CLINICAL VIGNETTE

Withdrawal Symptoms with Discontinuation in Selective Serotonin Reuptake Inhibitor Medications

Gregory J. Lam, MD and George C. Yen, MD

Case

A 26-year-old female with generalized anxiety and self-reported obsessive-compulsive disorder tendencies had been taking escitalopram initiated by an outside community psychiatrist. She had been doing well overall, reporting improvement in her symptoms since starting the medication. She denied any noticeable adverse effects since starting escitalopram. She was also taking spironolactone for her acne and an oral contraceptive pill. The patient called and reported she is no longer seeing her psychiatrist, and was interested in weaning off escitalopram. She had been taking 20mg daily for eight months total. She was counseled to wean down to 10mg for one week, and then 5mg for another week, and then to stop. About three weeks later, the patient complained of severe dizziness, lightheadedness, "brain shaking/rattling", headaches, and hot flashes. She had followed instructions regarding the tapering of escitalopram, and had last taken a 5mg dose four days prior. She was evaluated and had normal vital signs, normal neurologic examination, and normal otoscopic examination. We discussed whether she should restart on a low dose of 5mg of escitalopram to ameliorate her symptoms, but she declined. Two-weeks later, the patient emailed and stated her symptoms had completely resolved.

Discussion

Antidepressants including selective serotonin reuptake inhibitors (SSRIs) are commonly prescribed in the outpatient setting. In 2011-2014, approximately 12.7% of persons age 12 and over reported antidepressant medication use during the past month, including 19.1% in persons ages 60 and over.[1] Although antidepressants have assisted in treating various mood disorders including anxiety and depression, there are various adverse effects associated with these medications that can lead to challenges with medication adherence as well as patient quality of life. Commonly reported adverse effects including sexual dysfunction, insomnia, weight gain, and drowsiness.[2] The potential for withdrawal symptoms with the discontinuation of antidepressants also must be considered by both providers and patients. Descriptions of symptoms associated with cessation of SSRIs first appeared in case reports in the mid-1990's.[3] Zejecka et al proposed a definition of antidepressant discontinuation syndrome as the onset of a cluster of somatic and psychiatric symptoms following the discontinuation of an SRI (serotonin reuptake inhibitor), not attributable to other causes such as other medications or illness. The symptoms included dizziness, light-headedness, insomnia, fatigue, anxiety/agitation, nausea, headache, and sensory disturbance.[3] Black et al. proposed diagnostic criteria for SSRI discontinuation syndrome. These include: two or more of the following symptoms developing within 1-7 days of discontinuation or reduction in dosage of an SSRI after at least one month of use. The symptoms are severe enough to cause clinically significant distress and are not due to a general medical condition or recurrence of a mental disorder. Symptoms include dizziness, light-headedness, vertigo or feeling faint; shock-like sensations or paresthesia; anxiety; diarrhea; fatigue; gait instability; headache; insomnia irritability; nausea or emesis; tremor and visual disturbances.[4]

Studies report certain SSRIs have greater risk of discontinuation symptoms. Randomized controlled trials and retrospective studies demonstrated significantly greater withdrawal symptoms with patients taking paroxetine compared to those taking other SSRI's such as fluoxetine, sertraline, citalopram, escitalopram, although symptoms were reported in all forms of SSRIs.[5] A randomized control let trial using placebo substitution across all drug groups found a statistically significant relationship between the percentage reduction in plasma concentration of the drug and the appearance of discontinuation symptoms.[6] This led to the belief that discontinuation symptoms were more frequent after the abrupt cessation of medications with shorter half-lives. This was supported by paroxetine's mean half-life of 20 hours, compared to citalopram (36 hours) and fluoxetine (1-4 days) with longer half-lives and less frequent discontinuation symptoms.[7] Other factors associated with increased frequency of discontinuation symptoms include taking an SSRI for at least 5-8 weeks, higher dose of SSRI, taking an SSRI with non-linear pharmacokinetics, inconsistent compliance, and patients with prior discontinuation symptoms with other antidepressant medications.[8]

Various measures should be implemented to minimize the risk of developing discontinuation syndrome. Proper counseling when initiating an SSRI will prevent patients from self-discontinuation without proper guidance from a medical prescriber. Anticipatory guidance will also reduce patient distress if discontinuation symptoms do develop, and reduce anxiety surrounding thoughts of being addicted or dependent on psychotropic medications. Selection of an SSRI or any psycho-

tropic agent that has a longer half-life is key, particularly if a patient has a history of discontinuation syndrome or has inconsistent medication adherence or follow-up. Fluoxetine is one of the safest choices in these situations. There is no standard tapering regimen that is universally recommended for SSRIs, and recommendations may depend on the duration the patient has been on the medication. Generally, a progressive taper of the SSRI over at least four weeks is recommended, with a 25% reduction in dose every one to two weeks being reasonable.[9] Others have suggested a more conservative tapering schedule of 25% dose reduction per month for any antidepressant.[10] It is important to continue close monitoring and follow-up with the patient during the weaning period until the patient has completely discontinued the medication.

If discontinuation syndrome does occur, there are several management options. Reassurance that symptoms are generally self-limiting and non-life threatening will help to ease anxiety and distress. If symptoms are moderately or severely bothersome, the dose of the medication can be reverted back to the previously tolerated dose, and the taper regimen prolonged with longer periods between dose reductions of one to two months. Another option involves immediately stopping the current SSRI and starting fluoxetine at 10-20mg per day until symptoms abate, then proceeding to taper fluoxetine over 2-4 weeks.[9] If another antidepressant medication is needed to help continue management of anxiety or depression, direct switching to a different SSRI at an equivalent dose or cross titration to a different psychotropic agent should be considered.

Conclusion

With increasing attention to mental health in the general population, conditions like depression and anxiety are common chief complaints that primary care physicians need to be comfortable managing. Discontinuation syndrome has the potential to cause significant patient distress, particularly at a time when they are already experiencing severe depression or anxiety. An episode of discontinuation syndrome with one psychotropic agent may cause reluctance to consider other medications for future treatment. Careful initiation, titration, and tapering of pharmacotherapy is needed. Selecting a psychotropic agent with a long half-life, instituting a gradual taper schedule, and using fluoxetine as a bridge are methods to prevent and manage discontinuation syndrome.

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