

Risperidone and nocturnal enuresis as a rare side effect

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Özet

Risperidon ve nadir bir yan etki olarak enürezis nokturna

Çocuk ve gençlerde risperidon psikotik bozukluk, yaygın gelişimsel bozukluklar, davranım bozukluğu ve mental retardasyona eşlik eden davranış sorunları gibi birçok psikiyatrik bozukluğun tedavisinde etkin olabilecek bir ajan olarak belirtilmektedir. İştah artışı, kilo alımı ve sedasyon sık görülen yan etkiler olmasına rağmen risperidona bağlı gelişen enürezis nadir görülen bir yan etkidir. Risperidona bağlı enürezis nokturna gelişen bir olgu sunulup bulgularımız literatür bilgileri eşliğinde tartışılmıştır.

Anahtar kelimeler: Risperidon, enürezis nokturna, yan etki

Abstract

For children and adolescents, risperidone is proposed to be an effective agent for treating many psychiatric disorders such as psychotic disorders, pervasive developmental disorders, conduct disorder and behavioral problems accompanying mental retardation. Excessive appetite, weight gain, and sedation are among the most common adverse effects; on the other hand risperidone-induced enuresis is rarely reported. A case with risperidone-induced enuresis will be presented and the results will be discussed using a number of relevant case studies from the literature.

Key words: Risperidone, nocturnal enuresis, side effect

Introduction

Risperidone is an atypical antipsychotic agent with blockage effects on dopamine² and serotonin² (1). Due to the reduced risk of tardive dyskinesia and extrapyramidal symptoms, risperidone has started to replace the more traditional antipsychotic agents (2). Risperidone appears to be adequately tolerated and effective in reducing aggression and symptoms associated with disruptive behavioral disorders, in children with sub average IQ (3, 4). Excessive appetite, weight gain, and sedation are among the most reported adverse effects (5). The incidence of risperidone-induced enuresis is lower than 1% (6). Nocturnal enuresis is a rare adverse effect that reduces adherence to medication (2, 7). The study by Vokas et al. on 68 adults with schizophrenia revealed that 28% of the patients developed nocturnal enuresis after the initiation of risperidone treatment, whereas only 13% had such symptoms prior to risperidone (8).

Enuresis has been frequently reported in the literature in the use of risperidone in combination with selective serotonin reuptake-inhibitors (SSRI) or mood stabilizers in children (6, 9). Took suggests that the combined use of risperidone and SSRIs may increase the risk of nocturnal enuresis (2). There are a number of case reports in the literature about risperidone-induced enuresis in children (5, 6).

A case diagnosed with mental retardation, according to DSM-IV diagnostic criteria, who had risperidone-induced enuresis will be discussed in this report (10).

Case

A nine year-old girl was referred to child psychiatry clinic with hyperactivity, running away, anger outbursts, and aggressive behavior to her family and others. After the psychiatric and psychometric evaluations mental retardation was diagnosed. Due to hyperactivity and aggressive behavior, risperidone was initiated at 0.5 mg/day (morning dose) and increased to 1 mg/day (morning and evening dose) after a week. Immediately after the initiation of risperidone she began bed wetting. Her personal

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history revealed that she achieved urinary bladder control at 7 years of age, and since then she has had no urinary incontinence. Family history was negative for nocturnal enuresis. Urological and neurological evaluations were normal. Because of the nocturnal enuresis, risperidone's evening dose was changed to a midday dose without making any changes in the total dose. Behavioral interventions including limiting the intake of fluids in the evening, awakening of the patient to urinate by the parents, were initiated. A significant remission was observed after the arrangement of medication and behavioral therapy; the patient who was wetting the bed every night became wetting only three times a month. Because of the patient's excessive weight gain, risperidone was stopped and quetiapine initiated. No nocturnal enuresis was observed during the three month period of quetiapine treatment.

Discussion

The developing of nocturnal enuresis after starting risperidone, dramatic response to drug discontinuation and the absence of any other drug used by the case and the absence of an identifiable medical cause are suggestive of the causal effect of risperidone to enuresis.

While the pathophysiology of antipsychotic-induced enuresis remains unclear, a number of mechanisms have been proposed (5):

1. decreased tone of the internal bladder sphincter due to α 1-adrenergic blockage (5);
2. reduced dopamine transmission in the basal ganglia (5);
3. urinary retention and subsequent overflow incontinence due to antimuscarinic properties (5);
4. blockage of pudendal reflexes via antagonism of 5-HT₂ or 5-HT₃ (11).

Risperidone displays low affinity for the muscarinic receptors and due to its strong peripheral α -1 adrenergic, central dopaminergic and norepinephrinergic blockage effects; it may be the cause of enuresis (5, 7).

The sedative effects of antipsychotics may lead to inability to wake up during sleep and might cause enuresis (12). In our case, improvement of nocturnal enuresis complaint, after giving the evening dose at midday and the behavioral treatment including parents awakening the patient to urinate every night might be the indications of sedative effects of risperidone and might suggest that it plays an effective role in developing of enuresis.

Regarding the management of enuresis associated with antipsychotics, several interventions including behavioral modifications like reduction of fluid intake during evenings, awakening the patient to urinate, prescription of the minimal effective dose of the antipsychotic agent, cessation of the drug, and treatments with anticholinergic agents like oxybutynin, and trihexyphenidyl, α -adrenergic agonists like ephedrine, and/or desmopressin have been suggested (5,13).

In Took's case report (2), 5 cases were presented, 10 to 14 years of age, which had experienced enuresis after using risperidone combined with SSRIs. In one of the patients, enuresis lasted only two weeks, resolving spontaneously. In two of the patients discontinuation of the risperidone, resulted with a rapid resolution of the enuresis. One of these two resumed risperidone treatment after a two-month break, and the incontinence did not return. In the other two patients, behavioral interventions including reduction of fluids in the evening, parents awakening the patient to urinate were initiated and these were successful in only one of the two patients. Desmopressin was initiated for the other one and this resulted in an immediate cessation of the enuresis (2). In Herguner's two autistic cases, behavioral modification, lowering the dosage of the medication, and cessation of the drug did not seem to be effective approaches because of the fact that the cases had severe behavioral problems and communicational difficulties (5). In the case report of Kantrowitz et al., enuresis ceased after stopping only the nighttime dose of risperidone (11).

In our case, enuresis did not resolve spontaneously, and lasted for two months. Moreover, because of the severe behavioral problems, lowering the dosage of the medication did not seem to be effective option, and was not used. Instead, the evening dose was switched to a midday dose. Finally, a significant improvement was observed.

Changing risperidone with a less potent peripheral α -1 adrenergic antipsychotic (ex. quetiapine, olanzapine) may be a possible management strategy for risperidone-induced enuresis (5, 6, and 11). In our case, because of a different adverse effect, excessive weight gain, risperidone was changed to quetiapine and nocturnal enuresis ceased. Antipsychotic-induced enuresis is an embarrassing and distressing adverse effect that may lead to severe compliance problems. If care is not given, it is an adverse effect that may be overlooked. Since early

identification together with early prevention may increase medication adherence, this side effect must be inquired. Furthermore, due to the fact that it may be permanent, the family should be informed about the potential side effects.

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