Hallucinations Following Intravenous Use of Tapentadol

Gaurav Kumar Singh, MD, DM; Abhishek Khatri, MD; Ateev Sudhir Chandna, MD; Lekhansh Shukla, MD, DM; and Jayant Mahadevan, MD, DM

Tapentadol is a dual action, centrally acting synthetic opioid with modest agonism at the μ-opioid receptor and strong norepinephrine reuptake inhibition.[1] It is approved for oral use as an analgesic at 50–200 mg/d for immediate-release and 200–500 mg/d for sustained-release preparations. It is not currently approved for parenteral use due to lack of safety data.[2] However, studies have shown that it is frequently misused parenterally as a drug of abuse.[3] A systematic review of 18,028 adverse events found that neuropsychiatric events were most commonly seen, followed by respiratory and cardiovascular events.[4] Here, we describe 2 cases of individuals who developed tapentadol-induced hallucinations in clear consciousness following nonprescribed intravenous use.

Case 1

A 26-year-old man presented to the hospital with a 2-year illness characterized by intravenous use of tapentadol, starting with 200–400 mg/d, which in the span of 1 month increased to 4,000–5,000 mg/d in multiple sittings. He reported development of second- and third-person auditory hallucinations after the intake of 200 mg intravenously. The voices occurred around 30 minutes after the injection, when the feeling of "high" was maximum and lasted for an hour. There was significant acting out secondary to the hallucinations, with the patient searching for the source of these voices and replying to them. These hallucinations reduced in frequency and eventually stopped altogether following regular use of 200 mg for 3 months. Following this, the hallucinations would be present fleetingly for 2–3 seconds, at times when the patient would take doses ≥500 mg during a single injection, which would be much higher than his normal intake. At the time of presentation, the patient did not describe any hallucinations for the past 6 months, despite continuing heavy use.

Case 2

A 24-year-old man presented to the hospital with a 4-year illness characterized by opioid use in dependence pattern. He was predominantly using 100–150 mg of intravenous heroin in a day and tapentadol during periods when heroin was unavailable. On one such occasion, when he used a dose greater than 1,000 mg of tapentadol in a day, he developed second-person auditory hallucinations along with visual hallucinations that lasted for about 1–2 hours after use and resolved spontaneously. He reportedly became extremely fearful and stopped using tapentadol after the experience. There was no past history of psychotic symptoms or family history of psychosis in either of the cases.

Discussion

Opioid-induced psychotic symptoms have been reported with tramadol, pentazocine, fentanyl, morphine, hydromorphone, and oxycodone, with the data supporting the same derived primarily from pain and palliative care settings, suggesting that other factors may have played a role.[5] Our cases demonstrate the occurrence of hallucinations in clear consciousness in the context of intravenous tapentadol use, which has not previously been reported. In the first case, the patient developed hallucinations at therapeutic doses but then acquired "tolerance," with higher doses of tapentadol required to "provoke" hallucinations. In the second case, the patient developed hallucinations only at a supratherapeutic dose. Postmarketing surveillance studies of tapentadol have described hallucinations at both therapeutic and supratherapeutic doses. However, in general, previous reports have shown that the dose of tapentadol required to produce hallucinations was much higher.[6] The mechanism may be related to "opioid-induced dopamine dysregulation" where μ-opioid receptor–mediated inhibition of γ-aminobutyric acid interneurons leads to hyperactivation of the mesolimbic dopaminergic pathways contributing to the development of hallucinations.[5] Our cases highlight the importance of enquiring about specific neuropsychiatric symptoms secondary to tapentadol use.

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Author Affiliations: Department of Psychiatry, AIIMS, Bhubaneshwar, India (Singh); Department of Psychiatry, National Institute of Mental Health and Neurosciences, Bangalore, India (Khatri, Chandna); Centre for Addiction Medicine, Department of Psychiatry, National Institute of Mental Health and Neurosciences, Bangalore, India (Shukla, Mahadevan).

Corresponding Author: Jayant Mahadevan, MD, DM, Centre for Addiction Medicine, Department of Psychiatry, National Institute of Mental Health and

Neurosciences, Hosur Rd, Bangalore 560029, India (jayantmahadevan@gmail.com).

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