

Does Solifenacin solve the urgency symptoms in postpartum women?

By

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Abstract:

Background: It is widely accepted that antimuscarinics are considered first-line treatment for patients with overactive bladder (OAB). However, the mechanism by which antimuscarinics improve the symptoms of OAB remains to be fully elucidated. **Patients and methods:** This study is a clinical prospective follow up study carried out in Consultancy Clinic of Al-Elwiya Maternity Teaching Hospital in Baghdad-Iraq. duration(November, 2019-April, 2020). inclusion criteria were adult postpartum women at childbearing age with symptoms of overactive bladder treated by Gynecologist with Solifenacin tablets. **Results:**current study showed 34% of them were in age group 20-29 years. Mean parity history of women with OAB was (3); 32% of them had parity history of 1-3 para and 68% of them had parity history of 4-6 para. delivery mode for 84% of women with OAB was vaginal delivery, as well as 36% of women with OAB had ≤ 7 times of urinations at day, as well as a significant decline in score 2 observed after treatment with Solifenacin ($p=0.01$). No significant differences were observed in score 3 before and after Solifenacin treatment ($p=0.06$). A significant decline in score 4 was observed after treatment with Solifenacin ($p=0.001$). No significant differences were observed in women with OAB before and after Solifenacin treatment, so a highly significant increase in control of urination after treatment ($p<0.001$). **Conclusion:** solifenacin drug is effective in reduction of overactive bladder syndrome score three months after treatment.

keywords: solifenacin ,overactive bladder syndrome , after treatment.

الخلاصة

نبذة: تتميز فرط نشاط المثانة سريريًا بالإلحاح البولي وكثرة التبول وسلس البول مع عدم وجود عدوى. كان للمثانة المفرطة النشاط عبء كبير على صحة المرأة ونوعية حياتها.

هدف الدراسة: تقييم فعالية علاج سوليفيناسين للنساء البالغات بعد الولادة الذين يعانون من أعراض فرط نشاط المثانة.

المرضى وطرق البحث: دراسة متابعة مستقبلية سريرية أجريت في العيادة الاستشارية لمستشفى العلوية التعليمي للأومفة في بغداد - العراق خلال ستة أشهر طوال الفترة من 1 نوفمبر 2019 حتى 30 أبريل 2020 على عينة من 50 امرأة بالغة بعد الولادة مع فرط نشاط المثانة المعالجة بسوليفيناسين. كان تقييم علاج سوليفيناسين يعتمد على قياس نتائج أعراض فرط نشاط المثانة قبل وبعد العلاج.

النتائج: تم تسجيل نتيجة معيار أعراض فرط نشاط المثانة قبل علاج السوليفيناسين (7.6) بعد العلاج بسوليفيناسين إلى (5.6) مع وجود فرق احصائي متميز وكبير بينهما ($P < 0.001$). استمر العلاج لـ 84% من النساء المصابات بالمثانة المفرطة ، بينما توقف لـ 16% منهن. لوحظت استجابة جيدة للعلاج لـ 88% من النساء المصابات بالمثانة المفرطة النشاط ، بينما لوحظت استجابة ضعيفة لـ 12% منهن. لوحظت آثار جانبية لعلاج سوليفيناسين في 16% من النساء المصابات بالمثانة المفرطة النشاط. كانت الآثار الجانبية الشائعة جفاف الفم ، والإمساك ، وعدم وضوح الرؤية.

الاستنتاجات: العامل المضاد للمسكارين السوليفيناسين هو دواء فعال وآمن في علاج النساء المصابات بمتلازمة فرط نشاط المثانة.

الكلمات المفتاحية : سوليفيناسين , متلازمة فرط نشاط المثانة. العلاج بعد ثلاث اشهر

Introduction:

Lower urinary tract symptoms (LUTS), including urgency, frequency and nocturia, are common in the general population and increase in prevalence with ageing¹. Overactive bladder (OAB), the clinically defined symptom complex of urgency, with or without urgency incontinence, usually with frequency and nocturia, in the absence of infection or other pathology,² is the most common cause of incontinence in both men and women, and the prevalence of OAB increases with age¹.

