Pramipexole-Induced Peripheral Edema in a Patient With Bipolar Depression

To the Editor: Pramipexole (PX) is a potent nonergoline agonist at the D_2 dopamine-receptor group, with highest affinity to D_3 dopamine-receptors.[1–4] it has been shown to be an effective treatment for Parkinson's disease and restless legs syndrome.[2,3] recently, it has been reported that pramipexole is also effective for treatment-resistant depression or bipolar depression.[1,4] to our knowledge, this is the first report of a patient using PX for bipolar depression who developed pedal edema.

Case Report

"Ms. A," A 46-year-old married woman, had a 15-year history of bipolar II disorder according to DSM-IV-TR criteria. She had no history of other general medical disease or drug abuse. She had experienced at least two documented hypomanic episodes each year, and at presentation was undergoing a 10-month depressive episode. She showed feelings of guilt, loss of motivation, and suicidal ideation. Her medications included nortriptyline 50 mg/day, valproate 400 mg/day, and lithium 400 mg/day. Although her nortriptyline dosage was increased to 55 mg/day, her depressive symptoms persisted and she became overly sedated for 4 weeks. After that, pramipexole 0.25 mg/day was added, and nortriptyline was discontinued. Two weeks after the addition of pramipexole, she noticed difficulty wearing her shoes and walking. Physical examination revealed severe pitting edema of both lower limbs extending to the feet. Laboratory studies including serum glucose, creatinine, hemoglobin, total protein, albumin, and thyroid-stimulating hormone were normal. Chest X-ray was also normal, and doppler ultrasounds of both lower limbs were negative for deep-vein thrombosis. All data ruled out congestive heart failure, renal failure, nephritic syndrome, thyroid dysfunction, or obstruction to venous return as possible explanations for the pitting edema. Because of a suspicion of pramipexole-induced edema, pramipexole was discontinued immediately. Her pitting edema in both lower limbs was improved within 2 weeks. There was no recurrence of edema during 5 months of follow-up.

Discussion

In this case, the edema occurred within 2 weeks of adding pramipexole and disappeared 2 weeks after discontinuing pramipexole. All other potential causes of peripheral edema were ruled out. The appearance of edema implied pramipexole-induced pedal edema. The commonly reported adverse effects of pramipexole include nausea, visual hallucinations, fatigue, and somnolence.[1] Recent reports suggest that, in the patients with Parkinson's disease, pedal edema is also a relatively common adverse effect, with a prevalence of 5%–45%.[1,2] Previous literature has indicated the occurrence of pramipexole-induced peripheral edema several months after the start of pramipexole therapy, with rapid abatement roughly 1 week after discontinuation of the drug.[2] The pathophysiology of pramipexole-induced edema is unknown in Parkinson's disease patients.[2,3] In previous studies,[3] development of edema was concluded to be idiosyncratic, depending on the patients. In this case, the novel contribution is the occurrence of peripheral edema in a bipolar depression patient. However, the relationship between the presence of bipolar disorder and the occurrence of this adverse effect remains unclear. Clinicians must recognize this potential adverse effect when administering pramipexole in depressed patients, because quick recognition can avoid unnecessary investigations.

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