



Leg oedema due to low-dose risperidone during maintenance monotherapy of schizophrenia

Serhat Tunç & Hamit Serdar Başbuğ

To cite this article: Serhat Tunç & Hamit Serdar Başbuğ (2018) Leg oedema due to low-dose risperidone during maintenance monotherapy of schizophrenia, *Psychiatry and Clinical Psychopharmacology*, 28:1, 104-106, DOI: [10.1080/24750573.2017.1379718](https://doi.org/10.1080/24750573.2017.1379718)

To link to this article: <https://doi.org/10.1080/24750573.2017.1379718>



© 2017 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group



Published online: 21 Sep 2017.



Submit your article to this journal [↗](#)



Article views: 3723



View related articles [↗](#)



View Crossmark data [↗](#)



Citing articles: 1 View citing articles [↗](#)

CASE REPORT



Leg oedema due to low-dose risperidone during maintenance monotherapy of schizophrenia

Serhat Tunç ^a and Hamit Serdar Başbuğ ^b

^aDepartment of Psychiatry, Faculty of Medicine, Kafkas University, Kars, Turkey; ^bDepartment of Cardiovascular Surgery, Faculty of Medicine, Kafkas University, Kars, Turkey

ABSTRACT

Drug-related peripheral leg oedema is most commonly associated with steroids, nonsteroidal anti-inflammatory, antihypertensives, and immunosuppressive agents. The second-generation antipsychotic risperidone is rarely associated with such oedematous complications. This adverse effect of risperidone occurs with a higher incidence in higher doses according to its dose-dependent nature. In this paper, a rare case of small maintenance dose risperidone-induced peripheral leg oedema in a schizophrenia patient was reported.

ARTICLE HISTORY

Received 13 August 2017
Accepted 8 September 2017

KEYWORDS

Risperidone; drug side effects; leg; oedema

Introduction

Risperidone is a widely prescribed second-generation antipsychotic agent that is mostly used in the treatment of schizophrenia and schizoaffective disorders. It is a benzisoxazole derivative having a strong binding affinity to serotonin type-2 (5-hydroxytryptamine, 5-HT₂), dopamine (D₂), and α 1-adrenergic receptors causing antagonism at these receptors [1]. Risperidone seems to be very efficient also in childhood and adolescence behavioural disorders including hyperactivity, aggressiveness, self-injurious states, irritability, and stereotypes [2]. Although risperidone has several side effects, most of them are not serious such as increased appetite, drowsiness, agitation, anxiety, and insomnia [3]. However, oedema was introduced as a rare but severe adverse effect of risperidone mentioned in some case reports occurring in a dose-dependent manner [4]. Leg oedema is a rarely observed side effect of risperidone especially in small doses of maintenance treatment of schizophrenia [1]. In this paper, a subacute onset of a bilateral leg oedema after initiation of low-dose risperidone treatment in a schizophrenia patient was reported.

Case presentation

A 37-year-old man was referred to the psychiatry outpatient clinic with the complaints of bilateral leg oedema. The leg oedema started two weeks ago after his medication for schizophrenia treatment was altered. He was prescribed risperidone (2 mg/day) instead of aripiprazole (5 mg/day) to prevent the recurrent episodes that happened again in the last

two months. The patient had a 10 years history of schizophrenia with an psychotic episode-free period for the last 7 years after his initial diagnosis and hospitalization.

According to his physical examination, both feet and ankles were severely oedematous. There was a slight pretibial pitting oedema upwards through the distal one-third of both legs. The upper two-thirds of the legs were nearly non-oedematous. The patient was hospitalized to examine the symptoms and signs correctly with a multidisciplinary approach. The cardiovascular surgery consultation revealed no vascular pathologies including venous insufficiency and lymphoedema. Lower extremity venous doppler ultrasound imaging demonstrated no venous thromboembolic (VTE) state. Cardiology consultation was performed to exclude any cardiomyopathies or valvular pathologies. The echocardiography showed an ejection fraction of 65% which implicates no contractile dysfunction with normal cardiac valves. The urinalysis and biochemical tests including renal and hepatic function tests revealed no abnormalities. The haemoglobin was 14.6 mg/dl. D-dimer levels were evaluated to exclude a subclinical VTE. No protein C or S deficiency or any factor deficiencies were detected. Blood cell counts and the morphology were normal. The Immunoglobulin E (IgE) levels were detected to exclude an angioedema or any allergic reactions against the antipsychotic agent that demonstrated no abnormalities.

According to the Naranjo causality scale (which showed a score of 6), this adverse effect was probably induced by risperidone [5]. As the peripheral leg oedema was thought to be related to the medical treatment with risperidone, the risperidone was thus

CONTACT Serhat Tunç  drserhattunc@gmail.com  Department of Psychiatry, Faculty of Medicine, Kafkas University, Pasacayiri, Kars 36100, Turkey

© 2017 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

replaced by another second-generation antipsychotic agent amisulpride (400 mg/day). After the drug alteration, peripheral oedema on both legs was gradually subsided in four days revealing no residual swelling. The patient was discharged with no other complications.

