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USE OF CLOZAPINE IN POLYPHARMACY SITUATIONS IN A SCHIZOPHRENIC PATIENT WITH LOW THERAPEUTIC RESPONSE - CASE REPORT

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Abstract: OBJECTIVE: Case report of a schizophrenic patient maintaining clinical instability despite the use of polypharmacy with significant side effects, whose new therapeutic proposal aimed to reduce medication classes and dosage. **METHOD:** The case report in this work was obtained through a medical record review, interviews with the patient, family members and literature review; **FINAL CONSIDERATIONS:** The reported case brings into discussion the treatment of a complex situation and the use of polypharmacy with the aim of possible stabilization in resistant schizophrenic patients. Evidence that, when well executed, a therapeutic proposal with medication reduction, with assertive drugs, even if adopted by few, is possible and guarantees greater adherence and well-being to the patient.
Keywords: schizophrenia, polypharmacy, clozapine.

INTRODUCTION

Although it is discussed as if it were a single disease, schizophrenia encompasses a group of disorders with heterogeneous etiologies and includes patients with variable clinical presentations, treatment response and disease course. Signs and symptoms vary and include changes in perceptions, emotion, cognition, thinking and behavior. The expression of these manifestations varies between patients and over time, but the effect of the disease is always serious and generally long-lasting. Schizophrenia is one of the most common serious mental disorders, but its essential nature has not yet been clarified. [1]

Schizophrenia, internationally, has an annual incidence of around 15 to 42 per 100 thousand inhabitants.[2] It is equally prevalent in men and women. Both sexes differ, however, in terms of the onset and course of the disease. The onset is earlier among men. The peak ages of onset are between 10 and 25 years for men and between 25 and 35 years for women.[1] When an antipsychotic is administered to a patient with acute schizophrenia, approximately 60% will improve, in the sense that they have achieved complete remission or they will only have mild symptoms; the remaining 40% will improve but still demonstrate varying levels of drug-resistant positive symptoms.[1] Clinicians must understand that the diagnosis of schizophrenia is based entirely on psychiatric history and mental status examination. There is no laboratory test for this disorder. [1]

OBJECTIVE

Case report of a schizophrenic patient maintaining clinical instability despite the use of polypharmacy with significant side effects, whose new therapeutic proposal aimed to reduce medication classes and dosage.

METHOD

The case report present in this work was obtained through a medical record review, interviews with the patient, family members and literature review;

CASE REPORT

ANAMNESIS

Patient, D.E.M.V, male, 67 years old, retired truck driver, sought care at the Psychosocial Care Center/CAPS accompanied by a family member, due to an episode of psychomotor agitation, auditory hallucinations, aggressiveness with oscillations of improvement and clinical worsening. The patient was diagnosed with schizophrenia 39 years ago, after his first persecutory psychotic episode while working. During the treatment, it was said that during the treatment process there were three admissions to psychiatric hospitals, the last one being more than 5 years ago. It is important to emphasize that

the treatment continued over the years in psychiatric outpatient clinics and psychosocial care centers and, when stable, with significant social impairment, negative symptoms, hypersomnia and cognitive decline.

Non-alcoholic, denied smoking, as well as drug use throughout his life, frequent physical activity, but obesity BMI 31.3 kg/m², hypertensive on stable treatment, non-diabetic, non-dyslipidemic. Good social conditions with a structured family with a family history of schizophrenia. Using polypharmacy in recent years with the aim of clinical stabilization of persecutory psychotic symptoms, insomnia and sometimes verbal aggression. Using: Haldol 5mg 1-1-1; Levomepromazine 100mg 1-1-1; Carbamazepine 200mg 1-1-1; Risperidone 2mg 1-0-1; Escitalopram 10mg 1-0-0; Diazepam 10mg 0-1-1. All medications administered by a family member with a good level of education and adherence. Already being used in past therapies: Chlorpromazine, Thioridazide and Valproic Acid in various combinations.

MENTAL STATUS EXAMINATION

In good general condition, stable triage vital signs, neat appearance, dull face, sialorrhea, little communicative. Flat affect during the consultation, when questioned he referred to auditory hallucinations of voices with repetitive content of accusation, defamation and potential harm to the family. Delusions of persecution kept him at home most of the time with doors and windows closed, making it difficult to convince him to come for consultations, he said that "men would catch everyone". Shallow speech with short answers and loose ideas. Family members also reported sometimes agitated behavior at home when in contact with televisions and radios with a desire to escape and verbal aggression with spontaneous remission after family support or use of Diazepam in an extra dose. The patient performed simple household activities (sweeping sidewalks and drying dishes), *insight* was absent at the time of the consultation and poor most of the time. Family member also states that during episodes of stability the patient remains with very prominent negative symptoms.

DIAGNOSTIC ASSESSMENT

When the DSM-5 diagnostic criteria for schizophrenia are listed, the diagnosis is concluded and revised into: Paranoid Schizophrenia, multiple episodes, currently in an acute episode.

