

CASE REPORT

Medicine Science 2019;8(2):449-50

Management of obsessive compulsive disorder induced by the use of clozapine

Yunus Emre Donmez¹, Ozlem Ozcan², Fatma Kartal Sarioglu³, Sumeyra Gungoren⁴

¹Malatya Training and Research Hospital, Clinic of Child and Adolescent Psychiatry, Malatya, Turkey

²Inonu University, Faculty of Medicine, Department of Child and Adolescent Psychiatry, Malatya, Turkey

³Inonu University, Faculty of Medicine, Department of Psychiatry, Malatya, Turkey

⁴Harran University, Faculty of Medicine, Department of Child and Adolescent Psychiatry, Sanliurfa, Turkey

Received 17 July 2018; Accepted 19 September 2018

Available online 26.10.2018 with doi:10.5455/medscience.2018.07.8920

Copyright © 2019 by authors and Medicine Science Publishing Inc.

Abstract

The second generation antipsychotic of clozapine has superior efficacy compared to other antipsychotics especially for treatment-resistant schizophrenia. In up to 20% of patients receiving clozapine treatment, the side effect of obsessive compulsive symptoms or obsessive compulsive disorder occurs. These obsessive compulsive side effects sometimes cause cessation of the use of clozapine and sometimes causes difficulties in treating the psychotic symptoms due to dose reductions. This manuscript presents a case with resistant schizophrenia who developed obsessive compulsive disorder secondary to clozapine treatment and was successfully treated with clomipramine and aims to discuss the case accompanied by the literature.

Keywords: Atypical antipsychotics, clozapine, obsessive compulsive disorder, clomipramine, adolescent

Introduction

The second generation antipsychotic of clozapine has superior efficacy compared to other antipsychotics especially for treatment-resistant schizophrenia [1]. In up to 20% of patients receiving clozapine treatment, the side effect of obsessive compulsive symptoms (OCS) or obsessive compulsive disorder (OCD) occurs [2,3]. These obsessive compulsive side effects sometimes cause cessation of the use of clozapine and sometimes causes difficulties in treating the psychotic symptoms due to dose reductions. Additionally these obsessive compulsive side effects linked to clozapine may be interpreted as a worsening of the psychotic symptoms and clozapine dose may be increased and this results in a worsening of OCS/OCD. In the literature there are very few case reports about approaches to OCS/OCD linked to clozapine [4]. This manuscript presents a case with resistant schizophrenia who developed OCD secondary to clozapine treatment and was successfully treated with clomipramine and aims to discuss the case accompanied by the literature.

Case Report

The sixteen-year old male patient was monitored by our clinic for early-onset schizophrenia diagnosis. Psychiatric examinations of the patient observed that self-care had reduced, he had distrustful opinions, disorganized talk, grandiose and nihilistic delusions, visual and auditory hallucinations, and blunted affect. With no history of alcohol, drug or chronic medication use and with no chronic disease, the patient's family also had no history of psychiatric disease. The patient was examined by the neurology clinic for organic etiology and neurological pathology wasn't detected. The patient did not benefit from 4 mg/day risperdal treatment and treatment was discontinued because of the extrapyramidal system side effects. After the risperidon treatment the patient used haloperidol 10 mg / day, aripiprazole 20 mg / day and olanzapin 15 mg/day respectively. But the patient did not benefit from these treatments and some extrapyramidal side effects have been observed. As a result, in the fourth month the patient began clozapine treatment. Before the patient began clozapine treatment positive and negative syndrome scale (PANSS) scores were 53 for negative symptoms and 66 for positive symptoms. With periodic controlled dose increases, in two weeks the clozapine dose reached 225 mg. The patient responded positively to 225 mg/day clozapine dose and PANSS scores reduced to 25 for negative symptoms and 39 for positive symptoms. In the second

*Corresponding Author: Yunus Emre Donmez, Malatya Training and Research Hospital, Clinic of Child and Adolescent Psychiatry, Malatya, Turkey
E-mail: dryemredonmez@gmail.com

week of 225 mg/day clozapine treatment, the patient was observed cleaning and religious obsessions with hand washing and praying compulsions. As the patient had not responded to any other antipsychotics other than clozapine, treatment changes were not made and considering the benefit of 225 mg/day clozapine dose it was not reduced. The patient began clomipramine treatment of 75 mg/day for treatment of OCS. The patient's psychotic and obsessive-compulsive symptoms were monitored along with the possible hematologic side effects of clozapine and the possible cardiac side effects of clomipramine. Clomipramine dose was increased to 150 mg/day within two weeks. During six weeks of monitoring, the patient's psychotic symptoms were not observed to increase, with OCS largely reducing. With Children's Yale-Brown Obsessive-Compulsive Scale score of 27 before clomipramine treatment, scores reduced to 13 due to treatment. No side effects due to clomipramine were observed during the treatment of the patient. But depending on the use of clozapine, hypersalivation was observed. The patient's treatment successfully continues.

Discussion

In 25-64% of schizophrenia patients, OCS are observed and of these 8-26% abide by the criteria for clinically significant OCD [4]. A combinatorial meta-analysis and meta-regression study identified the OCD incidence with schizophrenia as 13.6% with OCS incidence of 30.3% [5]. Additionally only 1.7-14% of OCD patients have psychotic symptoms and 4-12% occur comorbidly with schizophrenia [4]. OCS are observed continuously during the progression of schizophrenic disorder, and may occur more clearly during chronic or late stage schizophrenia. The prevalence in first-attack patients is low, with rates of nearly 9% for OCS and 1.5% for OCD [6]. The low incidence of OCS and OCD in early schizophrenia is proposed to be linked to drug naivety or short-term treatment duration. Though comorbidities have not been clearly defined, epidemiologic findings lead to the consideration that antipsychotics used by schizophrenia patients contribute to the risk of OCS [4].

