A Risperidone Long-acting Injection Provoked Urinary Retention: A Case Report

Hao-Lun Luo, M.D., Wei-Chia Lee, M.D., Ph.D., Yao-Chi Chuang, M.D.

Division of Urology, Chang Gung Memorial Hospital, Kaohsiung Medical Center, Kaohsiung, Taiwan; College of Medicine, Chang Gung University, Taoyuan, Taiwan

ABSTRACT

Risperidone is commonly used to treat behavioral disturbance in elderly demented patients because it has less extrapyramidal effects than conventional antipsychotics. To increase compliance and reduced adverse effects among these patients, a risperidone long-acting injection has been developed. However, the elderly may be affected by a potential risk of detrusor underactivity. By inhibiting the central serotonergic and dopaminergic pathways, risperidone may cause urinary retention as the results of decreasing detrusor contractility and increasing sphincter resistance. We report here an older male patient, who previously had no obvious bladder outlet obstruction. He received a relatively safe dosage of long-term injection risperidone and developed urinary retention during the course of his antipsychotic therapy treatment.

Keywords: risperidone, serotonin, urinary retention, elderly.

INTRODUCTION

Risperidone, an atypical antipsychotic drug, is increasingly being used for the treatment of mental illness like schizophrenia, bipolar disorder, and irritability associated with autism. Risperidone is a serotonin-dopamine receptor antagonist that has a dual mechanism of inhibition on 5-hydroxytryptophan (5-HT) and dopaminergic (D) receptors [1]. The antagonistic activity of risperidone on the 5-HT_{2A} receptors of the presynaptic dopaminergic nerve terminals affects the nigrostriatal pathway. As a result of dopamine release and competition by risperidone for the D_2 receptor, D_2 blockade is reversed in the striatum. Therefore, risperidone can produce a significant antipsychotic effect and causes fewer extrapyramidal effects at lower doses than other more conventional agents.

To increase compliance and prevent symptoms worsening progressively among psychosis patients, a risperidone long-acting injection was developed. In previous studies, risperidone long-acting injection has been shown to have advantages in terms of assured compliance, sustained delivery and the proven efficacy of an atypical antipsychotic when treating the positive and negative symptoms of schizophrenia. Expert consensus guidelines indicate that risperidone long-acting injection 25 mg q 2 weeks is adequate for most patients. Risperidone long-acting injections are generally well tolerated and are associated with a low incidence of adverse effects. Some of the most common side effects seen with this drug include drowsiness, insomnia, priapism, and an increased appetite. However, the side effect of acute urinary retention has rarely been reported in the literature. A PubMed search revealed only two reports of risperidone induced urinary retention. We present here a case of acute urinary retention when a regular dose of risperidone long-acting injection was prescribed for an elderly man with acute psychosis.

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Address correspondence to: Dr. Wei-Chia Lee, Division of Urology, Chang Gung Memorial Hospital, Kaohsiung Medical Center, 123, Ta Pei Road, Niao Song Hsiang, Kaohsiung, Taiwan

E-mail: dinor666@ms32.hinet.net

BRIEF HISTORY

A 69 year-old male patient previously had suffered no obvious low urinary tract symptoms or overt risk factors of voiding dysfunction. He was noted to have frequent violent behavior events with hallucination and delusions. Acute psychosis was impressed and he was admitted to the psychiatric ward for an etiology survey and disease control. Risperidone, a serotonin-dopamine receptor antagonist, was prescribed in a loading dose of 25 mg intramuscular injection to control the acute psychosis. A maintenance dose of risperidone 1 mg per night was also used. However, an acute urinary retention episode occurred 3 days later. Regular clean intermittent catheterization every eight hours revealed a profuse residual urine volume around 500 mL even when the patient was treated with tamsulosin 0.4 mg per day for two days. Thus an indwelling Foley catheter was introduced. A digital rectum examination showed a walnut size prostate of elastic consistency and with a smooth surface.

CLINICAL INVESTIGATIONS AND TREATMENT COURSE

Videourodynamic studies were arranged to identify the etiology of the urinary retention and for a bladder function evaluation. The voiding phase of the videourodynamic studies revealed a patent urethra without any specific obstructive site (Fig. 1A). Therefore, chronic bladder outlet obstruction, such as benign prostate enlargement or urethral stricture, could be ruled out. Furthermore, the cystometrogram disclosed a decreased detrusor pressure at maximum uroflow rate and hesitancy in the initiation of voiding, which resulted in a poor uroflow rate and a remarkable post-void residual (Fig. 1B). Hence, detrusor underactivity with a delayed opening of the bladder neck was impressed in this male patient. Gradually tapering off of the risperidone was carried because of the patient's stable psychosis condition. No more urinary retention episodes occurred under a low dose of risperidone (3 mg per day) together with doxazosin 4 mg daily.

