To the Editor,

Escitalopram is a relatively new selective serotonin reuptake inhibitor (SSRI) and is one of the most widely used drugs to treat major depressive disorder. More common side effects of escitalopram are nausea, dry mouth, vomiting, dizziness, agitation and insomnia. Premarketing and postmarketing data also indicate infrequent incidence of menstrual disorders or irregularity and metrorrhagia. The underlying pharmacological mechanism of this effect is unknown but is thought to be related to the modulation of serotonin.

CASE

A 21-year-old woman with no comorbid medical conditions was diagnosed with major depressive disorder. Blood count and biochemistry including thyroid function tests and vitamin B12 levels were normal. Medical therapy was initiated with escitalopram 5 mg/day for 4 days; on the fifth day, the dose was increased to 10 mg/day. At the eighth-day follow-up visit, the patient reported intermenstrual spotting-like bleeding since the 6th day of treatment. She had no history of menstrual irregularity or intermenstrual bleeding. The patient was referred to the gynecology clinic for work-up. Blood and coagulation tests, radiologic studies and gynecologic examination did not reveal any underlying gynecologic pathology. The patient was lost to follow-up, and when she presented to the psychiatry outpatient clinic three weeks later, she reported that she had discontinued escitalopram and the vaginal bleeding had ceased one day later. The patient was briefed on possible side effects of escitalopram and after obtaining informed consent escitalopram 5 mg per day was reinitiated. The patient reported recurrence of vaginal bleeding on the second day of escitalopram rechallenge. The patient was asked to continue taking 5 mg per day, but vaginal spotting did not cease for the next two days. Escitalopram was discontinued and the patient’s vaginal bleeding stopped approximately 18 hours later.

DISCUSSION

Aside from the more common and mostly mild side effects which are often well tolerated by the patients, there is also potentially severe bleeding as a complication associated with SSRIs. There are reports indicating increased risk of gastrointestinal bleeding, and bleeding in non-gastrointestinal sites such as epistaxis and ecchymosis, albeit much rarer, has also been reported.

The serotonin reuptake mechanism is found also in non-neural cells such as platelets, and its inhibitory effect on platelet aggregation and vasoconstriction is the proposed etiology of hemostatic disturbances seen with SSRIs. Modulation of hormonal levels by stimulating luteinizing hormone, prolactin, estradiol, and progesterone secretion and inhibitory effects on gonadal steroid metabolism are also thought to play a role.

In the current literature, to our knowledge, intermenstrual vaginal bleeding associated with
Escitalopram has not been reported. The Naranjo adverse drug reaction probability scale yielded a score of 8 out of 13 points for escitalopram as a probable cause of the patient’s intermenstrual vaginal bleeding. Vaginal bleeding started after administration of escitalopram, stopped after discontinuation, recurred on escitalopram rechallenge, and ceased again after discontinuation. A definite association was not proven on the grounds that dose-dependent changes in the severity of adverse reaction was not observed and placebo challenge could not be utilized. Escitalopram’s mechanism of serotonin modulation as a cause of vaginal bleeding remains ambiguous. This case, however, supports premarketing and postmarketing data indicating escitalopram as a potential cause of menstrual disorders or irregularity and metrorrhagia.

References:


1M.D., Ercis State Hospital, Psychiatry Unit, Van - Turkey. 2M.D., Ercis State Hospital, Radiology Unit, Van - Turkey. 3M.D., Ercis State Hospital, Obstetrics and Gynecology Unit, Van - Turkey

Correspondence Address: Dr. Abdullah Yıldırım
Erciş Devlet Hastanesi, Psikiyatri Polikliniği, Erciş, Van - Türkiye
Email address: yldrmbullah@yahoo.com

This letter was accepted for publication in October 14, 2014.

Declaration of interest:
A.Y., D.T., E.K., Y.K.: The author reported no conflict of interest related to this letter.