Oxybutynin and Tolterodine in a Trial for Treatment of Overactive Bladder in Iranian Women

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Abstract

Objective: To evaluate the efficacy and side effects of Oxybutinin in comparison to tolterodine in treatment of overactive bladder (OAB) with detrussor overactivity (DOA) in Iranian women.

Materials and methods: One hundred Iranian old women with clinical symptoms of OAB who show IDO in the filling cystometry participated in this randomized double-blinded parallel-group by using two kinds of the drugs for 4- week course (2 mg tolterodine twice-daily, or oxybutinin 5 mg, three times a day) in alike packages. We collected data from 3-day FVC before and after the treatment course. The effectiveness of each drug was studied using the paired t-test and improvement after treatment between two groups was compared by independent T-test.

Results: Positive changes in urinary urgency, Frequency and Urge incontinence after treatment in both groups were seen but mean improvements in the all were larger in the patients who treated by oxybutinin especially in terms of urgency and Urge incontinence . Dry mouth was the most common side-effect in two groups. Unlike other studies it was higher in the tolterodine group but the difference was not significant.

Conclusion: Four week treatment with oxybutinin was better than tolterodine in improving urgency and urge incontinence but there were not statistically significance between them.

Keywords: Over Active Bladder, Oxybutynin; Tolterodine, Frequency Volume Chart, Urodynamic Study

Introduction

Oxybutynin and Tolterodin are two highly effective anticholinergic drugs suitable for treatment of overactive bladder (OAB) syndrome. Each drug has a different specificity to bladder muscarinic receptors, thus different adverse effect profiles should be considered. Additionally different individuals experience the symptoms of OAB and the adverse effect to different extents, therefore quality of life is affected differently in the patients with OAB. Previous findings supported similar efficacy of both drugs in different types and doses in improvement of symptoms of OAB, but in order to reduce the adverse side effects tolterodin was recommended and oxybutinine may minimize treatment costs (1-8). Determining the lowest therapeutic dose of the drugs helps in selecting different preparations regarding to the prominent symptom, cost and adverse effects. This study was designed to determine the effectiveness of oxybutinin (5 mg IR tablet t.d.s.) vs. Tolterodin (2 mg IR table b.i.d.) in treatment of the OAB.

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Materials and methods

In this randomized, double-blind, parallel-group trial conducted in a hospital related to Tehran University of Medical Sciences, Tehran, Iran, female outpatients with documented over active bladder syndrome [urinary frequency (>or=8 micturations /24 hours) plus urge incontinence (>or=5 episodes/week)] who show idiopathic detrussor overactivity (IDO) in the filling cystometry were randomized to receive oral treatment with oxybutynin hydrochloride tablet (5 mg, Iran Daru Co., Iran) every 8 hours or tolterodin tablet (2mg, Loghman Co., Iran) twice daily for 4 weeks. The study included all eligible patients from February 2011 till February 2012. A 3-day frequency volume chart (FVC) was obtained before and after the treatment course. Subjective and objective symptoms were assessed before, and one month after treatment.

The effectiveness of each drug was compared using the paired samples t-test.

Results

Totally 100 women with the age of 53 ± 12 years (mean ± SD) were included. Mean subjective daytime and night-time frequency, urgency and incontinency significantly decreased after treatment in both groups.

On a 3-day frequency-volume chart, after treatment with oxybutinin the daytime and the night-time frequency of patients decreased 22% (p= 0.000) and 17.6% (p= 0.035) respectively. In tolterodin group, the daytime and the night-time frequency of patients decreased 16.4 % (P=.000) and 24.3% (P=.006).

The evaluation of urinary urgency showed significant decrease in both groups. The urinary urgency and nocturnal urinary urgency were decreased by 58.8% (p= 0.008) and 39.7% (p= 0.001) respectively in Oxybutinin group and 41.8% (p= 0.000) and 39.1% (p= 0.001) respectively in Tolterodine group. There was a statistically significant decrease in episodes of incontinence with oxybutinin (46.7%; P = 0.001) also a significant decrease in patients treated with tolterodine (39.7%; p= 0.002).

In this study the discontinuation of treatment due to adverse events had no significant difference in two groups (6% and 8% in oxybutinin and tolterodine group respectively, p= 0.082) dry mouth was the most common side-effect in both groups (30% in oxybutinin group and 26% in tolterodine group).

