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LETTERS TO THE EDITORS

Naltrexone-induced psychosis in a patient with alcohol use disorder

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Naltrexone is a competitive antagonist of μ, δ, and κ opioid receptors, which are used for the targeted treatment of alcohol use disorders (AUD). Naltrexone-related psychotic symptoms are an uncommon side effect. We report a case of a patient with AUD who experienced auditory hallucinations after receiving naltrexone.

A 45-year-old divorced woman presented to the emergency room with auditory hallucinations, visual hallucinations of bugs, persecutory delusions, restlessness, hand tremor and cold sweating. She had unipolar depression in her 20s but never exhibited manic symptoms. She persistently drank various alcoholic beverages (e.g., whiskey, beer, and wine) over the last 10 years after becoming unemployed. During the COVID-19 pandemic, she became afraid of going outside, mostly stayed at home, and engaged in excessive drinking. Laboratory data revealed unremarkable findings except for mildly elevated concentrations of aspartate aminotransferase, alanine aminotransferase, and gamma-glutamyl transferase. During her most recent drinking session, which occurred several hours prior to hospital admission, she drank two bottles of sake (approximately 60 drinks). A psychiatric admission was arranged because of suspected alcohol-related psychosis and alcohol withdrawal symptoms.

She underwent inpatient detoxification, during which lorazepam (12 mg per day) and sulpiride (400 mg per day) were administered. The medications were tapered gradually over 2 weeks, and her psychosis subsided after detoxification. She agreed to receive naltrexone for maintenance treatment. One hour after receiving her first dose of naltrexone (25 mg), she experienced auditory hallucinations (voices) and dysphoria. These symptoms persisted for 4 hours and then subsided. Because auditory hallucinations are not a common side effect of naltrexone, the patient agreed to retake it, after which she reported similar experiences and symptoms that subsided without other medical prescriptions. Follow-up lab data and computed tomography of the brain revealed no notable findings. She was prescribed normal doses of mirtazapine and estazolam and a low dose of quetiapine after discharge. No further psychotic symptoms were reported.

Naltrexone has been used to treat the psychotic symptoms of patients with schizophrenia, but supporting evidence for this treatment is unavailable.[1] Naltrexone-induced psychotic symptoms are uncommon. A 24-year-old female patient with schizophrenia experienced visual hallucinations after receiving 50 mg of naltrexone daily for 2 to 3 days to achieve an anti-obesity effect. Her visual hallucinations disappeared 3 to 4 days after she stopped taking naltrexone.[2] Another 44-year-old female patient without schizophrenia reported auditory hallucinations, visual hallucinations, and persecutory delusions after receiving 50 mg of naltrexone daily for 3 days for alcohol dependence. Her psychotic symptoms resolved 2 days after she discontinued naltrexone.[3] In our patient, psychotic symptoms were noted after she received 25 mg of naltrexone, and her symptoms subsided after 4 h. In these three cases, they were young to middle-aged female patients. Our patient and another schizophrenic patient had pre-existing psychosis, while the third patient with AUD did not have psychosis before treatment. The mechanisms through which naltrexone causes hallucinations remain unclear and require further research.

Dopamine release in the medial frontal cortex and nucleus accumbens can be differentially modulated.[4] Although naltrexone reduces the dopamine level in the nucleus accumbens, resulting in a reduction in alcohol intake,[5] the antagonist effect of the κ opioid receptor on naltrexone may disinhibit dopamine release in the medial prefrontal cortex and induce psychosis.[4] Naltrexone-induced psychotic symptoms have not been reported in patients with opioid use disorder probably because of the rare occurrence rate, and more people have received treatment for AUD than for opioid use disorder.

Because our patient started receiving naltrexone during hospitalization, we were able to perform a differential diagnosis and observe her conditions closely. If she had started naltrexone as an outpatient, the side effects could have led to undesirable results. The prescription of naltrexone after alcohol detoxification is helpful for differentiating drug-induced psychosis from delirium caused by alcohol withdrawal. When naltrexone-induced psychosis is suspected, naltrexone must be discontinued instead of prescribing additional doses of antipsychotic agents.

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Disclosure

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Grief, interpersonal disputes, and role transitions: the breadth of interpersonal telepsychotherapy as a strategy to reduce mental health suffering due to the COVID-19 pandemic among health professionals

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The COVID-19 pandemic necessitated the rapid development of strategies to treat mental suffering among health professionals. Our letter reports the prevalence of problem areas used in interpersonal psychotherapy (IPT)[1] and the fitness of the IPT model as applied to health professionals seeking emotional support during the COVID-19 pandemic.

We investigated the appropriateness of IPT problem areas in a sample of participants in the TelePSI project.[2] TelePSI is a 3-arm randomized clinical trial started in May 2020 designed to evaluate the effects of ultra-brief IPT, cognitive behavioral therapy (4 sessions), and psychoeducation (1 session with reinforcing videos) to reduce symptoms of anxiety, depression, and irritability among health workers in Brazil.[2] TelePSI chose IPT due to its versatility and evidence of efficacy in psychiatric conditions with anxiety and depressive symptoms.[3] It is level-1 evidence in guidelines for treating depression, eating disorders, and bipolar disorders. IPT originally includes four problem areas, but three of them (grief, interpersonal disputes, and role transitions) are more suitable for brief treatment.[1]

We analyzed data from the first 300 participants in the TelePSI interpersonal arm. The participants were 83.6% female, with a mean age of 37.8 (SD = 9.7) years. Nine therapists provided online IPT for health professionals during the pandemic, with weekly supervision. The average score for the Clinical Global Impression - Severity scale, which ranges from 1 (asymptomatic) to 7 (among the most symptomatic patients), was 3.58 (SD = 1.29), and the functionality score, which ranges from 1 (no impairment) to 4 (severe impairment), was 1.96 (SD = 0.81).

A total of 69.4% participants only had one problem area, and 27.4% had two problem areas. A total of 5% had all three problem areas. Regardless of the combinations, a total of 12% (n=36) selected grief as the primary IPT problem area, 45.7% (n=137) selected interpersonal dispute as the primary IPT problem area, and 71.3% (n=214) selected role transition as the primary IPT problem area.

In a multiple regression model including all three problem areas and adjusting for the effects of co-occurrence, role transition as the IPT area was independently associated with higher severity in crude severity scores ($b = 0.51$, $p < 0.001$) and crude functionality scores ($b = 0.26$, $p = 0.025$). The role transitions group seems to have more diffuse difficulties in dealing with the pandemic as a whole than the other two groups.

The TelePSI project observed that the IPT model adequately fits most pandemic-associated clinical situations presented by health workers. The IPT problem area model was an excellent way to focus ultra-brief psychotherapy during the COVID-19 pandemic. In 95% of our sample, the therapist detected a primary IPT area problem, confirming the fitness of the IPT model for the COVID-19 pandemic. Role transition was the most prevalent IPT problem area, as expected, and was associated with greater symptom severity. IPT is a life-event psychotherapy,[4] and its model appears to be a promising approach for mental suffering during the COVID-19 pandemic.

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