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Penile anesthesia in Post SSRI Sexual Dysfunction (PSSD) responds to low-power laser irradiation: A case study and hypothesis about the role of transient receptor potential (TRP) ion channels

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ABSTRACT

Treatment of paroxetine-induced penile anesthesia in Post SSRI Sexual Dysfunction (PSSD) by Low-power Laser Irradiation (LPLI) is unknown in medical literature. The aim of the current article is to report partial efficacy of LPLI for paroxetine-induced persistent penile anesthesia. We report on a male patient who presented with a history of reversible loss of smell, taste and skin sensitivity occurring within a week after start of 20 mg/day paroxetine-hemihydrate for a depressive period. Concurrently, patient suffered from penile anesthesia, scrotum hypesthesia, anejaculation and erectile difficulties with normal sexual desire. During 2.5 years of paroxetine treatment and throughout 2 years after paroxetine discontinuation, genital and sexual complaints persisted. Penile anesthesia was treated by LPLI with single and multi diode pulsed laser probes. After 20 LPLI-treatment sessions of 15 min each, patient reported partial return of penile touch and temperature sensation. Clinical improvement of glans penis sensitivity was reported to 20% and 40%, compared to pre-paroxetine treatment penile sensitivity during erect and flaccid states, respectively. However, anejaculation and erectile difficulties remained unchanged. Briefly, in the current patient with early onset of PSSD, LPLI treatment reduced paroxetine-induced penile anesthesia. It is hypothesized that SSRI treatment induces disturbances of transient receptor potential (TRP) ion channels of mechano-, thermo- and chemosensitive nerve endings and receptors resulting in the penile anesthesia in PSSD. It is further hypothesized that there are two types of PSSD, one of which occurs soon after the start of SSRI treatment.

1. Introduction

Selective serotonin reuptake inhibitors (SSRIs) are well-known for their efficacy to treat depression, anxiety disorders and obsessive compulsive disorder, but also for their efficacy to treat lifelong and acquired premature ejaculation (Waldinger et al., 2004; Althof et al., 2014). On the other hand, the SSRIs are also well-known for their reversible sexual side effects, such as decreased sexual desire, impaired orgasm, delayed or lack of ejaculation, and erectile difficulties (Balon, 2006; Segraves, 2007). More rarely SSRIs and other serotonergic antidepresssants may also induce restless genital syndrome (ReGS) or persistent genital arousal disorder (PGAD) which may emerge during SSRI treatment and/or shortly after their discontinuation (Waldinger et al., 2010a, 2010b, 2011). ReGS is not a sexual disorder or a sexual side effect, but it is a separated genital disorder, presumably caused by a sensoric neuropathy of the end-branch of the pudendal nerve, and characterized by genital dysesthesias, pre-orgasmic or pre-ejaculatory genital sensations, with or without restless legs, with or without complaints of an overactive bladder that may persist for a very long time after SSRI discontinuation (Waldinger et al., 2010a, 2010b, 2011). In very rare cases, the common SSRI-induced sexual side effects may persist long after SSRI discontinuation (Csoka and Shipko, 2006; Bolton et al., 2006; Csoka et al., 2008; Bahrick and Harris, 2009; Bahrick, 2008; Farnsworth and Dinsmore, 2009; Kauffman and Murdock, 2007; Kauffman, 2008).

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This has been called Post SSRI Sexual Dysfunction (PSSD) (Csoka et al., 2008). So far, only a few case reports on PSSD have been published (Csoka and Shipko, 2006; Bolton et al., 2006; Csoka et al., 2008; Kauffman and Murdock, 2007). The symptomatology of PSSD varies but comprises both disturbances in sexual desire, sexual arousal, ejaculation, erection and genital anesthesia. The underlying neurobiological mechanism of PSSD is unknown.

In the current article, we describe the case of a male patient, who was referred to the first author for a diagnostic workup and treatment of PSSD, including the persistence of penile anesthesia for over two years after 2.5 years of daily paroxetine treatment. The patient provided written informed consent for publication of his case.

1.1. Case report

Mr. A. is a 43-year-old male with a university Master degree. For a depression related to his divorce he was prescribed 20 mg paroxetine HCL hemihydrate by a psychiatrist for about 2.5 years, e.g., from May 2008 until November 2010. Within 7 days after the start of 20 mg paroxetine, Mr. A. lost his smell and taste and he experienced diminished skin sensitivity over large parts of his body including his penis and scrotum together with the occurrence of anejaculation and difficulties in attaining an erection. Smell and taste fully returned after 2 months. Although he reported these side effects in an early stage to his psychiatrist, he was advised to continue taking paroxetine as it was assumed that the sexual side effects were a temporary phenomenon. As his depression improved, Mr. A. took the decision to gradually reduce the dosage of paroxetine and eventually he stopped taking paroxetine in November 2010. He did not experience complaints of a SSRI discontinuation syndrome. Skin sensitivity gradually returned but persisted in the genital area.

