Evaluation of the Clinical Efficacy and Complications of Duloxetine in Comparison to Solifenacin in the Treatment of Overactive Bladder Disease in Women: A Randomized Clinical Trial

Mahboubeh Mirzaei, Azar Daneshpajooh, Seyed Omidreza Anvari*, Salar Dozchizadeh, Mohamad Teimourian

Purpose: SNRIs (serotonin and norepinephrine reuptake inhibitors) like duloxetine are known to have a role in the treatment of anxiety disorder and stress urinary incontinence. According to the correlation of anxiety disorder and overactive bladder, this study aimed to evaluate the clinical efficacy and complications of duloxetine (SNRI) as a medication in the treatment of overactive bladder in female patients. We were interested to know the probable therapeutic effect and side effects of duloxetine in overactive bladder.

Materials and Methods: In this single-blinded interventional randomized clinical trial, 60 female patients with idiopathic overactive bladder (hyperreflexia) referred to the urology clinic, were divided into two groups as pilots. The first group was treated by 10mg/daily solifenacin and the second group received 20mg/daily duloxetine. The patients were evaluated by the ICIQ-OAB Questionnaire before and after a one-month follow-up period. The intervention primary outcomes were evaluated by the patient's presentation of the frequency, nocturia, urgency, urge urinary incontinence and the drugs side effects as secondary outcomes were checked.

Results: Sixty women with confirmed overactive bladder disease were evaluated. Solifenacin and duloxetine had the same effect on the treatment of overactive bladder (p value = 0.148). The clinical symptoms were obviously relieved in both groups after treatment. Side effects were insignificantly more common in the solifenacin group (p value > 0.05). However, the different frequency of blurred vision in the two groups was statistically significant (p value = 0.04). The most common complication in the solifenacin and duloxetine groups was anxiety.

Conclusion: The results showed that solifenacin and duloxetine improved overactive bladder symptoms. According to this evaluation, duloxetine can be a suitable alternative option for overactive bladder treatment, due to the acceptable therapeutic effect and side effects.

Keywords: solifenacin; duloxetine; overactive bladder (OAB); stress urinary incontinence (SUI)

INTRODUCTION

The International Continence Society (ICS) defines the overactive bladder (OAB) as a "symptom syndrome suggestive of lower urinary tract dysfunction." The disease is defined as "Urinary urgency, usually accompanied by increased daytime frequency and/or nocturia, with urinary incontinence (OAB-wet) or without (OAB-dry), in the absence of urinary tract infection or other detectable disease. "[1] Therefore, the patient usually suffers from the excess need to urinate frequently throughout the day. The disease presentations include the urinary urgency (sudden and severe urge to urinate), frequent urination (more than 8 times in 24 hours), and urge urinary incontinence[2]. Urge urinary incontinence (UUI) is defined as sudden and involuntary urine leakage associated with urgency.[3] More than 40% of patients with OAB have urinary incontinence. Also, about 40-70% of urinary incontinence is caused by overactive bladder[4].

The main cause of bladder overactivity disorder is not known[5]. The disease can be idiopathic[6,7] or caused by involuntary contractions of the bladder wall muscles (hyperreflexia) or a major underlying disorder such as supraspinal neurologic disorders, spinal cord injury, stroke, Parkinson's disease, Alzheimer's disease, multiple sclerosis, neurologic trauma, diabetes, prolonged recurrent bladder infections, etc. Although, the loss of bladder wall muscles elasticity could be due to tuberculosis, bladder stones, bladder tumors, prior prostate surgery in men, and multiple pregnancies in women[8]. The interactions of neurological and muscular causes result to bladder function impairment, and the number of urinations increases without any voluntary control. Overactive bladder also can be associated with poor autonomic nervous system function. Excess release of acetylcholine at the level of epithelial cells or parasympathetic fibers of the bladder muscle layer or detrusor muscles is one of the mechanisms.[9]

Prior researches showed that the disease has a high prevalence in the world and is more common among women and the elderly[5,10]. Prevalence of the disease varies between different populations and depends on age, sex, race, and ethnic group[11]. Although the disease can affect anyone of any age, its prevalence increases with age[12]. People over the age of 65 are 39.9 percent more likely to get the disease. Postmenopausal women are also more likely to develop the disease due to the

Department of Urology, Shahid Bahonar Hospital, Kerman University of Medical Sciences, Kerman, Iran.
*Correspondence: Department of Urology, Shahid Bahonar Hospital, Kerman University of Medical Sciences, Kerman, Iran.
Tel: +989396317557. Email: Omidr.anvari@gmail.com
Received May 2020 & Accepted July 2021

Table 1. Determination and comparison of demographic variables in the two groups.

