Case Report

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Ptosis after introduction of risperidone in a pediatric patient: case report and literature review

Abstract

Risperidone is an antipsychotic used in several psychiatric diseases and other disorders in adults and children. It is the most frequently prescribed antipsychotic drug in children and adolescents worldwide. This drug has several adverse effects, however, palpebral ptosis is rarely reported with its usage. In the few published case reports, palpebral ptosis after the administration of risperidone was considered a presentation or an exacerbation of myasthenia gravis.

The purpose of this case report is to present a 5-year-old boy who developed a palpebral ptosis after the initiation of 0.15 ml of risperidone for a sleep disorder (night terrors).

Keywords: risperidone, palpebral ptosis, pediatrics, drug adverse effect

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Introduction

Risperidone is a second-generation antipsychotic, initially developed for the treatment of schizophrenia. It acts as a serotonin-dopamine antagonist, binding to 5-HTA2A and D2 receptors-type but with higher affinity for the first. It is approved for pediatric bipolar disorder 1 (children age 10–17), irritability in autism (ages 5–27), and schizophrenia in children 10–17. However, it is frequently prescribed off label for indications such as attention deficit hyperactivity disorder (ADHD), Tourette syndrome, behavioral disturbances, and impulse control disorders.[1–3]

Adverse events are relatively frequent while taking risperidone. These are more studied in the adult populations but children are at higher risk compared to adults of developing them. The most frequently described are metabolic abnormalities and weight gain.[1,4]

Palpebral ptosis has been rarely reported as an adverse effect of risperidone.[5] Studies have been conducted with rats and Beagle dogs taking intramuscular risperidone-loaded microspheres during a 12-week period and the development of ptosis was observed with dose-dependent severity, incidence and onset time.[6,7] In an observational cohort study conducted in New Zealand with 420 children taking atypical antipsychotics, palpebral ptosis was reported in only one five-year-old girl receiving risperidone 4 mg/day, which resolved following dosage reduction.[3]

In this article, we present a case of a 5-year-old boy who developed unilateral palpebral ptosis after the initiation of 0.15 ml of risperidone for sleep disorder (night terrors).

Case description

A 5-year-old boy was observed in the emergency department (ED) after the development of a left palpebral ptosis associated in the day after initiating risperidone 0.15 ml once per day for a history of night terrors. Due to the progressive worsening even after the immediate suspension of the medication, the mother decided to bring him for emergent evaluation. She also reported 2 episodes of vomiting, but denied other systemic and ophthalmic signs or symptoms (such as diarrhea, respiratory symptoms, fever, blurred or double vision, red or yellow eye coloration). At the observation, we noted a palpebral ptosis of the left eye with no occlusion of the visual axis (Figure 1). Visual acuity was 20/20 on both eyes with no correction, there was no anisocoria, pupils were symmetrically reactive and there was no relative pupillary afferent defect. Ocular alignment and motility as well as confrontation visual fields were also normal. No alterations were observed at the optical coherence tomography (OCT). The patient had also a systemic and neurologic evaluation by the Pediatrician and the Neurologist on the ED and no other change was observed. A head and orbital computed tomography (CT) was obtained and nothing relevant was noticed.

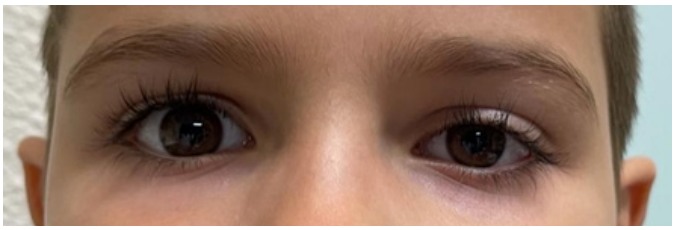

Figure 1 Palpebral ptosis of the left eye at presentation.

The child was observed 3 days later with a worsening of the palpebral ptosis and the mother also reported complaints of diplopia (the boy stated "seeing two mothers"). No other symptoms developed and there were no new episodes of vomiting. At this time, he already had an occlusion of the visual axis (Figure 2). Also, an anisocoria of 0.9 mm was observed with a bigger right pupil diameter in the dark (right eye 5.3 mm vs left eye 4.4 mm). Visual acuity was still preserved with 20/20 on both eyes and color testing was normal. No diplopia was observed (he could only see 4 images on the Worth 4 dot test) and ocular alignment and movements were still also normal.