OAB and other forms of urinary incontinence (UI) are stigmatizing conditions with significant impacts on quality of life ³ and are commonly under-reported by patients for multiple reasons, including belief that incontinence is normal post-partum or as part of ageing, or that treatment is not available ⁴. OAB is a disorder of the filling phase of the bladder, characterized by the presence of urgency, the sudden, compelling desire to void which is difficult to defer ².

The exact underlying cause of urgency and of OAB remains the subject of much debate in the literature, with there being evidence for the urothelium, detrusor and brain being involved in the pathophysiology of OAB⁵. In those without lower urinary tract dysfunction, voiding is under voluntary control and continence is maintained by a complex interaction between the bladder and numerous areas of the brain, including the frontal and prefrontal cortices, the periaqueductal grey matter and the pontine micturition centre ⁶. Neurological diseases, including the accumulation of white matter hyperintensities on magnetic resonance imaging, cerebrovascular disease and dementia are all strongly associated with the development of LUTS in later life⁷. As such, OAB cannot be considered simply as a disease of the bladder and lower urinary tract. Although conservative management options consider a whole-person approach, encompassing fluid intake, urgency suppression and bladder retraining, pharmacological agents are all directed at the bladder itself⁸.

Patients and methods:

Patients

This study is a clinical prospective follow up study carried out in Consultancy Clinic of Al-Elwiya Maternity Teaching Hospital in

Baghdad-Iraq. The duration of study was six months throughout the period from 1st of November, 2019 till 30th of April, 2020.

All postpartum women presented to Consultancy Clinic of Al-Elwiya Maternity Teaching Hospital with symptoms of overactive bladder (OAB) were the study population. The inclusion criteria were adult postpartum women at childbearing age with symptoms of overactive bladder (urinary frequency, urgency, incontinence) treated by Gynecologist with Solifenacin tablets. The exclusion criteria were younger or older age, current pregnancy, dysuria, stress incontinence, mixed incontinence with predominant stress incontinence, regular urethral catheterization, intermittent self catheterization, urinary retention, urinary tract infection, chronic cystitis in last two weeks, bladder calculus, history of previous or exciting pelvic malignant tumors, thyroid dysfunction, diabetes mellitus, hypertension and lactation.

After eligibility to inclusion and exclusion criteria, a convenient sample of 58 adult postpartum women with OAB treated with Solifenacin was selected from Consultancy Clinic of Al-Elwiya Maternity Teaching Hospital after taking their approval to participate in the study. After duration of treatment with Solifenacin, the side effects of drug started in eight women and they excluded from the study and women who completed the study were 50 58 adult postpartum women with OAB treated with Solifenacin.

Methods

The data collection was carried out by the researcher through direct interview with selected women, The women were assessed by the senior in Consultancy Clinic and the researcher. The diagnosis was confirmed according to symptoms of OAB and the senior prescribed 10 mg or 5 mg

of oral Solifenacin tablet once daily for women with OAB for duration of at least 3 months (the dose was dependent on severity of OAB symptoms). After this interview, the researcher followed them for maximum duration of 6 months. The researcher reported the OAB score questions before and after treatment in addition to assessing the treatment course, response to treatment and side effects of treatment.

Statistical analysis: The data of women were analyzed by application of Microsoft excel program and Statistical Package for Social Sciences (SPSS) version 23.

Results:

This study included 50 women with overactive bladder (OAB) presented with mean age of 31.5 ± 5.1 years; 34% of them were in age group 20-29 years and 66% of them were in age group 30-39 years. Mean parity history of women with OAB was (3); 32% of them had parity history of 1-3 para and 68% of them had parity history of 4-6 para. The delivery mode for 84% of women with OAB was vaginal delivery, while 16% of them were delivered by cesarean section. All these findings were shown in table 1.

Table (1): General characteristics of women with OAB.

