

Comparing the Effect of Tolterodine, Biofeedback (Pelvic Floor Muscles Training) and Drug plus Biofeedback on Quality of Life and Urge Urinary Incontinency in Patients Referred to Imam Khomeini Hospital in 2014

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Abstract

Background: Urgency is a characteristic for overactive bladder and is defined by a sudden obligatory need for urination, a feeling that can be hardly stopped. Many methods such as drug therapy and feedback have been used to treat urinary incontinency.

Objectives: The aim of this study was to assess and compare the effect of medication, biofeedback or biofeedback plus medication on urge- urinary incontinency and quality of life of patients.

Methods: This was a case-control randomized clinical trial performed on patients referred to Imam Khomeini hospital in 2014. Patients were divided into three groups of drug (Tolterodine), biofeedback, and biofeedback plus drug. Biofeedback group underwent two sessions of treatment weekly for four weeks, and the drug group received tolterodine (4 mg slow release) for four weeks. The third group received both of them. Quality of life and urinary incontinency symptoms were compared between the three groups and analyzed, using SPSS Version 16 software (IBM, Armonk, USA).

Results: Meaningful differences were observed between the three groups with respect to change in the total score of the questionnaire ($P < 0.001$). Between the groups, drug therapy had the most effect on improving the total score of the questionnaire, with a mean change of 25.44 ± 1.80 . No meaningful difference was observed between drug plus biofeedback and biofeedback group ($P = 0.114$). By comparing the mean incontinency score, we found a meaningful difference between the drug and biofeedback groups and the biofeedback and biofeedback plus drug groups ($P < 0.001$ and $P < 0.002$, respectively); however, no meaningful difference was found between the biofeedback plus drug group and the drug group in mean incontinency score ($P = 0.187$).

Conclusions: Our study results revealed that tolterodine and biofeedback both increased quality of life indices and decreased the severity of urinary incontinency significantly in our participants. However, drug plus biofeedback treatment improved the severity and quality of urinary incontinency, but did not improve quality of life of the patients. Therefore, physicians should consider improving the quality of life of patients as well.

Keywords: Tolterodine, Urinary Incontinency, Biofeedback

1. Background

Urgency is a characteristic for overactive bladder and is defined by sudden obligatory need for urination, a feeling that can be hardly stopped. Urge incontinency is one of the most prevalent types of inconsistency. Overactive bladder has been defined by the International Continence Society (ICS), with the following signs and symptoms: Urgency in urination with or without urge- urinary incontinency (UUI), which is usually accompanied with frequency and nocturia in absence of infection or any pathologic con-

dition, suggesting detrusor over-activity. Frequency is defined as eight times or more urination in 24 hours; also, nocturia is a need for urination more than one time during the night (1).

Urge incontinency has been shown to affect patients' quality of life to a large extent. Urge- incontinency can be due to detrusor myopathy, neuropathy or a combination of both. Idiopathic incontinency has no obvious cause. Laboratory investigations on the bladder muscles of patients with bladder over-activity have shown an increase in electrical stimulation response and an increased sensi-

tivity to stimulation with acetylcholine (2). Partial disruption of cholinergic nerves may justify some of the findings, which is the most acceptable mechanism of new onset detrusor over-activity following hysterectomy or other pelvic surgeries. Mills et al. compared electromyogram and some other variables of patients with detrusor over-activity and those without any urological disorders, and found the following results: Partial cut of detrusor nerve with some intact nerve areas and areas of decreased innervation by staining nerve fibers specific for acetylcholine esterase; decreased contractive response to electrical stimulants; over-sensitivity to potassium and diversity in electromyogram activity of the bladder (2).

Some central nerve system complications may also cause bladder over activity such as multiple sclerosis, Parkinson's disease, spinal cord injuries, dementia, diabetic neuropathy etc. (3). Moreover, detrusor over activity can occur without any neurologic cause. Bladder contractions can be spontaneous or due to rapid filling of bladder, postural changes or even walking and coughing. Some other conditions include urinary tract infection, bladder cancer, bladder stone, bladder inflammation, bladder outlet obstruction and some drugs such as diuretics and bethanechol (3, 4). Usually, there is no obvious reason for detrusor over activity (5, 6).

Risk factors of detrusor over- activity are white ethnicity, patients with diabetes Type 1, and patients with depression, those older than 75 years, patients with arthritis, those who consume oral hormonal replacement therapy and those with high body mass index (7).

Diagnosis of detrusor over- activity is based on clinical signs and symptoms. American Urologic Association (AUA) has suggested assessing underlying disorders that affect bladder function such as neurological diseases, diabetes mellitus, gross hematuria, previous pelvic or vaginal surgeries, pelvic cancers and radiation to pelvis and pelvic organs prolapse in women (8).

Bladder over-activity can be treated by some techniques (9-13). Any specific known cause should be treated first. For instance, urinary tract infection should be managed by appropriate antibiotics, and atrophic urethritis should be managed by vaginal estrogen ointment.