Figure 2 Worsening of the palpebral ptosis 3 days later.

A new observation was done 9 days after the ED episode and a total resolution of the clinical signs was observed (Figure 3). The child had no ptosis or anisocoria at this moment. Thorax CT and orbital magnetic resonance (MRI) were both normal. Acethylcholine receptor antibody (AChR) was negative.

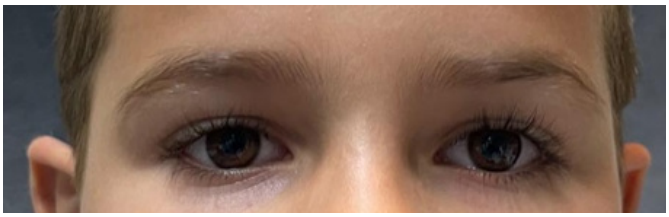

Figure 3 Improvement of the palpebral ptosis 9 days after the ED episode.

Discussion

Risperidone is the most frequently prescribed antipsychotic drug in children and adolescents worldwide and the most commonly reported side effects are weight gain, metabolic abnormalities, extrapyramidal symptoms, prolactin elevation and sedation.[8] In the literature, palpebral ptosis is a rare adverse effect reported following the administration of risperidone.[5] When revising published case reports in PubMed, three clinical cases were reported in which the palpebral ptosis after the administration of risperidone was considered a presentation or an exacerbation of myasthenia gravis (MG).[9–11] The first of a 29-year-old female with schizophrenia and with a previous diagnosis of MG, who started treatment with long-acting risperidone injection. She was stable for 7 years, but developed double vision, palpebral ptosis and generalized weakness following the initiation of this medication. She showed resolution of the symptoms only 7 weeks after her last injection.[9] The second case is of a 6-year-old female patient with no previous diagnosis of MG. She was started on risperidone 0.25 mg/day due to an ADHD and developed palpebral ptosis associated with extreme tiredness. She was diagnosed with an ocular MG after a positive AChR antibody (10 mg/dL) and a thymoma-compatible lesion was detected in a thorax–neck CT.[10] The third and more recent case was a 20-year-old male with schizophrenia who was taking risperidone oral 2 mg daily. He developed palpebral ptosis, muscle rigidity, sialorrhea and dysphagia and was diagnosed with MG.[11] Routinely used psychotropics such as antipsychotics in patients with MG are risk factors for exacerbating symptoms because of their anticholinergic effects. These effects are considered much lower with second-generation antipsychotic such as risperidone when compared to clozapine and olanzapine. However, these clinical cases illustrate that risperidone may be consider a trigger or an exacerbator for MG, even though schizophrenia for itself poses a possible risk factor of developing MG.[9,10] Inhibition of neuronal transmission and calcium influx at the presynaptic terminal (which inhibits ACh release); increased number of autoantibodies against postsynaptic AChR; and changes in postsynaptic ion permeability are proposed mechanisms for the relationship between antipsychotics and MG.[9]

Risperidone is metabolized into the active metabolite 9-hydroxyrisperidone (9-OH-RIS) mainly by cytochrome P450 enzymes 2D6 and also 3A4 (CYP2D6 and CYP3A4). Therapeutic response to this drug can be influenced by the plasma level and the concentration of 9-OH-RIS. CYP2D6 gene is highly polymorphic and its variations impact the metabolism of numerous medications, leading to alterations in their efficacy and adverse effects. Due to this polymorphism, risperidone plasmatic levels have great individual variations.[12,13] Studies show that CYP2D6 genotypes may serve as a predictor of adverse reactions with risperidone treatment.[13] Other medications can algo interfere with CYP2D6, which was also described in one of the clinical cases previously reported in which the patient was taking fluoxetine which is a potent inhibitor of CYP2D6, leading to an increase in risperidone plasma concentration by 2.5–2.8 folds.[9] However, in children, the relationships between risperidone dose and blood concentrations have not been clarified yet, but studies suggest a lower therapeutic concentration range when compared to the therapeutic window established for adults (between 20 and 60 ng/mL)[14] and also suggest that monitoring should be done to increase safety and effectiveness in children and adolescents.[8] In our clinical case, the child had a worsening of the clinical picture four days after suspending the drug, which made us believe that his drug metabolism was probably slower and he still had the drug or its active metabolite after that period. The patient was not diagnosed with MG, and we believe the ptosis was an isolated adverse drug reaction to risperidone. This is supported by the Adverse Drug Reaction (ADR) Probability Scale (Naranjo's scale)[15] which in this case is 8 – a probable adverse reaction. Similar cases reported in the literature were all diagnosed with MG and this is a differential diagnosis that must be always taken into account and excluded. Further research is needed to explore adverse effects of this psychotropic in children, determine its ideal therapeutic window in this population, its safety and efficacy.

