Duloxetine for the treatment of post-prostatectomy stress urinary incontinence

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Abstract

Objectives: Stress urinary incontinence (SUI) is a known complication following prostatectomy. Duloxetine, a combined serotonin/norepinephrine reuptake inhibitor, can decrease SUI by increasing urethral sphincter contractility. We examined the outcomes of patients with mild to moderate post-prostatectomy SUI treated with duloxetine.

Methods: We conducted a retrospective review of men treated with duloxetine to manage mild to moderate post-prostatectomy SUI from 2006 to 2012. All patients received oral duloxetine 30 mg once a week, then 60 mg thereafter. Patients were seen one month later to determine drug efficacy and side effects.

Results: In total, 94 men were included in the study. Daily pad usage decreased from 2.9 (range: 1-5) to 1.6 (range: 0-4) (p < 0.05). Incontinence Impact Questionnaire (IIQ-7) scores decreased from 13.0 (range: 6-18) to 7.9 (range: 2-16) (p < 0.05). Linear satisfaction scores improved from 0.8 (range: 0-2) to 2.0 (range: 1-3) (p < 0.05). Following a 1-month duloxetine trial, 33/94 (35%) men reported satisfactory SUI improvement and requested to continue the medication. The drug was discontinued in 61/94 (65%) patients due to poor efficacy in 32/94 (34%), intolerable side effects in 14/94 (15%) or both in 15/94 (16%). Reported side effects included fatigue, light-headedness, insomnia, nausea and dry mouth.

Conclusions: Duloxetine improved post-prostatectomy SUI in 47/94 (50%) men following a 1-month trial. However, only 33/94 (35%) patients were able to tolerate the drug. Duloxetine may be considered a treatment option for men with mild to moderate post-prostatectomy SUI.

Introduction

Stress urinary incontinence (SUI) is a known complication of radical prostatectomy that may persist in up to 90% of patients 1 year after the procedure.1 When compared to individuals who are continent, patients with incontinence have a higher level of anxiety, lower quality of life (QOL) and poorer life satisfaction.2 Traditionally, treatment options for post-prostatectomy SUI have involved surgical intervention. Placement of an artificial urinary sphincter remains the gold standard, with success rates up to 90%.3 However, the procedure is invasive and the need for surgical revision is common.4

Duloxetine, a selective serotonin (5-HT) and norepinephrine (NE) reuptake inhibitor, has been shown to decrease SUI by increasing urethral sphincter contractility.5 The drug inhibits the pre-synaptic reuptake of 5-HT and NE at Onuf’s nucleus in the sacral spinal cord. The result is an increase in rhabdosphincter activity due to increased post-synaptic receptor stimulation. This unique pharmacotherapy has demonstrated efficacy in the management of female SUI and has been approved for this use in Europe since 2004.6

The use of duloxetine in men is an active area of investigation and represents a potential nonsurgical therapy for post-prostatectomy SUI.5,7-10 The goal of our investigation is to evaluate the efficacy and reported side effects in patients with mild to moderate post-prostatectomy SUI treated with duloxetine.
pies, pre- and post-incontinence impact questionnaire (IIQ-7) scores, pre- and post-linear satisfaction score (0 [unsatisfied] to 3 [greatly satisfied]) and medication side effects. All patients received oral duloxetine 30 mg at bedtime for 1 week, then 60 mg at bedtime thereafter. Patients were seen 1 month after the start of pharmacotherapy to determine drug efficacy and side effects. Statistical significance was determined using Fisher’s exact test.

**Results**

Ninety-four patients were included in the study. Mean patient age was 64.3 years (range: 47-83). The average time since radical prostatectomy was 19.3 months (range: 9-49).

We tallied the pre- and post-treatment pad usage, IIQ-7 scores and linear satisfaction scores (Table 1). Following a 1-month trial of duloxetine, 51/94 (54%) patients reported a ≥50% reduction in daily pad usage. Satisfactory SUI reduction and drug tolerability was reported in 33/94 (35%) men. The improvement in daily pad usage, IIQ-7 scores and QOL scores all reached statistical significance (p < 0.05). The drug was discontinued in 61/94 (65%) patients due to lack of efficacy in 32/94 (34%), intolerable side effects in 14/94 (15%) or both in 15/94 (16%). Reported intolerable side effects included fatigue (12%), light-headedness (11%), insomnia (3%), nausea (3%) and dry mouth (2%).

**Discussion**

Multiple factors may contribute to the risk of SUI following radical prostatectomy including age, preoperative continence status, surgeon experience, education level, concomitant pulmonary disease and need for adjuvant radiation therapy to the prostatic bed. The etiologies of SUI after prostatectomy include injury to the nerve, muscle fibers or both. The somatic and autonomic neural innervation of the EUS arise from Onuf’s nucleus of the sacral cord. The post-synaptic autonomic neurons of the EUS have a high density of serotonergic and noradrenergic terminals. Blocking the reuptake of NE and 5-HT in the pre-synaptic adrenergic nerve results in increased EUS contractility secondary to increased stimulation of the post-synaptic 5-HT and NE receptors.

Several clinical studies investigating the role of duloxetine in post-prostatectomy SUI have been published. Filocamo and colleagues reported duloxetine and pelvic floor physical therapy may allow for earlier return to continence as compared to physical therapy alone following catheter removal in the immediate postoperative period. Similarly, two additional studies found an approximate 50% reduction in pad usage with patients taking duloxetine to manage post-prostatectomy SUI.

<table>
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<tr>
<th>Table 1. Changes in mean pad usage, IIQ-7 scores and linear satisfaction scores after one month of duloxetine pharmacotherapy</th>
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<tr>
<td><strong>Mean daily pad usage (range)</strong></td>
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<td>IIQ: Incontinence Impact Questionnaire.</td>
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<td>Mean daily pad usage (range)</td>
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<td>Mean IIQ-7 score (range)</td>
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<td>Mean linear satisfaction score (range)</td>
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Other pharmacologic agents have been investigated for the treatment of post-prostatectomy SUI. Alpha-adrenergic agonists, including midodrine, norephrine and ephedrine, as well as beta-2-antagonists, have been used. However, the lack of receptor selectivity and severe systemic side effects have limited their clinical use. Although imipramine, a tricyclic antidepressant with 5-HT and NE reuptake properties, has shown efficacy for post-prostatectomy incontinence, doses required to achieve success have significant anticholinergic side effects. Venlafaxine, a 5-HT/NE reuptake inhibitor similar to duloxetine, has also been studied with positive results.

Our study is limited by its retrospective nature and small sample size. Pad usage was used as an outcome measure, but this may not accurately quantify the magnitude of incontinence since the type of pad used was not standardized. As well, the follow-up is short and durability of the results is unknown. Clinically, our patients electing to continue duloxetine have not reported tachyphylaxis. The study, however, does add to the literature supporting further investigation of this medication for the treatment of post-prostatectomy stress incontinence.
Conclusion

The surgical complication of post-prostatectomy SUI can result in decreased QOL. Many patients are reluctant to undergo an additional surgical procedure to address this problem. Our data indicate that duloxetine is a promising non-invasive medical treatment option for mild to moderate post-prostatectomy incontinence.

Competing interests: None declared.

This paper has been peer-reviewed.

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