Letter to the Editor

Transient Ischemic Attack Associated With Trazodone Therapy: A Case Report

To the Editor: Trazodone is a tetracyclic antidepressant commonly prescribed for insomnia. We report the emergence of neurologic symptoms suggestive of transient ischemic attack (TIA) in a patient following the initiation of trazodone. To the best of our knowledge, no reports of such an occurrence have been published.

Case report. Mr A, a 40-year-old man with a history of mood disorder not otherwise specified (*DSM-IV* criteria), was admitted to a psychiatric inpatient unit in 2010 for suicidal ideation and depressed mood. He developed depressive symptoms about a year prior to this presentation when he got laid off from his job of over 4 years. Mr A had attempted suicide twice in the preceding year (the first time, he attempted to asphyxiate himself, and the second time, he overdosed on hydrocodone tablets) and was hospitalized at a psychiatric inpatient unit on both occasions. During his most recent admission (2 months prior to this presentation), he was started on fluoxetine treatment, which he discontinued after discharge. The stressors precipitating his current admission included homelessness, unemployment, financial constraints, and impending divorce. He endorsed depressed mood, decreased interest, poor energy, sleep difficulties, poor appetite, and suicidal ideation with a plan to stab himself. He denied auditory or visual hallucinations, psychotic symptoms, and drug or alcohol abuse. He had experimented with cocaine and marijuana during high school. There was no evidence of homicidal ideation or delusions. His medical history was significant for irritable bowel syndrome and tinnitus. Findings of his physical examination were unremarkable, and he was not taking any medications at the time of presentation.

He did not tolerate valproic acid and citalopram initiated during this admission. He tolerated lithium carbonate 300 mg 3 times daily but complained of insomnia. He reported a past history of nonresponse to zolpidem. Five days after the admission, he was started on trazodone 50–100 mg at bedtime as needed for insomnia. Twelve hours later, he developed slurred speech, neck pain, facial tingling sensations, vertigo, dizziness, lack of coordination, muscle weakness, blurred vision, and diplopia. His serum lithium level was 0.5 mEq/L. An immediate computed tomography scan of the head was performed, which was negative for hemorrhage or ischemia. He was unable to walk and required wheelchair support. We discontinued trazodone, which led to rapid resolution of all his neurologic symptoms, except for his dizziness, within 24 hours. Neurologic examination on day 2 revealed no abnormalities, but the neurologist recommended magnetic resonance imaging of the brain and angiography of the neck to rule out stroke; findings of both tests were within normal limits. He received a single 325-mg dose of aspirin and was started on meclizine 25 mg/d. His dizziness improved on day 2 after cessation of trazodone therapy. We decided to continue lithium since the serum lithium level was low and all his symptoms resolved.

A temporal relationship between drug initiation and emergence of neurologic symptoms and, most importantly, complete remission on discontinuation suggests TIA possibly as an adverse event following trazodone use.

The literature shows that serotonergic drugs cause cerebral vasoconstriction. Paroxetine, a selective serotonin reuptake inhibitor (SSRI), has caused TIA and stroke.[1–3] It was postulated that paroxetine and other SSRIs may result in changes of the vasculature and subsequent ischemic events in predisposed patients.[1] Normally, serotonin secreted by platelets stimulates 5-HT_{2A} receptors, which mediate vasoconstriction. This is counterbalanced by the release of the vasodilator nitric oxide upon serotonin stimulation of endothelial 5-HT_1 receptors. In addition to their serotonergic activity, SSRIs such as paroxetine weakly inhibit norepinephrine reuptake and nitric oxide production, which increases the risk of cerebrovascular events.[1]

The combination of lithium, trazodone, and paroxetine as well as the combination of lithium, trazodone, and bupropion has been implicated in stroke.[2] It is possible that the combination of lithium and trazodone in our patient has a role in the evolution of vasoconstriction, given their serotonergic effects. Similarly, ergot derivatives, amphetamine, and cocaine cause stroke due to their sympathomimetic and serotonergic effects.[4] Trazodone possibly increases the serotonin release from platelets by its antagonistic and reuptake inhibitor effect at serotonin receptor, which may cause vasoconstriction. Trazodone has an effect on vascular and coagulation system like that of SSRIs, which may implicate that trazodone is associated with cerebrovascular accidents. Our case emphasizes that when vasoconstriction is suspected, serotonergic drugs should be discontinued.

References

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