		Duloxetine Group. Mean	SD	Solifenacin Group. Mean	SD	*p*. value
Age		52.13	12.64	54.10	14.68	0.580
Weight		72.46	12.85	70.20	9.55 0.441	0.921
Number of Pregnancy		3.73	2.61	3.80	2.56	
		Prevalence	**%**	**Prevalence**	**%**	***p*. value**
Vaginal Atrophy	Yes	11	36.7	11	36.7	1
	No	19	63.3	19	63.3	

decreased estrogen level[13]. Milsom et al. showed that the prevalence of overactive bladder was 1.8-30.5% in Europe, 1.7-36.4% in the United States, and 1.5-15.2% in Asia[10]. Wein et al. estimated that at least 17 million Americans were affected by overactive bladder [2]. About 49 million in Europe and 33 million in the United States have symptoms of bladder overactivity. This ratio is higher than the prevalence of hypertension, asthma and diabetes[14].

Sometimes, the OAB disease severity disrupts the patient's individual life[15]. Untreated and frequent urination can affect physical, social and emotional health[2]. OAB affects daily activities such as traveling, physical activity, relationships, sexual function, and also the normal sleep[16]. Studies have shown that patients with overactive bladder have a lower quality of life. Urinary incontinence can lead to urinary tract infections, skin rashes, skin fragility, increased risk of hospitalization, embarrassment, mental distress, reduced social interactions, reduced quality of life, self-restriction, or avoidance of sexual activity[4]. As an example, the quality of life of patients with overactive bladder was lower than that of patients with diabetes in the social and functional areas[17].

The disease should not be mistaken for urinary tract infections due to the symptoms overlap[5,15]. The volume of urine is relatively small each time urinating. Pain during urination indicates that there is a problem other than overactive bladder[5].

The predisposing factors are perineal muscle weakness in women and BPH in men, along with other underlying and chronic disorders in the elderly[18].

Primary treatment options include medication, behavioral therapy, or a combination. In very rare cases, where patients do not respond to primary treatment, surgery such as detrusor myectomy, augmentation enterocystoplasty with continent urinary diversion is recommended[5]. Anticholinergic drugs, tricyclic antidepressants (TCAs), and calcium channel blockers (CCBs) are among the main drugs used[19].

Unfortunately, many people do not seek medical treatment, because they mistakenly believe that bladder control problems are an inevitable part of old age and that there is no cure for it, or that they are embarrassed to talk to the doctors and other health care providers about their problems[2]. Due to the attribution of its symptoms to the other diseases, only a few will benefit from appropriate treatment. They experience a sense of embarrassment and fear of being in a social environment, that isolates them from the workplace and society, ultimately leading to depression. The correlation between obsessive-compulsive symptoms and the OAB has been evidenced in the literature.[20] In our research, we proposed to try the drug, duloxetine to treat the OAB, to compare it with the standard treatment, and to evaluate the side effects, according to the correlation of the OAB and obsessive-compulsive disorder. Since duloxetine is known to have a therapeutic role in the treatment of anxiety disorders and stress or mixed urinary incontinence in adults, we were interested to know the probable therapeutic effect and side effects in OAB. If the drug proves to be effective, it could be used as a single medication in mixed urinary incontinence, instead of combination treatment with anticholinergics in these patients. There is no prior literature in this regard.

Patients and Methods

This research was a single-blinded randomized clinical trial study. This clinical trial was approved in the clinical ethics committee of Kerman university of medical sciences. (code: IR.KMU.AH.REC.1398.099) Iran clinical trial registration center approved the clinical trial. (Code: IRCT20191010045047N1) The study population was the women referred to the urology clinic in Kerman in 2018 who had bothersome urgency with or without other irritative urinary tract symptoms. We decided to evaluate 30 patients in each group as pilots. The patients under 18 years of age, the ones with known urinary tract infection, bladder stones, positive history

Table 2. Determination and comparison of the frequency of complications in the two groups.

