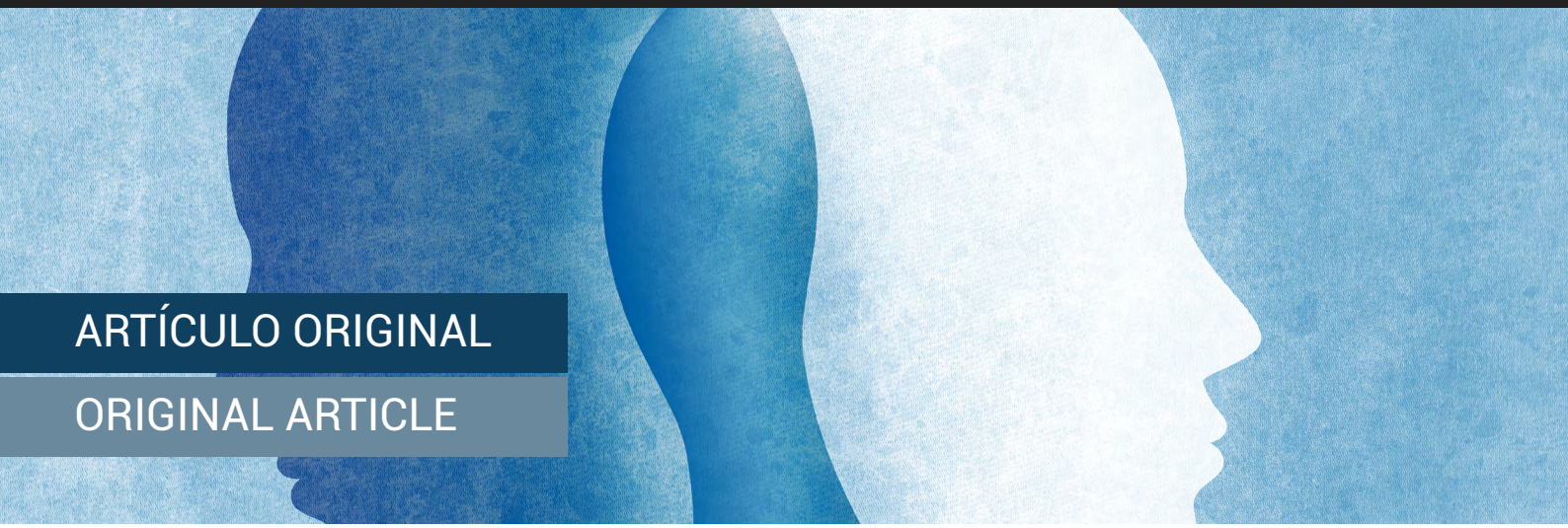
PSICOSOMÁTICA
Y PSIQUIATRÍA

22 / AÑO 2022
JULIO • AGOSTO • SEPTIEMBRE



ARTÍCULO ORIGINAL

ORIGINAL ARTICLE

Recibido: 13/07/2021. Aceptado: 15/04/2022

TRATAMIENTO DE LA PSICOSIS CON CLOZAPINA EN EL SÍNDROME VELOCARDIOFACIAL

PSYCHOSIS TREATMENT USING CLOZAPINE IN VELOCARDIOFACIAL SYNDROME

A. Raquel Faria[1], J. Mesquita Machado[2], C. da Costa Campos[2]

[1]Residente de Psiquiatría, Servicio de Psiquiatría, Hospital de Braga, Braga, Portugal.
[2]Especialista de Psiquiatría, Servicio de Psiquiatría, Hospital de Braga, Braga, Portugal.

Correspondencia: Raquel Faria raquelfaria@outlook.com

Conflict of interests
None declared.

SEMP Sociedad Española de Medicina Psicosomática
Sociedad Marcé Española (MARES)

ISSN 2565-0564
DOI: https://doi.org/10.34810/PsicosomPsiquiatrnum220402

ABSTRACT

Introduction: Velocardiovacial syndrome (VCFS) is a heterogeneous clinical entity caused, most of the times, by a microdeletion on chromosome 22. The main clinical features of this syndrome are: changes in facial and palate morphology, congenital heart abnormalities, hypoplasia of the thymus, immunodeficiencies with increased risk of infection, hypoparathyroidism, intellectual disability and psychiatric disorders. In most cases, the comorbid mental pathology falls into the psychotic disorder category.

