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Psychosis treatment: A case series report

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Abstract

In this report, we describe 3 clinical cases of patients with psychotic disorders in different stages of the disease, from the emergency ward evaluation, inpatient unit, and outpatient treatment. In all, a 6-month follow-up is detailed in the text. Patients reported variability of positive and negative symptoms, cognitive manifestation, and metabolic syndrome associated with the psychiatric disorders.

A novel therapeutic approach was administered. Our results show better control and improvement of positive and negative symptoms, a decrease in metabolic syndrome, better treatment tolerance, and strengthened therapeutic adherence, producing a faster recovery in social and work functioning.

Keywords: cariprazine, social functioning, schizophrenia, antipsychotic

Introduction

Background

Despite being one of the most severe and deteriorating mental disorders **[1]**, schizophrenia is still a point of debate in the present day. It is considered by most a complex and chronic mental disorder that implies high pharmacologic treatment needs, high economic costs, and personal and social needs **[2,3]**. Some perceive it as a homogeneous affection; others describe it as a group of disorders of heterogeneous etiology, which implies that patients present different clinical symptoms, treatment responses, and different disease progression. Also described as a syndrome, a group of schizophrenias, or, as stated in the DSM-V, schizophrenia spectrum disorder **[4]**.

Schizophrenia usually debuts before age 25 and affects between 0.4-1.5 % of the world population. Approximately 1 in every 100 people will develop the illness during their lifetime, with chronification being the norm, affecting all social statuses equally. A first-grade family member of a patient affected by schizophrenia will have a 10 times higher risk of developing the disease than the general population. Also, the risk of death is doubled over the general population; this could be related to many factors, such as long hospitalization periods, antipsychotic side effects, and difficulties in the diagnosis **[5,6,7]**.

This disorder affects all subject dimensions, provoking behavioural changes, passivity and irritability, disorganization of speech and daily activities (sleep, eating, etc.), lack of personal hygiene, unspecific somatic complaints, bizarre thoughts, and restricted concerns. The cognitive and motor levels present a neuromotor deficit; concentration and attention span are also affected. In the social and work areas, there is an essential deterioration of the overall functioning capabilities, social isolation, and perceived bizarre experiences **[8]**.

In an attempt to diminish the devastating effects of this illness, we have the option of antipsychotics. These treatments tend to be very efficient in controlling positive symptoms, but even with the development of new molecules, there is a substantial lack of beneficial effects on the rest of the symptoms **[9]**. Antipsychotics have been the base of schizophrenia treatment since the 1950s. Initially used for the Treatment of acute psychotic events, it eventually gained importance for avoiding relapse of symptoms and became a long-term maintenance treatment **[10]**.

In treating and controlling schizophrenia, antipsychotics are used for acute episodes; symptoms relapse prevention and emergency treatment for behavioural disorder control, and symptom reduction **[11]**.

Among the different therapeutic options, we have cariprazine, a new generation antipsychotic, approved by the EMA for use in Europe **[12]**, with an indication for the Treatment of schizophrenia, and previously approved by the FDA in the USA, for the Treatment of schizophrenia, bipolar disorder, and mixed episodes in adults **[13]**.

Clinical data and positioning reports have shown that cariprazine could be especially beneficial in patients with predominantly negative symptoms due to its excellent tolerance profile **[17]**. On a daily consult, our patients present a complex situation with various clinical elements and comorbid profiles that do not fit precisely with the published studies.

In this publication, we detail 3 different clinical cases, evaluated in the ER and then hospitalized in our Brief Hospitalization Unit. After discharge, the evaluation continued in our Mental Health Ambulatory Care Unit. One of the patients presented a first psychotic episode, the second presented prolactin-related secondary effects, and the third one was a chronic psychotic patient.

Clinical Case 1

53-year-old woman, single, has a son with whom she has little relationship, lives alone, pending incapacitation process—personal history of high blood pressure. No history of familial psychiatric disorders was known. Known personal psychiatric records by Mental Health, diagnosed with continuous paranoid schizophrenia, does not follow up by the mental health unit of Santa Cruz de la Palma; for more than 3 years, she has not attended an assessment by nursing and part of psychiatry. Multiple admissions to our short-term hospitalization unit last in July 2018. Current Treatment: paliperidone 9 mg 1-0-0-0, olanzapine 20 mg 0-0-0-1, recently abandoned.

According to the emergency service doctor, she was brought in by the civil guard to alter her behavior on public roads. Upon her arrival, she presented a seborrheic and somewhat incoherent speech. She did not admit why she was brought in and barely cooperated in the interrogation. With no current treatment, the patient recognized that she had abandoned it because she got "milk from her tits" and was like a cow.

