



## Comparison between efficacy of Solifenacin and Oxybutynin for the treatment of overactive bladder in women.

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**ABSTRACT... Objective:** To compare the efficacy of solifenacin and oxybutynin in the treatment of overactive bladder in female patients. **Study Design:** Quasi Experimental study. **Setting:** Department of Urology, Institute of Kidney Diseases, Peshawar. **Period:** Sept 2017 to Mar 2018. **Material & Methods:** After selection of 312 female patients with overactive bladder by convenience sampling, written informed consent was taken and pre-treatment overactive bladder symptoms (OABS) score was calculated. Patients were randomly distributed in two equal groups of 156 subjects, where Group A received Oxybutynin (3 mg, BD) and Group B received Solifenacin (5mg, OD) for a period 12 weeks. Patients were called for follow up visit to determine and compare the efficacy of study drugs. Those who showed improvement in at least 03 points in OABS score taken pre-treatment were considered as positive responders. **Results:** The mean age of patients was  $38.8 \pm 7.62$  years with age range from 20 to 50 years. 110 (70.5%) subjects in oxybutynin treated group while 126 (80.8%) subjects in solifenacin treated group reported significant improvement in OAB symptoms. **Conclusion:** Solifenacin is relatively more effective than oxybutynin for treating female patients with overactive bladder.

**Key words:** Efficacy, Oxybutynin, Overactive Bladder, Solifenacin.

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## INTRODUCTION

Overactive bladder (OAB) is a complex of symptoms, characterized by urinary urgency with or without urge incontinence, increased urinary frequency and nocturia, in the absence of underlying pathological condition explaining these features. This definition was proposed in a standardization of terminology report by international continence society (ICS).<sup>1</sup> Urgency is a mandatory component of this definition, describing the fact that urgency is the major driving force behind all other elements like incontinence, frequency and nocturia.<sup>2,3</sup> These symptoms are due to over activity of detrusor muscle as demonstrated by urodynamic tests but urethro-vesical dysfunctions can also cause similar clinical features.<sup>4</sup>

Globally, millions of people are suffering from OAB. In America, it is estimated that approximately seventeen million people are affected by this

disease with increasing prevalence as age increases. Studies reported OAB prevalence of 16.5% in US population aged  $\geq 18$  years and 16.6% in European individuals aged  $\geq 40$  years and by the year 2025, there will be substantial rise in this number.<sup>5</sup> The quality of life of patient is more negatively affected by OAB than by asthma, hypertension, cardiac diseases or diabetes mellitus. Even their quality of life is much poorer than the lives of people with depression.<sup>6</sup> Several reports have been published describing the association of urinary incontinence with significant healthcare cost. In the year 2000, estimated total economic cost associated with OAB was 12.6 billion dollars in USA while in Sweden, urinary incontinence alone accounts approx 2% of the total healthcare cost.<sup>7</sup>

As far as the management of OAB syndrome is concerned, various treatment options are available aiming to reduce the magnitude of

symptoms. Anti-muscarinics are considered as the first line agents i.e. Oxybutynin, Solifenacin, Darifenacin, Propiverine, Tolterodine, Trospium, Fesoterodine and Flavoxate. They block the muscarinic receptors of detrusor muscle, reducing its activity and hence the symptoms. In our setup, Oxybutynin and Solifenacin are more commonly prescribed. Oxybutynin has been in use for over 20 years and available in different dosage forms whereas Solifenacin is an anticholinergic drug which is more bladder selective and well-tolerated. These two drugs have been assessed in various randomized controlled trials against placebo or compared with other competitors where both found to be effective in patients of OAB.<sup>8,9</sup> In a clinical trial where 863 patients with OAB symptoms were randomized with solifenacin versus placebo, the former has shown significant reduction in the episodes of urinary urgency, with or without incontinence.<sup>10</sup> But a meta-analysis based on 50 randomized controlled trials including more than 27000 female patients revealed only modest reduction in OAB symptoms after treatment with anti-muscarinic drugs. They caused reduction in urge incontinence by 1.73 episodes/day and voids by 2.06/day whereas, placebo decreased the urge incontinence by 1.06 episodes/day and voids by 1.2/day. This analysis revealed no individual drug to be superior than other competitors.<sup>11</sup>

Hence, there is a lot of disparity in the data on efficacy of anti-muscarinic drugs in terms of urgency and episodes of urge incontinence. This study was an attempt to identify more efficacious agent between two commonly used anti-muscarinic drugs for OAB i.e. Oxybutynin and Solifenacin. The local data will help the clinicians in selecting most appropriate pharmacotherapy for overactive bladder in our population.