Side-effect		Duloxetine Group. Prevalence	%	Solifenacin Group. Prevalence	%	*p*. value
Dry Mouth	Yes	8	26.7	10	33.3	0.389
	No	22	73.3	20	66.7	
Constipation	Yes	10	33.3	10	33.3	1
	No	20	66.7	20	66.7	
Blurred vision	Yes	2	6.7	9	30	0.042
	No	28	93.3	21	70	
Anorexia	Yes	5	16.7	6	20	1
	No	25	83.3	24	80	
Sleep disturbances	Yea	5	16.7	11	36.7	0.143
	No	25	83.3	19	63.3	
Anxiety	Yes	11	36.7	17	56.7	0.195
	No	19	63.3	13	43.3	

Table 3. The average ICIQ-OAB questionnaire in the two groups.

	Duloxetine Group.		Solifenacin Group.		*p*. value
	Mean	SD	Mean	SD	
Before Treatment	13.90	3.19	14.86	2.89	0.225
After Treatment	8.76	2.14	9.66	2.59	0.148
p. value	< 0.001		< 0.001		

of urogynecological malignancy, Obesity (BMI>40), high grade cystocele and rectocele (more than 2 according to the pelvic organ prolapse quantification system (POP-Q)), residue of urine>100cc and or maximum flow rates of lower than 15ml/s, pregnant, suffering from underlying neurologic disorder such as spinal cord injury, stroke, Parkinson's disease, Alzheimer's disease, multiple sclerosis, neurologic trauma, and diabetes were excluded from the evaluation. After obtaining written ethical consent, patients were randomly divided into two groups using the random allocation software. Patients were allowed to use other treatments through the follow-up period.

The research was single blinded. As the 10 mg dosage for solifenacin had better clinical efficacy in prior researches, group 1 received the anticholinergic solifenacin 10mg/daily and group 2 received SNRI duloxetine 20mg/daily without knowing the drugs name and characteristics. These patients were followed up for one month and then the ICIQ-OAB Questionnaire was filled out to compare the drug's effectiveness after the intervention. The intervention outcomes were evaluated by the patient's presentation of the frequency, nocturia, urgency, urge urinary incontinence, and the drugs side effects. A clinical interview was conducted by a psychologist to assess the psychologic side effects, based on the criteria in the reference of diagnostic & statistical manual of mental disorders.

After collecting the questionnaires, the data were statistically analyzed by SPSS statistical software version 20 using bivariate analysis between the two groups. To provide descriptive results, frequency index, relative frequency and central mean index, statistical chi-square test and statistical regression test were used. Patients' enrollment algorithm is shown in **Figure 1**. (CONSORT flow diagram)

RESULTS

130 patients with urinary urgency were referred, in which, 60 patients met the criteria for evaluation after the exclusion criteria review, urine analysis, and uroflowmetry. Two groups of thirty patients were evaluated in this study (**Figure 1**). The mean age was insignificantly higher in the solifenacin group (54.10 years) compared to the duloxetine group (52.13 years) (*p* value=0.580). The two groups were completely identical in