Variable	No.	%
Age mean \pm SD (31.5 \pm 5.1 years)		
20-29 years	17	34.0
30-39 years	33	66.0
Total	50	100.0
Parity mean \pm SD (3 \pm 1)		
1-3 para	16	32.0
4-6 para	34	68.0

Total	50	100.0
Mode of delivery		
Vaginal delivery	42	84.0
Cesarean section	8	16.0
Total	50	100.0

Regarding question 1; 36% of women with OAB had ≤ 7 times of urinations at day, 40% of them had 8-14 times of urinations and 24% of them had ≥ 15 times of urinations before treatment with Solifenacin. For question 2; no women with OAB had 0 or 1 wake up for urination at night, but 16% of them had 2 times of wake up for urination at night and 84% of them had ≥ 3 times awake up for urination at night before treatment with Solifenacin. Regarding question 3; 44% of women with OAB had less than once a week sudden desire to urinate, 38% of them had once a week or more, 14% of them had once a day, 2% of them had 2-4 times a day and 2% of them had 5 times or more a day before treatment with Solifenacin. For question 4; 34% of women with OAB had less than once a week leak of urine, 34% of them had once a week or more leak of urine, 22% of them had about once a day leak of urine, 8% of them had 2-4 times leak of urine and 2% of them had 5 times or more leak of urine before treatment with Solifenacin. As a result, the mean OAB score before treatment with Solifenacin was 7.6 ± 2 . All these findings were shown in table 2.

Regarding question 5; reasons for urination were mild urge or desire (30%), moderate urge or desire (38%), severe urge or desire (28%) and desperate urge or desire (4%) before treatment with Solifenacin. For question 6; 18% of women with OAB postpone urination not more than one in 4 hours, 44% of them postpone it for about 30-60 minutes, 26% of them postpone it for about 10-30 minutes, 10% of them postpone it for

few minutes and 2% of them must go immediately before treatment with Solifenacin. Regarding question 7; 62% of women with OAB perceived poor bladder control and 38% of them perceived no control at all before treatment with Solifenacin. All these findings were shown in table 3.

Table (2): OAB score questions before treatment with Solifenacin.

Variable	No.	%
Q1: How many times do you typically urinate from waking in morning to sleeping at night?		
≤7	18	36.0
8-14	20	40.0
≥15	12	24.0
Total	50	100.0
Q2: How many times do you typically wake up to urinate from sleeping at night until waking in the morning?		
0	0	-
1	0	-
2	8	16.0
≥3	42	84.0
Total	50	100.0
Q3: How often do you have a sudden desire to urinate, which is difficult to defer?		
Not at all	0	-
Less than once a week	22	44.0
Once a week or more	19	38.0
About once a day	7	14.0
2-4 times a day	1	2.0
5 times a day or more	1	2.0
Total	50	100.0
Q4: How often do you leak urine because you cannot defer the sudden desire to urinate?		
Not at all	0	-
Less than once a week	17	34.0
Once a week or more	17	34.0
About once a day	11	22.0

2-4 times a day	4	8.0
5 times a day or more	1	2.0
Total	50	100.0
OAB score before Solifenacin treatment mean \pm SD (7.6 \pm 2)		

Table (3):OAB score questions before treatment with Solifenacin.

Variable	No.	%
Q5: What is the reason that you usually urinate?		
Out of convenience	0	-
Because I have mild urge or	15	30.0
Because I have moderate urge or desire	19	38.0
Because I have severe urge or	14	28.0
Because I have desperate urge or desire	2	4.0
Total	50	100.0
Q6: Once you get the urge or desire to urinate, how long can you postpone it comfortably?		
No more often than one in 4	9	18.0
About 30-60 minutes	22	44.0
About 10-30 minutes	13	26.0
A few minutes (less than 10	5	10.0
Must go immediately	1	2.0
Total	50	100.0
Q7: In your opinion, how good is your bladder control?		
Perfect	0	-
Very good	0	-
Good	0	-
Poor	31	62.0
No control at all	19	38.0
Total	50	100.0

