The positive impact of cariprazine in schizophrenia treatment management – case report

Lavinia Horosan, Adriana Ion, Diana-Elena Nistor

“Prof. Dr. Alexandru Obregia” Clinical Psychiatry Hospital, Bucharest, Romania

ABSTRACT

Schizophrenia, recognized as a leading cause of global disability, stands as a multifaceted challenge for mental health professionals. Despite advancements in the field, schizophrenia persists as a condition which needs ongoing research and the development of individualized approaches to enhance treatment outcomes. This case report illustrates the transformative effects of cariprazine on a patient with paranoid schizophrenia, highlighting improvements in functionality, quality of life, and treatment adherence. While current antipsychotics address positive symptoms effectively, they fall short in managing negative symptoms, creating a notable treatment gap. Cariprazine, with its unique receptor profile, emerges as a promising solution, demonstrating efficacy in improving both negative and cognitive symptoms. The importance of addressing negative symptoms introduces cariprazine as a valuable intervention and emphasizes the need for ongoing research to optimize schizophrenia treatment strategies.

Keywords: cariprazine, schizophrenia, negative symptoms, treatment adherence

INTRODUCTION

Schizophrenia, recognized as one of the top 15 leading causes of disability globally, exerts a profound impact on individuals’ well-being and societal health [1]. In recent studies, the estimated median prevalence rates of schizophrenia among non-institutionalized individuals were slightly lower than the figures commonly found in textbooks. Specifically, the rates were between 4.0 and 7.49 per 1,000 throughout a person’s lifetime (lifetime prevalence) and 7.2 per 1,000 the lifetime morbidity risk [2,3]. Even if the numbers are smaller, this complex mental health disorder significantly contributes to the burden of disability, prompting a need for deeper understanding and effective interventions to alleviate its consequences. The burden of disease in schizophrenia is notably influenced by the prominence of negative symptoms, which usually persist even with proper antipsychotic treatment and after the remission of positive symptoms [4,5].

The clinical manifestation of schizophrenia is characterized by heterogeneity, with classical associations encompassing positive, negative, and neuropsychiatric symptoms. Positive symptoms include delusions, hallucinations, thought disorder, disorganized thinking, and disorganized behavior [6]. Negative symptoms encompass alogia, anhedonia, difficulty in social relationships, flattened affect, reduced motivation, and attentional impairment [6,7]. Negative symptoms in schizophrenia fall into two categories: primary symptoms, inherent to the disorder, and secondary symptoms, which may result from factors like positive symptoms, depression, medication side effects, or substance abuse [8]. Neuropsychiatric deficits are frequently observable as impairments in higher-level thinking, decision-making, reasoning, planning, visual memory, working memory, executive functions, emotional recognition, and attention [9].

Currently, available antipsychotics show significant effectiveness in handling positive symptoms during acute phases and preventing relapse. However, their efficacy diminishes when faced with the complexities of negative symptoms, creating a notable gap in addressing these particular symptoms [10,11]. Negative symptoms can be severe enough to interfere with normal functioning, and they are only marginally responsive to antipsychotic treatment.
[5,12]. The primary indicators of diminished quality of life among individuals with schizophrenia are negative symptoms, and elevated scores on negative symptoms correlate with impaired psychosocial functioning [6,7]. Current drug trial guidelines for negative symptoms recommend a minimum 6-month treatment duration [13]. In acute phase trials, reductions in negative symptoms are observed, but these are often considered unspecific or linked to a decrease in secondary negative symptoms [14]. As patients often continue the same medication for extended periods to prevent relapses, evaluating the acute phase’s impact on negative symptoms remains a priority [15,16].

In recent years, the importance of treating negative symptoms has come into focus, leading to new studies and antipsychotics that predominantly address this issue. One of the medications that emphasizes improvement in both negative and cognitive symptoms of schizophrenia is cariprazine. It possesses a distinctive receptor profile marked by its preference for dopamine D3 receptors, exhibiting D3/D2 receptor partial agonism, along with serotonin 5-HT1A agonism 5-HT2B antagonism with moderate affinity for adrenergic, histaminergic, and cholinergic receptors [17,18]. Cariprazine has proven to be an effective medication in treating acute episodes as well as preventing relapses and has excelled in improving negative and cognitive symptoms, even in comparison to risperidone. It also showed an overall better quality of life with improved functional outcomes [17,19].

Based on the combined expertise and perspectives of an International Panel, the optimal candidates for cariprazine include individuals experiencing their initial episodes of psychosis, those exhibiting predominant negative symptoms in both acute and maintenance phases, and those facing significant side effects from other antipsychotics during stable periods. When considering the extended treatment of this chronic disorder, cariprazine emerges as one of the first-line medications [20]. As recommended in the medication’s brochure, the manufacturer suggests an initial dose of 1.5 mg/day and a maximum dose of 6 mg/day for schizophrenia [21]. The current recommended doses for cariprazine have proven to be effective, with 4 mg/day addressing negative symptoms and 6 mg/day managing positive symptoms [22].

