

2020; 6(2): 88-90



CASE REPORT/CASO CLÍNICO

Palmitato de Paliperidona num Adulto com Síndrome de Asperger Paliperidone Palmitate in an Adult with Asperger's Syndrome

TIAGO ANTUNES-DUARTE MD *1.2 FILIPA FERNANDES-ÓRFÃO MD 3

1. Serviço de Psiquiatria e Saúde Mental do Hospital de Santa Maria - Centro Hospitalar Universitário Lisboa Norte, Lisboa, Portugal

2. Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal

3. USF Cuidar Saúde - ACES Almada Seixal, Seixal, Portugal

Resumo

A síndrome de Asperger é uma perturbação caraterizada pelo compromisso da interação social e um padrão de comportamentos estereotipados. Estes incluem comportamentos repetitivos, irritabilidade, agressividade, hiperatividade e desatenção. O tratamento dos sintomas comportamentais constitui um desafio, com escassos estudos acerca da eficácia das diferentes abordagens terapêuticas. Este artigo é a primeira descrição do uso bem-sucedido de palmitato de paliperidona mensal no tratamento de sintomas comportamentais num adulto com síndrome de Asperger.

Abstract

Asperger's syndrome is a disorder characterized by impaired social interaction and a pattern of stereotyped behaviors. These include repetitive behaviors, irritability, aggressiveness, hyperactivity and inattention. The treatment of behavioral symptoms is a challenge, with few studies on the effectiveness of different therapeutic approaches. This article is the first description of the successful use of monthly paliperidone palmitate in the treatment of behavioral symptoms in an adult with Asperger's syndrome.

Palavras-chave: Adulto; Antipsicóticos; Síndrome de Asperger; Palmitato de Paliperidona; Pirimidinas

Keywords: Adult; Antipsychotic Agents; Asperger Syndrome; Paliperidone Palmitate; Pyrimidines

INTRODUCTION

Asperger's syndrome (AS) is a subtype of pervasive development disorders in the ICD-10.¹ It is characterized by an impairment in social interaction and a pattern of restricted or stereotyped behavior.² Patients show no language delay and their cognitive development is not marked by an overall delay but by specific impairments in certain areas such as the executive functions.^{3,4} Behavioral symptoms associated with AS include repetitive behaviors, irritability, aggression, hyperactivity, inattention, and social impairment. Irritability in AS may include severe temper outbursts and/or impulsive aggression towards one-self or others. Moderate-to-severe irritability is known to occur in up to 30% of the patients with AS.³

Behavioral symptoms associated with AS are most commonly treated with serotonin selective reuptake inhibitors (SSRIs), psychostimulants, and antipsychotics.² SSRIs are less effective than antipsychotics and while psychostimulants demonstrate some benefit for the treatment of hyperactivity and inattention in individuals with AS, they are also associated with more adverse effects than antipsychotics.² Antipsychotics, namely aripiprazole and risperidone, are the most effective medications for the treatment of behavioral symptoms in AS.⁵ Oral paliperidone appears effective

Recebido/Received: 2020-05-05

Aceite/Accepted: 2020-06-06

Publicado / Published: 2020-11-27

^{*}Autor Correspondente/Corresponding Author: Tiago Antunes-Duarte | tantunesduarte@gmail.com | Serviço Psiquiatria e Saúde Mental do Hospital de Santa Maria - CHULN | Av. Prof. Egas Moniz, 1649-035 Lisboa(ORCID - 0000-0002--9856-7376)

[©] Author(s) (or their employer(s))and RPPSM Journal 2020. Re-use permitted under CC BY-NC. No commercial re-use./© Autor (es) (ou seu (s) empregador (es)) e revista RPPSM 2020. Reutilização permitida de acordo com CC BY-NC. Nenhuma reutilização comercial.

for the treatment of irritability in children, adolescents, and adults with AS.⁶⁻⁹ A trial of oral paliperidone conducted in adolescents and young adults with autism demonstrated an 84% response rate in the treatment of irritability.¹⁰

In 2010, the European Medicines Agency approved a monthly sustained-release intramuscular (IM) formulation of the atypical antipsychotic paliperidone, paliperidone palmitate, for the treatment of adults with schizophrenia.¹¹ In this report, we report the first successful use of monthly paliperidone palmitate for the treatment of behavioral symptoms in an adult with AS.

