

Vortioxetine in schizophrenic patients with suicidal ideation

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Abstract

Introduction: The presence of suicidal ideation represents a challenge for clinicians, and it is essential to detect and treat it effectively to prevent the patient from taking his or her own life.

Case Presentation: Two clinical cases will be described, a 74-year-old man and a 19-year-old woman suffering from schizophrenic spectrum disorder, manifesting suicidal ideation. The patients were treated effectively and without adverse effects with vortioxetine.

Conclusion: Vortioxetine has proven effective in treating suicidal ideation in patients with schizophrenic spectrum disorders.

Keywords

Schizophrenia; Suicidal Ideation; Suicide; Vortioxetine.

Introduction

Suicidal ideation is a multifaceted and complex psychopathological symptom changing in intensity and duration. In schizophrenic patients, the lifetime prevalence of suicidal ideation was 34,5%; in comparison, point prevalence was 29,9% [1]. However, a clear suicide plan was observed between 6,4% and 13% of patients [1] and fortunately, only a tiny part of them pass suicidal intention and engage in self-injurious behaviour [2].

The term suicidal ideation refers to the presence of ideas of death characterized by fantasizing about own death and funeral, about the life after death or about ways to take their own life without however manifesting a clear intention to die. No specific signs or symptoms have been identified that would allow the clinician to predict a suicide event accurately. However, some psychopathological aspects, such as hopelessness, flat affect, insomnia, irritability and nihilistic delusions have been associated with increased suicide

risk [3]. Patients with suicidal ideation associated with delusions or hallucinations show a 6-fold increased risk of suicide respect to patients with suicidal ideation related to negative symptoms such as abulia, alogia and social inhibition, who conversely have a reduced risk of suicidal ideation [4,5]. In addition, patients with schizophrenia tend to commit suicide more frequently during periods of remission and in the early stages of psychosis, as they are often more prone to develop depressive episodes [6,7].

Where there is no straightforward self-injurious design or risk of committing suicidal acts, most patients with suicidal ideation are managed as outpatients. However, suicidal ideation persists despite drug treatment with antipsychotics used to manage positive or negative psychotic symptoms.

In this paper, we will describe two clinical cases in which suicidal ideation was treated with vortioxetine. Vortioxetine is a multimodal antidepressant that, in addition to the classic mechanism of serotonin reuptake inhibition, acts as an antagonist, full and partial agonist of the serotonin receptors. Indirectly by acting on serotonergic receptors, it increases dopamine levels, noradrenaline, histamine and acetylcholine. It also modulates the neurotransmission of glutamatergic circuits.

Case Presentations

Case 1

The first case concerns a 74-year-old man with residual schizophrenia. He had previously suffered from a productive form of schizophrenia with delusions of persecution, hallucinations and violent behaviour. The patient had been regularly taking olanzapine 10 mg/bid for about ten years with adequate control of psychotic symptoms and he did not present organic medical problems. After a long period of remission, in which he had no longer raised delusions, hallucinations or disorganized behaviour, he began to manifest apathy, complaints about his inability to remember and suicidal ideation. On the psychiatric examination, he appeared fairly cooperative; the speech was spontaneous but focused on some death issues. Thought content was within normal limits, while thought form seemed poor. The patient was oriented in time, space and person. The affect was flat.

The patient showed prevalent suicidal ideation without however presenting a clear suicidal intent. He stated that he would never harm himself, although the suicidal ideation was pervasive and persistent. He was administered the Suicidal Ideation Attribute Scale (SIDAS) (8) and the score obtained was 42 (the range score is between 0-50, higher scores correspond to more severe symptomatology). He was also well supported by his wife and sons and was rarely left alone or with objects that could be used for self-harm as a precaution. Vortioxetine was used, starting at 5 mg daily and moving to 10 mg/day after a week. One month after the start of treatment, the patient reported a substantial clinical improvement with a reduction in suicidal ideation and no longer complained of memory difficulties. Affect was more reactive and did not present psychotic symptoms such as delusions, hallucinations or violent behaviour. had improved and the score obtained at SIDAS had dropped to 24. After 12 months, the patient did not present with worsening suicidal ideation.

Case 2

This other case concerns a young 19-year-old girl suffering from a schizoaffective disorder, in which the psychotic component was pretty compensated with the use of long-acting injectable Aripiprazole lauroxil. She was also taking Lithium Carbonate at 300 mg/bid. The last reported value was 0.35. SIDAS [8] score was 46.

