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CASE REPORT Open Access

# Risperidone-associated enuresis—a case report

Ashish Sarangi*, Zachary Mkhantar and Preston Weaver

## Abstract

**Background:** Risperidone has been reported to be effective in treating both the positive and negative symptoms of schizophrenia, aggression, and behavioral disorders. While the metabolic side effect profile of this medication has been broadly studied, studies related to this medication's bladder effects are relatively rare. We present a case of risperidone-induced enuresis in an adult male with schizophrenia that resolved upon discontinuation of the offending medication.

**Case presentation:** We describe a case of a 32-year-old man with a primary psychotic disorder who developed debilitating enuresis secondary to taking risperidone. Enuresis resolved upon switching to Seroquel.

**Conclusion:** Enuresis secondary to risperidone is not commonly discussed prior to initiation by the treating psychiatrist however can be debilitating. Discussing this potential side effect is critical to informed decision making on the patient's part.

**Keywords:** Risperidone, Enuresis, Case report

## Background

Risperidone is the most commonly prescribed antipsychotic worldwide due to its broad clinical applications [1]. While generally well tolerated, risperidone can cause hyperglycemia, weight gain, dyslipidemia, metabolic syndrome, impaired concentration and recall, and hyperprolactinemia, well-documented side effects in the literature that are considered strongly prior to prescribing risperidone [2]. One study found that the incidence rate of NE in patients taking atypical antipsychotics was 20% for clozapine, 9.6% for olanzapine, 6.7% for quetiapine, and 6.2% for risperidone [3] (see Table 1). It is plausible that individuals who experience risperidone-induced enuresis will have similar effects with other antipsychotics therefore increasing the overall risk of non-compliance with their medications and increasing the likelihood of symptom relapse with a decline in quality of life. Several pharmacologic interventions for risperidone-induced enuresis such as anticholinergics, alpha-1 agonists, and desmopressin have been tried and varied in their success [4]. For risperidone-induced enuresis specifically, reboxetine, a selective noradrenaline reuptake inhibitor antidepressant, has been successful in resolving symptoms of enuresis, suggesting a central noradrenergic cause of risperidone-induced enuresis [5]. Desmopressin, as well, has improved enuresis in patients taking risperidone [6]. Various genetic polymorphisms in dopaminergic transmission and in proteins involved in crosstalk with serotonergic receptors have shown to be important in risk of developing schizophrenia and responsiveness to antipsychotics [7]. Likewise, these polymorphisms could explain the varied rates of adverse effects seen from atypical antipsychotic treatment. Below, we present a case of risperidone-induced enuresis in a 32-year-old male with schizoaffective disorder with symptom resolution upon discontinuation of the medication.

## Case presentation

Mr. CH is a 32-year-old man with a 10-year history of schizoaffective disorder, depressive type, who presented to our clinic in 2019 after a failed suicide attempt. He

* Correspondence: aks_sarangi@hotmail.com
Texas Tech University Health Sciences Center, Lubbock, TX, USA

**Table 1** Incidence of enuresis in varying antipsychotics

| Medication | Clozapine | Olanzapine | Quetiapine | Risperidone |
|---|---|---|---|---|
| Rate of nocturnal enuresis | 20% | 9.6% | 6.7% | 6.2% |

denied any past medical history, including primary enuresis. He endorsed auditory hallucinations, which he described as "static" with intermittent command auditory hallucinations telling him to end his life, as well as visual hallucinations consisting of "shadows". His hallucinations caused marked anxiety and impairment at work, forcing him to lose his job. His auditory hallucinations were moderately controlled with perphenazine 8 mg qhs and his depressive symptoms well-controlled with citalopram 40 mg qd. Despite treatment with benztropine 0.5 mg bid, he was still experiencing forced blinking and perioral movements, prompting discontinuation of the medication due to anticholinergic burden. These symptoms remained stable despite discontinuation of benztropine. He had no history of excessive water intake, diabetes, or other chronic medical conditions. The patient was not taking any other medications that could plausibly cause his urological symptoms.

After being relatively stable since August 2018, he experienced a decompensation in his hallucinations and depressive symptoms in July of 2020 without an identifiable trigger. He was agreeable to an increase in his perphenazine to 12 mg qhs, but due to lack of insurance coverage, the decision was made to cross-taper to risperidone. His dosage of perphenazine was decreased to 4 mg qhs for 1 week, after which perphenazine was discontinued and risperidone 1 mg bid was initiated. The patient experienced enuresis daily since risperidone was started until the day, he stopped taking it. The patient noted that his enuresis was very distressing. He was immediately switched to Seroquel 50 mg bid, which subsequently resolved his enuresis. Within a few days of starting Seroquel, he reported diminished frequency and intensity of his auditory hallucinations.

## Discussion

Mr. CH had no history of childhood or adult-onset enuresis prior to his treatment with risperidone. His enuresis presented rather acutely but rapidly resolved upon switching to quetiapine. There was no evidence of diuretic consumption during this time and no past history of polyuria secondary to diabetes mellitus.

