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Efficacy of Duloxetine in the Early Management of Urinary Continence after Radical Prostatectomy

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Key Words
Duloxetine • Urinary continence • Radical prostatectomy

Abstract
Aim: To evaluate the efficacy of early duloxetine therapy in stress urinary incontinence occurring after radical prostatectomy (RP). ***Material and Method:*** Patients that had RP were randomly divided into 2 groups following the removal of the urinary catheter. Group A patients (n = 28) had pelvic floor exercise and duloxetine therapy. Group B patients (n = 30) had only pelvic floor exercise. The incontinence status of the patients and number of pads were recorded and 1-hour pad test and Turkish validation of International Consultation on Incontinence Questionnaire–Short Form test were applied to the patients at the follow-up. ***Results:*** When the dry state of the patients was evaluated, 5, 17, 3, and 2 of 28 Group A patients stated that they were completely dry in the 3rd, 6th, 9th and 12th month respectively and pad use was stopped. There was no continence in 30 Group B in the first 3 months. Twelve, 6, and 8 patients stated that they were completely dry in the 6th, 9th and 12th month, respectively. But 3 of 4 patients in whom dryness could not be provided were using a mean of 7.6 pads in the first day and a mean of 1.3 pads after 1 year. When pad use of the patients was evaluated, the mean monthly number of pad use was determined to be 6.2 (4–8) in the initial evaluation, 2.7 (0–5) in the in 3rd month, 2 (0–3) in the 6th month and 1.6 (0–2) pad/d in the 9th month in the group taking medicine. The mean monthly number of pads used was determined to be 5.8 (4–8) in the initial evaluation, 4.3 (3–8) in the 3rd month, 3 (0–6) in the 6th month and 1.6 (0–6) pad/d in the 9th month in the group not taking medicine. ***Conclusion:*** According to the results, early duloxetine therapy in stress urinary incontinence that occurred after RP provided early continence.

Introduction

Surgical intervention of the prostate is the leading cause in the etiology of urinary incontinence of adult males. Radical prostatectomy (RP) performed for prostate cancer is the major reason for these interventions. RP is the gold standard treatment in localized prostate cancer for the patients with a life expectancy of more than 10 years [1]. However, urinary incontinence which can occur after RP is an important surgical complication that considerably worsens the quality of life [2, 3]. While the rate of postoperative urinary incontinence is 1% in patients in whom prostatectomy is performed due to benign causes, this rate after RP is reported to be between 2 and 66% [4]. Most common causes in the pathophysiology of post-prostatectomy urinary incontinence (PPI) are intrinsic sphincter deficiency, external sphincter insufficiency, and detrusor instability [5–8]. It is still controversial which factor is more responsible for incontinence.

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Table 1. Continence status of patients

	Duloxetine +PFE, month					PFE, month					p value
	1st	3rd	6th	9th	12th	1st	3rd	6th	9th	12th	
Incontinence, n	28	23	6	3	1	30	30	18	12	4	
Incontinence, %		82.1%	21.4%	10.7%	3.5%		100%	60%	40%	13.3%	0.0003

P value was obtained by comparing the 6th month improvement rates. P value obtained when the results of continent patients at the end of the 12th month were evaluated: 0.0254. The statistically significant difference was obtained during evaluation of number of pads, pad weights, and ICIQ-SF assessment in the 3rd month but this difference was not obtained at the end of the 12th month. When the continent patients were compared, a statistically significant difference was obtained in the 6th month and this difference continued at the end of the 12th month.

Although detrusor instability is seen in PPI patients with a high rate of 30–60%, continuation of incontinence of patients that benefited from anticholinergic treatment shows that the event is not only related to detrusor instability. It was reported that autonomic parasympathetic nerve and external sphincter damage that developed during surgery could be more important in PPI development. Urodynamic investigations showed that PPI patients had a high rate of sphincter deficiency [9].

Although different surgical and medical treatments are used for treatment of incontinence that develops after PR, there is still no standard treatment providing long-term cure. In studies performed in recent years, successful results were obtained with duloxetine treatment of stress incontinence due to intrinsic sphincter deficiency especially in women [10, 11]. Duloxetine is a highly efficient serotonin and norepinephrine reuptake inhibitor. It acts by increasing the stimulus sent to the urethral sphincter with its effect on Onuf's nucleus. There are no adequate studies to clarify the effect of duloxetine on stress incontinence in men.