Methods: In this study, we present the clinical case of a 34-year-old patient diagnosed with VCFS, with past history of ventricular septal defect with spontaneous closure in childhood and refractory psychosis. Due to the patient's treatment-resistant psychosis, treatment with clozapine has been put to practice. However, when taking into account the possible adverse effects of the drug in patients with VCFS, the authors conducted a non-systematic literature review on the treatment of psychosis in VCFS with clozapine in Pubmed, using the following keywords: velocardiofacial syndrome; clozapine.

Results: There are not many medical studies on the use of psychiatric drugs concerning the treatment of psychiatric disorders in patients with VCFS. Treatment with clozapine in these populations should be considered, always taking into account the particularities and vulnerabilities of these patients, especially in cases of refractory psychosis. Risks and benefits of different treatments should be considered, bearing in mind this population's great vulnerability to adverse effects of drugs.

Discussion: In this case study, we concluded that treatment of psychosis in patients with VCFS remains a major challenge, given clinical vulnerabilities of this specific population, thus further studies being needed.

Keywords: velocardiofacial syndrome; clozapine.

RESUMEN

Introducción: El síndrome velocardiovacial (velocardiofacial syndrome - VCFS) es una entidad clínica heterogénea causada, en su mayoría, por una microdeleción en el cromosoma 22. Las principales características clínicas de este síndrome son: cambios en la morfología facial y del paladar, anomalías cardíacas congénitas, hipoplasia del timo, inmunodeficiencias con mayor riesgo de infección, hipoparatiroidismo, retraso mental y trastornos psiquiátricos. En la mayoría de los casos, la patología mental comórbida suele estar dentro del rango de los trastornos psicóticos.

Métodos: Presentamos el caso clinico de una paciente de 34 años diagnosticada con SVCF con patologia cardíaca (comunicación interventricular con cierre espontáneo desde la infancia) y psicosis refractaria a varios antipsicóticos. Por tratarse de una paciente con mala respuesta al uso de varios antipsicóticos, inició tratamiento con clozapina. Teniendo en consideración los posibles efectos adversos del fármaco sobre la comorbilidad de VCFS, se realizó una revisión bibliográfica no sistemática en Pubmed sobre el tratamiento de la psicosis en VCFS con clozapina, con las palabras clave: síndrome velocardiofacial; clozapina.

Resultados: No hay muchos estudios sobre el uso de psicofármacos en el tratamiento de la comorbilidad psiquiátrica en pacientes con VCFS. El tratamiento con clozapina en pacientes con VCFS debe considerarse teniendo en cuenta las particularidades de cada caso, sobre todo en casos con una mayor propensión a la psicosis refractaria, y, sobre todo, evaluando los riesgos y beneficios de su administración, siempre teniendo en cuenta que existe una mayor vulnerabilidad a los efectos adversos en la administración de fármacos en esta población.

Discusión: En base al presente trabajo, se concluyó que el tratamiento de la psicosis en pacientes con VCFS sigue siendo un gran desafío dadas las vulnerabilidades clínicas de esta población.

Palabras clave: velocardiofacial syndrome; clozapine.

INTRODUCTION

Velocardiofacial syndrome (VCFS) is a congenital syndrome caused by the most common microdeletion found in humans - 22q11.2 microdeletion.

VCFS is clinically heterogeneous, with some common characteristics between affected patients, namely: delayed psychomotor development, cardiac anomalies (conotruncal type), hypoparathyroidism and hypocalcemia, palate anomalies, immunodeficiencies, facial morphological changes (long face with tubular nose, fine palpebral fissures and a small mouth), short stature, urinary system malformations, psychiatric disorders.

Psychiatric disorders most frequently associated with SVCF are psychotic ones, particularly psychotic disorders. It is estimated that around 30-40% of these patients end up developing psychosis during their lifetime. It is also estimated

that 2% of all of the population diagnosed with schizophrenia has 22q11.2.1.4 microdeletion.