Secondary enuresis is a relatively rare side-effect that is seen among different classes of psychiatric medications. SSRIs alone, as well as SSRIs when used in conjunct with risperidone, have been shown to cause enuresis in both adolescent and young adult patients with a variety of psychiatric conditions. Enuresis resolved upon discontinuation of the drug or switch to a different agent within the same pharmacological class [8, 9]. Possible mechanisms of action include serotonin reuptake inhibition causing potentiation of cholinergic neurotransmission in human detrusor muscle [10], central action, or possible peripheral action on modulation of voltage-dependent calcium channels in smooth muscle [8]. Despite these cases, in 2000, enuresis was reported to be the 6th most common reason for prescribing SSRIs to children [11]. A 61-year-old man and a 42-year-old man both developed diurnal enuresis after addition of bupropion HCL SR and XL, respectively, to their medication regimen for depression. In both patients, urinary symptoms resolved after discontinuation of bupropion [12, 13].

After review of the literature, it appears that pharmacological treatment of psychiatric medication-induced enuresis has rarely been attempted except in the context of patients with psychiatric conditions well-controlled with atypical antipsychotics. Trihexyphenidyl, an M1 antagonist, has been effective in treatment of both clozapine-induced enuresis and sialorrhea [14]. Aripiprazole has been used to treat clozapine-induced enuresis, possibly due to D2 agonist activity in the clozapine-induced hypodopaminergic state within the basal ganglia [15]. TCAs have established antienuretic properties and have been effective in resolving SSRI and clozapine-induced enuresis [16]. Methylphenidate was shown to cause enuresis in two adolescent boys, one with ADHD, the other with ADHD with comorbid methylphenidate-induced anxiety. In the patient with only ADHD, discontinuation of MPH and initiation of atomoxetine resolved his enuresis. In the patient with ADHD and comorbid anxiety and enuresis, addition of milnacipran improved both methylphenidate response in the patient, while improving his anxiety and completely resolving his enuresis [17].

Different mechanisms have been proposed for how certain atypical antipsychotics can cause enuresis. It is possible that the anticholinergic properties of atypical antipsychotics cause decreased detrusor function, leading to increased post-void residuals and overflow incontinence [18]. Risperidone specifically has had Ki values reported as high as 10,000 nM, indicating that there is no significant interaction between risperidone and muscarinic receptors. It is possible that serotonergic blockade could cause nocturnal enuresis, as clozapine, risperidone, and olanzapine all have relatively high affinity for the 5-$HT_{2a}$ receptor [19]. Functional studies have shown that serotonergic antagonists stimulate parasympathetic activity and suppress sympathetic and somatic

activity, which could lead to increased detrusor function and decreased internal urethral sphincter tone [10, 20, 21].

For risperidone specifically, alpha-1-adrenergic blockade has been implicated as a possible mechanism of pathologic enuresis [22]. However, many of the therapeutic benefits of risperidone are due to its conversion to its active moiety 9-hydroxyrisperidone. 9-hydroxyrisperidone can be administered directly through the newer atypical antipsychotic paliperidone. Paliperidone has been shown to exhibit weak affinity for alpha-1 and alpha-2 adrenergic receptors when compared to risperidone in vivo [19, 23]. It is possible that the reason only a certain subset of patients experiences enuresis when given risperidone is because of differences in metabolism of risperidone to its active moiety. Risperidone is converted to its active moiety by *CYP2D6* and to a lesser extent by *CYP3A4*. Poor metabolizers of risperidone are known to have two inactive copies of the *CYP2D6* gene, causing accumulation of risperidone instead of its active moiety. While these patients have been shown to have larger decreases in symptoms of schizophrenia, they are also more likely to experience extrapyramidal symptoms and likely enuresis [24]. Thus, it is possible that patients who saw large improvement in their psychotic symptoms on risperidone that were forced to switch medications due to enuresis lacked functional *CYP2D6* enzymes, leading to a larger than normal blockade of alpha-1-adrenergic receptors. It seems likely that 9-hydroxyrisperidone may lead to less enuresis.

However, risperidone has also been shown to treat urinary incontinence [25], giving strength to the idea that atypical antipsychotic-induced pathologic enuresis has a multifactorial cause.

## Conclusion

The exact relationship between antipsychotics and nocturnal enuresis is not completely understood. No single treatment has been shown to be the most effective for treatment of enuresis caused by atypical antipsychotics. Some patients experience remission of symptoms simply by discontinuing the medication. However, others risk loss of symptom control when switching to another antipsychotic medication, requiring additional pharmaceutical treatment for their enuresis. Enuresis decreases the quality of life for patients and negatively impacts treatment compliance Therefore, it is important for physicians to be aware of the risk of enuresis in patients taking atypical antipsychotics and to be prepared to consider alternative causes of enuresis outside of their prescribed psychiatric treatment plan. The risk of enuresis should be fully discussed prior to initiating treatment with this medication.

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### Authors' contributions

AS developed the idea and provided case information and edited draft versions. PW wrote major sections of the manuscript and worked on table. ZM wrote the "Discussion" section of the manuscript. The authors read and approved the final manuscript.

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## Declarations

### Ethics approval and consent to participate

Not applicable

### Consent for publication

All patients included in this research gave written informed consent to publish the data contained within this study. If the patient was less than 16 years old, deceased, or unconscious when consent for publication was requested, written informed consent for the publication of this data was given by their parent or legal guardian.

### Competing interests

The authors declare that they have no competing interest.

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## Publisher's Note