In this study, we tried to determine whether duloxetine was effective in the early period of men with urinary incontinence after PR.

Materials and Methods

Fifty-eight patients out of 112 patients aged 55–75 year-old (median age 61.2 years) with various degrees of stress incontinence and undergoing nerve-sparing retroperitoneal laparoscopic RP due to prostate cancer between 2010 and 2013 were included in the study. Patients were excluded from the study on the basis of the following criteria: BMI score greater than 30 kg/m^2, central and peripheral neuropathy, ongoing treatment for diabetes mellitus, history of radiotherapy for the pelvic floor, history of urethral stricture, known neurological disease, presence of preoperative incontinence, or preoperative use of serotonin and norepinephrine reuptake inhibitors. The patients were randomly divided into 2 groups after removal of the catheter in the postoperative third week and recalled for follow-up. Baseline incontinence status of the patients was evaluated by using the number of pads, pad weight, and International Consultation on Incontinence Questionnaire–Short Form (ICIQ-SF).

Twenty-eight patients in Group A were given duloxetine (60 mg tablet once daily) and pelvic floor exercise (PFE), 30 patients in Group B were given only PFE for 12 months. The patients were recalled for follow-up at 3 months intervals. Incontinence status of the patients, number of pads was controlled, and 1-hour pad test and Turkish validation of ICIQ-SF test were applied to the patients at the follow-up. Attention was paid to use of pads with similar characteristics during pad use. A 25% decrease in the number of pads and a 3-point decrease in ICIQ-SF total scores was considered to be an improvement. All of the patients were informed about efficacy and adverse effects of duloxetine. Both intra-group and inter-group comparisons were performed with Mann Whitney U and Kruskal-Wallis tests by using obtained results. We used oral instructions and then used biofeedback once to teach PFE.

Results

When the dry state of the patients was evaluated, 5, 17, 3 and 2 of 28 patients in Group A stated that they were completely dry in the 3rd, 6th, 9th, and 12th month respectively and stopped pad use. Dryness could not be provided in 1 patient who developed a urethral stricture and internal urethrotomy surgery was performed in the advanced period (table 1).

There was no incontinence in 30 patients in Group B in the 3rd month. Twelve, 6 and 8 patients stated that they were completely dry in the 6th, 9th, and 12th month, respectively, while 3 of 4 patients in whom dryness could not be provided, were using a mean of 7.6 pads in the first day and a mean of 1.3 pads after 1 year. Urethral stricture developed in 1 patient and internal urethrotomy surgery was performed.

Table 2. Comparison of pad weights, pad numbers, and ICIQ–SFs of all groups

	Duloxetine +PFE, month				PFE, month				p value
	1st	3rd	6th	9th	1st	3rd	6th	9th	
Pads	6.2 (4–8)	2.7 (0–5)	2 (0–3)	1.6 (0–2)	5.8 (4–8)	4.3 (3–8)	3 (0–6)	1.6 (0–6)	
Improvement rate		56%	67%	74%		25%	48%	72%	0.0038
Pad weight, g	30.1 (8–55)	15.1 (3–40)	14 (0–30)	7.6 (0–11)	25.7 (9–58)	18.8 (4–45)	13.3 (0–20)	7.9 (0–12)	
Improvement rate		50.1%	53.4%	74.7%		26.8%	48.2%	69.2%	0.0196
ICIQ–SF	19.5 (18–21)	11 (8–13)	8.1 (6–11)	10 (10–10)	19.3 (18–21)	15.2 (12–19)	13 (6–16)	9.6 (8–12)	
Improvement rate		43.5%	58.4%	48%		21.2%	32.6%	50.2%	0.0174

P value was obtained by comparing the 3rd month improvement rates. 12th month values are not given because there were not enough patients to evaluate.