Regarding adverse reactions, the most commonly reported were akathisia, tremor and restlessness, with headaches and insomnia particularly noted during long-term use [23]. Doses over 6 mg/day correlated with weight gain and elevated creatine kinase and transaminase levels. Hence, the maximum recommended dose was established at 6 mg/day, as the risks outweigh the benefits at higher doses [23]. Although there is no proven increase in cardiovascular risk, it has been observed that elderly patients with psychosis associated with dementia have an elevated risk of death. Therefore, the medication’s brochure includes a dedicated warning box highlighting this risk, and the drug is contraindicated in this patient category [21,23].

**CASE REPORT**

We present the case of a 34-year-old patient diagnosed with paranoid schizophrenia since the age of 29. Over time, the patient has had multiple admissions to our clinic and has undergone various treatment regimens, as shown in Table 1. During the latest admission, he was brought to the hospital by the ambulance and the police, accompanied by his aunt, who sought the assistance of authorities because the patient had locked himself inside his house and could not be reached. According to the police reports, the patient has received multiple complaints from neighbors due to his disruptive behavior, consistently causing disturbances.

In our initial assessments, the patient displayed a highly tense body posture with limited movements. Strikingly, there was a significant reduction in blinking, giving the impression that he almost didn’t blink, with wide, bulging eyes. The speech was informationally poor, with a low tone and a slow rhythm. The patient reported experiencing complex auditory hallucinations that disturbed him, along with occurrences of physical and mental automatism, stating, “I make gestures without wanting to; I feel like making this gesture with my hand, but I don’t know why... I feel like screaming, and I can’t control myself”. As for the physical examination, no other pathological changes were observed apart from reduced weight. His blood tests were also within normal limits, and the toxicology report was negative.

According to the Positive and Negative Syndrome Scale (PANSS), the patient exhibited a high severity of negative symptoms, showing impaired affective responsiveness, social withdrawal, and diminished motivation. While the patient displayed some positive symptoms, the severity was comparatively lower than the negative symptoms. Hallucinations and delusions were present but did not dominate the clinical picture. The category of general psychopathology within the PANSS scale showed the interplay of symptoms beyond the positive and negative dichotomy. Disorganized thinking was evident in the patient’s speech and communication, and he demonstrated cognitive deficits, including impaired attention and concentration, inappropriate emotional responses, insomnia, and lack of movement coordination.

The psychological examination yielded the following conclusions: the patient exhibits reduced cooperation, lack of spontaneity and conversational
flow, emotional blunting, apathetic social withdrawal, significantly narrowed sphere of interests and concerns, passivity, adaptation difficulties, lack of emotional flexibility and affective resources, psychological fragility, and markedly diminished overall functional performance (Global Assessment of Functioning Scale = 30/100).

From the patient’s history, we learn that previous hospitalizations were also a consequence of the patient’s hetero-aggressive behavior towards objects during psychotic episodes. He destroyed the windows of a bank, threw objects from his apartment through the windows, and consistently had issues with neighbors who were disturbed by his yelling and throwing objects around the house. In one of the previous hospitalizations, it was noted that the patient constantly hit himself in the face with his fists and claimed that he could not control himself. Although the clinical picture of hospitalizations varies, one aspect continues to recur consistently, namely the persistence of negative symptoms. Because he lives alone, it is challenging to monitor whether he is correctly taking his treatment or if he is taking it at all.

The last admission was about one week ago, and the treatment regimen included olanzapine 5 mg/day, valproic acid 500 mg/day, and gabapentin 600 mg/day. Additionally, a flupentixol long-acting injection at 20 mg every two weeks was initiated a month ago, with the patient having received two injections at the time of our evaluation. With this treatment, his positive symptoms persisted, leading to a modification in his behavior that led to this current admission. I kept the same therapeutic regimen but decided to discontinue flupentixol treatment. With this treatment, no improvement was observed in the patient’s symptoms. The patient continues to report the presence of voices and a lack of control over his own body.

There was an abundance of negative symptoms, as demonstrated by the patient’s lack of interest in any activity, spending the entire time in bed, claiming that even at home, lying in bed was the main activity. Since the age of 29, when he was diagnosed, he ceased working and retired on medical grounds. The patient was socially isolated living alone. Throughout the admission, he did not communicate with any other patient and did not express a desire to participate in clinic activities, content with staying in bed. He also exhibited reduced appetite, reflected in his low weight for his height and age. There was a lack of emotional flexibility with a pronounced affective blunting. The patient had difficulties in performing daily tasks, had poor personal hygiene, and a lack of interest in eating sufficiently and appropriately.