Discussion

Anticholinergics are the mainstay of pharmacotherapy for OAB. Evidence for their efficacy is mostly derived from short-term phase III randomized drug trials (9).

Different patients experience the symptoms of OAB (frequency, urgency, urge incontinency) to different extents. These findings remind the importance of selecting the drug which most effectively improves the prominent complaints impressing the quality of life in people with OAB especially in elderly (1, 2). Therefore researches are being conducted on different types and the lowest therapeutic dose of anticholinergic drugs.

Although it acts on all types tolterodine is more commonly known to act on M2 and M3 subtypes of muscarinic receptors (10). In comparison to oxybutynin (M3 and M1 selective, but more so in the parotid than in the bladder) tolterodine is claimed to have fewer side effects as it targets the bladder more than other areas of the body (10).

Treatment with oxybutynin and tolterodin as different anticholinergic types (immediate-release or extended-release tablets) have shown a similar efficacy in improving urination diary variables in patients with overactive bladder (7, 8, 11, 12).

Previous studies said the discontinuation rates caused by adverse events were similar between the two formulations. But extended release (ER) preparations are more expensive than the others (12).

In addition to similar efficacy and adverse effects, cost and the effect on the most prominent symptom have essential roles in choosing the appropriate treatment.

There is a trend for detecting the lowest therapeutic dose of anticholinergic drugs in the treatment of OAB in elderly because of 32% reported rate of using other drugs with anticholinergic effects in elderly which leads to cumulative adverse effects (13). There were not statistically significant differences between the different doses of oxybutinin and tolterodin [(5 vs. 10 mg ER tablet of oxybutinin) (4,12), (5 mg IR tablet of oxybutinin three times a day vs. 2mg IR tablet of tolterodin two times a day) (7,8,12) and (2 x 2 mg IR tablet vs. 4mg ER of tolterodin) (11, 12)].

Although differences were found in the length of the studies but regarding to achieve an appropriate improvement in OAB symptoms, the 4-week treatment course was recommended (11, 12).

More severe and frequent dry mouth episodes was seen in whom took oxybutynin immediate-release (IR) compared to other preparations (11). In this study 2.5mg IR tablet of oxybutinin three times a day was used and statistically significant differences for improvement in frequency, urgency and urge incontinence episodes were seen.

This recommended dose of oxybutinin (5mg IR tablet three times a day) is associated with therapeutic effect and fewer adverse effects especially dry mouth, and may thus be preferable. Thus determining the lowest therapeutic dose of the drugs is mandatory in treatment designation with different preparations regarding to cost effectiveness and decreased adverse effects.

In this study the adverse events resulted in discontinuation of treatment were similar in two groups. This result is in contrast to some other studies concerning tolterodine to have fewer adverse effects in comparison to oxybutinin (7, 12). Different age groups under study and ethnic disparities may interpret the distinction.

OAB is presented with various symptoms. Urgency in 54% and urge incontinence in 36% of patients with OAB were seen (13). In present study improvements in urinary urgency, frequency and urge incontinence after treatment were seen in both groups. Improvement score in patients treated by oxybutinin was larger especially in terms of urgency and urge incontinence. Therefore in patients with OAB with the chief complain of urgency or urge incontinence oxybutinin regimen should be recommended. Night-time frequency was shown to be improved by a significantly larger score by tolterodin. Respectively for elderly patients in whom the most troublesome complaint is mentioned to be nocturnal frequency and disturbed sleep pattern prescription of tolterodin is suggested. Mostly the studies have implemented that applying FVCs of ≥3 days can be used to monitor therapeutic outcomes of drugs in OAB (14). Our data collected from micturation diaries of 3 days were recorded by the patients being educated by a selected gynecology resident. If this method is used, it is recommended to train the patients and monitor for chart fulfilling method in a continuous manner.

In conclusion, difference in the symptoms of patients which reduce their quality of life in planning a course of treatment should be considered. Physicians should consider the patients' prominent symptom in selecting a kind of antimuscarinic drug for treatment of overactive bladder syndrome.

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Disclosure

Authors have no relationships with any companies for any financial interests.

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