THERAPEUTIC INTERVENTION

The doctor-patient-family bond began, the patient's clinical condition was reported and explained and the need to review pharmacological therapy, given the polypharmacology already used and the low stabilization of the clinical picture. The family condition of 24-hour care and the absence of acute life-threatening conditions allowed the patient to not be hospitalized immediately and attempt stabilization in an outpatient environment. Therefore, after formulating the Singular Therapeutic Project (PTS), the patient was referred for blood collection (blood count, lipid profile, TSH, T4, vitamin b12, vitamin d, fasting blood glucose, glycated hemoglobin, creatinine, TGO, TGP, troponin, CRP, partial urine test). The change in pharmacological prescription started with Clozapine 50mg 1-1-1, doubling the dose after 72 hours, reaching 300mg per day divided into 100mg three times a day. Carbamazepine 200mg 1-1-1, Levomepromazine 25 mg 1-1-1 (reduced) and Diazepam 10mg were maintained in cases of agitation. Haldol 5mg 1-1-1 was then suspended; Risperidone 2mg 1-0-1 and Escitalopram 10mg 1-0-0 (gradually). Maintained daily telephone contact to observe the patient's clinical progress.

EVOLUTION

The patient remained agitated during the first 48 hours of the new therapeutic proposal, but without clinical worsening of the initial condition. After 72 hours, he returned for a face-to-face consultation and significant sedation was observed, remaining drowsy most of the day. Slowed thoughts with reduced flow, maintaining dullness, sialorrhea present, speech when provoked with more cohesive content, reported a decrease in auditory hallucinations and delusions, family member reported nights of peaceful sleep without awakenings as before. At the end of the first week, laboratory tests were repeated, which remained without significant changes. After 10 days of starting a new therapy, the patient shows good adaptation, absence of reported hallucinations and delusions, maintaining a state of dullness, cohesive speech with a still slow flow of thought, but allopsychically and autopsychically oriented. Motor slowness and impoverishment present, but without signs of extrapyramidal exacerbation. It was then decided to withdraw Levomepromazine 25mg 1-1-1 and clinical observation. Behavioral measures of physical activity initiated according to the patient's condition.

At the end of 30 days of treatment, the patient remained stable without episodes of hallucinations, delirium and agitation, a good response to the withdrawal of Levomepromazine 25mg 1-1-1 due to drowsiness, however, the patient still had frequent complaints during consultations. Laboratory tests remained without noteworthy changes. At the end of the fourth week, the daytime dose of Clozapine was reduced to 50mg 1-1-2, resulting in a daily dose of 150mg per day associated with Carbamazepine 200g 1-1-1. Patient returns at the end of 45 days of treatment with maintenance of clinical stability, absence of delusions and hallucinations, improvement in dullness and negative symptoms, cohesive but slowed flow of thought, without leaks of ideas. Choosed to reduce Clozapine 50mg 0-0-2, obtaining a daily dose of 100mg, maintaining clinical observation and physical activity, returning in 60 days with exams.

After 100 days of treatment with scheduled return, the patient maintains a good standard of laboratory tests, continues performing routine physical activities and improves his disposition at home by carrying out domestic activities. Improvement of speech and affective dullness, family reports notable clinical improvement. Follow-up occurred with a further reduction of Clozapine 50mg 0-0-1 and maintenance of this dosage, associated with Cabarbamazepine 200mg 1-1-1 and return of Escitalopram 10mg 1-0-0 (due to episodes of sadness and anhedonia). Patient has remained stable for 8 months with class and reduced doses of psychotropic drugs, undergoing routine exams and physical activity.

DISCUSSION

It is common in clinical practice to find polypharmacy in patients diagnosed with schizophrenia with low response or inadequate response to medications, causing great damage in several aspects, including biological, social and psychological. Assertiveness in therapeutic conduct depends on several factors, including: length of illness, existing clinical conditions, side effects, doctor-patient-family relationship, among others. In the clinical case presented, taking into account the time since the onset of the comorbidity and the various drug trials already instituted, it was decided to use Clozapine as a foundation treatment for schizophrenia, even taking into account the existing metabolic risk. Clozapine is effective for patients who respond poorly to dopamine receptor antagonists. Double-blind studies

that compared it with other antipsychotics indicated that it had clearer advantages over conventional medications in patients with more severe psychotic symptoms, as well as in those who had previously responded poorly to other antipsychotics. [1]

Clozapine is the only atypical antipsychotic recognized as particularly effective when other antipsychotic agents fail. Therefore, it is considered the "gold standard" for its effectiveness in schizophrenia. Clozapine is also the antipsychotic associated with the highest risk of developing a life-threatening and occasionally fatal complication called agranulocytosis, in 0.5 to 0.2% of patients. For this reason, it is necessary to monitor the blood count of these patients. It also presents a greater risk of seizures, can be very sedating, a greater risk of myocarditis and weight gain.[3]

Even in the face of Clozapine's therapeutic challenges, it was an essential drug for the acute event and clinical stabilization of the patient, even at reduced doses. Thus ensuring the initial objective of the therapeutic proposal of reducing classes and pharmacological dosage in the patient and consequent improvement in quality of life.

FINAL CONSIDERATIONS

The reported case brings into discussion the treatment of a complex situation and the use of polypharmacy with the aim of possible stabilization in resistant schizophrenic patients. Evidence that when well executed a therapeutic proposal with medication reduction, with assertive drugs, even if adopted by few, it is possible and guarantees greater adherence and well-being to the patient.

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