## MATERIAL & METHODS

This experimental study was carried out at Institute of Kidney Diseases (IKD), Peshawar from Sept 2017 to Mar 2018. A sample size of 312 patients was determined by WHO calculator, using 38% efficacy of oxybutynin, 52% efficacy of solifenacin, 95% confidence level and 80% power of test.<sup>12</sup> After taking approval from the hospital

ethical committee and written informed consent, female patients visiting urology OPD fulfilling the inclusion criteria i.e. 20-50 years of age, urinary frequency of >07 times/day, at least 01 episode of urinary urgency/week with or without urinary incontinence, nocturia at least 01 episode/night, with duration of these symptoms more than three months and baseline OABS score of 04 were enrolled in the study. (The OABS score is a symptom assessment questionnaire designed to quantify OAB symptoms into a single score.<sup>13</sup> The questionnaire consists of 4 questions on OAB symptoms with maximum scores ranging from 2 to 5: daytime frequency (2 points), night-time frequency (3 points), urgency (5 points), and UUI (5 points). The total score ranges from 0 to 15 points, with higher scores indicating higher symptom severity).

To minimize the confounding and biasness in the outcome, pregnant women, patients of stress incontinence, malignancy in the pelvic organs, pelvic organ prolapse, bladder stones, UTI, neurological conditions (e.g. spinal injury, multiple sclerosis, parkinson disease, diabetic neuropathy) and medical conditions contraindicating the use of study drugs were excluded from the study. After detailed history, physical examination and calculating pre-treatment OABS score, necessary investigations like Ultrasound abdomen and pelvis, Post void residual urine volume (PVRV), retrograde urethrogram, Micturating cystourethrogram (MCUG) and MRI were performed where needed. Patients were randomly allocated two groups (156 in each) where Group A received Oxybutynin (3mg, BD) and Group B received Solifenacin (5mg, OD) for a period of 12 weeks. They were called for follow up visit to determine the drug efficacy by observing significant difference in OABS score before and after treatment. Patients showing an improvement in at least 03 points in pre-treatment OABS score was considered positive responders. All the relevant data was recorded in a predesigned proforma.

## Data Analysis

The collected data was analyzed in SPSS version 20. Numerical variables like age and duration

of symptoms were described as Mean ± SD. Categorical variables like efficacy were described in terms of frequency and percentages. Chi-square test was applied to compare the efficacy of oxybutynin and solifenacin among different groups, keeping p value <0.05 as significant. Efficacy was stratified against age and duration of OAB symptoms to see effect modification.

**RESULTS**

A total of 312 female patients of overactive bladder comprising of age range from 20 to 50 years, with mean age of 38.8 ± 7.62 years were observed. In oxybutynin treated group, 10(6.4%) patients were of age ≤25 years, 70(44.9%) patients were in age range of 26-40 years and 76(48.7%) patients were of age >40 years with mean age 38.5 ± 7.78 years. In solifenacin treated group, 4(2.6%) patients were of age ≤25 years, 66(42.3%) patients were in age range of 26-40 years and 86(55.1%) patients were of age >40 years with mean age 39.3 ± 7.47 years. The distribution of age between two groups was statistically insignificant with p value 0.191. (Figure-1).

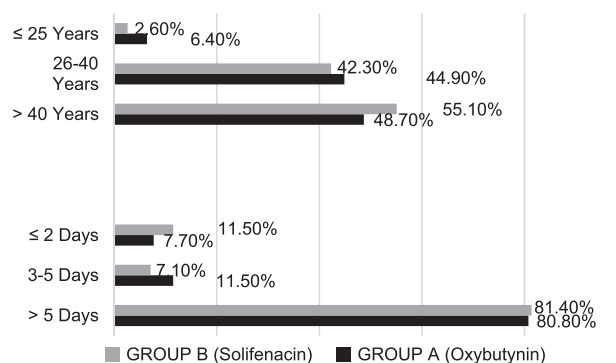
In oxybutynin treated group, the average duration of symptoms was 6.9 ± 2.11 days with 12(7.7%) patients having duration ≤2 days, 18(11.5%) patients having 3-5 days and 126(80.8%) patients having symptoms for >5 days. While in solifenacin treated group, the average duration of symptoms was 7 ± 2.23 days with 18(11.5%) patients having duration ≤2 days, 11(7.1%) patients having 3-5 days and 127(81.4%) patients having symptoms for >5 days. This distribution of duration of symptoms between two groups was also statistically insignificant with p value 0.235. (Figure-1)

Distribution of efficacy between two groups is demonstrated in Figure-2, where oxybutynin was found to be effective in 110(70.5%) patients while solifenacin in 126(80.8%) patients. The response of both drugs was statistically significant with p value 0.024.

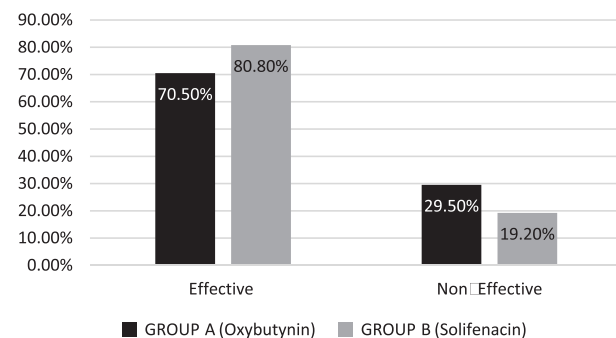
Age wise distribution of efficacy in both groups revealed efficacy greater in younger patients which decreased with increasing age i.e. among

patients of age ≤25 years, oxybutynin showed efficacy in 90% subjects and solifenacin in 75% subjects whereas among patients of age >40 years, oxybutynin showed efficacy in 69.7% subjects and solifenacin in 61.6% subjects. This age wise distribution of efficacy between two groups was statistically insignificant with p value >0.05. When efficacy was stratified over duration of symptoms in both groups, the results were insignificant except for duration of symptoms >5 days where oxybutynin reported greater efficacy than solifenacin. (Table-I)

