

Case report

Rapid anti-suicidal effect of intravenous ketamine in resistant schizophrenia: a case report

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Summary

Suicide in schizophrenia is a major risk of premature death. Ketamine has been frequently shown to have immediate antidepressant effect and has a significant role to prevent suicidal attempt and plan in unipolar and bipolar depression. Though use of ketamine in severe depression with psychosis has been proven but the use in psychotic diseases has been generally ignored due to the risk of exacerbating dissociative or psychotic symptoms. We provided a case of a 43-years-old female patient suffering from schizophrenia with significant suicidal ideation and showed that ketamine infusions intravenously at a subanesthetic dose of 0.5mg/kg with a syringe pump infusion had a strong anti-suicidal impact. Importantly, no relevant psychotic or dissociative symptoms occurred during the duration of the augmentation treatment, resulting in prolonged remission of suicidality. This intervention with ketamine was safe and showed significant alleviation of suicidality which might inspire future studies.

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Introduction

Suicide is the leading cause of early death among the patients with schizophrenia.¹ The life time prevalence of suicide in schizophrenic patients is about 34.5%.² According to a study, approximately 5-6 % of the patients with schizophrenia die by suicide.³ An effective treatment for suicide in schizophrenia and other major psychiatric disorders like depression, personality disorder remains a challenge.

Ketamine is classified as a dissociative anesthetic since it causes the user to be awake but insensitive to their surroundings.¹ It is also known as a psychedelic drug and is commonly used in clubs.⁴ Ketamine has caused renewed interest in treating refractory depression as well as severe suicidal thoughts and attempts. In 2019, the United States Food and Drug Administration (USFDA) approved ketamine nasal spray for the treatment of resistant depression.⁵ Intravenous ketamine is used for resistant depression and suicidal ideation with the existing drug, thrice weekly for 2 weeks, once a week for 4 weeks, and then as needed.⁶ Although ketamine has been shown to have powerful anti-suicidal and antidepressant effects in the treatment of unipolar and bipolar,⁷ its use in psychotic illnesses has been generally avoided due to the risk of inducing dissociative or psychotic symptoms and little is known about its therapeutic effects in schizophrenia.⁸

Case summary

We described the case of a 43-years-old female patient with severe, persistent, chronic schizophrenia. Suicide attempts occurred as a result of command hallucinations. She was given a clozapine trial and was unable to tolerate the side effects of the increased dose, which included drowsiness, sialorrhea and weight gain. As a result, the dose of clozapine was reduced to 250 mg and risperidone was added. She was taking 12 mg of risperidone plus 250 mg of clozapine every day at one time. Despite these therapies, the patient's positive symptoms of command hallucination and frequent, strong suicidal thoughts continued resulting in significant distress and impairment in functioning. She attempted suicide by injecting a large dosage of insulin intravenously and became unconscious. She received psychotherapy twice in the hospital for suicidality and psychotic symptoms. Her psychotic symptoms eased, yet she tried suicide anyway. She was given an augmentation session of intravenous ketamine at a subanesthetic dose of 0.5mg/kg via a syringe pump because she did not respond to conventional psychopharmacotherapy. Intravenous ketamine was administered via a syringe pump in order to maintain it at a much slower rate in order to avoid any anesthetic dangers, all while being closely monitored by a consultant anesthesiologist with extensive experience with ketamine. Her syringe pump was

administered in a high density unit (HDU) in a general hospital with an intensive care unit (ICU) setup, while a heart monitor was used to monitor any side effects. The patient weighed 60 kg. In a syringe pump, 30 mg of ketamine were injected into 30 ml of normal saline (intravenous ketamine anesthetic dose 1-2mg/kg body weight). She had only one hurdle during the process: she became nauseated at one point. The syringe pump was slowed further and supplied over 80 minutes from start to end. For the next two hours, the patient was monitored in an HDU bed. When her vitals were confirmed to be normal, she was told to go home with an emergency phone number to contact if she felt sick at any moment. She was interviewed the next morning, then every 12 hours for the next two days, then every week for four weeks. Her suicidal plans and intensity were significantly reduced. We intended to give the patient intravenous ketamine in accordance with the resistant depression regimen outlined previously, but she only received one dosage. We quickly noted a robust anti-suicidal reaction following the intravenous ketamine treatment. Within the same time span, the Columbia- suicide severity rating scale (C-SSRS) revealed a significant drop in moderate to no suicidal thinking. However, no apparent dissociation phenomena were observed. There was no notable changes in the patient's vital signs during or after ketamine administration. There was a persistent remission of suicidality for a follow up period of three month. Notably, there was no production of positive psychotic symptoms during or after ketamine administration.



Figure 1: Severity of suicidal symptoms before, during and after ketamine augmentation treatment by total scores of the C-SSRS

Discussion

Suicide was a severe mental health problem, with over 800,000 suicide deaths worldwide each year and around 16 million suicide attempts.⁹ The most common diagnosis of suicidal behaviour

were mental diseases, particularly depression, substance abuse and schizophrenia.¹⁰ Treatment options for improving features of suicidality were limited. Conventional interventions such as antidepressants, cognitive behavioral therapy and electroconvulsive therapy had been shown to reduce suicidal ideation and behavior in people suffering from depression, but this effect took weeks, leaving a significant proportion of patients at risk of suicide for an extended period of time.¹¹ Furthermore, only lithium had been shown to reduce suicide completion in those with mood disorders.¹²

Fortunately, multiple randomized control trials (RCTs) conducted during the last two decades had proven that ketamine, a glutamate N-methyl-D-aspartate (NMDA) receptor antagonist, exhibits rapid-onset antidepressant effects.¹³ Replicated research also suggested that ketamine could lessen suicidality symptoms quickly.¹⁴ Suicidal ideation decreased often occur within a few hours, with some patients responding as soon as 40 minutes after the initial infusion.¹⁵ Currently, The USFDA had approved ketamine nasal spray, the S-enantiomer of ketamine, for the treatment of depressive symptoms in adults with major depressive disorder (MDD) who had acute suicidal ideation or behaviour.⁷ Most clinical studies found a significant decrease in suicidal ideation and overall depressive symptom severity after ketamine treatment, implying that ketamine's anti suicidal effects were mediated to some extent by improvements in overall depressive symptom severity.¹⁶ In an open-label ketamine experiment, it was shown that a substantial decrease in suicidal ideation after six ketamine infusions. After adjusting for total depressed symptom intensity, the anti-suicide effects reached significance, showing that the anti-suicide benefits of ketamine were independent of the antidepressant effects.¹⁷

Although there were numerous studies regarding the anti-suicidal and antidepressant effect of ketamine in affective disorder, to the best of our knowledge, this was the first report in our country on an antidepressant augmentation treatment with intravenous ketamine in schizophrenia leading to rapid anti-suicidal and antidepressant effects without any accompanying meaningful psychotic or dissociative phenomena.

Conclusion

We encouraged scientists and clinicians to broaden the application range of ketamine beyond the diagnosis of depression after experiencing a safe and effective treatment with ketamine in schizophrenia. More research, including greater doses and different methods of administration, will be needed to increase our present understanding of ketamine's effects in psychotic illnesses. The findings highlighted the necessity for further study in the form of controlled studies to determine the efficacy, safety and long term outcomes of ketamine in this particularly challenging patient population.

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