Beneficial Sexual Side-effects From Fluoxetine

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We report cases of several side-effects from the antidepressant fluoxetine. We suggest that, at therapeutic doses, fluoxetine may have a beneficial effect on sexual function in some men with erectile failure and premature ejaculation.

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The bicyclic propylamine antidepressant, fluoxetine hydrochloride, is a potent serotonin reuptake blocker with an affinity for muscarinic, α_1 adrenergic and H_1-histamine receptors with little, if any, effect on the reuptake of other monoamines (Stark *et al*, 1985). The reported rate of treatment-related sexual dysfunction ranges from 5% (Stark *et al*, 1985) to 8% (Herman *et al*, 1990), although under-reporting of fluoxetine's sexual side-effects due to patient or doctor reticence, or both, has been suggested (Musher, 1990). Recognised problems include anorgasmia in women and anorgasmia, delayed or inhibited orgasm and ejaculation in men (Kline, 1989; Lydiard & George, 1989; Herman *et al*, 1990; Zajecka *et al*, 1991; Musher, 1990).

Modell (1989) reported a case of a woman developing spontaneous yawning, clitoral engorgement and multiple orgasms. Although these sexual side-effects were universally experienced as unpleasant, few patients elect to stop fluoxetine as a result, provided their depressive symptoms responded (Mendels, 1987).

Case reports

Case 1

B, a 67-year-old married man, presented with a 12-week history of major depression, meeting DSM–III–R criteria (American Psychiatric Association, 1987). He had discontinued imipramine, started by his general practitioner, because of hypotensive side-effects three weeks earlier. He denied any sexual difficulties, admitting only to loss of libido for approximately the last eight weeks. Treatment with fluoxetine (20 mg, daily) was commenced.

Within 12 days the depressive symptoms improved, abating after seven weeks. Treatment was then continued for six months. B reported no side-effects (sexual effects were specifically denied) at any time during the treatment phase. Three weeks after the drug was discontinued B returned to the clinic accompanied by his wife demanding reinstitution of fluoxetine because his pre-depressive illness level of sexual functioning had returned. There was no recurrence of depressive symptoms. He had had erectile impotence, as opposed to premature ejaculation, for 17 years. However, while on fluoxetine the duration of satisfactory erection was approximately 15 minutes (wife's estimate) and when drug free it reduced to a few seconds (too short to allow penetration). They refused the sex therapy which was offered after elimination of organic aetiological causes for the erectile difficulty. One week after the reintroduction of fluoxetine sexual function returned to a satisfactory level.

Case 2

C, aged 78, presented with depression and subjective memory impairment. On examination, cognitive function was found to be normal but his depressive symptoms fulfilled DSM–III–R criteria for major depression. He complained of loss of libido for nine months, which coincided with his dysphoria and poor memory. He had long-standing, poor-quality erection (semi-flaccid) with premature ejaculation and associated anxiety in sexual situations. The history was confirmed by his (male) sexual partner. After four weeks of treatment with fluoxetine, both his depressed mood and subjective memory impairment resolved. The couple's sexual problems were treated with sensate focus (Masters & Johnson, 1970) and exploration of underlying guilt about homosexuality. Termination of fluoxetine after six months resulted in a return of poor-quality erection, failure to maintain erection, and premature ejaculation without situational anxiety. There was no recurrence of depressive symptoms. The sexual difficulties resolved two weeks after reintroduction of fluoxetine (20 mg, daily).

Discussion

Because fluoxetine exerts little if any effect on cholinergic and adrenergic receptors, the direct or indirect effects of increased amounts of serotonin on spinal, peripheral or central receptors, either individually or in combination, may be inhibiting ejaculation. Serotonin has been shown to cause inhibition of ejaculation within central and spinal pathways in animals (Svensson & Hanson, 1984). Serotonin may directly relax the smooth muscles involved in orgasm and ejaculation via a similar mechanism by which it relaxes vascular smooth muscle (Vanhoutte & Lischer, 1986). Serotonin may, on the other hand, be playing an inhibitory role on the noradrenergic excitatory mechanisms of orgasm (Brindley, 1981).

Fluoxetine does not have a product licence for treatment of erectile disorders. In both of these cases the sexual difficulty did not have an underlying organic cause. C and his partner underwent routine sex/relationship therapy (Masters & Johnson, 1970), which did not resolve the problem, whereas B and his partner refused sex therapy as an alternative.

The alternative treatments for erectile impotence (in case 1 and secondary to premature ejaculation in case 2) were considered and discussed with the patients and their partners, for example vacuum-pump devices, surgical implantation of penile prosthesis, and the intracavernosal injection of vasoactive substances (e.g. papaverine (Virag, 1982)).

Papaverine, either alone or in combination with phentolamine, is effective in about 70% of patients but the disadvantages are significant. There is a 40–50% treatment drop-out rate, mainly due to low patient acceptability, priapism, reduced erection quality with prolonged use, and tissue fibrosis (Krane *et al*, 1989).

Intracavernosal injection of prostaglandin E1 is less likely to produce tissue fibrosis but causes pain at the injection site in 20–30% of users (Artoux & McQueen, 1991).

These case reports raise the possibility that fluoxetine may have a beneficial clinical effect on erectile function in some patients. In these cases a beneficial effect was achieved in both premature ejaculation and poor-quality erection. Both patients also claimed to have improved libido while taking fluoxetine, and, as there was no recurrence of depressive symptoms, the reduction on stopping the fluoxetine was unlikely to be depressive.

By the age of 75, as many as 55% of men have periods of erectile difficulty (Krane *et al*, 1989), while general population estimates range from 3–10% across all age groups (Spector & Carey, 1990; Riley, 1990). The lack of reports of advantageous effects on sexual function may be due to the same factors that lead to under-reporting of sexual side-effects in general. It is possible that if fluoxetine is treating an age-related problem, ageist attitudes of both doctors and patients may prevent discussion of the sexual aspects of both depression and its treatment (Power-Smith, 1991).

These cases suggest that further investigation of the role of specific serotonin reuptake inhibitors on sexual functioning may usefully add to the understanding of sexual dysfunction and its treatment possibilities.

If fluoxetine proved an effective treatment it would be beneficial because of the greater aesthetic acceptability of an oral preparation over the other available treatment options.

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