Ir J Psych Med 1998; 15(2): 76-79

Amitriptyline-induced anorgasmia reversed by nefazodone

Sir – Delayed or absent ejaculation and/or orgasm is the commonest sexual side-effect of antidepressant drugs, matched only by decreased libido. Attempts to treat antidepressant-induced anorgasmia with cyproheptadine, amantadine, methylphenidate, yohimbine, dosage reduction, drug holidays and drug substitution had mixed results.[1] We report a case of amitriptyline-induced anorgasmia reversed by switching over to nefazodone.

A 31 year old married man was referred with a first episode of major depression of six months duration. Prior to the onset of depression he was sexually active. He had decreased libido and decreased frequency of sexual intercourse since the onset of the depression. His depression as well as his libido improved on treatment with amitriptyline 200mg for four weeks. However, he was unable to attain ejaculation/orgasm even after trying for 30 minutes and caused his wife genital soreness. This increased the strain on their marriage which was already affected by his depression. Therefore we stopped the amitriptyline and commenced him on nefazodone. Six weeks after being on nefazodone 400mg/day, he reported complete return of normal sexual functioning while his depression remained in remission.

This is the first report of successful reversal of antidepressant-induced anorgasmia by substitution with nefazodone. Nefazodone inhibits serotonin reuptake and blocks 5-HT_2 receptors, resulting in the facilitation of 5-HT_{1A} neurotransmission. Both 5-HT_2 blockers[1] and 5-HT_{1A} agonists[2] facilitate male rat sexual behaviour. This may explain the reports of nefazodone causing spontaneous ejaculations[3] and correcting sertraline-induced anorgasmia when used as an adjunct.[1]

All antidepressant drugs have the potential to cause sexual side-effects which can cause distress, impair quality of life and reduce compliance with treatment. An adverse effect in one patient may be used beneficially in another.

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Extrapyramidal reactions from concurrent SSRI and atypical antipsychotic use

Sir – In a recent letter, Farragher and Walsh[1] report what they believe is a delayed onset of extrapyramidal side-effects in a patient concurrently receiving paroxetine and risperidone. In their letter they explain that their patient had a diagnosis of paranoid schizophrenia, had received at least three antipsychotics (separately) prior to receiving risperidone, and had never experienced an extrapyramidal reaction. Further, this 45 year old man had safely taken risperidone up to 6mg/day for a duration of one year and had also initially tolerated the eventual addition of paroxetine 20mg/day to risperidone 4mg/day for a total of 18 days. This patient then presented 48 days post-discharge with bucco-facial rigidity and involuntary movements of the same area. The authors essentially conclude by attributing this extrapyramidal reaction to paroxetine. I believe that additional points are worth raising.

First, the authors line of reasoning for determining that paroxetine was the 'likely causative factor' of this patient's delayed EPR is incomplete. In their letter, Farragher and Walsh contend that because their patient had tolerated higher previous risperidone doses for one year, that risperidone could not have played a role. Further, because their patient was able to tolerate this higher dose of risperidone previously, the authors rule out the possibility that a pharmacokinetic drug-drug interaction between paroxetine and risperidone may have contributed to this patient's EPR. The extrapolation here would be that paroxetine, through its inhibition of the CYP-450 2D6 isoenzyme, may elevate plasma risperidone levels which would in turn mimic a higher dose of risperidone.

In considering the cause of this EPR, we should not lose sight of the fact that risperidone is a potent D_2 receptor antagonist[2,3] and that because the patient was taking the risperidone, that some degree of D_2 antagonism was occurring because of this drug. In addition to possibly raising plasma risperidone levels, paroxetine may have been causing an indirect inhibition of dopaminergic activity,[4] this may manifest in some patients as an EPR. The concurrent pharmacodynamics of risperidone and paroxetine (with or without the said pharmacokinetic interaction) was not proposed in the letter by Farragher and Walsh. The only way that paroxetine could have been assessed to be the sole cause of this patient's EPR is if paroxetine was re-administered alone and the same reaction occurred. It is therefore reasonable to assert that this reaction could not have occurred without the degree of D_2 receptor antagonism being exerted by the risperidone.

Second, the above presumes that the patient was diligent in following his prescribed dosing regimen. Farragher and Walsh do not address the reliability of their patient to remain compliant with the prescribed pharmacotherapy. Non-compliance being a realistic concern for any pharmacotherapeutic regimen, it is certainly plausible to consider that their patient was not reliably taking either or both medications as prescribed. Given this, we do not truly know whether the reported EPR was in fact due to paroxetine, risperidone, both, or neither.

A final comment involves the extent to which extra-