When pad use of the patients was evaluated the mean monthly number of pad use was determined to be 6.2 (4–8) in the initial evaluation, 2.7 (0–5) in the in 3rd month, 2 (0–3) in the 6th month, and 1.6 (0–2) pad/d in the 9th month in Group A. Mean monthly number of pad use was determined to be 5.8 (4–8) in the initial evaluation, 4.3 (3–8) in the 3rd month, 3 (0–6) in the 6th month, and 1.6 (0–6) pad/d in the 9th month in Group B.

When the pad weight was evaluated, the baseline pad weight was determined to be 30.1 g (8–55 g), 15.1 g (3–40 g) in the 3rd month, 14 g (0–30 g) in the 6th month, and 7.6 g (0–11 g) in the 9th month in Group A, and the baseline pad weight was determined to be 25.7 g (9–58 g), 18.8 g (4–45 g) in the 3rd month, 13.3 g (0–20g) in the 6th month, and 7.9 g (0–12g) in the 9th month in Group B (table 2).

The score obtained when the inquiry form of quality of life was evaluated was 19.5 (18–21) at the baseline, 11 (8–13) in the 3rd month, 8.1 (6–11) in the 6th month, and 10 (10–10) in the 9th month in Group A, while it was 19.3 (18–21) at the baseline, 15.2 (12–19) in the 3rd month, 13 (6–16) in the 6th month, and 9.6 (8–12) in the 9th month in Group B (table 2).

All of the patients regularly attended pelvic exercises during incontinence but they also stopped pelvic exercises after stopping pad use.

No life-threatening adverse effects developed in the patients due to the medicine. The most commonly reported side effect was a feeling of tiredness (6 of 28 patients), dry mouth (5 of 28 patients), and nausea and constipation (2 of 28 patients). No patient discontinued the medicine due to adverse effects. Drug use was gradually discontinued after 1 month following creation of continence.

Discussion

The most important cause of urinary incontinence occurring after prostatectomy is sphincteric deficiency. While urinary incontinence due to detrusor overactivity is determined at a rate of 3–40% after prostatectomy, sphincteric deficiency is the most common cause either alone or together with urinary bladder dysfunction in 40–88% of the cases. Since the proximal urethral sphincter is removed during RP, creation of continence or prevention of urinary incontinence becomes completely dependent on the distal urethral sphincter [12, 13]. Mostwin [14] suggested that urinary incontinence occurring during or after RP was due to sphincteric disorder caused by ischemia and immobilization occurring in the postoperative period, direct pudendal nerve damage, and shortening of the length of the urethra more than the critical dimension. In similar studies, urinary incontinence not occurring in the preoperative period but occurring in the postoperative period has been attributed to partial urinary bladder decentralization or desensitization or mobilization of the seminal vesicles after surgery, possibly to fibrosis, infection, and changes in the urinary bladder wall [15, 16].

While history, physical examination, inquiry forms, and simple tests are enough in patients with PPI in whom conservative or medical treatment are administered, the patients should to be evaluated with detailed investigations and urodynamic tests in sphincter, urethral sling surgery, or other invasive procedures [1]. The definition of urinary incontinence, when it occurs, day/night incontinence, its severity, and factors causing or increasing urinary incontinence, should especially be determined. One of the most important issues here is heterogeneity in the definition of incontinence (full dryness, pad weight,

number of pads, and social continence) and uncertainty in time until regaining of continence after removal of the catheter. Some investigators defined cases continuing more than 1 year as delayed incontinence by considering the first 3 months after surgery as the early period. The rate of incontinence after RP varied from 8 to 87% at 6 months and from 5 to 44.5% 1 year after the operation [17]. There are personal preferences in the rationale of the approach which is generally accepted. In our study, we also accepted the first 3 months after surgery as the early period. Similarly, while continence was defined to be non-enuresis in some studies, pad wetting to a certain weight or "social continence" was considered to be enough in some studies. Also in our study, while we accepted the decrease in the number of pad as social continence, we accepted non-enuresis as continence. Physical, psychological, and social well-being of patients are determined by using the quality of life and/or disorder criteria forms for patients and the method which will be selected in treatment of urinary incontinence occurring after prostatectomy is determined in the light of these results [2, 3, 17]. The most commonly used inquiry form related to this subject is the ICIQ-SF. We also used the Turkish validation of ICIQ-SF form in our study.