The management protocol of overactive bladder by the Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU) is as follows (14, 15):

First line treatment includes behavioral treatments and education. Antimuscarinic treatment together with behavioral management can be helpful. Second line treatment is antimuscarinic agents; slow release medications should be used instead of rapid release. Transdermal oxybutynin can be effective clinically. Third line treatment includes sacral neuromodulation or peripheral tib-

ial nerve stimulation (PTNS) for selective patients with resistant signs and symptoms. Moreover, injection of onabotulinumtoxinA into detrusor is another modality. Selection of a specific modality is based on the severity of signs and symptoms, and the resulted complications affect the patients' quality of life (16). The three main treatment modalities are drug therapy, behavioral therapy, and surgery (17).

Different medications used include anticholinergic agents such as tolterodine, trospium chloride (Sanctura) (18, 19), propiverine hydrochloride, solifenacin (Vesicare), Darifenacin (Enablex), oxybutynin patch (Oxytrol) and fesoteridone (Toviaz) beta-2 agonists, botulinum, tricyclic antidepressants (TCA), capsaicin and some others (18-24).

Oxybutynin (Ditropan) and tolterodine (Detrol) are two commonly used anticholinergic drugs for treating overactive bladder, with good and documented effects (25). However, they may cause xerostomia in many patients. Tolterodine can be substituted with less effect on saliva secretion and good response (26, 27).

Pelvic floor muscle training (PFMT) includes special exercises for increasing the function of pelvic muscles. It is considered as programs of repetitive and voluntary contractions of pelvic muscles, trained by a specialist. To be effective, PFM should be repeated 30 - 80 times a day (28).

Biofeedback is a rehabilitative program in which some electrodes are placed on patients' abdomen and anal area. It helps patients to control muscle normal physiological reactions that lead to inconsistency.

Finally, augmentation cystoplasty is rarely used for idiopathic overactive bladder. In this method, a part of intestine is excised and used as part of bladder.

2. Objectives

The aim of this study was to assess and compare the effect of medication, biofeedback, and biofeedback plus medication on urinary incontinency and quality of life of patients.

3. Methods

This was a case-control randomized clinical trial performed on patients referred to Imam Khomeini hospital. Patients were divided into three groups of drug (Tolterodine), biofeedback and biofeedback plus drug. The biofeedback group underwent two sessions of treatment weekly for four weeks, the drug group received tolterodine (4 mg slow release) for four weeks, and the third group received both of them. All participants filled the quality of life questionnaire and urination timetable at initiation

and four weeks later. Inclusion criteria were as follows: Patients aged 18 to 75 years with urgent incontinency, who referred to the gynecology clinic of Imam Khomeini hospital, not receiving any treatment before enrollment, not having any chronic systematic diseases such as diabetes, chronic kidney diseases, cancer etc. and living in Tehran and the ability to refer for follow-up sessions. Exclusion criteria were stress incontinency, urgent incontinency fewer than three times a day, receiving diuretics or alpha blockers, history of pelvic surgery, acute urinary tract infection, age below 18 years and more than 75, having chronic diseases such as MS (Multiple sclerosis), CHF (Congestive heart failure), DM (Diabetes mellitus), COPD (Chronic obstructive pulmonary disease), dementia and etc., fecal inconsistency and smoking. Sample size was calculated based on Kafri et al. (29) as 54 patients for each group.

The quality of life questionnaire has 24 items in four categories of physical health domain, psychological domain, social relationship domain, and environmental domain; it is filled by self-report method. The study was approved by the institutional ethical review board at Tehran University of Medical Sciences, Tehran, Iran (1395 - 326). A written informed consent was obtained from all patients before enrollment, and they were assured of the confidentiality of their responses. Finally, data were analyzed, using SPSS software, version 16 (IBM, Armonk, NY, USA), using qualitative and quantitative measures. P-value less than 0.05 was considered statistically significant in all analyses.

4. Results

This study was performed on 154 patients with urinary inconsistency in three groups of tolterodine, biofeedback, and biofeedback plus drug. All patients were female, with the mean age of 45.25 ± 13.30 years. Most patients had elementary school education. No significant difference was observed between the three groups with respect to age, education level, and immigration, history of physical or mental disease or history of drug use, which shows acceptable randomization between the three groups. Patients' characteristics are summarized in Table 1.

Kolmogorov-Smirnov (KS) test was used to assess normal distribution of data, and all data had normal distribution. In biofeedback group, the total score of the questionnaire before the intervention was 74.71 ± 15.01 , which increased to 79.71 ± 13.19 ; this increase was statistically meaningful ($P < 0.001$). However, in tolterodine group, there was a significant increase in the total score of the questionnaire (73.03 ± 2.95 before the intervention to 98.48 ± 2.61 , $P < 0.001$). In biofeedback + drug group, the total score was not significantly increased (72.71 ± 17.51 before the intervention to 74.58 ± 13.99 , $P = 0.228$).