METHODS

In this study, we present the clinical case of a 34-year-old patient diagnosed with VCFS, with past history of ventricular septal defect with spontaneous closure in childhood and refractory psychosis. Due to the patient's treatment-resistant psychosis, treatment with clozapine has been put to practice. However, when taking into account the possible adverse effects of the drug in patients with VCFS, the authors conducted a non-systematic literature review on the treatment of psychosis in VCFS with clozapine.

RESULTS

CASE REPORT

Patient description

This article is based on the observation of a patient in the psychiatric ward of *Hospital de Braga*, a 34-year-old woman, single and without children. She had completed the 9th grade of school, resorting to special education. The patient was diagnosed with VCFS in childhood, manifested as velopharyngeal insufficiency, ventricular septal defect with spontaneous closure and intellectual developmental disorder. Her follow-up took place at *Centro Hospitalar Universitário do Porto*.

Case history

In 2012, at the age of 24, she started treatment in the psychiatric unit for anxious and depressive symptoms, but it was not until 2013 that she showed the first behavioral changes - throwing away her clothes, hiding personal belongings at home and starting a self-injurious behavior. Around this time, the patient quit her job. Still in 2013, she had her first hospitalization for psychotic symptoms, namely delusions with persecutory content and auditory hallucinations in the form of compelling voices.

That same year, she began antipsychotic medication, which was changed several times, sometimes before the maximum therapeutic dose was reached, as she was prone to medication side effects. From 2013 to 2021, the patient took several antipsychotic medications for a period of at least eight weeks each, namely: Aripiprazole 10 mg orally, Risperidone 3 mg orally, Paliperidone 6 mg orally, Quetiapine 200 mg orally, Sulpiride 50 100 mg orally, Melperone 75 mg orally, Olanzapine 20 mg orally, Haloperidol 5 mg orally, Chlorpromazine 100 mg orally, Aripiprazole 15 mg orally, Paliperidone 100 mg IM once a month, Trevicta 350 mg 3/3 months, Levomepromazine 150 mg, Haloperidol 100 mg IM once a month. Due to her behavioral symptoms, she was also treated with mood stabilizing medications, namely topiramate 50 mg, valproic acid 500 mg and carbamazepine 400 mg. Due to the occurrence of depressive episodes, which usually followed psychotic decompensations, she was also treated with various antidepressants over the years: Mirtazapine 15 mg, Sertraline 50 mg, Fluvoxamine 50 mg, Fluoxetine 20 mg. The biggest challenge in treating this patient was the frequency and susceptibility to medication side effects. During the nine years she has been in our care, she was hospitalized and admitted to the emergency service multiple times for behavioral changes characterized by heteroaggressiveness and psychotic decompensation with persecutory and erotomanic delusions and auditory hallucinations in the form of command voices. In December 2020, her medication was switched and she started treatment with haloperidol 100 mg IM 2 in 2 weeks, carbamazepine 200 mg 2/day, lorazepam 2.5 mg 3/day, levomepromazine 50 mg 3/day, and biperiden 2 mg 2/day. She exhibited a new psychotic decompensation. Since this was a patient who met the criteria for treatment-resistant psychosis (at least two antipsychotics, one of them second generation, at the appropriate dosage and duration to achieve a response), it was decided to start with clozapine at a dose of 25 mg. After two weeks, an analytical examination was performed, which revealed thrombocytopenia, so it was decided to continue the inpatient treatment. In this context, an initial examination was performed with complete blood count, evaluation of renal function and ionogram, liver function, troponins, lipid profile, glycosylated hemoglobin, C-reactive protein, erythrocyte sedimentation rate, pro-BNP and electrocardiogram. After initiation of treatment, vital signs and possible occurrence of symptoms indicative of adverse effects were monitored. Thrombocytopenia was detected at the first examination, so carbamazepine was discontinued. The clozapine dose was titrated up to 150 mg. However, around the second week of treatment, the patient began to develop fever, with a total of two febrile episodes. She immediately underwent an analytical workup with monitoring of the previously described parameters and septic screening, with no significant changes noted. The patient also complained of

marked sialorrhea, which even affected food intake. For this reason, it was decided to discontinue clozapine.