In the psychiatry interview, the patient was hostile, refused to be questioned, and tried to intimidate with gestures or looks; she was evasive and only commented that she "is waiting for a woman" and did not want to see us, that we should have left. She stands out in the observation with a foul physical appearance and a dishevelled, dirty attitude that suggest the presence of sensorial-perceptual alterations and delusions, although she had not been open about them. A clinical decompensation was suspected.

The prolactin level was 2034 ng/mL, while the other analysis reported average values. Cranial CT was standard.

Upon admission, cariprazine 1.5 mg was started and gradually increased to 6 mg over 7 days for acute control of symptoms in the inpatient setting.

During the first days of hospitalization, the patient presented soliloquies and auditory hallucinations in addition to referential delusions. After starting the new antipsychotic Treatment, these manifestations were more controlled, chronic, and at a secondary level. Effect and behavior varied very little compared to admission, which was disorganized and dysphoric.

After 32 days of Treatment and hospitalization, the patient was discharged with appropriate behavior, fair criticism of the disorder, commitment to the Treatment, and the promise to keep up-to-date, and she expressed her joy after the galactorrhoea stopped. Other symptoms, such as headache and muscle aches, possibly associated with hyperprolactinemia, also ceased. Prolactin levels at discharge were at 28 ng/mL, the weight in one month was reduced by 5 kg, from 97 to 92 kg, and no side effects were reported.

Treatment at discharge was cariprazine 6 mg, one tablet for breakfast; losartan 50 mg, one tablet for breakfast and dinner; hydrochlorothiazide 12.5 mg, one tablet for breakfast.

The diagnosis was episodic paranoid schizophrenia with a stable defect. After discharge, she has attended three outpatient controls; the first is 15 days after release, and the following two have been monthly. The doctor reports psychiatric clinical stability, with progressive weight loss, currently, 86 kg; she is being followed up with the endocrine physician due to slightly elevated blood glucose levels and prolactin in the normal range. She has already attended court, not gone to the subpoenas for a year, and a relative has been assigned as her guardian.

Clinical Case 2

The 46-year-old man lived with his partner, the mother of his 8-year-old son, who is not currently working—on the personal background of pathologies known. There was no previous personal psychiatric history. The patient had been under Treatment for one week with risperidone 6 mg/day, prescribed by his primary care physician for behavioural disturbances. Schizoid personality traits, according to his companion, he has always been very lonely and "weird.".

The patient arrived at the ER accompanied by his family at their initiative for presenting behavioural disturbances in the last week. According to his wife, the patient delivered mutations and soliloquies for six days and claimed to be in contact with God since he was communicating with him.

During the interview with the family, no psychiatric history was reported. After his father's death, he worked sporadically, but since 2018 he stopped working because he said he was fine doing his things at home. The patient's wife said he did not seem normal and noticed that he had changed his way of being.

He presented global insomnia and emotional lability with unmotivated laughter alternated with crying episodes. His wife perceived him as abstracted and informed he said that a lawyer had bewitched him. The symptoms had progressively intensified in recent days. As a possible trigger, the patient reported that two days before, he received a notification of denial of free legal services (he had been for years in legal proceedings for an inheritance).

An organic screening was performed in the emergency department to rule out medical etiology from the symptoms. A brain scan was

performed without relevant clinical findings—blood test within normality, including PCR, liver profile, CPK, and blood count.

After being admitted to the psychiatry ward, risperidone was suspended due to a lack of clinical response, and the patient started Treatment with cariprazine 1.5 mg.

The dose of cariprazine was progressively increased to 3 mg on the third day and 4.5 mg after seven days for acute control of symptoms in the inpatient setting with good tolerance, only referred to drowsiness as a secondary symptom. The clinical response began to be evident on the 5th day of Treatment, and, at the moment of discharge, 17 days later, he was asymptomatic, criticizing what had happened, recognizing his symptoms as "paranoia."

The diagnosis at discharge was paranoid schizophrenia; the patient took cariprazine 4.5 mg, one tablet for breakfast. He attended a check-up fifteen days after release, taking cariprazine 4.5 mg with good tolerance. Asymptomatic defining himself as active and happy, "I'm normal; it's me." The family reported that he had started attending an INEM course (job training) and the gym, and he began to meet friends. After 6 months of follow-up, the patient remains asymptomatic, with no reported drug side effects—current dose cariprazine 4.5 mg at breakfast.

Clinical Case 3

A 34-year-old female patient from Germany who had been visiting the island (La Palma) since last January, doing photography work, no known previous medical history. No current treatment was prescribed, and no family psychiatric history was known.

