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**Dadić-Hero, Elizabeta; Ružić, Klementina; Grahovac Juretić, Tanja; Hero, Lucija**

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## Priapism – a possible side-effect of olanzapine

### *Prijapizam – moguća nuspojava olanzapina*

Elizabeta Dadić-Hero, Klementina Ružić, Tanja Grahovac Juretić, Lucija Hero\*

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#### Summary

The evaluation of the effects of antipsychotics on sexual function in patients with schizophrenia is complex because it is difficult to discern whether a particular dysfunction is a consequence of the disease itself or it is a side effect of a particular medication. One of such dysfunctions is priapism. We will present a case of a patient who has been in treatment for schizophrenia for the last 26 years. As extrapyramidal side effects have occurred over the past two years, the first generation antipsychotics were replaced with olanzapine. At the same time the patient was involved in a multidisciplinary psychosocial treatment program consisting of psychoeducation, social skills training and therapeutic community. After three months of group treatment, he mentioned painful penile erection. Olanzapine was reduced and risperidone introduced by gradual titration (4 mg daily). Four weeks after having administered risperidone, the painful erection subsided completely. This case illustrated the importance of psychosocial interventions, especially psychoeducation, in timely recognition and reporting all symptoms/side effects. Also, in cases of possible antipsychotic-induced priapism, a medication with less alpha-1 antagonism should be considered and used at the lowest effective dose.

**Key words:** schizophrenia, antipsychotics, olanzapine, painful erection (priapism)

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#### Sažetak

Procjena učinaka antipsihotika na spolnu funkciju bolesnika sa shizofrenijom je složena, pogotovo stoga jer je teško razlučiti je li određena disfunkcija posljedica same bolesti ili je nuspojava određenoga lijeka. Jedna od takvih disfunkcija je priapizam. Predstaviti ćemo slučaj bolesnika koji se posljednjih 26 godina liječi od shizofrenije. Kako su se tijekom posljednje dvije godine pojavile ekstrapiramidalne nuspojave, prva generacija antipsihotika zamijenjena je olanzapinom. Istodobno je bolesnik bio uključen u multidisciplinarni psihosocijalni program koji se sastojao od psihoeukacije, treninga socijalnih vještina i terapijske zajednice. Nakon tri mjeseca grupnog tretmana spomenuo je problem s bolnom erekcijom penisa. Olanzapin je smanjen, a risperidon uveden postupnom titracijom (4 mg dnevno). Četiri tjedna nakon uvođenja risperidona, bolna erekcija se potpuno povukla. Ovaj slučaj ilustrirao je važnost psihosocijalnih intervencija, posebno psihoeukacije, u pravodobnom prepoznavanju i prijavljivanju svih simptoma/nuspojave. Također, u slučajevima mogućeg priapizma izazvanog antipsihotikom, potrebno je razmotriti uvođenje lijeka s nižim antagonizmom za alfa-1 receptore i koristiti ga u najmanjoj učinkovitoj dozi.

**Ključne riječi:** shizofrenija, antipsihotici, olanzapin, bolna erekcija (prijapizam)

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\* **The University of Rijeka, Faculty of Medicine** (Assoc. prof. Elizabeta Dadić-Hero, MD, PhD; Assoc. prof. Klementina Ružić, MD, PhD; Assoc. prof. Tanja Grahovac Juretić, MD, PhD); **Clinical Hospital Centre Rijeka, Psychiatry Clinic** (Assoc. prof. Klementina Ružić, MD, PhD, Assoc. prof. Tanja Grahovac Juretić, MD, PhD); **The Josip Juraj Strossmayer University of Osijek, Faculty of dental medicine and health** (Lucija Hero)

Correspondence address / Adresa za dopisivanje: Tanja Grahovac Juretić, KBC Rijeka, Klinika za psihijatriju, Krešimirova 42, 51 000 Rijeka, Tel. 051-658-333. E-mail: tanjagj1@gmail.com

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## Introduction

Schizophrenia is a mental illness that can occur as early as adolescence or in young adulthood. The illness is characterised by distinctive psychopathology. Patients with schizophrenia are oriented towards their inner world where delusional events prevail, thus making them apathetic towards the reality they tend to isolate themselves from. Clinical manifestations of the illness, as well as its types can vary. However, in a psychopathological sense, their common features are thought and affective disorder and failure to function adequately. Human sexual function is complex and affected in many different ways by schizophrenia and the antipsychotic drugs used in its treatment. Sexual dysfunction is a common problem in people with schizophrenia, especially in men, with reported prevalence rates of 16.8% to 70%.<sup>1</sup> The evaluation of the effects of antipsychotics on sexual function in patients with schizophrenia is also complex because the deleterious effects of conventional antipsychotics are superimposed on the effects of the disease itself.<sup>2</sup> Priapism is defined as a persistent, often painful penile erection not associated with sexual stimulation. Although relatively uncommon, priapism represents a urologic emergency because without prompt recognition and treatment it can result in urinary retention, cavernosa fibrosis, impotence, or even gangrene.<sup>3</sup> Priapism as a medication side effect accounts for 25%-40% of all cases, with the most commonly associated categories of drugs being antipsychotics and antihypertensives.<sup>4</sup> Atypical antipsychotics, also known as second-generation antipsychotics, owing to their favourable side effect profile, are the first line of treatment for schizophrenia. Second generation antipsychotics have their advantages in comparison to typical antipsychotics, but can also cause serious side effects including priapism.<sup>5</sup> Priapism is a rarely reported, underappreciated side effect which has been documented with nearly all the atypical antipsychotic medications including olanzapine.<sup>6,7</sup> The mechanism of priapism associated with antipsychotics agents is thought to be related to alpha-adrenergic blocking properties. Detumescence is sympathetically mediated, and alpha1-adrenergic antagonism (within the corpora cavernosa) inhibits detumescence. The propensity of individual antipsychotics to induce priapism can presumably be estimated on the basis of alpha1-adrenergic blockade affinities.<sup>6</sup>

