Intramuscular ketamine in acute depression: A report on two cases

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ABSTRACT

It takes about 2 weeks for the onset of antidepressant action of drugs while electroconvulsive therapy though faster, is a cumbersome procedure requiring an anaesthetist and at least a minor operation theatre. Recent studies have shown that Ketamine, when given to severely depressed patients in the dose of 0.5 mg/kg as a slow intravenous infusion over 40 minutes, brought about acute relief from depression and amelioration of suicidal risk within a few hours. The improvement, however, was transient and lasted for up to a week but could be sustained by further weekly or biweekly injections. As the dose of ketamine administered was found to be safe, it was now tried in the intramuscular route in two severely depressed patients with similar rapid improvement. The cases are reported here which pave way for an easier mode of treating acute depression.

Key words: Acute depression, intramuscular ketamine, suicidality

INTRODUCTION

Several medications are effective for treating depression; however, they take weeks or months to achieve their full effects. A more rapidly acting antidepressant would have a significant impact on the management of depression. Recently, case reports and studies have brought to light, the short term efficacy of intravenous ketamine on severe depression and suicidality. Considering the favorable safety profile of parenteral ketamine, it was tried in the same dose in the intramuscular route in two acutely depressed and suicidal patients with similar rapid response. The two cases are reported here.

BACKGROUND

While so far, the focus has been on neurotransmitters and related neuro-modulation, recent interest has been on the role of neuro-plasticity. Depression is now believed to be characterized by stress- and cortisol-induced impairment of neuro-genesis, dendritic arborization, and new synapse formation in the hippocampus and prefrontal cortex along with opposite changes in the amygdala. Antidepressant treatments are now believed to restore normalcy by restoring hippocampal, pre-frontal cortex, and amygdala functioning through promotion of neuro-genesis, dendritic arborization, and synaptic connectivity. Relearning and re-adaptation may be an essential part of the healing process, imprinting healthy cognitions and behaviors on the newly-formed connections.

There is a growing evidence that glutamate-driven neuro-plasticity may be the final common pathway in antidepressant action with both conventional drugs and Electro-convulsive therapy (ECT).

A few case reports and small randomized clinical trials using intravenous infusions of ketamine have shown significant, rapid, but short-lived antidepressant benefits. In these studies, ketamine was shown to produce a rapid antidepressant effect within hours, but the effect lasted less than 1 week. In a recent article, Andrade has reviewed the
various case reports and studies on the short term efficacy of intravenous ketamine on severe depression and suicidality. In most of these studies, ketamine was administered in the dose of 0.5 mg/kg as an intravenous infusion in 50-100 ml of normal saline over a period of 40 minutes. Understanding how ketamine works may lead us to a better understanding of the causes of depression and may facilitate designing a rapidly acting yet longer lasting antidepressant.

Ketamine is an N-methyl D-aspartate (NMDA)-receptor antagonist. It is widely used as an anesthetic drug with wide therapeutic index. It has an addiction potential and is classified in UK as class C drug. It has half-life of just 17 mins and its urinary excretion occurs in just 2 hours. When administered parenterally, it is totally eliminated from the body in 24 hrs.

Ketamine in the dose of 1 mg/kg i.m. has been used with proven safety for narcoanalysis in what has been termed “Ketamine Abreaction”.

However, little is known about the potential role of intramuscular (i.m.) ketamine in the treatment of major depression.

**CASE REPORTS**

**Case 1**
A 23-year-old bachelor reported with symptoms of Obsessive Compulsive Disorder (OCD) of over 5 years duration characterized predominantly by obscene thoughts leading to guilt feelings and consequent depression. His depression became intense over the last few months along with suicidal thoughts. He was, therefore, placed on fluoxetine 40 mg/day and bupropion 150 mg bid. However, due to the stress of ensuing exams and the unbearable guilt feelings caused by his obsessive thoughts, he attempted suicide on December 27, 2010 by slashing his throat with a blade. Luckily, he immediately informed his friend on phone, who promptly rushed him to the casualty and got him saved in time. He returned to the psychiatrist for a review the same morning. He was still harboring suicidal thoughts while his Hamilton Depression Rating Scale (HDRS) was rated at 17.

His bupropion was hiked to 150 mg tid and fluoxetine to 60 mg/day. ECT was considered, but, in view of his ensuing exams, it was not favored.

He was therefore, administered inj ketamine in the dose of 0.5 mg/kg intramuscularly and kept under observation for the following two hours. He manifested no side-effects. After two hours, his HDRS score dropped down to 4 i.e., an improvement by over 70%.

Three days later, he was again given a similar dose of i.m. ketamine, which brought down his HDRS scores from 10 to 7 within 2 hours i.e., a 30% improvement.

During the subsequent weekly ratings of HDRS for a month, while his medication was continued, he was found to be maintaining the remission while suicidal thoughts never returned. He appeared in his final year examinations of Bachelor of Medicine and Surgery (MBBS) and did well to his satisfaction.

**Case 2**
A 21-yr-old bachelor, a medico, suffering from recurrent depressive episodes since last 5 years, has reported with a recent worsening of his symptoms along with suicidal ideas. He was on bupropion 150 mg tid and fluoxetine 20 mg cm. His HDRS score was 21 with a high score on the suicidality item. As he did not like to inform his family due to depressive illnesses in all of them, and as he was not willing for ECT, he was taken up for ketamine injection to induce a quick relief from depression.

A dose of 0.5 mg/kg of i.m. ketamine was administered to him and closely monitored for the next 2 hours. After 2 hours, his HDRS score dropped down to 6 i.e., an improvement of over 70%. He did not manifest any side effects.

On January 8, 2010, i.e., after 3 days, his HDRS was scored at 13. He was given a second dose of ketamine in the same dose and route. After 2 hours, his HDRS dropped to 6 signifying an improvement by over 50%. He reported nausea that evening, which subsided with oral domperidone. There were no other side-effects.

**DISCUSSION**

In the two cases described, the subjects were suffering from severe depression with suicidal intent. They had a promising career ahead of them which faced jeopardy due to their illness. The response to drugs was rather slow and both were not willing for ECT due to risks of cognitive impairment just before their exams and for other social reasons. At this juncture, an injection of ketamine brought about dramatic improvement especially with regards to their suicidal ideation and saved them.

It can be seen that the improvement with the first injection was much greater than that after the second injection. Nevertheless, the improvement was continued in both of them and appeared to have speeded up the action of the ongoing antidepressant medication.

It is likely that their glutamatergic action had certainly brought about a rapid relief from their suicidal ideation as well as from depression.

It can also be noted that intramuscular route of administration was much easier method than an i.v. infusion, and could be taken up as an emergency procedure especially as in the first case, where it was given soon after the suicidal attempt.
without waiting for pre-operative preparation of a day as is required for ECT. Even in the second case, as there were practical hurdles in giving ECT due to lack of availability of his next of kin, i.m. ketamine was administered as an emergency procedure to control his suicidal ideas.

CONCLUSION

Intramuscular ketamine injection has been found to bring about rapid relief from depression, especially the suicidal ideation comparable to administration as an i.v. infusion. It is thus foreseen as a promising tool in the emergency kit of not only psychiatrists but also primary care physicians. It is also envisaged as an effective alternative to ECT in severe depression especially where ECT is not preferred due to its related cognitive side effects and other social reasons. Well designed studies comparing i.v. vs. i.m. ketamine and ECT would elucidate the issue and possibly give us an important gadget in our armamentarium against severe depression.

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