The patient was brought into the emergency service by ambulance; the doctor described that she felt people around her were saying bad things about her, heard voices criticizing and intimidating her, and turned very agitated. Personnel at the hostel where the patient was staying informed us that she was sometimes crying, others dancing, with a distrustful attitude, and she was not sleeping or eating. The patient tried to escape from the ER, and although she spoke some Spanish, the interview was difficult, and the admission was decided for control and adequate Treatment.

Good physical appearance. Mistrustful attitude towards emergency staff. She was very agitated and nervous, fearing and distrusting everyone who approached her. Coherent and fluent speech to the questions asked intrusion phenomena paranoid-like related to the hostel's companions; she believed that everyone spoke badly of her and behind her back. In auditory hallucinations, the patient described people who speak badly about her and post bad things on her social networks.

In the first psychiatry interview (the patient is questioned in the presence of a German translator since her English is essential and she does not speak Spanish fluently), the patient was in great psychotic distress. However, she was approachable and described herself as quite lonely, with a particular hypersensitivity to people who felt their emotions and managed to acquire them. Laboratory exams and cranial CT were regular.

Upon admission, antipsychotic medication (cariprazine 1.5 mg) was established with excellent tolerance and clinical response. The delusional hallucinatory symptoms started to improve after 96 hours of Treatment with a 4.5 mg cariprazine dosage; the final dose of cariprazine was up-titrated to 6 mg for best control of symptoms.

At discharge, which occurred 9 days later, the patient was calm and adequate, with euthymic, consonant, and reactive mood, good criticism of the episode, and no delusional activity; no side effects were reported.

The diagnosis at discharge was paranoid schizophrenia. After two months, the patient, still on cariprazine 6 mg, remained without psychotic symptoms; she resumed her photographic work and lived alone in a rental apartment.

Discussion

In this publication, we described 3 different clinical cases of patients with psychosis treated with cariprazine, a third-generation antipsychotic drug; its mechanism of action is based on a partial agonism on the dopamine D3 and D2 receptors, with a preference for the D3 receptor. It shows a high affinity for the 5HT1A and 5HT2B receptors, a moderate affinity for the 5HT2A and H1 receptors, and a very low affinity for the α 1adrenergic receptor. It has no relationship with the muscarinic cholinergic receptors **[14,15]**.

Another advantage is that cariprazine decomposes in two principal metabolites (DCAR and DDCAR), both with similar receptor binding profiles as the original drug but with a different half-life which is very useful for first episodes and relapses18. Half-lives based on time to reach a steady state are 2–4 days for cariprazine, 1–2 days for DCAR, and 1–3 weeks for DDCAR; the effective half-life of total CAR (molar sum of cariprazine, DCAR, and DDCAR) is approximately 1 week. Moreover, cariprazine and its metabolites (DCAR and DDCAR) bind intensively to the plasma protein (92-97 % range) **[16]**.

Schizophrenia is a severe and disabling disorder, treated with pharmacology and a global approach. This approach aims to improve positive, negative, and cognitive symptoms of the disease and the overall functioning and quality of life of the patient.

The patients in the clinical cases described in this publication were treated with cariprazine in monotherapy. The Treatment was initiated in the Mental Health Inpatient Unit, taking advantage of the plasma concentrations of the DCAR metabolite, which resulted in a rapid improvement of the behavioural disturbance, hallucinations,

delirious thoughts, dissociative thoughts, and affected progress and conduct. We also noted an improvement in patient-doctor relationship and disease awareness, resulting in better patient implications in their Treatment and recovery. Additionally, the patient presented improved negative and cognitive symptoms that are critical for better adaptation and integration in their social life.

The efficacy of cariprazine is accompanied by a good safety profile that causes no alteration of the prolactin levels. Moreover, cariprazine doesn't induce metabolic effects, sedation was not described, the Q-T interval was not incremented, and the patients claimed no sexual dysfunctions.

The limitations of this study rely on the 6 months period of observation, which can be seen as a short time-lapse. Nevertheless, in this short time, we could ascertain the rapid improvement and stabilization of the clinical symptoms and the re-integration of the patients in their social life, which is strong evidence of the efficacy of cariprazine for the Treatment of positive, negative, and cognitive symptoms of schizophrenia.

Conclusion

As the clinical cases described showed, cariprazine is a convenient option for treating positive, negative, and cognitive symptoms in patients with a psychotic disorder, demonstrated by a good tolerability profile and common side effects.

Consent for Publication

Written informed consent has been obtained from all patients to publish the case details. Institutional approval was not required for publication.

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Disclosure

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