1.1.1. Loss of penile sensitivity

For about 4 months after the last dosage of paroxetine, he got acquainted with his new girlfriend. In April 2011 he had sexual contact with her for the first time, the first partnered sexual activity in about 3 years. During this sexual contact he experienced a complete loss of penile sensitivity. Specifically, the glans penis and shaft were insensitive for touch and temperature whereas the scrotal sensitivity was reduced compared to the time before taking paroxetine. Regarding sexual activity prior to paroxetine treatment, Mr. A. reported highly responsive erections to the slightest penile stimulation, early ejaculations within a minute since puberty, and immediate penile detumescence after ejaculation, suggesting a hypertonic state of lifelong premature ejaculation with erectio praecox and detumescentia praecox (Waldinger, 2014).

After the onset of paroxetine treatment, not only did he develop loss of taste and smell, loss of generalized skin sensitivity, including penile anesthesia and scrotum hypesthesia, he also lost the ability to ejaculate both intravaginally and during masturbation. Moreover, he experienced difficulties in attaining an erection. Sexual desire remained normal and with 50 mg sildenafil he still managed to attain erections.

1.1.2. Tiger balm

Mr. A. also reported that at some point he tested his penile sensitivity by applying Tiger Balm, a menthol and camphor containing ointment that is known to give a local heat sensation when applied to the skin. Application of Tiger Balm on the genitals is presumably intensely unpleasant or painful, but scientific information on its genital application is not available. Nevertheless, Mr. A. did not feel anything of the Tiger Balm at his glans penis except a vague sensation over his scrotum. The sexual difficulties led to a decreased sexual satisfaction, emotional problems and most of all relationship problems. For these complaints, the general physician of Mr. A. referred him and his female partner to a sexual therapist, who referred the couple to the first author after unsuccessful counseling sessions.

Mr. A. was seen by the first author in September 2012 approximately two years after he had stopped taking paroxetine 20 mg daily and 4.5 years after he had started paroxetine treatment. His medical history previous to paroxetine treatment did not report a particular disease or disorder. The sexual history revealed lifelong premature ejaculation since the age of 14 with early ejaculations occurring within about 1 min after vaginal penetration, facilitated early erections and immediate penile detumescence after ejaculation. At the time of testing, Mr. A. was not overweight or obese, he reported to be a non-smoker, and to limited use of alcohol. Mr. A. had a somewhat lower mood, but he did not feel depressed like in 2008 before he started paroxetine treatment. The penile anesthesia, scrotum hypesthesia (albeit less at the ventral part of the scrotum), anejaculation and difficulties in attaining an erection in the presence of a normal sexual desire were present in the same extent as he experienced in the last 4.5 years. He reported to use 50 mg sildenafil to attain an erection. Without sildenafil, attaining an erection took much longer than previous to paroxetine treatment but penile rigidity remained normal. Mr. A. was diagnosed as having PSSD induced at the very onset of 2.5 years of daily treatment of paroxetine HCL hemihydrate 20 mg. A general laboratory investigation in May 2012, on request of his general physician, did not show any abnormalities, e.g., fasting glucose, HbA1C, TSH, ESR and cholesterol were normal. However, at the time testosterone was not examined. Mr. A. was informed about the lack of evidence-based treatment for genital anesthesia and that his anesthesia could be contributive to his anejaculation and erectile difficulties.

1.1.3. Low-power laser irradiation

Since no effective medical treatments for PSSD are available, Mr. A. agreed to experimental treatment by the local application of low-power laser irradiation (LPLI, also known as Low Level Laser Therapy or Cold Laser Therapy). For LPLI treatment Mr. A. was referred to the second author.

At the first visit in October 2012, Mr. A. was treated with a 915 nm 100 mW, energy density: 0.80 $W/cm^2 = 48$ J/cm^2, class 3B laser probe (Omega XP) in multipulse mode (73,146,700 Hz alternating), applied transcutaneously. The probe was placed on the ventral side of the glans penis, on both lateral nerve branches at the base of the penis and with a 46 diode cluster probe (mix of wavelengths 660 nm, 820 nm, 870 nm, 880 nm, 940 nm, 950 nm) energy density: 0.075 $W/cm^2 = 9.7$ J/cm^2 on the lower back over the spinal nerve roots.

After the first five LPLI treatments, which all took place in October 2012, Mr. A. reported slight tingling at the glans penis which lasted for about two hours after which they disappeared again. These sensations at the glans penis had been absent since the use of paroxetine.

1.1.4. Improvement of penile sensitivity

In January 2013, after 20 LPLI treatments, Mr. A. reported an improvement of 10–15% of the sensitivity of particularly the glans penis, compared to the penile erection state prior to paroxetine treatment. He could feel the touch of his hand and that of his partner and also regained the capacity to distinguish warm and cold penis stimulation at the glans penis. Mr. A. was relieved by this improvement, but still was not able to ejaculate, neither intravaginally nor by masturbation. Also the difficulties attaining an erection were unchanged in the presence of normal sexual desire. Laboratory