A Case of Ketamine-Associated Prolonged Psychosis in the Perioperative Setting:

Clinical Course and Management

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Ketamine is increasingly utilized as an anesthetic for procedural sedation, owing to its benefits in maintaining hemodynamic stability, dissociative analgesic properties, and minimal respiratory depression.[1,2] However, the use of ketamine is also associated with potential adverse psychotropic effects, such as hallucinations and emergence agitation from anesthesia.[3] While prolonged psychosis following a single ketamine administration is rare, we present a unique case of extended postoperative psychosis after intraoperative ketamine induction for analgesia.

Case Report

A 56-year-old woman was admitted for surgery due to sudden right lower leg fracture. She had no psychosis on presentation to the emergency department. An open reduction internal fixation of the right lower leg was performed, during which ketamine 50 mg was administered intravenously. After surgery, upon returning to her room, the patient exhibited altered cognition and aggression. Psychiatry was consulted due to this abrupt behavioral change. Her psychiatric examination was notable for hyperactivity, inattention, auditory and visual hallucinations with responses to internal stimuli, delusional thought content, disorganized thoughts, impaired cognition and reasoning, and inability to recognize family. Over the course of 3 days, the patient displayed pervasive paranoia with no fluctuation in the levels of consciousness expected with delirium. The patient had delusions of persecution, evidenced by consistent refusal of wound checks, blood draws, vital sign assessments, medication, and participation in physical and occupational therapy. While the patient did display some features of delirium (inattention, altered cognition), she did not display fluctuation levels of consciousness and had persistent psychotic symptoms suggestive of a primary psychotic state.

A thorough psychiatric history obtained from the family revealed a brief episode of visual hallucinations 12 years ago lasting 2 days, which resolved without medical intervention. Risperidone was initiated postoperatively for psychotic symptoms and titrated to 3 mg/day by post-op day 3. On post-op day 4, the patient showed significant improvement in her psychiatric examination, cognition, mood, and affect. Risperidone was tapered and maintained at 1 mg daily for the rest of her hospitalization, with instructions to discontinue 1 week after discharge. Full symptom resolution was achieved within 6 days. Given her minimal psychiatric history, abrupt onset of psychosis, use of ketamine for anesthesia, and rapid recovery, we concluded that ketamine was likely a contributing factor.

Discussion

A review of the literature revealed no other cases of protracted psychosis after a single dose of ketamine in either an experimental or health care setting. While the case by Zuccoli et al[4] is quite different regarding patient demographics and usage pattern, their patient had prominent pervasive delusions similar to those found in our case report. These pervasive delusions were the most alarming feature of our case, as they were most disruptive to providing adequate postoperative care in the most safe and efficient manner. Our patient's persecutory delusions led to mistrust of health care staff, noncompliance, and distress in the form of fear and anxiety.

Several mechanisms have been proposed to explain ketamine's ability to induce psychosis in both healthy controls and patients with a history of psychosis, including the glutamate, dopamine, and glutamate-dopaminergic interaction hypotheses.[5–7] As *N*-methyl-D-aspartate (NMDA) receptor antagonists, both phencyclidine hydrochloride and ketamine can reproduce symptoms of schizophrenia.[6,8] Likewise, in patients with schizophrenia, postmortem studies have evidenced lower glutamate receptor density, as well as decreased cerebral spinal fluid concentrations of glutamate, suggesting some degree of glutamate dysfunction.[5] Increased indirect mesolimbic dopamine release may also play a role in ketamine-induced psychosis.[6,9] Aalto et al[6] used an exogenous ligand of the D2/D3 receptor to evaluate its binding potential in humans dosed with subanesthetic doses of ketamine and found decreased D2/D3 ligand binding versus controls (no ketamine). They suggest that this finding may be due to cortical dopamine release induced by ketamine, decreasing available D2/D3 receptor sites.[6] Ketamine may induce psychosis via 2 separate or coupled mechanisms involving anti-NMDA receptor activity and increased dopamine release.[5,6,9]

Due to her psychosis, our patient's hospital stay was prolonged an

additional 7 days, in addition to the need for psychotropic medication and psychiatric follow-up. This extended postoperative psychosis placed an additional medical, financial, and psychological burden on the patient, family, and health care system with potentially prolonged sequelae.

Conclusion

We present the first known case, to our knowledge, of protracted psychosis after a single dose of ketamine used for intraoperative pain control. Clinicians may consider a brief inquiry about a patient's past psychotic experiences; however, more prospective studies are needed to elucidate ketamine's potential to contribute to psychosis in certain patient populations.

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