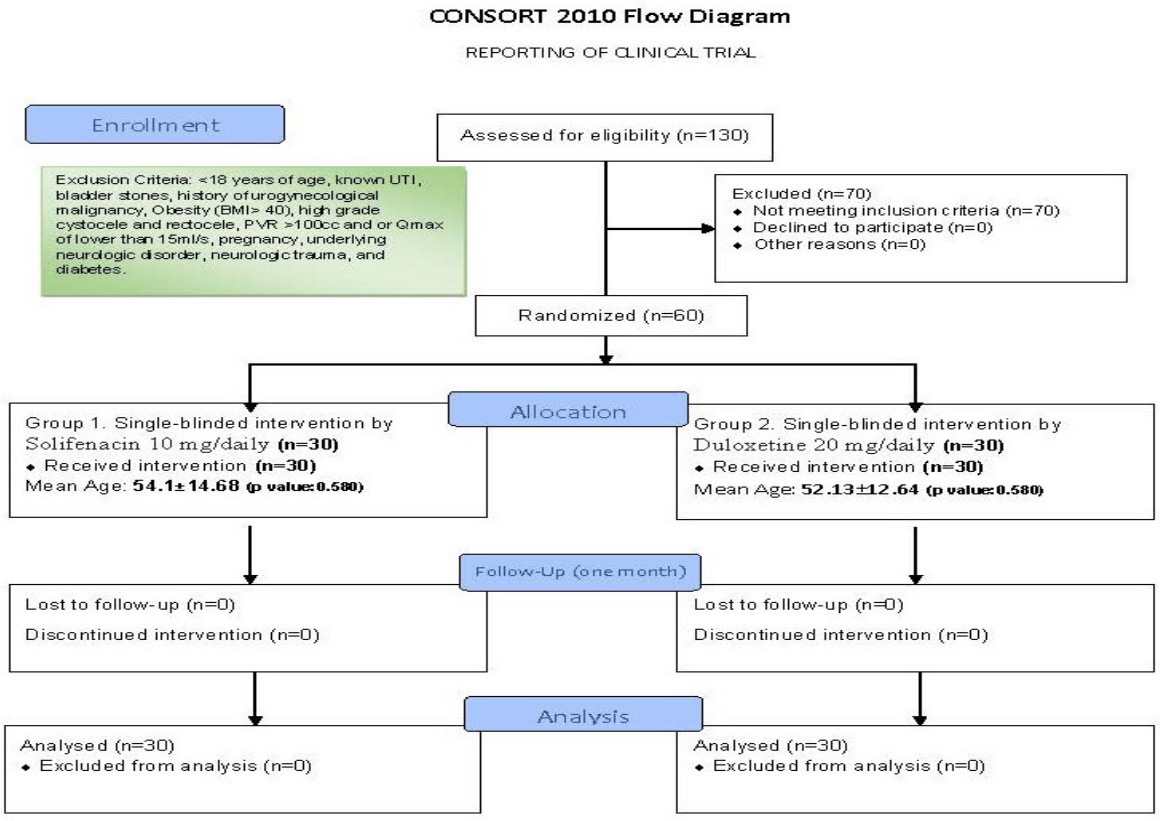

Figure 1. CONSORT Reporting Diagram of the clinical trial.

terms of demographic variables. Eleven patients in the duloxetine group and Eleven patients in the solifenacin group had concomitant atrophic vaginitis, who were treated with topical estrogen at the same time (**Table 1**). The clinical disorders like frequency, nocturia, urgency and urge urinary incontinence were obviously relieved in both groups after treatment. The mean of questionnaire score in the solifenacin group was 14.86 before the intervention and 9.66 after the treatment, respectively. These scores were 13.90 and 8.76 in the duloxetine group. This difference was not statistically significant (p value = 0.148). The scores in both groups decreased after the intervention. This difference was statistically significant (p value < 0.01) (**Table 3**). The prevalence of complications like dry mouth, blurred vision, anorexia, sleep disturbance, and anxiety was higher in the solifenacin group than in the duloxetine group. But, only the frequency of blurred vision was statistically significant (p value = 0.042). Gastrointestinal side effects were equal in both groups (**Table 2**).

DISCUSSION

Our results showed that SNRI, duloxetine relieved the overactive bladder symptoms. According to this evaluation, duloxetine may be a suitable alternative option for overactive bladder treatment, due to the acceptable therapeutic effect and side effects.

Overactive bladder disease is one of the main causes of medical expenses for the patient and the health care systems in the world. Early diagnosis and treatment of the disease will play a better and more effective role in the patient care and cost reduction.

The exact disease diagnosis includes the patient history, physical examination, and laboratory tests to rule out the differential diagnoses. Diagnostic cystoscopy, urine cytology, and diagnostic ultrasound of the kidneys and bladder are not recommended in the early stages of disease diagnosis[5]. Urodynamic test purpose is to distinguish between different types of incontinency; therefore, it is the most effective diagnostic method[21]. Many patients who suffer from bladder overactivity need long-term treatment to relieve the symptoms [12]. Different treatments can be used, depending on the patient's condition and the physician's decision, to improve the quality of life. But specific treatment for the disease is not always necessary[5]. The pelvic floor muscle exercises, bladder training, and other behavioral therapies are sometimes recommended[5,15]. The bladder training teaches the patient how to resist the urge to urinate. In some cases, the patient must have a plan to empty the bladder. Weight loss for overweight patients, reducing caffeine consumption (tea and coffee), and balancing fluid intake can also be beneficial[5, 22]. Decreased sensitivity of the bladder nerve fibers by the use of capsaicin or the use of Botox, potassium channel blockers, beta-adrenergic agonists, muscle relaxants, and neurotransmitter blockers are also used to treat overactive bladder[23,24].