The psychotic symptoms onset dates back to adolescence, characterized by depressive episodes and predominantly disorganized psychotic symptoms, a tendency to social withdrawal and relational difficulties. She was still in school, failed twice and failed to graduate.

She had many hobbies like music, writing and painting, but she did not care. She had prevailing and persistent suicidal ideas and was forced to the hospital twice because of these ideas. On the psychiatric examination, she appeared uncooperative, mutated, thought and perception adequate and oriented in space, time and person. She had been treated with 150 mg sertraline a day with little benefit, although she complained of ideas of death. After one month of ineffective treatment with sertraline, she has been treated with Escitalopram 15 mg daily with poor results. Even with venlafaxine 225 mg/day, there was no improvement, and the idea of death persisted.

Given the various therapeutic failures, it was decided to treat the patient with to start treatment with 10 mg of vortioxetine. Within 8 weeks, suicidal ideation was less pervasive and persistent, and the patient felt relief at having freed herself from this onerous burden. SIDAS [8] score was 30. She resumed her hobbies, and she began singing again. Twelve months later, the improvement related to suicidal ideation persists.

Discussion

Although these two cases are different regarding sex, age and diagnosis, both share continuous and pervasive suicidal ideation. The administration of vortioxetine 10 mg was effective in reducing suicidal ideation without worsening the psychotic symptoms. While the antipsychotic clozapine has a well-documented effect in preventing suicide in patients with schizophrenia [9], data are beginning to emerge that have analyzed the effect of vortioxetine on suicidal ideation in schizophrenia. A clinical trial investigating several studies ruled out that vortioxetine increases suicidal ideation or induces self-injurious behaviour [10].

Suicidal ideation is a problem not to be underestimated in the schizophrenic patient and should be evaluated routinely in this category of patients. The risk of committing suicide in schizophrenic patients indeed is 4.5 times higher than that for the general US population [11]. Identifying patients at risk and investigating the presence of suicidal ideation in patients with schizophrenia should be a part of every psychiatric assessment to intervene early and avoid a negative outcome since the presence of suicidal ideation in schizophrenic patients is a predictor of future suicidal behaviour [12]. Treatment with vortioxetine is effective in countering suicidal ideation, has lasting efficacy and without worsening effects on psycho-

tic symptoms. These clinical cases are limited to extending vortioxetine to all schizophrenic patients with suicidal ideation. Randomized placebo-controlled longitudinal studies would be needed to evaluate the efficacy of vortioxetine on suicidal ideation, tolerability and the absence of adverse effects on psychotic symptoms.

Vortioxetine is a multimodal agent that increases the release of serotonin, norepinephrine and acetylcholine mediated by blockade of the 5HT₃ receptor and by agonism on the 5HT_{1A}, 5HT_{1B}, 5HT_{1D} and 5HT₇ receptors [13]. Some authors also described that vortioxetine acts as an antagonist of the 5HT₇ receptor; indeed, subchronic administration of vortioxetine tends to down-regulated 5HT₇ receptor that determines the decrease of thalamocortical glutamate transmission [14]. A hyper-connectivity between the thalamus and frontal regions was observed in schizophrenia and it is associated with the severity and course of schizophrenia [15]. Moreover, increased neuronal glutamate transporter expression that induces neuronal and glial cell loss in the dorsolateral prefrontal cortex has been associated with a higher risk of committing suicide [16].

Some scientific evidence has shown that adding vortioxetine to treatment with antipsychotics such as risperidone [17] and clozapine improves both negative and positive symptoms [18]. However, care should be taken when using antidepressants as they may worsen delusions and hallucinations.

Vortioxetine effectively treated suicidal ideation in the two reported cases, without worsening psychotic symptoms and with no significant side effects.

Suicide is a process that goes through several stages that begins with the presence of ideas of death, followed in many cases by suicidal thoughts and can end with the last step, which is the enactment of self-harming behaviours [19]. Therefore, it should be mandatory to assess the presence of suicidal thoughts and check for suicidal risk factors in patients with schizophrenia to prevent self-injurious conduct.

Conclusion

To date, these are the first cases reported in the literature describing the use of vortioxetine in patients with schizophrenic spectrum disorders who manifest suicidal ideation. The reported clinical cases, although effectively and safely treated with vortioxetine, are by no means conclusive and have limited clinical value; nevertheless, given the magnitude of the problem, it would be of hope that randomized clinical trials would be conducted to test the efficacy of vortioxetine in the treatment of suicidal ideation.

Conflicts of interest: The authors declare that they have no conflicts of interest.

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