

Results. The desired result was reduced preoccupation with sexuality, but there were various side effects including a serious amount of bone loss.

Conclusion. We believe that more attention should be given to the adverse effects of long-term treatment with triptorelin. In our view the drug regime needs to be revised. **Hoogeveen J, and Van der Veer E. Side effects of pharmacotherapy on bone with long-acting gonadorelin agonist triptorelin for paraphilia. J Sex Med 2008;5:626–630.**

Key Words. GnRH agonist; Gonadotr opin-releasing Hormone Agonist; Osteoporosis; Side Effects; Triptorelin

Introduction

A recent Cochrane meta-analysis has shown that research into the use of libido inhibitors for the treatment of patients with a paraphilia is very limited [1]. Although no controlled randomized clinical research results have been published, case studies and minor open research programs indicate that libido inhibitors are an effective treatment for paraphilia [2–4]. The American Psychiatric Association also state that treatments without hormonal pharmacotherapy are clearly less effective in the sense of preventing recurrences than treatment with at least one component of a hormonal therapy [5].

Objectifying and quantifying the reduction in deviant sexual conduct is difficult during the medicinal treatment of paraphilia, given that a desirable response is beneficial to the patient. The patients' perception, activities, and sexually oriented conduct are charted based on clinical interviews, questionnaires, and observations. The level of experience of the person carrying out this type of questionnaire has a positive impact on the reliability of the results. On the other hand, this method has not yet been sufficiently substantiated through the use of equipment such as polygraphs and plethysmographs.

In the Dutch guidelines for treatment of paraphilia, one or two selective serotonin reabsorption inhibitors (SSRIs) are administered, where applicable in combination with cyproteron acetate, following psychotherapy treatment. If this fails to generate any effect, the last step is the administration of gonadorelin (*gonadotropin-releasing hormone*; GnRH agonists), such as

triptorelin. Triptorelin is a strong acting, synthetic analog of the hypothalamus hormone gonadorelin (in this case *luteinizing hormone-releasing hormone* [*LHRH*]), which stimulates the hypophyse to produce luteinizing hormone (LH) and follicle-stimulating hormone (FSH). Continued use results in a suppression on account of the depletion and desensitizing of the gonadotrope hypophyse cells. This generates a reduction in the testosterone levels in a male to castration level within 3 weeks. For the physiological aspects of hormones involved in sexual function, see review [6].

Androgen deprivation therapy is primarily prescribed in relation to a metastases testosterone-sensitive prostate carcinoma. This therapy lengthens the life expectancy of patients with prostate cancer, but causes a hypogonadal status. Gonadal hormones are essential for the integrity of the skeleton and hypogonadism also generates a significant risk of osteoporosis [7]. The androgen deprivation therapy is not a registered treatment for the indication paraphilia and sexual preoccupation or hypersexuality. Therefore triptorelin may only be prescribed in the event that it is used on a voluntary *informed consent* basis. An internist endocrinological consultant is indispensable in such a situation.

The triptorelin patient information sheet states numerous potential side effects, varying from excessive perspiration, hot flashes, and gynecomastia to light trabecular bone loss. Bone loss is generally reversible within 6 to 9 months after stopping treatment (patient information sheet text). The standard Dutch protocol is to prescribe a bisphosphonate for the prevention of osteoporosis. In addition to triptorelin, intramuscular dosage of 3.75 mg per month, our institute (Hoeve Boschoord) also administers a weekly dosage of 70 mg of alendronate, and calcium carbonate on a daily basis. The administration of the last two medicines is controlled.

The available information about the long-term use of antihormonal pharmacotherapy in combination with bisphosphonate for patients with a paraphilia is limited. This case study shows that there are potential side effects. A modification of the protocol is proposed.

Case Study

A 35-year-old male with a mild mental retardation (IQ = 75) was admitted with sexual obsessive behavior. In the past, this person acted out his sexual preoccupation through sexual contact with small children generally while he was under the influence of substances (primarily alcohol), for which he has been charged. Following unsuccessful treatment in accordance with the internationally accepted treatment protocol for paraphilia (including psychotherapy, antipsychotics, SSRI), the use of triptorelin appeared to show a reduced preoccupation with sexuality. This was established based on comprehensive self-reporting, questionnaires, and observations. A decrease in testosterone levels from 22.8 to 1.3 nmol/L was observed following the triptorelin injections. However, the patient reported (side) effects, such as hot flashes, perspiration attacks, erection and ejaculation disorders, and regularly asked whether the medication could be stopped.

Treatment with a weekly dosage of 70 mg of alendronate and a daily dosage of calcium carbonate/cholecalciferol (500 mg/400 IE) was commenced 2 months after the triptorelin treatment was started. As an additional standard test, a quantitative computer tomography (QCT) of the spinal column was made. The results showed an average spinal column bone mineral density (BMD) of 175.9 mg/mL calcium hydroxyl apatite at Th.12 up to and including L.4, with a T-score of 0.04 SD (standard deviation).

The BMD was 166.4 mg/mL with a T-score of –0.31 SD, 18 months after starting the treatment. Thirty-seven months after commencing the triptorelin treatment, he had a strongly deviating BMD for his age and was at threshold osteopenia to osteoporosis levels, namely 134.2 mg/mL with a T-score of –1.53 SD, in spite of the preventative prescription of a bisphosphonate and vitamin D, which were subject to controlled administration. This resulted in the decision to cease the triptorelin medication. Erections and pedophilic sexual fantasies returned almost immediately after halting the medication, which resulted in limiting measures with respect to the freedom of movement of the patient.

Discussion

The measures taken to prevent osteoporosis for this patient through the administration of a bisphosphonate did not work as effectively as required. Various explanations can be given. Bisphosphonates generate 50% fracture risk reduction [8]; it is possible that the patient in question belongs to the other 50%. The load-bearing activities of the patient were too limited during the 16 months of triptorelin use. The nutritional situ-