Although many studies have been performed to estimate in which PPI could be seen, the evidence level of most of them is low. Parameters such as prostate volume, age of the patient, and body weight were evaluated and contradictory results were found [18–21]. Although there is deficiency regarding controlled randomized trials, generally it is considered that advanced age increases the risk of PPI [19, 22]. Sphincter atrophy and neural degeneration occurring together with aging were described to be a risk factor for PPI [22, 24]. In the present study, it was observed that urinary incontinence was more severe especially in patients over 70 years of age. The cause of this condition could be co-morbidities increasing with the age, or detrusor or sphincteric deficiencies increasing with the age. It was stated that the physically active (intensive activity more than 1 hour a week) patients and the patients with low body mass index (BMI, 30 kg/m^2) had low risk for PPI [25]. However, there are also studies indicating BMI has no impact on PPI [20]. In the present study, no correlation was seen between BMI and the severity of urinary incontinence.

Treatment of urinary incontinence occurring after prostatectomy is performed by using various methods ranging from conservative methods to invasive interventions [1]. Determination of the type of urinary incontinence is important for treatment. Sphincteric deficiency, urinary bladder overactivity, or a combination of them may require different interventions. Treatment of urinary incontinence due to sphincter deficiency can use various methods ranging from conservative interventions to minimal invasive or artificial urinary sphincter surgeries. PFE, pharmacological treatment, injection treatments, perineal sling procedure, adjustable urethral sling, strengthening of the urinary bladder neck, artificial urinary sphincter, and new interventions are among these methods. Conservatively, fluid restriction and behavioral methods are preferred at the beginning. PFE can be beneficial in some cases. Pelvic floor muscle exercises are performed to strengthen pelvic floor muscles to provide urethral support in order to prevent urine leakage. PFE which were first suggested by Kegel are the simplest and most widely performed one among stress incontinence treatment options [26]. In the study performed by van Kampen et al. [27] including 102 randomized RP patients (placebo vs. PFE), the authors found significant difference for the PFE group both in return time to continence (56 vs. 88% in 3rd month) and in amount of incontinence. It was stated that PFE accelerated the return to continence especially in the early period and no difference was seen in efficacy in the treatments initiated after 6 weeks [28]. In their study, Filacomo et al. [29] found a significant difference in the PFE group in the 6th month after randomly dividing 300 patients (65 vs. 95%), and the rates of total continence was found to be same with the untreated group at the end of 1 year. The present results are consistent with this study. In our study, while no continent patient was determined in the patients that performed only PFE in the first 3 months, it was seen that efficacy and improvement occurred in the 6th month.

The most promising development in medical treatment of PPI in recent years is duloxetine, which is approved in many countries for female stress incontinence [30, 31]. Duloxetine which acts as a selective serotonin and norepinephrine reuptake inhibitor located at the presynaptic neuron in Onuf's nucleus of the sacral spinal cord produces neuronal output to the urethral sphincter and provides increase in the tone of smooth muscle and improvement in continence. In their study including 20 patients (15 RP and 5 radical cystectomy), Schlenker et al. [32] obtained full dryness with 40 mg duloxetine twice a day in 7 patients (35%), and the mean number of pads used by the patients decreased from 8.0 to 4.2 pads/d. Filcamo et al. [33] compared patients treated with duloxetine and exercise (30%) and exercise alone (11.5%) regarding full dryness ($p = 0.01$). In a similar study performed by Serra et al. [34], the treatment was initiated in 68 patients in

whom urinary incontinence continued after 1 year after RP and the percentage of patients without pads decreased to 37% by the second visit in the 3rd month after initiation of the treatment and reached 65% at the end of the study. When the overall studies performed in this field were investigated, the short-term results related to use of duloxetine after RP seemed to be promising. In the study performed by Chapple et al. [35], it was reported that this drug could not be included in the treatment modalities of urinary incontinence occurring after RP without adequate follow-up, and placebo-controlled randomized group studies. In their study including 112 patients, Fink et al. [36] obtained a significant decrease in mean use of pads from 3.3 to 1.5 pads/d in 49 patients. Only one of a limited number of studies performed in PPI patients was a prospective randomized trial. In this study, duloxetine and PFE groups were compared with a placebo and PFE and while better continence rates were observed in the duloxetine group at the end of 16 weeks, surprisingly the rate reversed after 8 weeks following discontinuation of the treatment (post-prostatectomy 24th week) [33]. In conclusion, there is no study with a high level of evidence and no agent with a high level of recommendation in the medical treatment of PPI.

