



Intravenous Ketamine-induced Affective Switch in a Patient of Major Depressive Disorder with Suicidal Ideation: A Case Report

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Abstract

In treatment-resistant unipolar and bipolar depression, there is increasing evidence to support the fast, although the short-lived antidepressant effect of ketamine, a non-competitive glutamate N-methyl-D-aspartate receptor antagonist. Ketamine has been shown to cause transient mood elevation or euphoria, dissociative symptoms and psychotomimetic effects when administered in unipolar or bipolar depression. Still, it has not been shown to cause an affective switch resulting in persistent hypomania/mania or a manic-like state. We report the case of a 47-years-old man who developed a switch to mania while receiving a sub-anaesthetic dosage of ketamine intravenously for his third episode of recurrent, non-psychotic severe major depression with suicidal ideation. This case indicates that a polarity switch should be acknowledged as a possible side effect when using ketamine for depression.

INTRODUCTION

Major depressive disorder (MDD) is a widespread, typically chronic mental illness that is a primary cause of disability around the world. Despite 50 years of study focused on finding effective treatments, antidepressant treatment resistance remains a clinically significant issue. In MDD, bipolar depression, treatment-resistant depression (TRD) and depression with suicidal ideation, research reviews have established the rapid, but somewhat short-lived antidepressant effect of subanaesthetic doses of ketamine, a non-competitive glutamate NMDA receptor antagonist.^{1,2} There is still a lack of data on the effectiveness and risk of polarity switch in unipolar depression patients treated with ketamine. We report the case of a male patient with severe depression and suicidal ideation who developed mania while being treated with a sub-anaesthetic dosage of intravenous ketamine.

CASE

A 47-years-old man was admitted to an inpatient psychiatric institution due to acute suicidality following his third episode of major depressive disorder, (MDD) without psychotic symptoms for two months. Past history of 2 similar episodes in 2010 and 2016 was present. During the 2010 episode, the patient

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also attempted suicide by slitting his wrist and ingesting acid. Psychiatric consultation was done, and patient took medications for one month only. Family history was not significant for any psychiatric or neurological disorder. Patient is a chronic smoker and smokes around 20 to 30 bidis/day. There were no history of any drug intake for any chronic medical illness or other substance use. Laboratory investigation parameters were within normal range. For the present condition, the patient was already on psychotropics, Escitalopram which was increased up to 20 mg on further visits and Clonazepam 0.5 mg at night. His condition had not improved and was rapidly deteriorating.

At the time of presentation, he rated 34 (very severe) on 17-item Hamilton Rating Scale for Depression (HRSD) and 40 (severe) on modified Scale for Suicidal Ideation. To terminate acute suicidality, the patient was advised for Electroconvulsive therapy, but patient and family members denied consent. We then administered intravenous ketamine after the patient consented to the same at the dose of 0.5 mg/kg in 100 mL NS over 40 minutes period. After 4 hours of administration, patient was re-evaluated. His mood became cheerful with clear sensorium. He complained of dizziness and blurring of vision. There were no other side effects reported. On the HAM-D, he scored 7 (normal), and on the MSSI, he scored 0 (no suicidal ideation) when scales were reapplied. He scored 19 on the Young Mania Rating Scale. Escitalopram was decided to be discontinued.

Ketamine injection was repeated on day 3 and day 7 in the same dose. On day 3 HAM-D was 18 (moderate depression), MSSI was 0, and YMRS was 14 pre-injection. HAM-D became 5, and YMRS was 18 after 4 hours of ketamine administration. On day 7, pre-treatment HAM-D was 16 (moderate depression), MSSI was 17 (mild-moderate ideation), and YMRS was 13. Post administrations, HAM-D was 8 (mild depression), MSSI was 0, and YMRS was 17.

After every injection, the patient-reported euphoria with increased energy in the body and motivation with no suicidal ideations. Family members complained that he has become overtly talkative, uninterruptible, restless, hyper-religious, over-familiar and making big claims. Even after the discontinuation of Escitalopram, there was a continuous

increase on YMRS scale. From this, it can be stated that the patient had an affective switch from depression to mania due to ketamine.

When the ketamine was stopped, depressive symptoms returned, along with suicidal ideation, after 12 days. Patient was then advised Tab Lithium 300 mg twice daily.

DISCUSSION

Even after discontinuing antidepressant medication, a polarity switch was observed in our patient with major depression who was treated with three doses of intravenous ketamine. When at least two manic symptoms last more than 50% of the day for two days, and the YMRS is more significant than 12, the International Society for Bipolar Disorders Task Force classifies a treatment-emergent affective switch as "likely."³ After a two-month follow-up, the patient showed no signs of manic or hypomanic symptoms.