Consent: Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Discussion

In most cases of risperidone-induced oedema, the immunological and hematological blood tests reveal no abnormal findings and the actual mechanism of pathogenesis remains unclear [1]. Risperidone acts as a vasodilator with its action on the α -receptors of the peripheral vascular system. This vasoactive effect may cause an increased hydrostatic pressure on the capillary system which would eventually result in tissue oedema [6]. Likewise, risperidone may induce the 5-HT receptor blockade which can potentially increase the plasma cyclic adenosine monophosphate levels that relax the vascular smooth muscle [7]. The dopaminergic blockade also plays a significant role in producing oedema by intervening the renal maintenance of fluid and electrolyte balance [8]. Also, several probable mechanisms may also be involved in the onset of risperidone-induced oedema such as the allergic reactions, receptor supersensitivity, and drug interactions [9]. The allergic reactions may be caused either by mast cell degranulation or activation of the kallikrein-kinin cascade. In the former case, angioedema is caused by the IgE-mediated hypersensitivity which usually coexists with urticaria and more generalized anaphylactic reactions [10]. The complement system involvement with C4-C2 activation in a patient with a previous C1 inhibitor deficiency was reported as a possible mechanism of angioedema [1]. The Type I and Type IV hypersensitivity reactions were also documented in another patient [11]. The allergic drug reaction should always be considered after the clinical signs of facial or pedal oedema, disseminated skin eruptions or urticaria. The blood C3, C4, and IgE levels may elucidate the hypersensitive and allergic nature of the aetiology [9]. The side effects of risperidone such as leg oedema may occur more prominently when the risperidone is reinstated after a drug-free period. This phenomenon may be explained by the supersensitivity of the α -receptors of neurons [12]. Risperidone is frequently used in combination with other drugs such as benzodiazepines, sodium valproate, and other antipsychotics. Thus the reactions may also occur due to drug interactions [9].

The risperidone-related leg oedema occurs as an infrequent adverse effect in between 1/100 and 1/1000

patients [1]. In our clinical practice, more than 200 patients with risperidone medication are being followed, but no other case of leg oedema was observed so far. However, this low incidence may solely be the result of being unawareness or underestimation of this relatively rare side effect of risperidone. In the present case, the aetiology of oedema was not clearly defined. The patient was treated with a risperidone monotherapy, and thus no possibility of drug interaction or additive effect of another agent were considered. The IgE levels were also normal revealing no diagnostic implications for allergic or hypersensitivity reactions.

Regarding the treatment, prescribing a diuretic is only partially effective despite causing intravascular volume depletion [13]. Therefore, the treatment of risperidone-induced oedema primarily depends on the discontinuation and substitution of the drug with another agent. However, if the drug is proven to be irreplaceable and appears to be effective, it would be appropriate to lower the dose until the oedema resolves with a closer follow-up [1].

In conclusion, leg oedema is a rare but serious side effect of risperidone. Although it has a dose-dependent nature and usually associates with high doses, it may also present with small maintenance doses as in this case. The patients especially who are receiving high doses of risperidone should be warned and monitored for these side effects. Despite the low incidence of oedema due to the risperidone administration, the likely occurrence of this adverse effect should always be taken into consideration by the psychiatrists, as it may affect patients' compliance with the prescription.

Disclosure statement

No potential conflict of interest was reported by the authors.

ORCID

Serhat Tunç  <http://orcid.org/0000-0002-2057-4074>

Hamit Serdar Başbuğ  <http://orcid.org/0000-0002-1363-6783>

References

- [1] Tamam L, Ozpoyraz N, Unal M. Oedema associated with risperidone. *Clin Drug Invest.* 2002;22(6):411-414.
- [2] Troost PW, Lahuis BE, Steenhuis MP, et al. Longterm effects of risperidone in children with autism spectrum disorders: a placebo discontinuation study. *J Am Acad Child Adolesc Psychiatry.* 2005;44(11):1137-1144.
- [3] Gunes F, Batgi H, Akbal A, et al. Angioedema – an unusual serious side effect of risperidone injection. *Clin Toxicol.* 2013;51(2):122-123.

- [4] Ravasia S. Risperidone-induced edema. *Can J Psychiatry*. 2001;46(5):453–454.
- [5] Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther*. 1981;30(2):239–245.
- [6] Yang HN, Cheng YM. Peripheral edema associated with risperidone oral solution. *J Clin Psychopharmacol*. 2012;32(1):128–130.
- [7] Franco K, Tamburrino M, Campbell N, et al. Dopaminergic activity and idiopathic edema. *Hosp Community Psych*. 1991;42(3):309–310.
- [8] Knox ED, Stimmel GL. Clinical review of a long-acting, injectable formulation of risperidone. *Clin Ther*. 2004;26(12):1994–2002.
- [9] Akdag ST, Fettahoglu EC, Ozatalay E. Pedal edema induced by low-dose risperidone monotherapy in a child. *J Child Adolesc Psychopharmacol*. 2009;19(4):481–482.
- [10] Kaplan AP, Greaves MW. Angioedema. *J Am Acad Dermatol*. 2005;53(3):373–388.
- [11] Terao T, Kojima H, Eto A. Risperidone and allergic reaction. *J Clin Psychiatry*. 1998;59(2):82–83.
- [12] Feroz-Nainar C, Selvaraj P, Roy M. Risperidone induced oedema in a child with learning disability and autism. *Autism*. 2006;10(3):308–310.
- [13] Sanders RD, Lehrer DS. Edema associated with addition of risperidone to valproate treatment. *J Clin Psychiatry*. 1998;59(12):689–690.