Conclusion

Duloxetine inhibits the reuptake of serotonin and noradrenaline in Onuf's nucleus. Pudental motor neurons are localized in Onuf's nucleus. These regulate the urethral striated muscles and the activity of these muscles increases after duloxetine use.

In our study, duloxetine treatment was initiated in patients after removal of the catheter. It was observed whether the 1-year period until return of normal continence could be shortened. Although the number of patients in our study group was low, according to our initial results, dryness with duloxetine + PFE treatment was usually provided in the 6th month. In the untreated group, continence was generally provided at the end of first year. Despite that patients discontinued the drug and left the pelvic exercise after provision of continence, maintenance of continence was provided. Further large-scale studies including more patients are required in this field.

References

1 Walsh PC: Anatomic radical retropubic prostatectomy; in Walsh PC, Retik AB, Vaughan ED, Wein AJ (eds): Campbell's Urology, ed 7. Philadelphia, WB Saunders, 1998, pp2565–2588.
2 Herr HW: Quality of life of incontinent men after radical prostatectomy. J Urol 1994; 151:652– 654.
3 Litwin MS, Hays RD, Fink A, Ganz PA, Leake B, Leach GE, Brook RH: Quality of life outcomes in men treated for localized prostate cancer. JAMA 1995;273:129–135.
4 Kao TC, Cruess DF, Garner D, Foley J, Seay T, Friedrichs P, Thrasher JB, Mooneyhan RD, McLeod DG, Moul JW: Multicenter patient self-reporting questionnaire on impotence, incontinence and stricture after radical prostatectomy. J Urol 2000;163:858–864.
5 Groutz A, Blaivas JG, Chaikin DC, Weiss JP, Verhaaren M: The pathophysiology of post-radical prostatectomy incontinence: a clinical and video urodynamic study. J Urol 2000;163:1767–1770.
6 Chao R, Mayo ME: Incontinence after radical prostatectomy: detrusor or sphincter causes. J Urol 1995;154:16–18.
7 Kielb SJ, Clemens JQ: Comprehensive urodynamics evaluation of 146 men with incontinence after radical prostatectomy. Urology 2005;66:392–396.
8 Leach GE, Trockman B, Wong A, Hamilton J, Haab F, Zimmern PE: Post-prostatectomy incontinence: urodynamic findings and treatment outcomes. J Urol 1996;155:1256–1259.
9 John H, Hauri D, Leuener M, Reinecke M, Maake C: Evidence of trigonal denervation and reinnervation after radical retropubic prostatectomy. J Urol 2001;165:111–113.
10 Patel-Gadhia R, Bhal K, Patil P: Retrospective audit on tolerability and efficacy of duloxetine for stress urinary incontinence. J Obstet Gynaecol 2011;31:258–259.
11 Basu M, Duckett JR: Update on duloxetine for the management of stress urinary incontinence. Clin Interv Aging 2009;4:25–30.
12 Groutz A, Blaivas JG, Chaikin DC, Weiss JP, Verhaaren M: The pathophysiology of post-radical prostatectomy incontinence: a clinical and video urodynamic study. J Urol 2000;163:1767–1770.
13 Ficazzola MA, Nitti VW: The etiology of post-radical prostatectomy incontinence and correlation of symptoms with urodynamic findings. J Urol 1998;160:1317–1320.
14 Mostwin JL: Urinary incontinence [editorial]. J Urol 1995;151:352–353.
15 Hellstrom P, Lukkarinen O, Kontturi M: Urodynamics in radical retropubic prostatectomy. Scand J Urol Nephrol 1989;23:21–24.
16 Foote J, Yun S, Leach GE: Post prostatectomy incontinence: Pathophysiology, evaluation and management. Urol Clin North Amer 1991;18:229–241.
17 Walsh PC, Partin AW, Epstein JI: Cancer control and quality of life following anatomical radical retropubic prostatectomy: results at 10 years. J Urol 1994;152:1831–1836.
18 Foley CL, Bott SR, Thomas K, Parkinson MC, Kirby RS: A large prostate at radical retropubic prostatectomy does not adversely affect cancer control, continence or potency rates. BJU Int 2003;92:370–374.
19 Eastham JA, Kattan MW, Rogers E, Goad JR, Ohori M, Boone TB, Scardino PT: Risk factors for urinary incontinence after radical prostatectomy. J Urol 1996;156:1707–1713.

