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Excessive yawning and SSRI therapy

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As we become more experienced with the long-term use of selective serotonin reuptake inhibitors (SSRIs), more subtle side-effects may become evident. Clinicians may be aware of yawning as a side-effect of antidepressant therapy, however sparse literature exists on the topic. We present two cases in which excessive daytime yawning was associated with SSRI treatment.

Case 1

Mr S. is a 32-yr-old computer analyst who began treatment for a major depressive episode with 10 mg/d fluoxetine. His depression responded rapidly to treatment, however following 1–2 wk therapy, he began to experience excessive daytime yawning. The patient estimated that yawning occurred 20–30 times daily. The yawning was not associated with sedation or a feeling of needing sleep. He was disturbed by this effect, as yawning occurred during business meetings and interpersonal interactions. This led the patient to become concerned that others would interpret this as a sign of boredom or lack of attention and interest.

Because of inhibition of ejaculation, fluoxetine was discontinued after 9 months. At the patient's request, no medications were given during the following 3 months and yawning quickly diminished to 3–4 times per day. The subject's depression recurred however, and 10 mg/d citalopram was prescribed. Excessive yawning resumed 1–2 wk following citalopram initiation at a frequency of 20–30 times per day. Again, adverse sexual effects occurred and citalopram was discontinued. Treatment with 100 mg/d bupropion SR was begun and the excessive yawning has not recurred.

Case 2

Dr L. is a 46-yr-old physician who began treatment of a major depressive episode with 50 mg/d sertraline. Following 1–2 wk treatment, he began to experience 75–100 yawning episodes daily. This was very distressing to him, as the yawning occurred in the presence of patients, co-workers and during meetings. Frequently, patients made

comments regarding the physician's yawning. This was so bothersome to him that discontinuation of the sertraline was necessary. The excessive yawning remitted within 1 wk and has not recurred following 18 months of treatment with 150 mg/d bupropion SR.

Discussion

In the cases presented, yawning occurred with three different SSRI agents and remitted following SSRI discontinuation. In one case, the excessive yawning returned upon re-challenge with a different SSRI and remitted again following its discontinuation. Neither patient experienced this side-effect with bupropion therapy. The yawning did not seem to be associated with daytime sleepiness or sedation and was moderately to severely bothersome to both patients.

In preliminary studies, up to 11% of patients receiving fluoxetine reported yawning as a side-effect of treatment, compared with 0% taking placebo [*Physicians Desk Reference* (PDR), 1999a]. This appeared to be more common in patients with bulimia and obsessive-compulsive disorders than in depression (PDR, 1999a). In fact, no patients in early studies of fluoxetine in depression reported yawning as a side-effect (PDR, 1999a). Initial studies of citalopram demonstrated only 2% of patients reporting yawning as a side-effect compared to < 1% on placebo (PDR, 1999c). Yawning was not assessed in placebo-controlled trials of sertraline use (PDR, 1999b). Excessive yawning has been reported in humans taking clomipramine (McLean et al., 1983) and in rats treated with desipramine (Mogilnica et al., 1986). In the desipramine-treated rats, yawning was reduced with haloperidol administration leading the authors to postulate that a dopaminergic mechanism may be involved. They also theorized that noradrenergic stimulation (through antidepressant treatment) may play a role in yawning induction. Serotonin reuptake inhibitor administration did not lead to increased yawning in rats. In our cases however, a serotonergic mechanism may have played a role. Complex neurotransmitter systems make pinpointing an exact mechanism of yawning induction difficult and conflicting data exist regarding the role of specific neurotransmitters.

In the two cases presented here, yawning seemed to be particularly frequent and bothersome. Although activation can be commonly experienced by some patients receiving SSRIs, others report daytime sleepiness as a

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side-effect. In both of our subjects, insomnia or sleep difficulty was not associated with the excessive yawning, nor was a sense of daytime sedation or sleepiness. Although the mechanisms of the excessive yawning remain unclear, it seems to be related to something other than simple fatigue associated with depression, insomnia, or sedation associated with SSRI therapy. We look forward to future reports of this interesting side-effect in association with psychotropic agents.

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