A study by Lin et al. about clozapine treatment of 102 schizophrenia patients reported the prevalence of OCS was 38.2%. Of patients 28.4% began to have OCS after clozapine treatment, with 5.9% developing OCD [7]. Ertugrul et al. in a study of 50 schizophrenia patients receiving clozapine treatment reported 20% of these patients had OCS after clozapine [8]. The OCS mechanism due to clozapine is not fully known. However, it is proposed that 5HT_{2A} receptor antagonism in key brain regions related to OCD including the anterior cingulate cortex, dorsal lateral prefrontal cortex and orbitofrontal cortex may cause OCS [9,10]. Additionally a variety of gene (SLC1A1, GRIN2B and GRIK2) polymorphisms have been proposed to cause clozapine-sourced OCS/OCD [11].

Strategies applied in clozapine induced OCS management at case reports may be listed as reducing the clozapine dose, use of serotonergic antidepressants and electroconvulsive therapy [4]. In some case reports, dose reductions facilitated by augmentation with valproic acid have also been shown to improve OCS outcomes [12,13]. In the literature there are two case reports encountered where clozapine-linked OCS was treated with clomipramine [14, 15]. However, these two cases were adult patients, with our case being the first adolescent case report in the literature treated with clomipramine for clozapine-linked OCS. There is only one case report of the treatment of clozapine-linked OCS in the adolescent age group in the literature, and sertraline was used for treatment

[16]. In the light of the case and literature data that we have shared, we are in the opinion that clozapine linked OCS/OCD can be treated by the use of clomipramine in adolescents and further studies regarding this matter are required.

Competing interests

The authors declare that they have no competing interest

Financial Disclosure

The financial support for this study was provided by the investigators themselves.

Yunus Emre Donmez ORCID:0000-0002-7785-2805

Ozlem Ozcan ORCID:0000-0003-3267-2648

Fatma Kartal Sarioglu ORCID:0000-0002-5379-0021

Sumeyra Gungoren ORCID:0000-0002-2806-807X

References

- Kane J, Singer MD, Meltzer MD. Clozapine for the treatment-resistant. Arch Gen Psychiatry. 1988;45:789-96.
- Bleakley S, Brown D, Taylor D. Does clozapine cause or worsen obsessive compulsive symptoms? An analysis and literature review. Ther Adv Psychopharmacol. 2011;1:181-8.
- Schirmbeck F, Zink M. Clozapine-induced obsessive-compulsive symptoms in schizophrenia: a critical review. Curr Neuropharmacol. 2012;10:88-95.
- Fonseka TM, Richter MA, Müller DJ. Second generation antipsychotic-induced obsessive-compulsive symptoms in schizophrenia: a review of the experimental literature. Curr Psychiatry Rep. 2014;16:510.
- Swets M, Dekker J, van Emmerik-van Oortmerssen K, et al. The obsessive compulsive spectrum in schizophrenia, a meta-analysis and meta-regression exploring prevalence rates. Schizophr Res. 2014;152:458-68.
- Sterk B, Lankreijer K, Linszen DH, et al. Obsessive-compulsive symptoms in first episode psychosis and in subjects at ultra high risk for developing psychosis; onset and relationship to psychotic symptoms. Aust N Z J Psychiatry. 2011;45:400-6.
- Lin SK, Su SF, Pan CH. Higher plasma drug concentration in clozapine-treated schizophrenic patients with side effects of obsessive/compulsive symptoms. Ther Drug Monit. 2006;28:303-7.
- Ertugrul A, Yagcioglu AEA, Eni N, et al. Obsessive-compulsive symptoms in clozapine-treated schizophrenic patients. Psychiatry Clin Neurosci. 2005;59:219-22.
- Milad MR, Rauch SL. Obsessive-compulsive disorder: beyond segregated cortico-striatal pathways. Trends Cogn Sci. 2012;16:43-51.
- Menzies L, Chamberlain SR, Laird AR, et al. Integrating evidence from neuroimaging and neuropsychological studies of obsessive-compulsive disorder: the orbitofronto-striatal model revisited. Neurosci Biobehav Rev. 2008;32:525-49.
- Cai J, Zhang W, Yi Z, et al. Influence of polymorphisms in genes SLC1A1, GRIN2B, and GRIK2 on clozapine induced obsessive compulsive symptoms. Psychopharmacology. 2013;230:49-55.
- Zink M, Englisch S, Knopf U, Kuwilsky A, Dressing H. Augmentation of clozapine with valproic acid for clozapine-induced obsessive-compulsive symptoms. Pharmacopsychiatry. 2007;40:202-3.
- Canan F, Aydinoglu U, Sinani G. Valproic acid augmentation in clozapine-associated hand-washing compulsion. Psychiatry Clin Neurosci. 2012;66:463-4.
- Biondi M, Fedele L, Arcangeli T, et al. Development of obsessive-compulsive symptoms during clozapine treatment in schizophrenia and its positive response to clomipramine. Psychother Psychosom. 1999;68:111-2.
- Leung JG, Palmer BA. Psychosis or Obsessions? Clozapine Associated with Worsening Obsessive-Compulsive Symptoms. Case Rep Psychiatry. 2016.
- Coskun M, Zoroglu S. Clozapine induced obsessions treated with sertraline in an adolescent with schizophrenia. Klinik Psikofarmakol Bulteni. 2009;19:155-8.