As said, primary treatment options include medication, behavioral therapy, or a combination[5]. There are very effective medications for treating overactive bladder which can help the patient return to normal life. However, no drug is as beneficial to lifestyle changes as it is for elder patients[5,22]. Anticholinergic drugs are the mainstay and the first line treatment medications, including Trospium, Fesoterodine, Solifenacin, Darifenacin, Oxybutynin, Tolterodine, and Hyoscyamine[25]. These drugs reduce the range of bladder contractions and voluntary contractions. The common side effects include confusion, dry mouth, constipation, prolonged QT interval, hypotension in the elderly, and papillary dilatation.

These drugs should not be used if the patient has closed-angle glaucoma and myasthenia gravis[26]. Solifenacin, a specific muscarinic receptor antagonist (M3) has a high selectivity for the urinary and bladder secretory glands. The drug reduces the elasticity of bladder smooth muscle and allows more urine to be retained in the bladder. Solifenacin is administered orally at 5 and 10 mg. doses, and the full therapeutic effects will be seen 2-4 weeks after treatment. Solifenacin is not recommended in people with severe renal or liver failure. Dry mouth is one of the most common side effects of solifenacin[27].

Another class of drugs is SNRIs (serotonin and norepinephrine reuptake inhibitors), including Duloxetine (Cymbalta)، Desvenlafaxine (Pristiq)، Tofenacin (Elamol, Tofacine) ، Milnacipran (Ixel, Savella) ، Levomilnacipran (Fetzima), and Venlafaxine (Effexor). The side effects are sexual dysfunction, generalized anxiety disorder, dyspepsia and panic attacks (28, 29). Duloxetine has been used to treat severe depressive disorders and generalized anxiety disorder in adults and to control diabetic neuropathic pain. It significantly increases the capacity of the sphincter muscle in the phase of urinary filling and storage. Therefore, it is known to have a therapeutic role in the treatment of anxiety disorders and stress or mixed urinary incontinence in adults. In a study of 306 women with OAB, by Steers. et al., it was found that the group receiving duloxetine had a significant improvement over the group receiving placebo. The most common adverse events with duloxetine (nausea, 31%; dry mouth, 16%; dizziness, 14%; constipation, 14%; insomnia, 13%; and fatigue, 11%) were the same as those reported by women with SUI and were significantly more common with duloxetine than placebo.[30]

Wang et al. evaluated the condition of a 17-year-old female suffering from OAB for 2 years. The results showed that duloxetine improved the bladder capacity and decreased urinary frequency[31]. Ghanbari et al. examined the efficacy and side effects of oxybutynin and tolterodine in the treatment of overactive bladder. The results showed that both oxybutynin and tolterodine improved the patient's quality of life. In that study, the effectiveness of these two drugs did not differ significantly[32]. Basu and Duckett examined the condition of a 47-year-old patient with urinary incontinence. The results showed that treatment of this patient with duloxetine was successful[33].

According to the prior researches, there are various treatments for OAB. The 10 mg dosage for solifenacin had better clinical efficacy at 12 weeks. Although the 5mg is starting dose.[34] As the results of our study showed, patients with OAB treated with duloxetine had side effects including dry mouth (26.7%), blurred vision (7.6%), anorexia (16.7%), sleep disturbance (16.7%), anxiety (7.36%) and constipation (33.3%). These results showed the duloxetine same efficacy and adverse effects of the Steers., et al. research with a little more incidence.[30] These side effects have also been reported in people treated with solifenacin. However, the

