

Case report / Olgu sunumu**A hypothermia case with early onset schizophrenia treated with clozapine****Gonca ÖZYURT,¹ Neslihan İNAL EMİROĞLU,² Burak BAYKARA²****ABSTRACT**

The usage of antipsychotics in children and adolescents increase in the general of the world and it was reported that 90% of these antipsychotics were atypical antipsychotic by researchers. Clozapine is considered to be the prototype of the atypical antipsychotics, as it was the first to be recognized as having less extrapyramidal side effects, not causing tardive dyskinesia, and not elevating prolactin. Clozapine is not a first choice antipsychotic but it can be used when other antipsychotics cannot be effective. Atypical antipsychotics, also clozapine, alter ability of body to regulate response to changes in temperature and humidity, patients may become hypothermic or hyperthermic; more likely in temperature changes due to inhibition of the hypothalamic control area. Transient temperature alteration can occur with clozapine in up to 50% of patients, usually within the first three weeks of treatment. In this article we present a 17 years old male adolescent with early onset schizophrenia. Although three different atypical antipsychotics were used and there was no treatment response in that case. After clozapine was administered, transient thermoregulation alteration was seen at the beginning of the treatment. (*Anatolian Journal of Psychiatry* 2015; 16(5):375-377)

Key words: Early onset schizophrenia, hypothermia, clozapine

Klozapinle tedavi edilen erken başlangıçlı şizofrenili bir hipotermi olgusu**ÖZET**

Çocuk ve ergen yaş grubunda antipsikotik ilaç kullanımı dünya genelinde artmaktadır. Araştırmacılarca antipsikotik ilaç kullanımının %90'ının ikinci kuşak antipsikotik ilaçlar olduğu bildirilmiştir. Klozapin atipik antipsikotiklerin prototipi olarak kabul edilmektedir, ilk az ekstrapiramidal yan etkili, geç diskineziye yol açmayan, prolaktini yükseltmeyen antipsikotik olarak tanınmıştır. Klozapin ilk seçenek olarak değil de, diğer antipsikotiklerin etkin olmadığı durumlarda kullanılan bir antipsikotiktir. Atipik antipsikotikler beden sıcaklığı ve nemdeki değişikliklere göre kendini düzenlemesini etkilerler, hastalar muhtemelen hipotalamik kontrol alanındaki inhibisyona bağlı olarak gelişen sıcaklık değişiklikleri ile hipotermik veya hipertermik duruma gelebilirler. Geçici sıcaklık değişiklikleri klozapin ile hastaların %50'sinde genellikle tedavinin ilk üç haftasında görülebilir. Bu sunumda üç farklı antipsikotik kullanmasına rağmen yeterli cevap alınamayan, klozapin kullanımına geçildikten sonra tedavinin başlangıcında geçici termoregülasyon değişiklikleri görülen 17 yaşında erken başlangıçlı şizofreni bir erkek ergen olgu sunulmuştur. (*Anadolu Psikiyatri Derg* 2015; 16(5):375-377)

Anahtar sözcükler: Erken başlangıçlı şizofreni, hipotermi, klozapin

INTRODUCTION

The usage of antipsychotics in children and adolescents increase in the general of the world¹. Clinical data about increasing of diagnosis of bipolar disorder and schizophrenia in childhood, extrapyramidal side effects, including tardive dyskinesia, of first-generation antipsychotics,

positive contributions of second-generation antipsychotic drugs on the attention, memory, and cognitive systems cause increasing of atypical antipsychotic usage.²⁻³

Clozapine is considered to be the prototype of the atypical antipsychotics, as it was the first to be recognized as having less extrapyramidal

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side effects, not causing tardive dyskinesia, and not elevating prolactin. Clozapine was defined as 'gold standard treatment' especially in treatment resistance schizophrenia. Clozapine also has the only risk of a life threatening and occasionally fatal complication called as agranulocytosis. Clozapine can cause an increased risk of seizures, high sedation and weight gain, it has the most cardiometabolic risks among the antipsychotics. Clozapine is not a first choice antipsychotic but it can be used when other antipsychotics cannot be effective for that reasons. It's biochemical mechanism of action that accounts for its special efficacy as well as its side effects have been still investigated by researchers.⁴ Atypical antipsychotics alter ability of body to regulate response to changes in temperature and humidity, patients may become hypothermic or hyperthermic; more likely in temperature changes due to inhibition of the hypothalamic control area. Transient temperature alteration can occur with clozapine in up to 50% of patients, usually within the first three weeks of treatment.⁵