His clinical evolution was unfavorable, so the decision to start a trial with cariprazine was made. The switch was made from olanzapine to cariprazine, from 1.5 mg of cariprazine per day and gradually increasing to a dose of 3 mg per day. Valproic acid was retained in the treatment regimen, with the dose increased to 1000 mg per day. After a week of treatment with cariprazine 3 mg/day, there has been a favorable change in the patient’s condition. The patient is now showing interest in being discharged, which is a positive outcome considering his previous indifference to being in the hospital. Additionally, there has been a noticeable change in appetite, with the patient craving enjoyable foods such as French fries. The conversational flow has improved, making it easier to engage in conversation compared to the time of admission when he responded monosyllabically or with brief answers to the examiner’s questions. Another change was the patient’s desire to take walks instead of staying in bed. Positive symptoms improved from the early days of transitioning from olanzapine to cariprazine.

The patient did not experience any adverse reactions. He was discharged with cariprazine 3 mg/day and valproic acid 1000 mg/day. Two weeks after discharge, he came for a follow-up appointment at the hospital on his own. He stated that the sensation of losing control over his thoughts and body did not occur, and he did not hear any voices during this peri-

TABLE 1. Patient’s medication and hospital admission history

<table>
<thead>
<tr>
<th>Admission date</th>
<th>Discharge date</th>
<th>Medication on discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>16 October 2019</td>
<td>11 December 2019</td>
<td>Clozapine 50 mg, Sertraline 100 mg, Valproic Acid 1500 mg, Risperidone long-acting injection 50 mg every two weeks</td>
</tr>
<tr>
<td>25 August 2020</td>
<td>11 September 2020</td>
<td>Risperidone 6 mg, Valproic acid 1000 mg</td>
</tr>
<tr>
<td>31 March 2021</td>
<td>21 April 2021</td>
<td>Amisulpride 800 mg, Zolpidem 10 mg, Switching Amisulpride with Olanzapine 10 mg because of hypotension</td>
</tr>
<tr>
<td>7 May 2023</td>
<td>24 May 2023</td>
<td>Olanzapine 20 mg, Valproic Acid 500 mg</td>
</tr>
<tr>
<td>21 October 2023</td>
<td>03 November 2023</td>
<td>Flupentixol long-acting injection at 20 mg every two weeks, Valproic Acid 1500 mg, Gabapentine 600 mg, Diazepam 20 mg</td>
</tr>
<tr>
<td>10 November 2023</td>
<td>22 November 2023</td>
<td>Flupentixol long-acting injection at 20 mg every two weeks/two doses, Valproic Acid 500 mg, Gabapentine 600 mg, Diazepam 20 mg, Olanzapine 5 mg</td>
</tr>
<tr>
<td>Recommendations at discharge</td>
<td>Cariprazine 3 mg, Valproic Acid 1000 mg</td>
<td></td>
</tr>
</tbody>
</table>
od. He started watching a new TV series and took daily walks. He cooked French fries, a food he had been craving in his last days in the hospital. At home, he faced some issues related to heating the house but managed to seek help and handle it independently without his aunt’s assistance. The patient is scheduled for a new follow-up, and we hope that during this time, the progress will continue to be as favorable as it has been so far.

**DISCUSSIONS**

In the case presented, we discussed a patient who, prior to treatment with cariprazine, had reduced functionality affecting his quality of life. Following the transition to cariprazine, an improvement in his functionality is observed. Quality of life is an essential aspect to be considered in the therapeutic management of any medical condition. Therefore, maintaining functionality in all areas of life should always be a priority for clinicians. Patients with schizophrenia need assistance in the process of being reintegrated into society and to lead the best possible life. Positive symptoms are quickly controlled by antipsychotic medication, but it is the negative symptoms that are the main predictor factor for the quality of life of patients with schizophrenia [24].

Cariprazine represents a notable advancement in the pharmacological landscape for schizophrenia, specifically addressing the challenging domains of cognitive and negative symptoms. As the field of psychiatry continues to acknowledge the unique challenges posed by cognitive and negative symptoms, the importance of ongoing research and the development of medications like cariprazine cannot be overstated. These studies contribute to refining our understanding of the disorder and offer hope for more effective and comprehensive therapeutic approaches, ultimately paving the way for improved outcomes and a better quality of life for individuals with schizophrenia.

Nonadherence to antipsychotic treatments presents a significant challenge for clinicians treating schizophrenia, influenced by factors such as poor insight, negative attitudes towards medication, chronicity of illness, complex treatment regimens, medication side effects, cost, and social functioning [25]. Cariprazine has very good tolerability, with reduced adverse reactions, a neutral metabolic profile, and no significant impact on the cardiovascular or endocrine system [26]. Cariprazine demonstrated markedly prolonged sustained remission periods, elevated remission rates, and enhanced probability of maintaining remission for at least six consecutive months, showing improved treatment adherence [27]. Upon starting cariprazine, our patient exhibited a significant enhancement in treatment adherence. The medication effectively alleviated his symptoms, instilling a sense of stability. Due to minimal side effects, the patient was more inclined to adhere to the medication regimen, recognizing the pivotal role of cariprazine in supporting patients during their long-term recovery process.

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**REFERENCES**


