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Letter to the editor

Paroxetine-induced enuresis

I would like to include one case to the literature on children and adolescents who have developed enuresis while taking paroxetine. Up to now, the fact that enuresis may have occurred as a result of the side effect of using paroxetine was not reported in some articles and letters.

A 14-year-old girl presented at the Department of Child and Adolescent Psychiatry had obsessive–compulsive disorder (OCD) agoraphobia according to DSM-IV [1]. Her obsessive–compulsive symptoms, including contamination, controlling and checking started approximately at the age of eight. After the patient and her family were informed about the disorder, treatment with paroxetine was started at a dosage of 20 mg/d. When she was being treated with 20 mg paroxetine, nocturnal and diurnal enuresis symptoms started on the second day. The frequency of diurnal enuresis was four or five times a day, whereas the frequency of nocturnal enuresis was two or three times in the night. Due to the occurrence of enuresis after treatment with paroxetine, it was stopped on the fifth day and diurnal and nocturnal enuresis decreased and stopped in 2 d.

Enuresis is the repeated voiding of urine onto a child's clothes or bed; voiding may be involuntary or intentional. The term is often used alone, imprecisely, to describe wetting that occurs only at night, during sleep. It is more accurate, however, to refer to nighttime wetting as nocturnal enuresis; this distinguishes it from daytime wetting [1,4].

Psychopharmacological treatment of psychiatric disorders in children and adolescents is not as well established as that in adults. Data on pharmacodynamics, pharmacokinetics, efficacy and tolerability are relatively scarce. Selective serotonin re-uptake inhibitors (SSRIs) are an effective component of treatment for depression and anxiety disorders in children and adolescents [10].

Paroxetine, one of the SSRIs, inhibits serotonin re-uptake very selectively and it is free of anticholinergic, antihistaminic and antiadrenergic side effects. However, it somewhat inhibits presynaptic re-uptake of dopamine [3], and noradrenaline [9]. Paroxetine is approximately 95% protein bound. The elimination half-life of paroxetine is approximately 24 h. It is highly lipophilic and accumulates in fat-rich tissues, including in cells of the CNS, and is metabolized primarily in the liver by cytochrome P-450 (CYP-450). The potential for accumulation effects may be important with respect to long-term unwanted effects and also in terms of continuation of effects after withdrawal [8].

Despite extensive research and a voluminous body of literature, a simple explanation for enuresis does not exist. Serotonin (5-HT) may participate in the peripheral neural control of the bladder and urethra, although its central effects are probably more substantial. Immunochemical techniques demonstrate small intensely florescent (SIF) cells in pelvic ganglia which are immunoreactive for 5-HT. 5-HT immunoreactive fibers also surround ganglion cells [7].

As has occurred with most receptors, 5-HT binding sites were first characterized using non-specific, then relatively specific ligands, leading to four subfamilies, namely, 5-HT1, 5-HT2, 5-HT3 and 5-HT4. Among the 5-HT1 subfamily, 5-HT1A, 5-HT1B, 5-HT1C and 5-HT1E receptors were found [5].

5-HT or its agonists primarily inhibit, and occasionally facilitate, cholinergic ganglionic transmission in pelvic ganglia [6]. Furthermore, 5-HT facilitates neurally evoked bladder contractions by increasing the release of acetylcholine from nerve terminals in the bladder wall. 5-HT has also been shown to contract the bladder body and relax the bladder neck [2]. The excitatory effects on bladder smooth muscle are blocked by 5-HT2 antagonists [5].

According to this biochemical mechanism, enuresis would have occurred. In this case, only the association between paroxetine and enuresis was investigated. Therefore, further study is needed to investigate this issue for SSRIs.

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