Add-on Subanesthetic Ketamine in Electroconvulsive Therapy: A Case Report of a Patient with Bipolar Depression

The evidence showed that add-on ketamine anesthesia in electroconvulsive therapy (ECT) enhances the treatment effect, but this is a rare practice in clinical settings because of some safety concerns [1, 2]. We are presenting a case of a male patient with a recurrent difficult-to-treat major depressive episode, who received a course of ECT with ketamine as the anesthetic agent.

Case Report

A 57-year-old successful businessman patient experienced his first major depressive episode at the age of 42 years. During the age of 43–45 years, he had an elevated mood, during which he had had a buying spree having spent about 100 million New Taiwan dollars in three years. He retained occupational function during that time, and the hypomanic condition was remitted spontaneously. After that, he remained in a persistent dysphoric state for 10 years, and he retired from his job at 50 years of age. He had his second major depressive episode when he was 55 years old, and he attempted suicide with a drug overdose. His third major depressive episode began at the end of 2018. The symptoms and signs included all-day depressive mood, loss of interest, intense anxiety, poor appetite with bodyweight loss, insomnia, low motivation with poor energy, psychomotor retardation, and attempted suicide with another drug overdose again in June 2019. He was then admitted to our psychiatric inpatient ward.

Tracing back to his medication record, the patient had received psychotropic treatment since the first episode. He had received many kinds of antidepressants, mood stabilizers, and several types of antipsychotic drugs. The regimen of daily venlafaxine (225 mg) combined with mirtazapine (30 mg) and olanzapine (10 mg) as augmentation was effective before but was ineffective for the third major depressive episode.

Under the impression of treatment-resistant bipolar depression, we decided to treat him with bitemporal ECT plus intravenous ketamine as added on anesthetic after his giving written informed consent. During the admission, we maintained his main daily medication as venlafaxine (225 mg), agomelatine (25 mg), and olanzapine (10 mg). We arranged six sessions of ECT with two-seizure episodes in one session. We did ECT twice per week with an anesthesiologist's assistance in every session. Every week, we rated him with the Hamilton Depression Rating 17 (HAMD-17) score before and after the treatment to assess the therapeutic effect.

The patient was treated with a seizure threshold of 120 millicoulombs (mC) in the first session of ECT. For evaluation of response to anesthesia, we used only propofol (80 mg, 1 mg/kg) and succinylcholine (20 mg, 0.25 mg/kg) in the first ECT session (the first and the second seizures). From the second to the sixth session, we added on ketamine (40 mg) with the same dose of propofol and succinylcholine in every session. After using ketamine, we noted that he showed elevated blood pressure (around 180–220 mmHg of systolic blood pressure) and tachycardia (about 120 beat/minute) after ECT, and this condition sometimes persisted for 20–30 min. We considered to give nicardipine (0.5 mg). His blood pressure and heart rate would have declined to normal ranges. Despite hypertension and tachycardia, he only complained about impaired memory without other discomforts. The weekly HAMD-17 score was declined from 30 points to 25, 21, and finally, 10 points after the treatment course of the ECT. The HAMD-17 score was decreased from the suicidal ideation domain first, and then, it was declined globally. After 12 seizures of ECT, he was discharged from our ward without complications.

Comment

ECT is a promised treatment for severe or treatment-resistant major depression or bipolar depression [3]. Treatment-resistant depression still remains an operational definition, and several different definitions have been suggested [4]. We defined treatment-resistant depression here as "failure of three or more adequate antidepressant or psychotherapy trials from different classes (either in combination or succession) in the current episode [5]."

In the challenging cases, the use of ECT has generally shown a response rate of 60%–80% and a remission rate of 50%–60% [3]. Ketamine, an anesthetic agent with *N*-methyl-D-aspartic acid receptor antagonist and opioid receptor agonist properties, can rapidly and transiently improve treatment-resistant depression, including suicide ideation [6]. The optimal method and dose of giving ketamine and for those treatment-resistant depressions have not been established [7, 8]. But the dosage of 0.5 mg/kg with an intravenous method has been used in the majority of studies, and one study revealed that doses below 0.5 mg/kg are not efficacious [8, 9]. Clear evidence existed to confirm that the efficacy of a single infusion of ketamine can have a remarkable antidepressant effect [8, 10]. A few studies suggested that repeated giving ketamine can improve and maintain the antidepressant effect [11, 12].

Some evidence suggested that ketamine can hasten the response of depressive symptoms to ECT [1]. The antidepressant effect of add-on ketamine anesthesia in ECT is remarkably higher than that of other anesthetics in both the short term (1–2 weeks) and long term (3–4 weeks) [2].

Compared to other anesthetics, those given with ketamine group have a higher risk of hallucinations, confusion, hypertension, tachycardia, and a longer recovery time from anesthetic agent [2].

In our patient, the average seizure duration according to an electroencephalogram was 26.5 s, which has been considered long enough in previous studies [13]. Although the combined anesthetic of propofol has remarkable seizure threshold-elevating properties [14], another anesthetic containing ketamine has the effect of lowering the seizure threshold in contrast [1]. The effect of lowering the seizure threshold is related to seizure quality [1]. This patient had a positive response to our treatment protocol with the HAM-D 17 score declining more than 50% (30 to 10), and the suicidal ideation was declined immediately after two sessions of ECT. We did identify hypertension and tachycardia after ECT treatment and needed hypertensive drugs for those side effects, but we did not observe hallucinations or confusion. Generally speaking, those side effects in this patient were manageable and acceptable. Under the consideration of those side effects, the prescription of add-on ketamine anesthesia in ECT should be carefully given and monitored by anesthesiologists, especially in elderly patients and those with heart failure or other physical problems.

Our case report here is limited to be only one patient. To our best knowledge, we have not found any other published reports. But we have experienced a successful case of a patient treated with add-on ketamine combined with bitemporal ECT. We cannot attribute the antidepressant effect to ECT, intravenous ketamine, or a combination of these methods. (The institutional review board at Kaohsiung Veterans General Hospital approved the publication of this case report (protocol number = VGHKS19-CT12-11 and date of approval = December 5, 2019) with the waiver to obtain written consent from the patient.)

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Conflicts of Interest

All authors declare no potential conflicts of interest in writing this case report.

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