20 Hsu EI, Hong EK, Lepor H: Influence of body weight and prostate volume on intraoperative, perioperative, and postoperative outcomes after radical retropubic prostatectomy. Urology 2003;61:601–606.
21 Steiner MS, Morton RA, Walsh PC: Impact of anatomical radical prostatectomy on urinary continence. J Urol 1991;145:512–514.
22 Catalona WJ, Basler JW: Return of erections and urinary continence following nerve sparing radical retropubic prostatectomy. J Urol 1993;150:905–907.
23 Burnett AL, Mostwin JL: In situ anatomical study of the male urethral sphincter complex: elevance to continence preservation following major pelvic surgery. J Urol 1998;160:1301–1306.
24 Hollabaugh RS, Dmochowski RR, Kneib TG, Steiner MS: Preservation of putative continence nerves during radical retropubic prostatectomy leads to kore rapid return of urinary incontinence. Urology 1998;51:960–967.
25 Wolin KY, Luly J, Sutcliffe S, Andriole GL, Kibel AS: Risk of urinary incontinence following prostatectomy: the role of physical activity and obesity. J Urol 2010;183:629–633.
26 Kegel AH: Physiologic therapy for urinary stress incontinence. J Am Med Assoc 1951;146:915–917.
27 Van Kampen M, De Weerdt W, Van Poppel H, De Ridder D, Feys H, Baert L: Effect of pelvic-floor re-education on duration and degree of incontinence after radical prostatectomy: a randomised controlled trial. Lancet 2000;355:98–102.
28 Franke JJ, Gilbert WB, Grier J, Koch MO, Shyr Y, Smith JA Jr: Early postprostatectomy pelvic floor biofeedback. J Urol 2000;163:191–193.
29 Filocamo MT, Li Marzi V, Del Popolo G, Cecconi F, Marzocco M, Tosta A, Nicita G: Effectiveness of early pelvic floor rehabilitation treatment for postprostatectomy incontinence. Eur Urol 2005;48:734–738.
30 Schlenker B, Gratzke C, Reich O, Schorsch I, Seitz M, Stief CG: Preliminary results on the off-label use of duloxetine for the treatment of stress incontinence after radical prostatectomy or cystectomy. Eur Urol 2006;49:1075–1078.
31 Zahariou A, Papaioannou P, Kalogirou G: Is HCl duloxetine effective in the management of urinary stress incontinence after radical prostatectomy? Urol Int 2006;77:9–12.
32 Schlenker B, Gratzke C, Reich O, Schorsch I, Seitz M, Stief CG: Preliminary results on the off-label use of duloxetine fort he treatment of stress incontinence after radical prostatectomy or cystectomy. Eur Urol 2006;49:1075–1078.
33 Filocamo MT, Li Marzi V, Del Popolo G, Cecconi F, Marzocco M, Tosto A, Nicita G: Pharmacologic treatment in post-prostatectomy stress urinary incontinence. Eur Urol 2007;51:1559–1564.
34 Collado Serra A, Rubio-Briones J, Puyol Payás M, Iborra Juan I, Ramón-Borja JC, Solsona Narbón E: Postprostatectomy established stress urinary incontinence treated with Duloxetine. Urology 2011;78: 261–266.
35 Chapple CR: Duloxetine for male stress incontinence. Eur Urol 2006;49:958–960.
36 Fink KG, Huber J, Würnschimmel E, Schmeller NT: The use of Duloxetine in the treatment of male stress urinary incontinence. Wien Med Wocheschr 2008;158:116–118.
37 Newman DK: Pelvic floor muscle rehabilitation using biofeedback. Urol Nurs 2014;34:193–202.