10md/daily solifenacin may have more side effects than the 5mg/daily dosage. The most common complication in both groups was anxiety. This research compared the medication duloxetine with the standard treatment, solifenacin in OAB. However, prior researches did not compare the two treatments and the efficacy was compared with the placebo. Our follow-up period was one month, that was less than some prior researches. Since the aim of this study was to replace duloxetine, alone as the first line of treatment, instead of combination therapy of duloxetine and anticholinergics in patients with mixed urinary incontinence, the follow-up time for the evaluation of the effects of duloxetine on OAB was considered as one month. However, longer follow-up periods may present more drug's efficacy and also side effects. The results of the study of solifenacin and duloxetine in the treatment of OAB in women referring to urology clinic in Kerman in 2018 showed that the clinical efficacy of these two drugs was the same and no preference was observed between the two drugs. Since, both can be suitable options in the treatment of OAB. Future researches with larger populations are needed to confirm the clinical efficacy of duloxetine to be used.

CONCLUSIONS

Our results showed that solifenacin and duloxetine relieved the overactive bladder symptoms. According to this evaluation, duloxetine can be a suitable alternative option for overactive bladder treatment, due to the acceptable therapeutic effect and side effects. We recommend to try other SNRIs for the OAB treatment to figure out the efficacy and complications in the future research.

ACKNOWLEDGMENTS

The clinical trial was approved in the clinical research center of Kerman university of medical sciences. We appreciate all the people who contribute in the preparation and fulfillment of this evaluation.

CONFLICT OF INTEREST

None declared by the authors.

REFERENCES

1. Haylen BT, de Ridder D, Freeman RM, Swift SE, Berghmans B, Lee J, et al. An International Urogynecological Association (IUGA)/ International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. Int Urogynecol J. 2010;21:5-26.
2. Wein AJ, Rovner ES. The overactive bladder: an overview for primary care health providers. Int J Fertil Womens Med. 1999;44:56-66.
3. Demaagd GA, Davenport TC. Management of urinary incontinence. P & T : a peer-reviewed journal for formulary management. 2012;37:345-61H.
4. Gibbs CF, Johnson TM, 2nd, Ouslander JG. Office management of geriatric urinary incontinence. Am J Med. 2007;120:211-20.
5. Gormley EA, Lightner DJ, Burgio KL, Chai TC, Clemens JQ, Culkin DJ, et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline. J Urol. 2012;188:2455-63.
6. Yarker YE, Goa KL, Fitton A. Oxybutynin. A review of its pharmacodynamic and pharmacokinetic properties, and its therapeutic use in detrusor instability. Drugs Aging. 1995;6:243-62.
7. Hebjørn S, Andersen JT, Walter S, Mouritzen Dam A. Detrusor Hyperreflexia. Scand J Urol Nephrol. 1976;10:103-9.
8. Liu HT, Jiang YH, Kuo HC. Increased serum adipokines implicate chronic inflammation in the pathogenesis of overactive bladder syndrome refractory to antimuscarinic therapy. PLoS One. 2013;8:e76706.
9. Torimoto K, Matsumoto Y, Gotoh D, Morizawa Y, Miyake M, Samma S, et al. Overactive bladder induces transient hypertension. BMC Res Notes. 2018;11:196-.
10. Milsom I, Coyne KS, Nicholson S, Kvasz M, Chen CI, Wein AJ. Global prevalence and economic burden of urgency urinary incontinence: a systematic review. Eur Urol. 2014;65:79-95.
11. Coyne KS, Sexton CC, Bell JA, Thompson CL, Dmochowski R, Bavendam T, et al. The prevalence of lower urinary tract symptoms (LUTS) and overactive bladder (OAB) by racial/ethnic group and age: Results from OAB-POLL. Neurourol Urodyn. 2013;32:230-7.
12. Milsom I, Stewart W, Thüroff J. The prevalence of overactive bladder. Am J Manag Care. 2000;6:S565-73.
13. Robinson D, Cardozo L, Milsom I, Pons ME, Kirby M, Koelbl H, et al. Oestrogens and overactive bladder. Neurourol Urodyn. 2014;33:1086-91.
14. Stewart WF, Van Rooyen JB, Cundiff GW, Abrams P, Herzog AR, Corey R, et al. Prevalence and burden of overactive bladder in the United States. World J Urol. 2003;20:327-36.
15. Gormley EA, Lightner DJ, Faraday M, Vasavada SP. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline amendment. J Urol. 2015;193:1572-80.
16. Abrams P, Kelleher CJ, Kerr LA, Rogers RG. Overactive bladder significantly affects quality of life. Am J Manag Care. 2000;6:S580-90.
17. Komaroff AL, Fagioli LR, Doolittle TH, Gandek B, Gleit MA, Guerriero RT, et al. Health status in patients with chronic fatigue syndrome and in general population and disease comparison groups. Am J Med. 1996;101:281-90.
18. Bear M, Dwyer JW, Benveneste D, Jett K, Dougherty M. Home-based management of urinary incontinence: a pilot study with both frail and independent elders. J Wound Ostomy Continence Nurs. 1997;24:163-71.
19. Ouslander JG. Management of overactive bladder. N Engl J Med. 2004;350:786-99.
20. Ahn K-S, Hong H-P, Kweon H-J, Ahn A-L, Oh E-J, Choi J-K, et al. Correlation between Overactive Bladder Syndrome and Obsessive