The mean incontinency severity was scored from 0 to 10. In biofeedback group, the mean scores before and after the intervention were 7.06 ± 2.17 and 3.22 ± 2.30 , respectively, showing a significant decrease ($P < 0.001$). In tolterodine group, it decreased from 6.06 ± 1.47 to 4.2 ± 1.17 , which was statistically significant ($P < 0.001$). In drug plus biofeedback, the mean score decreased from 7 ± 2.17 to 4.48 ± 2.82 , which was statistically significant ($P < 0.001$).

A significant difference was detected between the three groups in the questionnaire's total score ($P < 0.001$). Between the groups, the drug therapy group had the most effect on improving the total score of the questionnaire with the mean change of 25.44 ± 1.80 . However, no significant difference was found between the drug plus biofeedback and biofeedback groups ($P = 0.114$).

By comparing the mean of the incontinency score, we found a significant difference between the drug and biofeedback groups, and biofeedback and biofeedback plus drug groups ($P < 0.001$, and $P < 0.002$, respectively); however, we found no significant difference between the biofeedback plus drug and drug alone group in mean incontinency score ($P = 0.187$).

However, no meaningful association was found between age ($P = 0.081$), educational level ($P = 0.581$), patient or her family immigration ($P = 0.873$), history of physical or mental disease ($P = 0.264$) and drug history ($P = 0.862$) with quality of life score.

5. Discussion and Conclusion

Our study results revealed that tolterodine and biofeedback both increased quality of life indices, severity, and quality of urinary incontinency significantly in our participants. However, drug plus biofeedback treatment improved severity and quality of urinary incontinency, but it did not improve quality of life of the patients. Therefore, physicians should consider improving the quality of life of patients as well. Ghanbari et al. approved the effect of tolterodine and oxybutynin on severity of urinary incontinency and overactive bladder (30).

Kashanian et al. assessed the effect of pelvic floor muscles exercises by patient herself and exercises with pelvic floor muscles training device. They showed that both methods improved patients' quality of life and severity of urinary incontinency; this was in accordance with our study showing the effect of non-drug treatments (31).

Two studies were performed by Wang et al. to assess pelvic floor training exercises and biofeedback and compare it with invasive electrical stimulation of pelvic floor muscles. They found that non-invasive methods had equal effects on urinary incontinency with invasive electrical

Table 1. Patients Characteristics in the Three Groups^a

	Biofeedback Group	Tolterodine Group	Biofeedback + Drug Group	P-Value
Age	45.64 ± 12.92	47.82 ± 12.23	42.24 ± 14.28	0.443
Education level				0.104
Illiterate	12 (24)	8 (16)	7 (14)	
Elementary school	16 (32)	8 (16)	12 (24)	
Guidance school	9 (18)	12 (24)	6 (12)	
Diploma	6 (12)	14 (28)	10 (20)	
Bachelor	0	6 (12)	9 (18)	
Master	5 (10)	1 (2)	3 (6)	
Doctorate	1 (2)	0	1 (2)	
Student	1 (2)	1 (2)	2 (4)	
History of physical or mental disease	21 (42)	20 (40)	15 (30)	0.413
History of drug use	20 (40)	14 (28)	14 (28)	0.332

^aValues are expressed as mean ± SD or No. (%).

stimulation method (32, 33). Kafri et al. investigated the effect of drug therapy and different techniques of training pelvic floor muscles on 184 patients with urinary incontinence. They found that the effect was most achieved after three and 12 months (29). In addition, in our study, a positive effect was shown for pelvic floor training exercises.

Furthermore, Hirakawa et al. compared the effect of pelvic floor muscle training with or without biofeedback on stress urinary incontinence in quality of life. Their results showed the effect of PFMT on stress urinary incontinence (SUI) (34). However, biofeedback alone was effective on reducing signs and symptoms and improving quality of life, similar to our study.

Our results revealed that tolterodine was the best modality on urinary incontinence by improving scores of all the indices and mentioned variables in this study. After that, biofeedback had a positive effect on quality of life indices and urinary incontinence symptoms. Adding biofeedback to drug therapy improved disease symptoms relatively, but did not improve quality of life of the patients. However, biofeedback exerts its most effect in long-term and our study follow-up was short. Short-term follow-up may not show the effect of biofeedback and it was one of our limitations. However, these methods are cost-effective and reduce the need for medications used for urinary incontinence.

Our study had other limitations. Following-up patients was difficult and some patients did not refer to the hospital despite explanations about the necessity of follow-up visits. However, collecting sample size a long time for us. Therefore, it is suggested to conduct further studies with

larger sample size and longer follow-up time and assess the cost-effectiveness of non-drug therapies on urinary incontinence.

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Footnotes

Authors' Contribution: All authors participated equally in all the steps of the study.

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Conflicts of Interest: There was no conflict of interest to be reported.

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