Wada *et al.* found that 13.1% of hospitalised MDD patients experienced manic/hypomanic switch following acute antidepressant treatment, with manic/hypomanic episodes lasting 1 to 8 weeks and the switch happening more frequently in males.⁴ After a three-year follow-up of moderate/severe unipolar MDD patients who had mood switch during acute antidepressant treatment, no subject developed spontaneous mania/hypomania (once antidepressant maintenance treatment was completed).⁵

Niciu *et al.* analysed data from three separate studies (including a total of 98 treatment-resistant unipolar or bipolar depression patients) for treatment-emergent manic-like symptoms as measured by the YMRS while receiving subanaesthetic doses of ketamine.⁶ They concluded that there was insufficient evidence to support the idea that ketamine causes a polarity switch from depression to mania. Furthermore, they questioned the authors' attribution of the mood switch to ketamine in the case given by Ricke *et al.*,⁷ which claimed induction of sustained mania in a patient undergoing ketamine therapy for reflex sympathetic dystrophy with concomitant depression and insomnia.⁶

About three studies of unipolar and bipolar patients with treatment-resistant depression (TRD) who were randomised to subanaesthetic ketamine or placebo

found transient mood elevation in three of 44 (7%) placebo patients and five of 52 (10%) ketamine patients. Still, none met the criteria for International Society for Bipolar Disorders Task Force. According to the investigators, the findings did not indicate a permanent substance-induced syndrome because the patients' moods reverted to baseline the next day and without further intervention.⁸

Banwari *et al.* reported in 2015 that a patient with unipolar depression was given 0.3 mg/kg ketamine intramuscularly three times over six days, with YMRS scores of 17, 18, and 20 after each injection. Mania developed in this case despite the lack of concurrent medicines.⁹

Despite the lack of evidence, it appears that an effective switch is a possible complication of ketamine treatment.

CONCLUSION

This case study shows that polarity switch should be considered a possible side effect while using ketamine to treat treatment-resistant (MDD). More research on the safety and efficacy of ketamine in the treatment of depression is a significant need.

REFERENCES

1. Naughton M, Clarke G, O'Leary OF, Cryan JF, Dinan TG. A review of ketamine in affective disorders: Current evidence of clinical efficacy, limitations of use and pre-clinical evidence on proposed mechanisms of action. *J Affect Disord* 2014;156:24-35.
2. Serafini G, Howland RH, Rovedi F, Girardi P, Amore M. The role of ketamine in treatment-resistant depression: A systematic review. *Curr Neuropharmacol* 2014;12:444-461.
3. Tohen M, Frank E, Bowden CL, Colom F, Ghaemi SN, Yatham LN, *et al.* The International Society for Bipolar Disorders (ISBD) Task Force report on the nomenclature of course and outcome in bipolar disorders. *Bipolar Disord* 2009;11:453-73.
4. Wada K, Sasaki T, Jitsuiki H, Yoshimura Y, Erabi H, Hada Y, *et al.* Manic/hypomanic switch during acute antidepressant treatment for unipolar depression. *J Clin Psychopharmacol* 2006;26:512-5.
5. Navarro V, Gastó C, Guarch J, Penadés R, Pintor L. Treatment and outcome of antidepressant treatment-associated hypomania in unipolar major depression: A 3-year follow-up study. *J Affect Disord* 2014;155:59-64.
6. Niciu MJ, Luckenbaugh DA, Ionescu DF, Mathews DC, Richards EM, Zarate CA Jr. Subanesthetic dose ketamine does not induce an affective switch in three independent samples of treatment-resistant major depression. *Biol Psychiatry* 2013;74:e23-4.
7. Ricke AK, Snook RJ, Anand A. Induction of prolonged mania during ketamine therapy for reflex sympathetic dystrophy. *Biol Psychiatry* 2011;70:e13-4.
8. Niciu MJ, Luckenbaugh DA, Ionescu DF, Mathews DC, Richards EM, Zarate CA Jr. Subanesthetic Dose Ketamine Does Not Induce an Affective Switch in Three Independent Samples of Treatment-Resistant Major Depression. *Biol Psychiatry* (2013) 15(74(10)):e23-4. doi: 10.1016/j.biopsych.2013.01.038.
9. Banwari G, Desai P, Patidar P. Ketamine-induced affective switch in a patient with treatment-resistant depression. *Indian J Pharmacol* 2015;47:454-455.