Compulsive Disorder in Women. Korean journal of family medicine. 2016;37:25-30.
21. Arnold J, McLeod N, Thani-Gasalam R, Rashid P. Overactive bladder syndrome - management and treatment options. Aust Fam Physician. 2012;41:878-83.
22. Ruxton K, Woodman RJ, Mangoni AA. Drugs with anticholinergic effects and cognitive impairment, falls and all-cause mortality in older adults: A systematic review and meta-analysis. Br J Clin Pharmacol. 2015;80:209-20.
23. Babu R, Vaidyanathan S, Sankaranarayan A, Indudhara R. Effect of intravesical instillation of varying doses of verapamil (20 mg, 40 mg, 80 mg) upon urinary bladder function in chronic traumatic paraplegics with overactive detrusor function. Int J Clin Pharmacol Ther Toxicol. 1990;28:350-4.
24. Liu H, Liu P, Mao G, Chen G, Wang B, Qin X, et al. Efficacy of combined amlodipine/terazosin therapy in male hypertensive patients with lower urinary tract symptoms: a randomized, double-blind clinical trial. Urology. 2009;74:130-6.
25. Sussman DO. Overactive Bladder: Treatment Options in Primary Care Medicine. The Journal of the American Osteopathic Association. 2007;107:379-85.
26. Staskin DR. Overactive bladder in the elderly: a guide to pharmacological management. Drugs Aging. 2005;22:1013-28.
27. Luo D, Liu L, Han P, Wei Q, Shen H. Solifenacin for overactive bladder: a systematic review and meta-analysis. Int Urogynecol J. 2012;23:983-91.
28. Medarov BI, Chaudhry H, Sun JH, Rane N, Judson MA. Effect of SSRIs and SNRIs on Nocturnal Urinary Frequency. Ann Pharmacother. 2016;50:471-4.
29. Stahl SM, Grady MM, Moret C, Briley M. SNRIs: their pharmacology, clinical efficacy, and tolerability in comparison with other classes of antidepressants. CNS Spectr. 2005;10:732-47.
30. Steers WD, Herschorn S, Kreder KJ, Moore K, Strohbehn K, Yalcin I, et al. Duloxetine compared with placebo for treating women with symptoms of overactive bladder. BJU Int. 2007;100:337-45.
31. Wang S-M, Lee H-K, Kweon Y-S, Lee CT, Lee K-U. Overactive Bladder Successfully Treated with Duloxetine in a Female Adolescent. Clinical psychopharmacology and neuroscience : the official scientific journal of the Korean College of Neuropsychopharmacology. 2015;13:212-4.
32. Ghanbari Z, Esmaeili M, Eftekhar T, Esmaeili M, Miri E. COMPARISON OF EFFICACY AND SIDE-EFFECTS OF OXYBUTYNIN AND TOLTERODINE IN THE TREATMENT OF OVERACTIVE BLADDER. TEHRAN UNIVERSITY MEDICAL JOURNAL (TUMJ). 2011;69:302-8.
33. Basu M, Duckett JR. Detrusor overactivity successfully treated with duloxetine. J Obstet Gynaecol. 2007;27:438-40.
34. Madhuvrata P, Cody JD, Ellis G, Herbison GP, Hay-Smith EJ. Which anticholinergic drug for overactive bladder symptoms in adults. Cochrane Database Syst Rev. 2012;1:Cd005429.