CASE

Seventeen years old male adolescent applied to Dokuz Eylül Medical School Child and Adolescent Psychiatry Outpatient Unit with the symptoms arguing with his grandmother and father, not eating anything, fear of poisoning, thoughts about being damaged by someone He had had these symptoms for three months. In psychiatric examination he was conscious, cooperative, orientation of time, location and people were full, mood and affect were depressive and anxious, attention decreased, judgment, abstract thinking, and assessing the fact were damaged, he was explaining auditory hallucinations in perception. In the content of his thought he had persecution and reference delusions. The risperidone treatment (4 mg/day) was initiated and his symptoms were reduced in two months. After that he went to her mother's house for summer holiday and stopped to use his antipsychotics. His psychotic symptoms recurred two months after he stopped the drug. Risperidone was initiated again and its dose was increased to 6 mg per day but his symptoms became resistant so he was hospitalized to inpatient unit, biperidene 4 mg and diazepam 5 mg was initiated for his rigidity and akathisia symptoms. Cross titration amisulpride to risperidone was made because he had not had adequate response to risperidone. His prolactin level was 90 ng/mL and he had galactore while he was taking 400 mg

Anatolian Journal of Psychiatry 2015; 16:375-377

amisulpride per day so amisulpride dose was decreased and aripiprazole was initiated. In the eighth week of his hospitalization he was taking 200 mg amisulpride and 30 mg aripiprazole but he had not had adequate response so treatment resistant schizophrenia was thought and clozapine treatment was planned. Amisulprid was stopped with 50 mg/day decreasing once in three days. Biperidene 4 mg/day and diazepam 5 mg/day treatment was continued, rigidity was seen during that time. Aripiprazole 30 mg/day treatment was continued. Clozapine 12.5 mg/day was started and per clozapine dose was increased 12.5 mg every day. On the day when he took 75 mg clozapine his body temperature increased to 39.3°C and after 8 hours decreased to 33.3°C. He only took 500 mg paracetamol in the beginning of fever. In pediatric consultation they thought central fever and hypothermia due to clozapine and they suggested to use if we did not have any other option. He did not take clozapine twice and then he continued to take clozapine with the dose of 25 mg/day after pediatric consultation. Clozapine dose was increased to 300 mg/day and his psychotic symptoms reduced and then he was discharged.

DISCUSSION

In this article we present a 17 years old male adolescent with early onset schizophrenia. Although he used three different atypical antipsychotics and there was no treatment response. After clozapine was administered, transient thermoregulation alteration was seen at the beginning of the treatment.

Clozapine is suitable in the treatment of schizophrenia in children and adolescents, especially in treatment resistant schizophrenia. However, rarely, it can cause thermoregulation problems. Clozapine can cause hypothermia as if it can cause hyperthermia which may reach to neuroleptic malignant syndrome.⁶ Hypothermia, is the decreasing of body temperature to 35°C below it is a serious life-threatening dysfunction that can be associated with the usage of antipsychotic drugs. Both typical and atypical antipsychotics can decrease body temperature associated with central thermoregulatory mechanisms. There are both clinical and experimental data about hypothermic effects of clozapine.⁷ Due to experimental studies of clozapine, hypothermia related with clozapine can be associated with dopaminergic effects of clozapine. Hypothermia effect completely disappears as a response for selective D1 receptor antagonist.⁸ Due to Millan's

study especially D3 receptor induces hypothermia in rats and clozapine has high affinity to D2 and D3 receptors in rats and human beings.⁹ Clozapine is D2 and D3 receptor antagonist, so in our case clozapine may have influenced thermoregulation by binding D2 and D3 receptors in hypothalamus. Recent studies have revealed some risk factors in hypothermia which is caused by the usage of antipsychotic. These risk factors are usage of antipsychotics due to schizophrenia, endocrine problems such as hypothyroidism, epilepsy, organic brain damage such as mental retardation, medical illnesses, additional medications such as benzodiazepines

and β -blockers, beginning days of atypical antipsychotic treatment.¹⁰ In our case, usage of benzodiazepines, combination with the clozapine may cause the hypothermia. Hypothermia was revealed at the beginning of the treatment and disappeared after taper the dosage and never happened again, this was a useful experience for the decision of the maintenance of the clozapine treatment. Clinicians should not discontinued the clozapine treatment urgently when they meet the hypothermia, especially in treatment of the adolescents with treatment resistance schizophrenia.

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