CASE REPORT

A 29-year-old man diagnosed at the age of 4 with AS by a child and adolescent psychiatrist using ICD-10 criteria (F84.5).¹ At the age of 3, there were relevant delays in social interaction, as well as intense irritability including frequent severe tantrums and self-directed aggressive behavior, on the count of one every two days. He was administered thioridazine until the age of 9 with incomplete behavior control, and thus a switch for risperidone 2 mg daily was made. There was unremitting hyperactivity, psychomotor agitation, as well as moderate difficulties in reading and writing, and the dose was progressively increased towards 6 mg daily until he was around 14 years old. At this age, after 2 generalized tonic-clonic seizures he was diagnosed with epilepsy and started valproic acid 1500 mg/day. For the next two years there were around 3 to 4 seizures per month, and topiramate 300 mg/day was added. Due to incomplete seizure control, at 18 years old clobazam 10 mg/day was given on top of the other medications, with complete epilepsy control. At the age of 20, the self and hetero-aggressive episodes, especially towards his mother, became more frequent and violent, with between two and three episodes per day. There were erotomaniac delusions regarding his female neighbors and sexualized behaviors towards strangers, and therefore risperidone was increased to 9 mg/day. Until the age of 27, tantrums of irritability, bingeing episodes, stereotyped motor behaviors, coprolalia and echolalia were present. Amisulpride 25 mg/day, escitalopram 5 mg/day and haloperidol 10 mg/ day were intermittently given on the top of the previous medications, with no significant improvement. His Patient Global Impression of Change Scale (PGIC-VP) score was 2, despite full adherence to the medication, as stated by his mother, and verified by serum valproic acid levels regularly within the therapeutic range.¹²

At the age of 28, he was switched to oral paliperidone 6 mg/day, while maintaining valproic acid, topiramate, and

clobazam. All other medications were stopped. After 2 weeks, his mother referred an improvement in his behavior and also in the intellectual depth of his conversations. There was no reappearance of motor symptoms, and he became responsible for his own medication. Because of the increased capacity in impulse control, namely in controlling food binges, there was a 5 kg weight lost. Due to the maintained gains in behavior control, five months later he was transitioned to the long-acting formulation, and did the induction scheme of 150 mg, plus 100 mg eight days later, followed by paliperidone palmitate 75 mg monthly. He was able to start voluntary work at a clinic, and for some of the weekdays he managed to live by himself at a family house next to the clinic. After 3 months of therapy with palmitate paliperidone had elapsed, the reemergence of irritably and motor stereotypies one week before the next administration was due were noticed, and thus he started taking palmitate paliperidone 100 mg monthly. He was also taking valproic acid 2000 mg/day, topiramate 150 mg/day, and clobazam 10 mg/day. Twelve months have elapsed and, since he started palmitate paliperidone, improvements both in irritability and motor behavior have been maintained, with no episodes of self or hetero aggression ever since. At present, his Patient Global Impression of Change Scale (PGIC-VP) score is 6.12

DISCUSSION

Paliperidone is the active metabolite of risperidone but is not metabolized extensively in the liver,¹³ thus having fewer pharmacokinetic interactions. It usually lacks the drowsiness, dizziness, lightheadedness, and confusion risperidone produces when administered with valproic acid, especially when administered by injection. Another advantage is that paliperidone is provided in a sustained--release formulation, even in the oral form, making it possible to be administered once-daily and reducing the side effects related to the rapid absorption of risperidone. A lower equivalent-dose is thus also possible, in comparison with other antipsychotics (e.g. haloperidol, risperidone, etc.).¹⁴⁻¹⁶

This case reports the successful use of paliperidone in its oral formulation, and maintenance of the remission of behavioral symptoms with an equivalent dose of its long-acting injectable formulation in an adult with AS. The three-monthly paliperidone palmitate will probably also be successful in AS.

To the best of our knowledge, it is the first described case of paliperidone palmitate in an adult with AS and the results are compelling.

Responsabilidades Éticas

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho. **Fontes de Financiamento:** Não existiram fontes externas de financiamento para a realização deste artigo.

Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

Consentimento: Consentimento do doente para publicação obtido.

Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

Tiago Antunes-Duarte

Ethical Disclosures

Conflicts of Interest: The authors have no conflicts of interest to declare.

Financing Support: This work has not received any contribution, grant or scholarship.

Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

Patient Consent: Consent for publication was obtained.

Provenance and Peer Review: Not commissioned; externally peer reviewed.

References

- 1. The International Statistical Classification of Diseases and Related Health Problems. Tenth Revision. Geneva: World Health Organization; 1992.
- Doyle C, McDougle, C. Pharmacologic treatments for the behavioural symptoms associated with autism spectrum disorders across the lifespan. Dialogues Clin Neurosci. 2012;14:263-79.
- Lecavalier L. Behavioral and emotional problems in young people with pervasive developmental disorders: relative prevalence, effects of subject characteristics, and empirical classification. J Autism Dev Disord. 2006;36:1101-14. doi: 10.1007/s10803-006-0147-5.
- Mirkovic B, Gérardin P. Asperger's syndrome: What to consider?. L'Encéphale. 2019;45:169-74. doi: 10.1016/j.encep.2018.11.005.
- LeClerc S, Easley D. Pharmacological therapies for autism spectrum disorder: a review. P T. 2015;40:389-97.
- McDougle CJ, Holmes JP, Carlson DC, Pelton GH, Cohen DJ, Price LH. A double-blind, placebocontrolled study of risperidone in adults with autistic disorder and other pervasive developmental disorders. Arch Gen Psychiatry. 1998;55:633-41. doi: 10.1001/ archpsyc.55.7.633.
- Stigler KA, Erickson CA, Mullett JE, Posey DJ, McDougle CJ. Paliperidone for irritability in autistic disorder. J Child Adolesc Psychopharmacol. 2010;20:75-8. doi: 10.1007/s00213-012-2711-3.
- Kowalski JL, Wink LK, Blankenship K, Habenicht CD, Erickson CA, Stigler KA, et al. Paliperidone palmitate in a child with autistic disorder. J Child Adolesc Psychopharmacol. 2011;21:491-3. doi: 10.1089/ cap.2011.0035.
- 9. Stigler KA, Mullett JE, Erickson CA, Posey DJ, McDougle CJ. Paliperidone for irritability in

adolescents and young adults with autistic disorder. Psychopharmacology. 2012;223:237-45. doi: 10.1007/s00213-012-2711-3.

- Stigler KA, Mullett JE, Erickson CA, Posey DJ, Mc-Dougle CJ. Paliperidone for irritability in adolescents and young adults with autistic disorder. Psychopharmacology. 2012;223:237-45.
- European Medicines Agency, Committee for Medicinal Products for Human Use. Summary of opinion (initial authorization) for Xeplion (paliperidone palmitate). [cited 2020 May 4]. Available from: https:// www.ema.europa.eu/en/documents/smop-initial/ chmp-summary-positive-opinion-xeplion en.pdf.
- 12. Domingues L, Cruz E. Adaptação Cultural e Contributo para a Validação da Escala
- 13. Patient Global Impression of Change. IfisiOnline. 2011;2:31-7.
- 14. Stahl SM. Stahl's essential psychopharmacology: Neuroscientific basis and practical applications. 4th ed. New York: Cambridge University Press; 2013.
- Rado J, Dowd SM, Janicak PG. Paliperidone ER: Reformulated antipsychotic for schizophrenia Tx. Curr Psychiatry. 2007;6:75-82.
- Leucht S, Samara M, Heres S, Patel MX, Woods SW, Davis JM. Dose equivalents for second-generation antipsychotics: the minimum effective dose method. Schizophr Bull. 2014;40:314-26. doi:10.1093/ schbul/sbu001
- McEvoy JP, Byerly M, Hamer RM, Dominik R, Swartz MS, Rosenheck RA, et al. Effectiveness of paliperidone palmitate vs haloperidol decanoate for maintenance treatment of schizophrenia: a randomized clinical trial [published correction appears in JAMA. 2014;312:1473]. JAMA. 2014;311:1978-87. doi:10.1001/jama.2014.4310