REVIEW RESULTS

VCFS is clinically heterogeneous, with some common characteristics between affected patients, namely: delayed psychomotor development, cardiac anomalies (conotruncal type), hypoparathyroidism and hypocalcemia, palate anomalies, immunodeficiencies, facial morphological changes (long face with tubular nose, fine palpebral fissures and a small mouth), short stature, urinary system malformations, psychiatric disorders.

There are not many studies regarding the use of psychotropic drugs in the treatment of psychiatric comorbidities in patients with VCFS, although standard treatment regimens are generally recommended. However, one must never lose sight of existing comorbidities, as well as two other decisive aspects when choosing an antipsychotic: propensity for treatment-refractory psychosis in this population and greater vulnerability to medication adverse effects. This vulnerability is due to the highly variable phenotypic aspects of VCFS, which include: cardiac malformations that may increase the risk of prolongation of the QT interval; association between this syndrome and hypoparathyroidism and hypocalcemia with an increased risk of seizures; vulnerability to develop type 2 diabetes mellitus and obesity; and, finally, immunodeficiencies that condition a great risk of developing potentially serious infections (particularly important in the use of clozapine).

In general, it is recommended that special care should be taken in this group of patients when starting antipsychotic treatment. Complementary diagnostic tests and adjustments in drug dose should be carried out in order to reduce the risk of adverse effects, including: EKG, metabolic risk evaluation, parathyroid function evaluation and calcium dosage. The practicing physician should also consider the need for adjuvant treatment with anticonvulsants, antidyslipidemics or other drugs, depending on each particular case.

Adverse effects of Clozapine may be particularly frequent in these patients, including mainly the risk of seizures, severe neutropenia and myocarditis. Although the use of clozapine is considered relatively safe in this population, it is recommended dose titration up to a maximum of 250 mg/day. Even taking these measures into consideration, about half of these patients are affected with severe adverse effects of Clozapine, which may lead to treatment discontinuation and, therefore, the need for alternatives.

DISCUSSION

From the present study, it can be concluded that treatment of psychosis in patients with SVCF is still a great challenge. It is imperative to continue to investigate and invest in the study of the treatment of psychiatric comorbidity (particularly psychosis) in this population. The clinical idiosyncrasies we have been discussing make this clinical entity challenging for psychiatrists and other physicians treating these patients, which leads to the need for a multidisciplinary approach.

Further studies are needed in order to achieve a safe and effective treatment of psychosis concerning these patients in the future, particularly in cases of treatment-refractory psychosis.

CONFLICT OF INTERESTS

None declared.

REFERENCES

1. Choi, SH. Kang, SG; Kim, HY; Bae, JN; Lee, JS; Kim, WH. (2020). *Important Consideration in Choosing Antipsychotics in the Treatment of Patients with 22q11.2 Deletion Syndrome: Risk of Convulsion.* Clinical Psychopharmacology and Neuroscience; 18(3), 454–457. DOI: 10.9758/cpn.2020.18.3.454.
2. Murphy, KC. (2002). *Schizophrenia and velo-cardio-facial syndrome.* The Lancet, 359(9304), 426–430. DOI: 10.1016/S0140-6736(02)07604-3.
3. Murphy, KC; Owen, MJ. (2001). *Velo-cardio-facial syndrome: a model for understanding the genetics and pathogenesis of schizophrenia.* British Journal of Psychiatry, 179(5), 397–402. DOI: 10.1192/bjp.179.5.397.
4. Kendler, KS, Eaves, L. (2005). Genetics of Schizophrenia, Riley, B, Kendler, KS. *Review of Psychiatry Series - Psychiatric Genetics.* (116-117). Washington DC: American Psychiatric Publishing.
5. Taylor, DM, Barnes, TRE, Young, AH. (2021). Drug Treatment of Psychiatric Symptoms Occurring in the context of Other Disorders, Taylor, DM, Barnes, TRE, Young, AH. *The Maudsley Prescribing Guidelines in Psychiatry 14th ed.* (794-796). West Sussex: Wiley-Blackwell.
6. Taylor, DM, Barnes, TRE, Young, AH. (2021). Schizophrenia and Related Disorders, Taylor, DM, Barnes, TRE, Young, AH. *The Maudsley Prescribing Guidelines in Psychiatry 14th ed.* (190-244). West Sussex: Wiley-Blackwell.