Introduction

Treatment-resistant depression (TRD) clinically refers to unsatisfactorily response to at least one adequate antidepressant therapy (1). Although TRD episodes are most commonly related with major depressive disorder (MDD), they are also seen in the depressed phase of bipolar disorder (2).

Ketamine is a glutamate N-methyl-D-aspartate (NMDA) receptor antagonist and is used as an anesthetic agent (3); it has hypnotic, analgesic and amnestic effects (4). Recent studies show that subanesthetic infusion of ketamine is efficient for the treatment of depression (4, 5). The antidepressant effects were characterized by a rapid onset of action (6) even after a single dose and were effective in treatment-resistant patients (7). The rapid effect of ketamine may be an advantage in the management of suicide risk (5). Antidepressant effects of ketamine have been found to be short-lived and its psychomimetic properties may limit the use of ketamine in depressive patients (4).

Previous studies have shown that ketamine can improve the depression symptoms of patients successfully, mainly with a single intravenous injection (8, 9).

We present a case of a treatment resistant depressed patient with frequent intravenous injections of ketamine with satisfying results. We also would like to point out that the maintenance of ketamine can prevent the recurrence without dependence or tolerance as well as its rapid effectiveness.

Case Study

A 59-year-old female patient was referred to our clinic with the complaints of anhedonia, boredom and bulging in the stomach. She was anxious about not being able to feel better and had crying spells while at home.

These complaints were triggered by daily stress. Her medical history was significant for long-standing major depressive disorder and chronic anxiety. In summary, the treatment that the patient had received during her illness included the following: imipramine, duloxetine, quetiapine, citalopram, lamotrigine, paroxetine, bupropione, mianserin, sulpirid and carbamazepine. The blood drug levels were checked regularly and they were all in a therapeutic range, and she was found to be sensitive to all the psychotropic drugs after drug sensitivity tests. Because she did not benefit from these therapies, she was given 10 sessions of electroconvulsive therapy (ECT) and due to lack of adequate response 20 sessions of transcranial magnetic stimulation (TMS) was applied.

Four month after ECT, she had the same complaints and her symptoms worsened although she was taking her medication regularly. According to her psychiatric evaluation she was conscious and oriented. Her Clinical Global Impression score (CGI-S) was 6 and her Hamilton Depression score was 26. She had cognitive behavioral psychotherapy during medication. Due to her psychomotor retardation, behavioral activation techniques were applied. No improvement was observed during these treatments.

Three months after ECT, she had the same depressive symptoms again with even more suicidal thoughts. Her Hamilton score was 32 and ECT started again but stopped after the third procedure because the patient fell down and broke her hand. Therefore ketamine infusion treatment (0.5 mg/kg) was started. After the third infusion symptoms improved and suicidal thoughts diminished. Without any drug change Hamilton depression score decreased to 6.

Taking into consideration that the patient relapsed very quickly, weekly ketamine infusions continued for
four weeks and monthly maintenance infusions were also applied for six months. She hasn’t had any symptoms for two years and she did not have any dependence or tolerance to ketamine.

Discussion

Recently, ketamine infusion treatment has received attention, especially for severely depressed patients with suicidal thoughts, because of rapidly decreasing suicidality and depressive symptoms (10). We summarized some of recent studies examining the antidepressant effects of repeated dose of ketamine in Table 1. Response rates show more diversity and vary between 41.7% and 91.6%.

Grunebaum et al. (11) showed that ketamine infusion was associated with clinically significant reduction in suicidal ideation more than midazolam control. Aan het Rot et al. (12) studied the efficacy of repeated ketamine infusion (six infusions over 12 days) in symptomatic patients with TRD who had previously shown a satisfying response to a single dose. They found that eight of nine patients relapsed and one patient remained antidepressant-free with minimal depressive symptoms for >3 months. But in our case, not only the rapid recovery of symptoms but also repetitive severe depression and anxiety signs diminished without any relapses for two years of observation. The differences between the results of these two studies can be due to multimodal treatment approach.

In summary, we have shown ketamine infusion treatment successfully replaced ECT with even lower health expenses without hospitalization. No cognitive impairment was observed compared to ECT. During the maintenance treatment no tolerance was observed and no increase in the dosage was needed. In our case no signs of dependence on ketamine were detected. However, more study is required to identify the optimal dosing schedules and treatment methods.

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References


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<td>Zheng et al. [13]</td>
<td>BD/MDD</td>
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<td>MADRS, SSIS, HAMA, BPRS, and CADSS</td>
<td>36</td>
<td>68%</td>
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<tr>
<td>Murrough et al. [14]</td>
<td>MDD/TRD</td>
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<td>Rasmussen et al. [15]</td>
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<td>Shiroma et al. [16]</td>
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<td>1</td>
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<td>Cusin et al. [17]</td>
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<td>3</td>
<td>41.7%</td>
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Abbreviations: BD = bipolar depression, MDD/TRD = major depressive disorder/treatment-resistant depression, F/U= follow up, MADRS=Montgomery-Asberg Depression Rating Scale, SSIScale for Suicidal Ideations, HAMA=Hamilton Anxiety Scale, BPRS=Brief Psychiatric Rating Scale, CADSS=Clinician Administered Dissociative States Scale, QIDS-SR16=Quick Inventory of Depressive Symptoms, Self-Report Version, YMRS=Young Mania Rating Scale, HAM-D28=Hamilton Depression Rating Scale–28 items


