

Comparison of Side Effects of Solifenacin Vs Tolteridine in Patients with Urinary Incontinence

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ABSTRACT

Background: Urinary incontinence is a distressing condition affecting million of women all over the world and prevalence is on rise in old age. Anti-muscarinic agents are used to treat this disease. Effective treatment modality with minimum side effect remains a major challenge in these women.

Aim: To compare the side effects of Tolterodine and Solifenacin Succinate in patients with urinary incontinence.

Study design: Randomized controlled trial

Sampling technique: Non Probability purposive sampling

Methods: 830 women, aged 35-90 years presenting in OPD of Sharif Medic And Dental college /SMCH fulfilling the inclusion criteria were randomly treated with Solifenacin Succinate 5mg (Group-A) and Tolterodine 4mg (Group B) in duration of 5 years. Demographic characters including age, duration and pattern of urinary complaints were inquired. Both groups were followed for 3 months. All information analyzed using SPSS version 18. Frequency of side effects were noted in both groups and was assessed using Chi-Square test and p value ≤ 0.05 . Mean \pm SD calculated for quantitative data like age and qualitative data like side effects (Dry Mouth, Constipation).

Results: Mean age of patients was 57.34 \pm 11.54 years. Dry mouth was observed in 123(29.64%) patients in Group-A and 101(24.34%) in Group-B (p-value 0.085), while constipation was observed in 41(9.88%) patients in Group-A and 21(5.96%) patients in Group B. (p-value 0.000)

Conclusion: Solifenacin succinate (5mg) had significantly higher occurrence of constipation as compared to Tolterodine (4mg) while occurrence of dry mouth was also higher but not significant. These results showed that difference in side effects between Tolterodine and Solifenacin succinate in patients with urinary incontinence.

Keywords: Anti muscarinic, Solifenacin, Tolterodine, Overactive bladder, Dry Mouth, Constipation

INTRODUCTION

Overactive bladder, a syndrome comprised of frequency, urgency with or without urge incontinence and nocturia. Over 10-13 million people in United State and 200 million people worldwide suffers from this disorder. With an overall prevalence of 27.6% in developed countries while 28.7% in developing countries with a range from 5.2-72.8^{2,3}.

Regarding prevalence of urinary incontinences in Sindh Pakistan 11.56% suffers from urinary incontinence out of which 2.8% suffers from overactive bladder⁴. Several studies have shown that the burden of urinary incontinence may vary across the racial groups. Various, cross sectional studies reported a lower prevalence of overall incontinence in Black and Asian population when compared with white women⁵.

Bladder contraction is primarily under the direct control of parasympathetic nervous system so anticholinergic agents have been the first line

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treatment of overactive bladder. These agents work through non selective inhibition of muscarinic (M) receptors in smooth muscles throughout the body. Bladder smooth muscles contain mainly M3 receptors⁶. In addition these M3 receptors mediate saliva production, gastrointestinal smooth muscles and iris sphincter function; therefore expected side effects like dry mouth, constipation and miosis was observed in patients⁷.

Solifenacin and darfenacine are two new agents for OAB which have strong affinity for M3 receptors so comparable efficacy with lower side effects as compared to other anti-cholinergic agents. STAR trial comparing efficacy of Tolterodine with Solifenacin in OAB by Chapel and colleagues showed greater efficacy with mild to moderate side effects in both groups^{8,9}.

HO Chang TC conducted study comparing the Solifenacin and Toletrodine, equal efficacy in reducing the number of micturation (-2.56 \pm 3.31 vs -2.44 \pm 4.56, p=0.58) with no major difference in quality of life. Incidence of dry mouth (18% vs 8.3%, p=0.31) and constipation (12.8% vs 2.8%, p=0.20) was not significantly different¹⁰.

The results are also comparable to study by Basra the incidence of side effects such as dry mouth was greatest in the Solifenacin treated group (38%), followed by the Tolterodine (24%) $p < 0.05$, while another study showing the incidence of dry mouth was 17.5% in Solifenacin treated and 14.8% $p > 0.05$ (insignificant) in Tolterodine treated group.¹¹ In the same study the incidence of constipation was (3.2% in Solifenacin treated while 1.3%, $p > 0.05$ (insignificant) in Tolterodine group. Another study was done showing the incidence of constipation 7% in Tolterodine treated group alone¹².

The rationale of this study is to see the side effects of Solifenacin and Tolterodine as there is variability in side effects of Tolterodine and Solifenacin succinate in literature. In developing countries like Pakistan where basic health care is out of reach of common man a problem like urinary incontinence is largely overlooked and those who seek medical help remain non-compliant due to side effect if drug prescribed. Therefore, a study is required to choose a drug with lesser side effects to cope with the problem that makes a woman's religious, marital and social life miserable and poses economic burden on family.

The objective of this study was to compare the side effects of tolterodine and solifenacin succinate in patients with urinary incontinence.

MATERIAL & METHODS

This randomized controlled trial was conducted in the Department of Obstetrics and Gynecology, Sharif medical And Dental College /SMCH Lahore in 5 year duration. The sampling technique used was non Probability purposive sampling. The study was conducted in the Department of Obstetrics and Gynecology, Sharif medical And Dental College /SMCH Lahore in 5 year duration. A sample size of 830 cases (415 in each group) was calculated with 80% power of test, 5% level of significance and taking expected percentage of constipation in both groups i.e., 3.2% in Solifenacin group versus 7% Tolterodine group in patients with urinary incontinence.