## Case report

A 54-year-old male patient has been receiving psychiatric treatment for 26 years. Mental illness was diagnosed in an outpatient clinic and confirmed while hospitalized at the age of 28. Having finished college, the patient has never been employed, lives with his parents, and his emotional relationships have been rare and short-lived.

Following the last hospitalization 11 years ago, the patient regularly attended ambulatory psychiatric treatment and took his medications regularly. Over the past 4-5 years, the patient's preoccupation with emotional (i.e. sexual) relationships which he couldn't realize became apparent, and at times he expressed eroticised feelings. After 25 years of therapy with typical antipsychotics, tremor and akathisia were noticed as side effects of having been treated for years with fluphenazine 5 mg, biperiden 2 mg and clozapine 75 mg daily. The patient agreed the aforementioned psychopharmaca to be completely discontinued and for olanzapine to be introduced, with the dosage titrated to 7.5 mg, as well as diazepam 10 mg daily. Eventually, stable remission was established. Seven years later, alcohol abuse was noticed, which caused the patient to be uncritical and lacking adequate insight. Over the course of three months, the patient was motivated into a group treatment, which he joined in. The psychosocial program consisted of 3 components: 1) a psycho-education group led by a psychiatrist; 2) social skills training group lead by a trained nurse and a social worker and 3) therapeutic community where all members of the therapeutic team participated together. The weekly schedule consisted of one psychoeducational session, one social skills training and one session of the therapeutic community. Psychoeducation consisted of providing structured information on the illness and treatment, specifically about a) symptoms – how to recognise them, how to cope and what to do in case of deterioration; b) medication – information about pharmacotherapy, possible side effects and the importance of adherence; and c) how to improve general social functioning. Three months later, encouraged by the group, the patient mentioned painful penile erection, which he used as an excuse for his alcohol abuse. Olanzapine was gradually reduced in therapy and risperidone introduced by gradual titration (4 mg daily), taking into consideration the fact that risperidone can also have sexual side effects. Four weeks after having administered risperidone, the painful erection subsided completely.

## Discussion

People with schizophrenia often experience some kind of sexual dysfunction, however, due to the complex nature of the disease and the wide range of side effects of antipsychotics making it difficult to determine their aetiology. In the described case, remission was maintained with olanzapine, but painful penile erection occurred, which gave no indication whether it was a side effect caused by olanzapine or psychopathology. Olanzapine was gradually replaced with risperidone and within four weeks the painful erection subsided completely. Many medications have been associated with priapism, which is thought to be related to alpha-adrenergic blockade. Detumescence is sympathetically mediated, and alpha-adrenergic antagonism (within the corpora cavernosa) inhibits detumescence. Olanzapine has a pharmacological profile similar to that of clozapine, with a high affinity for dopamine D1, D2, and D4, serotonin (5-HT) 5-HT<sub>2A</sub>, 5-HT<sub>2C</sub>, and 5-HT<sub>3</sub>, muscarinic, alpha<sub>1</sub>-adrenergic, and histamine H<sub>1</sub> receptors. On the other hand, studies also suggest that risperidone and ziprasidone have the highest antagonism at alpha-1, and olanzapine has the lowest.<sup>8</sup> Risk factors for the development of priapism include recent dose changes, recent medication changes, reinitiation of medication after periods of noncompliance, concomitant substance use, and/or the use of other medications which also cause priapism.<sup>6</sup> Patients tend to find it difficult to speak about the sexual side effects, as was the case with our patient who took three months, along with alcohol abuse, to gain courage and verbalize the problem. Furthermore, the long-term patients in stable remission are perhaps not given adequate attention when it comes to all life segments and life quality, especially the quality of sexual life. This case illustrated the importance of psychosocial interventions as a complementary approach to the pharmacological treatment of schizophrenia. Proper patient education on side effects, as well as obtaining complete historical information on side effects from other medications, can help prevent recurrence. Also, group psychotherapy can encourage patients to talk about their sex life and sex related side effects in order to prevent serious consequences. From the pharmacological side,

a medication with less alpha-1 antagonism should be considered and used at the lowest effective dose.<sup>9</sup>

## Conclusion

Patients with schizophrenia can experience side effects which are easily observed and diagnosed. Some side effects, such as priapism, can be difficult to tell apart from psychopathology at times, as was the case with this patient. The choice of the antipsychotic was a risky one, especially given the well-known sexual side effects of risperidone. In this case, however, risperidone proved to be a good choice, as the painful penile erection disappeared.

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