**DISCUSSION**



**Figure-1. Distribution of age and duration of symptoms between two groups**



**Figure-2. Distribution of efficacy between two groups**

Overactive bladder is a common deplorable urological condition, poorly affecting the quality of life of many patients.<sup>14</sup> While managing the patients of overactive bladder syndrome, anti-muscarinic agents are considered as mainstay of treatment with aim to maintain the bladder’s conservative and retaining functions.

AGE		Group A	Group B	P-Value
≤ 25 years	Effective	9 (90%)	3 (75%)	0.5055
	Not Effective	1 (10%)	1 (25%)	
Total		10 (6.4%)	4 (2.6%)	
26-40 years	Effective	64 (91.4%)	54 (81.8%)	0.0804
	Not Effective	6 (8.6%)	12 (18.2%)	
Total		70 (44.9%)	66 (42.3%)	
> 40 years	Effective	53 (69.7%)	53 (61.6%)	0.1795
	Not Effective	23 (30.3%)	33 (38.4%)	
Total		76 (48.7%)	86 (55.1%)	
Duration of Symptoms		Group A	Group B	P-Value
≤ 2 Days	Effective	11 (91.7%)	13 (72.2%)	0.2044
	Not Effective	1 (8.3%)	5 (27.8%)	
Total		12 (7.7%)	18 (11.5%)	
3-5 Days	Effective	14 (77.8%)	11 (100%)	0.1288
	Not Effective	4 (22.2%)	0 (0%)	
Total		18 (11.5%)	11 (7.1%)	
> 5 Days	Effective	101 (80.2%)	86 (67.7%)	0.0171
	Not Effective	25 (19.8%)	41 (32.3%)	
Total		126 (80.8%)	127 (81.4%)	

**Table-I. Stratification of drug efficacy with age & duration of symptoms.**

Various anti-muscarinic drugs such as tolterodine, solifenacin, oxybutynin, trospium chloride, propiverine and fesoterodine have been widely used since long due to their proven efficacy, tolerability and stability.<sup>15,16</sup> The basic mechanism of action of these drugs is antagonism of muscarinic (M3) receptors located in the smooth muscles of bladder. Though, anti-muscarinics are commonly in use for treating OAB patients but which drug is more effective, is not yet clear.<sup>17</sup>

Many studies have been done previously regarding OAB prevalence in women with reported value of 16.9% which increased with advancement in age i.e. 4.8% in women with age <25 years, rising to 30.9% in those with age >65 years.<sup>18</sup> Another epidemiological survey done in Europe revealed OAB prevalence of 16.6% in a population of age ≥40 years and again was found to increase with age.<sup>19</sup> These findings resemble the results of our study where only 6.4% and 2.6% OAB cases were of age ≤25 years in oxybutynin and solifenacin treated groups, respectively but increased to 48.7% and 55.1% in those having age more than 40 years.

As far as efficacy is concerned, in this study solifenacin 5mg OD appeared to be relatively more efficacious than oxybutynin, resembling the results of trials done previously revealing solifenacin 5mg OD as drug of choice for treating OAB symptoms. Moreover, if 5mg OD solifenacin fails as primary drug, then 3mg TDS oxybutynin need to be considered as it offers efficacy similar to 10mg OD solifenacin.<sup>20</sup> There are various studies including randomized controlled trials which justified the superiority of solifenacin when compared with placebo and other anti-muscarinic drugs accounting its safety, clinical efficacy and cost.<sup>21</sup>

In contrast, there are reports which denies the superiority of solifenacin over oxybutynin. Kakar et al compared oxybutynin, solifenacin, fesoterodine and tolterodine with a conclusion that while tolterodine and solifenacin were equally effective for treating OAB, the oxybutynin and solifenacin showed improved efficacy, but more adverse effects were also reported.<sup>22</sup> In clinical trials, differences in the efficacy of various anti-muscarinic agents have often reached to

statistical significance. However in routine clinical practice, the magnitude of these differences are not readily appreciable and many clinicians labeled the efficacy of these drugs “comparable”.

In this study, some shortcomings which are worth to mention includes lack of data regarding tolerability of the study drugs and assessment of drug responses at various doses.

## CONCLUSION

It is concluded that solifenacin at a dose of 5mg OD appears to be slightly more favorable than oxybutynin at a dose of 3mg BD for the treatment of overactive bladder in women.

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2	Muhammad Saleh Faisal	Manuscript writing.	
3	Samiullah Opal	Data collection.	
4	Ahmad Nawaz	Concept and design of study.	
5	Muneeb Hassan	Statistical analysis and critical review.	
6	Sikandar Hayat	Statistical analysis and critical review.	