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Methylphenidate-induced spontaneous ejaculation

Bedriye Öncü, Burçin Çolak and Okan Er

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Correspondence to:
Burçin Çolak, MD
Department of Psychiatry, Ankara University, Ankara, Turkey
burcincolak@hotmail.com

Bedriye Öncü, MD
Okan Er, MD
Department of Psychiatry, Ankara University, Ankara, Turkey

Introduction

Methylphenidate (MPH) is the most commonly prescribed medication for attention deficit hyperactivity disorder (ADHD). Besides common side effects such as insomnia and loss of appetite, there are some rare side effects such as sexual dysfunction. Priapism, hypersexuality and excessive masturbation in children and spontaneous erection in adults have been reported with MPH [Bilgiç *et al.* 2007; Kelly *et al.* 2013]. Oosterhuis and colleagues reported spontaneous ejaculation in a 25-year-old man with MPH [Oosterhuis *et al.* 2009]. To our knowledge pubertal children have not been studied in this respect. Here we will present an adolescent with ADHD who reported spontaneous ejaculation during short-acting MPH therapy.

Case report

A 16-year-old boy with complaints of inattention, careless mistakes, lower than expected academic achievement and a childhood history of ADHD was diagnosed as ADHD predominantly inattentive type according to the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR). This young boy was 172 cm in height and 56.4 kg weight and was prescribed 30 mg of MPH daily. İn the first 2 months there were improvements in attention and concentration, the only side effect was feeling sleepy when the effects of the medication wore off. After 2 months of treatment, he reported an increase in anxiety, especially during written examinations. When the examinations were about to end, he also had spontaneous ejaculation with increasing anxiety. This incident happened twice: in the first examination he had three spontaneous ejaculations and in the second examination he had two spontaneous ejaculations. Neither salient erections nor sexual arousal were associated with the ejaculations. Concomitant medication use was not reported. The patient also reported a single spontaneous ejaculation that seemed to be associated with MPH 4 years earlier. Following cessation of the drug spontaneous ejaculations disappeared.

Discussion

Facilitating effects of psychostimulants and MPH on sexual function have been shown previously [Bilgiç *et al.* 2007; Kelly *et al.* 2013]. However, psychopharmacological mechanisms of stimulant-related ejaculation are not well studied.

MPH is a piperadine derivative, which binds to the dopamine transporter and noradrenaline transporter in the presynaptic cell, blocking dopamine and noradrenaline reuptake and increasing their extracellular levels [Schweri *et al.* 1985; Kuczenski and Segal, 1997]. Whereas an MPH-induced increase in synaptic dopamine levels is comparable with amphetamines, increase of noradrenaline is less than amphetamines with no significant effect on serotonin [Kuczenski and Segal, 1997; Markowitz *et al.* 2006]. Dopamine has been related with libido and sexual arousal associated with hypersexuality and spontaneous erections [Melis and Argiolas, 1995]. The sexual side effects of antiparkinsonian drugs confirm this mechanism [Klos *et al.* 2005]. Apomorphine (a dopaminergic agonist) was found to be effective in erectile dysfunction [Mulhall *et al.* 2001]. Another recent study showed that levodopa, another dopamine agonist, enhances activations in brain-reward systems associated with subliminal sexual stimuli [Oei *et al.* 2012]. So, spontaneous ejaculations in this patient might be mediated through the dopaminergic system. Nevertheless it would be a reductionist approach if we claimed that the exact mechanism of this side effect is directly due to dopamine increase. İn recent case reports, some sexual side effects, such as priapism and hypersexual behaviour, associated with MPH

was related to the cessation of the drug [Kelly *et al*. 2013; Coşkun and Zoroglu, 2009]. Furthermore, dopamine is more related to the first (libido) and the second stage of sexual response (arousal and erection). İn the third phase (orgasm; ejaculation in men), the effects of dopamine seem to be less important [Coşkun and Zoroglu, 2009; Stahl, 2012].

The central and peripheral pathways of ejaculation are associated with noradrenaline and MPH is also a reuptake inhibitor of noradrenaline [Stahl, 2012]. İn this respect, the noradrenergic effects of MPH may have a role in spontaneous ejaculation by peripheral effects on the sympathetic system, that is by reducing ejaculatory latency time [Oosterhuis *et al*. 2012; Coşkun and Zoroglu, 2009]. There are case reports of spontaneous ejaculation with the use of norepinephrine-reuptake inhibitors like milnacipran, reboxetine and zotepine [Oosterhuis *et al*. 2012]. Spontaneous ejaculation in this young man might have occurred through the aforementioned mechanism. Spontaneous ejaculation occurred when the patient became more anxious towards the end of the examination. Considering the activity of the sympathetic system in anxiety, MPH might have become an enhancer of this unusual side effect.

After cessation of MPH, the side effect disappeared but ADHD symptoms became apparent again. Adding a concomitant selective serotonin reuptake inhibitor (SSRI) instead of cessation of the stimulant might be a treatment option. Bartlik and colleagues showed that MPH apparently reversed sexual dysfunction secondary to SSRIs [Bartlik *et al*. 1995]. If we consider the opposite, it would be a reasonable option. Serotonin is an inhibitor of the orgasm phase [Stahl, 2012]. Consequently it is widely misused for premature ejaculation. İt makes more sense to use an SSRI for an undesired ejaculation such as spontaneous ejaculation, which suggests a more causal relationship with the peripheral pathways of ejaculation. However, there are not enough data that support this opinion.

Conclusion

This case report suggests that clinicians should be aware that MPH may induce some unusual side effects such as spontaneous ejaculation. Further research is needed to understand the exact mechanism and treatment options for this rare side effect.

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Conflict of interest statement

The authors declare that there is no conflict of interest.

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