Inclusion Criteria

- Patients having complaint of urinary incontinence
- Patients having complaints of nocturia
- Patients having complaints of frequency (The number of times a women voids during her waking hours. Normally it is between 4-7 voids per day)

Exclusion Criteria

- Patients with urinary tract infection (on urine complete examination)
- Patients with fistula (History of continuous dribbling of urine)
- Pregnancy
- Uterovaginal prolapse
- Patients with diabetes (BSF >126 mg/dl and BSR >200 mg/dl)

Data Collection Procedure: Patients fulfilling the inclusion criteria were registered through OPD of Sharif Medical And Dental College/SMCH. After informed consent demographic information like name, age address was recorded. Patients were randomly divided (using lottery method) in both study groups. Group-A patients were treated with Solifenacin Succinate (5mg) and Tolterodine (4mg) in Group-B patients. Side effects i.e., constipation and dry mouth (as per operational definitions) were noted after 3 months post treatment.

Data analysis procedure: All collected information was entered and analyzed using SPSS version 18. Quantitative data like age was presented in form of Mean \pm SD and qualitative data like side effects (Dry Mouth, Constipation). Chi Square was used to determine the frequency of side effects in both groups with $p \leq 0.05$.

RESULTS

During this study 830 women were enrolled 415 in each group mean age of all 830 patients was 57.34 \pm 11.54 years out of which mean age was 58.31 \pm 12.09 years in Group-A patients and 56.38 \pm 10.89 years in Group-B patients respectively.

When frequency of side effects were compared dry mouth was observed in 123(29.64%) Group-A patients vs 101 (24.34%) in Group-B patients (P value 0.085) NS (Table 1).

When frequency of constipation were compared 41(9.88%) patients in Group-A and 21(5.06%) in Group-B patients had this complaint. This difference in both treatment groups was statistically significant. (p-value=0.000) (Table 2)

Table 1: Frequency of Dry Mouth In Treatment Groups

	Group-A	Group-B
Yes	123 (29.64%)	101 (24.34%)
No	292 (70.36%)	314 (75.66%)
Total	415	415

Chi-Square Test= 2.959

p-value=0.085

Table-2: Frequency of Constipation In Treatment Groups

	Group-A	Group-B
Yes	41 (9.88%)	21 (5.06%)
No	374 (90.12%)	394 (94.93%)
Total	415	415

Chi-Square Test= 6.872

p-value= 0.008

DISCUSSION

Urinary incontinence is a major problem identified in women all over the world which affect their quality of life. This dilemma is commonest around the age of perimenopause and gradually worsen in old age¹³.

Antimuscarinics are established first line treatment options for overactive bladder. Therefore search of ideal antimuscarinic is going on which effectively relief the symptoms of patient without increasing the side effects and easy dose adjustment¹⁴.

As the number of antimuscarinic are increasing, number of double blind randomized controlled are pitching one against other to show efficacy and tolerability of these agents Despite good efficacy antimuscarinic have significant side effects and compliance with treatment is at best average¹⁵.

Since the advent of solifenacin succinate 2005 numbers of trials are coming to compare with tolterodine regarding efficacy, and tolerability¹⁶.

The therapeutic profile however may differ because antimuscarinics have differing profiles of receptor interaction on the five subtypes of muscarinic receptor that represent targets for OAB treatments.^{17,18} The major difference in efficacy and tolerability of different drugs is due to varied tissue absorption in peripheral tissue and selective action on bladder smooth muscle.

In our study frequency of dry mouth was 29.64% in Solifenacin vs 24.34% in tolterodine (p-value=0.085) patients .C.R. Chapple in STAR trial compared solifenacin- and tolterodine ER and analysis of adverse events showed dry mouth in 30% of the patients who were given solifenacin and 24% in tolterodine group⁸. In this study constipation was observed in 6.4% in solifenacin- and 2.5% in tolterodine group. In our study frequency of constipation was 9.88% in solifenacin treated patients versus (5.96%) in tolterodine treated group (p-value=0.000)

The results are also comparable to another study by Chapple C¹⁹.

In this study dry mouth occurrence was higher in solifenacin succinate i.e. 29.64% as that of 24.35% in Tolterodine group. Both these percentages were high as that of reported in Chapple C study but the trend for high dry mouth occurrence in solifenacin succinate group was same as that of results of this study.

Fred Govier in his Double-Blind, Placebo-Controlled Phase III Pivotal Trial investigated the efficacy and safety of solifenacin succinate 10 mg, a once-daily (OD) oral antimuscarinic agent, in overactive bladder syndrome. In his results he

reported that constipation and dry mouth occurred 38% and 19% of patients²⁰.

Michael B. Chancellor evaluated in his study reported occurrence of dry mouth and constipation in 17.5% and 11.6% patients²¹.

In different studies different trend was seen for the occurrence of constipation and dry moth for both drugs^{22,22,3}. However in this study both adverse effect (constipation and dry mouth) were observed to be high in solifenacin group but a dry mouth was significantly high in solifenacin group.

CONCLUSION

Solifenacin Succinate (5mg) had significantly higher occurrence of side effects than Tolterodine (4mg) in patients with urinary incontinence.

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