Acknowledgments

None.

Ethical considerations

Written informed consent for the publication of this clinical case was obtained from the parents of the individual reported here.

Conflicts of interest

The authors have no conflicts of interest to declare.

References

1. Rossow KM, Oshikoya KA, Aka IT, et al. Evidence for pharmacogenomic effects on risperidone outcomes in pediatrics. *J Dev Behav Pediatr*. 2021;42(3):205–212.
2. DeVane CL, Charles JM, Abramson RK, et al. Pharmacotherapy of autism spectrum disorder: results from the randomized BAART clinical trial. *Pharmacotherapy*. 2019;39(6):626–635.
3. Harrison-Woolrych M, Garcia-Quiroga J, Ashton J, et al. Safety and usage of atypical antipsychotic medicines in children: a nationwide prospective cohort study. *Drug Saf*. 2007;30(7):569–579.
4. Mano-Sousa BJ, Pedrosa AM, Alves BC, et al. Effects of risperidone in autistic children and young adults: a systematic review and meta-analysis. *Curr Neuropharmacol*. 2021;19(4):538–552.
5. Janssen Science™. Adverse event of risperdal - vision disorders. 2024.
6. Zhang J, Ye L, Wang W, et al. A 12-week subchronic intramuscular toxicity study of risperidone-loaded microspheres in rats. *Hum Exp Toxicol*. 2015;34(2):205–223.
7. Tian J, Wang W, Ye L, et al. A 12-week intramuscular toxicity study of risperidone-loaded microspheres in Beagle dogs. *Hum Exp Toxicol*. 2014;33(5):473–487.
8. 8. Kloosterboer SM, de Winter BCM, Reichart CG, et al. Risperidone plasma concentrations are associated with side effects and effectiveness in children and adolescents with autism spectrum disorder. *Br J Clin Pharmacol*. 2021;87(3):1069–1081.

9. Al-Hashel JY, Ismail II, John JK, et al. Worsening of myasthenia gravis after administration of injectable long-acting risperidone for treatment of schizophrenia; first case report and a call for caution. *Neuromuscul Disord*. 2016;26(4-5):309–311.

10. Ogutlu H, Karayagmurlu A, Esin IS, et al. Myasthenia gravis attack after oral risperidone treatment: A case report. *Eurasian J Med*. 2018;50(2):128–129.

11. Abualkhair L, Almaghrabi A, Al Edrees N, et al. Unmasking of Myasthenia Gravis after introduction of oral risperidone in a schizophrenic saudi male: a case report. *Cureus*. 2021;13(12):e20541.

12. Wang X, Huang J, Lu J, et al. Risperidone plasma level, and its correlation with CYP2D6 gene polymorphism, clinical response and side effects in chronic schizophrenia patients. *BMC Psychiatry*. 2024;24(1):41.

13. Lu J, Yang Y, Lu J, et al. Effect of CYP2D6 polymorphisms on plasma concentration and therapeutic effect of risperidone. *BMC Psychiatry*. 2021;21:70.

14. Taurines R, Fekete S, Preuss-Wiedenhoff A, et al. Therapeutic drug monitoring in children and adolescents with schizophrenia and other psychotic disorders using risperidone. *J Neural Transm (Vienna)*. 2022;129(5-6):689–701.

15. Adverse drug reaction probability scale (Naranjo) in drug induced liver injury. 2024.

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