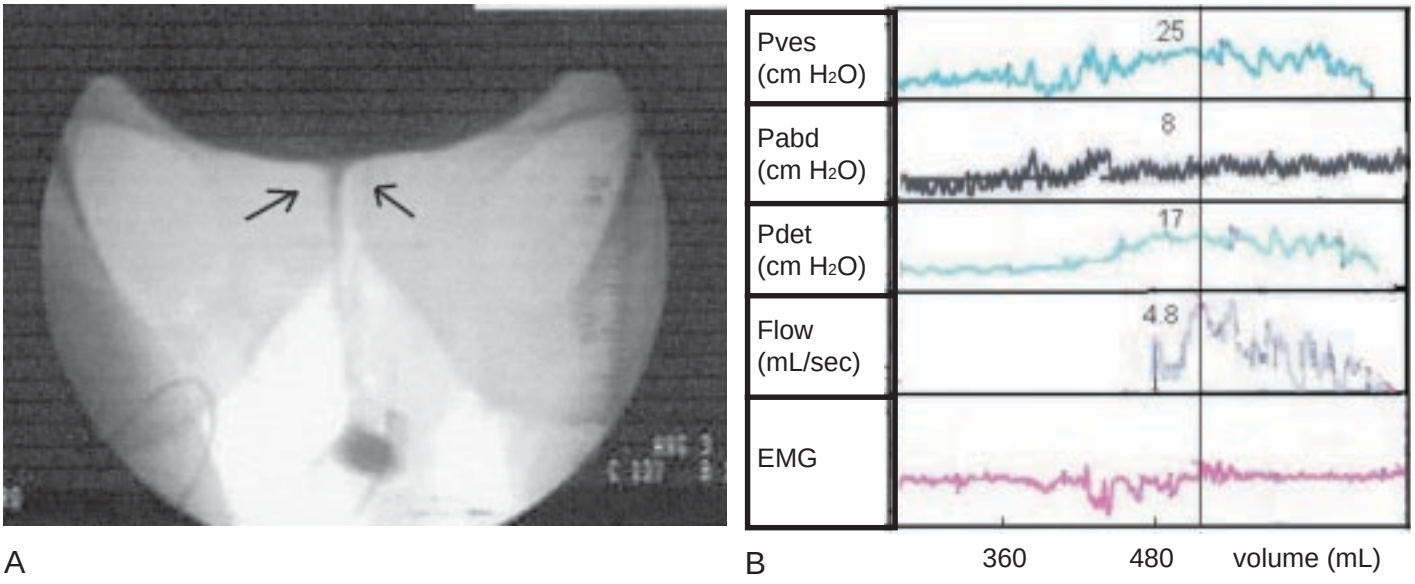

Fig. 1. The videourodynamic findings of this 69 year-old male patient. (A) During voiding, the bladder neck was open and the prostate urethra was also wide (arrow heads). (B) Detrusor underactivity was noted in this case. The urodynamic study revealed a delayed first sensation of bladder filling and an adequate bladder capacity of 480 mL at which time he voided with decreased detrusor pressure and hesitancy in the initiation of voiding. The maximum uroflow rate of this patient was 4.8 mL/sec and a remarkable PVR of 350 mL was noted. Pabd, abdominal pressure; Pdet, detrusor pressure; Pves, intravesical pressure.

DISCUSSION

Our patient developed acute urinary retention three days after a loading dose of long-acting risperidone was given and his voiding function improved when the dose of risperidone was tapered off. We suggest that risperidone can provoke bladder neck dysfunction and detrusor underactivity in some elderly patients.

It was known that the 5-HT- containing pathway plays an important role in the control of micturition. The descending serotonin pathway from the raphe nuclei can inhibit bladder contractility and increases sphincter resistance [2]. This mechanism may explain the efficacy of serotonergic-based antidepressants, such as duloxetine, in the treatment of urgent incontinence and stress urinary incontinence. 5-HT_{1A} receptor activation can promote detrusor contractions at sub-threshold bladder volumes in the rat. The sympathetic autonomic nuclei, as well as the sphincter motor nuclei, also receive a serotonergic input from the raphe nucleus. Activation of both the $5HT_{2A/2C}$ and α1-adrenergic receptors of the pudendal motor neurons in the ventral horn of the sacral spinal cord has been shown to increase the activity of the striated urethral sphincter. Recently, it has been reported that the serotonergic system is involved in blocking the afferent pathway of the micturition reflex [3].

The pharmacological effects of risperidone on bladder function are consistent with the urodynamic findings of detrusor underactivity and delayed opening of the bladder neck in this patient. Pharmacologically, risperidone can act as an antagonist affecting $5HT_{1A}$, $5HT_{2A}$, $5HT_{2c}$, α1-adrenergic, D_2 and histaminergic (H_1) receptors. These effects can inhibit detrusor contraction and increase striated urethral sphincter activity. In addition, risperidone can stimulate dopamine secretion through 5-HT_{2A} blockade. It has been found that agonists of D_1 receptors suppress an overactive bladder and agonists of D_2 receptors stimulate detrusor overactivity. As a result, stimulation of central D_1 receptors and blockade of D_2 receptors may be one of the mechanisms that caused detrusor underactivity in our patient.

Although risperidone long-acting injection is considered to have a low incidence of adverse effects, we suggest that an adequate evaluation of voiding function in elderly patients is necessary if risperidone is used as a neuroleptic. Particularly this is true for patients who are being treated with risperidone in combination with a potent psychoactive drug (e.g. fluoxetine-risperidone) [4]. Bladder emptying results involve a balance between detrusor muscle contraction and bladder outlet resistance. Provoked bladder outlet functional obstruction and detrusor underactivity can cause acute urinary retention in some individuals. Clinically, detrusor underactivity is usually underestimated and has a high prevalence in the older members of the population. Even without overt neurological disease, the aging process may result in modest declines in detrusor contractility [5]. Among men and women aged 60 years and older, 22.1% and 10.8%, respectively, report difficulty emptying their bladder. Furthermore, the elderly may have other coexisting conditions that can deteriorate the bladder emptying function, such as diabetes mellitus, cerebral vascular accident, and benign prostatic hyperplasia.

CONCLUSION

The serotonergic system seem to play a role in micturition and patients treated with neuroleptics and 5-HT antagonists may have noticeable urinary retention that is related to detrusor underactivity and higher sphincter resistance.

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