

Urinary Retention After Haloperidol Decanoate and Fluoxetine Combination Reversed After Discontinuation of Fluoxetine

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ABSTRACT

Introduction: Urinary retention is a side effect not commonly observed during the use of psychotropics, although it has been reported that 2% of acute urinary retention episodes are induced by drugs, including some psychotropic agents as antidepressants and antipsychotics. This report describes a case of a young adult with a premorbid schizoid personality disorder, who evolved with urinary retention after using combined therapy with haloperidol decanoate and fluoxetine.

Case Report: JFG, 24 years old, with pre-morbid schizoid personality disorder and probable intellectual disability, admitted to a psychiatric ward due to a severe depressive episode with loss of self-care and food refusal. About nine days before admission to the psychiatric ward, he had used 01 intramuscular ampoule of haloperidol decanoate. On admission, olanzapine 5 mg/d was prescribed (in the presence of psychotic symptoms: probable audiovisual hallucinations), fluoxetine 20 mg/d and Clonazepam 0.5 mg/d at night. After six days, olanzapine was suspended to maintain the use of haloperidol decanoate as antipsychotic monotherapy. On the tenth day of hospitalization, he developed dysuria, voiding effort and reduced urinary output, without an increase in nitrogen slag, signs of infection or other changes in the urine summary. After about two days without maintenance of satisfactory debt and with the exclusion of other causes, the hypothesis of urinary retention due to the combination of psychotropics, and fluoxetine was withdrawn, and around two days after the suspension of fluoxetine, the patient evolved with resolution of the urinary retention.

Discussion: It is already known that both fluoxetine and haloperidol are metabolized by the hepatic enzyme CYP450 2D6,2,3, and that fluoxetine is an important inhibitor of this same enzyme, so that their concomitant use, due to these pharmacokinetic interactions, predisposes to increased serum levels of both, augmenting adverse effects, especially in patients with a low Body Mass Index like the one of this report. Some cases with similarities were previously reported in the literature, including one that reported urinary retention also in a young patient, but due to fluoxetine and oral haloperidol combination, that was reverted after haloperidol discontinuation, emphasizing that this is the first report of a case of urinary retention with fluoxetine/haloperidol combination reverted with the maintenance of haloperidol use.

Conclusion: To our knowledge, this is the first report of urinary retention with haloperidol decanoate associated with fluoxetine, reverted after discontinuation of fluoxetine and maintenance of haloperidol, considering that haloperidol couldn't be suspended because of its long-acting presentation. This report emphasizes the importance of the knowledge of pharmacokinetic interactions in the management of psychiatric patients, by bringing an infrequent side effect, managed with the help of the concepts of drug interactions.

Introduction

Defined as the inability to completely empty the bladder [1], urinary retention is a side effect not commonly observed during the use of psychotropics, although it has been reported that 2% of acute urinary retention episodes are induced by drugs [2]. A variety of classes of drugs can interfere with the physiology of the lower urinary tract, contributing to the development of urinary retention, including some psychotropic agents [3]. A previous review of the literature observed that there were several case reports of selective serotonin reuptake inhibitors (SSRI) causing urinary retention in combination. They hypothesized that these combinations may have affected the hepatic metabolism of the other drugs, like the case of fluoxetine impairing the cytochrome CYP2D6 enzyme metabolism of risperidone when administered in combination, increasing the plasma levels of risperidone and therefore contributing to its side effects [4]. Overall, there is good evidence that urinary retention is very rarely if at all associated with SSRI used in monotherapy [3]. Concerning the effects of typical antipsychotics, haloperidol promoted urinary retention in 5% of patients, but the lack of homogeneous definitions of urinary retention among these studies make it hard to conclude the real role of haloperidol for the development of urinary retention, with a possibility that the typical antipsychotics only caused mild voiding dysfunction instead [3]. This report describes a case of a young adult with a premorbid schizoid personality disorder, who evolved with urinary retention after using combined therapy with haloperidol decanoate and fluoxetine.

Case Report

A man, 24 years old, only child, Body Mass Index 15.16 kg/m², with pre-morbid schizoid personality disorder and probable intellectual disability, admitted to a psychiatric ward due to a severe depressive episode with loss of self-care and food refusal. About nine days before admission to the psychiatric ward, he had used 01 intramuscular ampoule of haloperidol decanoate, and started biperiden 2 mg/d orally for three days, after an outpatient consultation with a psychiatrist. There was no report of previous use of psychotropic drugs. On admission, olanzapine 5 mg/d was prescribed (in the presence of psychotic symptoms: probable audiovisual hallucinations), fluoxetine 20 mg/d and Clonazepam 0.5 mg/d at night. On the sixth day of hospitalization, olanzapine was suspended to maintain the use of haloperidol decanoate for greater therapeutic adherence after hospital discharge, with 1 ampoule administered intramuscularly, maintaining an interval of fifteen days from the applied dose prior to admission. On the tenth day of hospitalization, he developed dysuria, voiding effort and reduced urinary output, without an increase in nitrogen slag, signs of infection or other changes in the urine summary. After about two days without maintenance of satisfactory debt and with the exclusion of other causes, the hypothesis was raised that such an occurrence could be related to adverse effects due to the combination of psychotropics, and fluoxetine was withdrawn, considering the impossibility of suspension of the depot antipsychotic. Around two to three days after the suspension of fluoxetine, the patient evolved with resolution of the urinary retention, a time interval that coincides with the half-life of fluoxetine (2 to 4 days)1(Figure 1).



Figure 1: Case report timeline.

Discussion

It is already known that both fluoxetine and haloperidol are metabolized by the hepatic enzyme CYP450 2D6 [5,6], and that fluoxetine is an important inhibitor of this same enzyme, so that their concomitant use, due to these pharmacokinetic interactions, predisposes to increased serum levels of both, augmenting adverse effects, especially in patients with a low Body Mass Index like the one of this report. This knowledge derives from studies with oral formulations, but the interaction between oral fluoxetine and haloperidol decanoate was already described in the literature, with one study showing the 14 days after the addition of fluoxetine, a very significant increase in haloperidol concentrations (100%) was observed, reinforcing the knowledge that the pharmacokinetic interactions with haloperidol of fluoxetine is clinically significant, either by inhibiting its hepatic metabolism or and by displacing it from protein binding sites [7]. Some cases with similarities were previously reported in the literature [8,9], including one that reported urinary retention also in a young patient, but due to fluoxetine and oral haloperidol combination, that was reverted after haloperidol discontinuation, emphasizing that this is the first report of a case of urinary retention with fluoxetine/haloperidol combination reverted with the maintenance of haloperidol use. The recovery of spontaneous diuresis after only two days of fluoxetine suspension in our case report emphasizes the hypothesis that the major mechanism underlying this interaction was the probable fluoxetine property of displacing haloperidol from protein binding sites, knowing that as stated before, both medications are substrates of the same cytochrome P450 enzyme, CYP 2D6 [5,6].

Conclusion

To our knowledge, this is the first report of urinary retention with haloperidol decanoate associated with fluoxetine, reverted

after discontinuation of fluoxetine and maintenance of haloperidol, considering that haloperidol couldn't be suspended because of its long-acting presentation. This report emphasizes the importance of the knowledge of pharmacokinetic interactions in the management of psychiatric patients, by bringing an infrequent side effect, managed with the help of the concepts of drug interactions.

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