Regarding question 1; 82% of women with OAB had ≤ 7 times of urinations at day, 16% of them had 8-14 times of urinations and 2% of them had ≥ 15 times of urinations after treatment with Solifenacin. For question 2; no women with OAB had 0 or 1 wake up for urination at night, but 38% of them had 2 times of wake up for urination at night and 62% of them had ≥ 3 times awake up for urination at night after treatment with Solifenacin. Regarding question 3; 70% of women with OAB had less than once a week sudden desire to urinate, 26% of them had once a week or more, 4% of them had once a day, no woman had 2-4 times a day and no woman had 5 times or more a day after treatment with Solifenacin. For question 4; 54% of women with OAB had less than once a week leak of urine, 46% of them had once a week or more leak of urine, no woman had about once a day leak of urine, no woman had 2-4 times leak of urine and no woman of them had 5 times or more leak of urine after treatment with Solifenacin. As a result, the mean OAB score after treatment with Solifenacin was 5.6 ± 1 . All these findings were shown in table 4.

Regarding question 5; reasons for urination were mild urge or desire (42%), moderate urge or desire (50%), severe urge or desire (8%) after treatment with Solifenacin. For question 6; 30% of women with OAB postpone urination not more than one in 4 hours, 54% of them postpone it for about 30-60 minutes, 14% of them postpone it for about 10-30 minutes, 2% of them postpone it for few minutes and no woman must go immediately after treatment with Solifenacin. Regarding question 7; 98% of women with OAB perceived poor bladder control and 2% of them perceived no control at all after treatment with Solifenacin. All these findings were shown in table 5.

Table (4): OAB score questions after treatment with Solifenacin.

Variable	No.	%
Q1: How many times do you typically urinate from waking in morning to sleeping at night?		
≤7	41	82.0
8-14	8	16.0
≥15	1	2.0
Total	50	100.0
Q2: How many times do you typically wake up to urinate from sleeping at night until waking in the morning?		
0	0	-
1	0	-
2	19	38.0
≥3	31	62.0
Total	50	100.0
Q3: How often do you have a sudden desire to urinate, which is difficult to defer?		
Not at all	0	-
Less than once a week	35	70.0
Once a week or more	13	26.0
About once a day	2	4.0
2-4 times a day	0	-
5 times a day or more	0	-
Total	50	100.0
Q4: How often do you leak urine because you cannot defer the sudden desire to urinate?		
Not at all	0	-
Less than once a week	27	54.0
Once a week or more	23	46.0
About once a day	0	-
2-4 times a day	0	-
5 times a day or more	0	-
Total	50	100.0
OAB score after Solifenacin treatment(5.6±1)		

Table (5): OAB score questions after treatment with Solifenacin.

Variable	No.	%
Q5: What is the reason that you usually urinate?		
Out of convenience	0	-
Because I have mild urge or	21	42.0
Because I have moderate urge or desire	25	50.0
Because I have severe urge or	4	8.0
Because I have desperate urge or desire	0	-
Total	50	100.0
Q6: Once you get the urge or desire to urinate, how long can you postpone it comfortably?		
No more often than one in 4	15	30.0
About 30-60 minutes	27	54.0
About 10-30 minutes	7	14.0
A few minutes (less than 10	1	2.0
Must go immediately	0	-
Total	50	100.0
Q7: In your opinion, how good is your bladder control?		
Perfect	0	-
Very good	0	-
Good	0	-
Poor	49	98.0
No control at all	1	2.0
Total	50	100.0

There was a highly significant difference in score 1 before and after treatment with Solifenacin ($p < 0.006$). A significant decline in score 2 was observed after treatment with Solifenacin ($p = 0.01$). No significant differences were observed in score 3 before and after Solifenacin treatment ($p = 0.06$). A significant decline in score 4 was observed after treatment with Solifenacin ($p = 0.001$). All these findings were shown in table 6 and figure 1.

Table (6): Distribution of OAB scores before and after Solifenacin treatment.

Variable	Before		After		P
	No.	%	No.	%	
Score 1					<0.001^{*S}
≤7	18	36.0	41	82.0	
8-14	20	40.0	8	16.0	
≥15	12	24.0	1	2.0	
Score 2					0.01^{*S}
2	8	16.0	19	38.0	
≥3	42	84.0	31	62.0	
Score 3					0.06 ^{**NS}
Less than once a week	22	44.0	35	70.0	
Once a week or more	19	38.0	13	26.0	
About once a day	7	14.0	2	4.0	
2-4 times a day	1	2.0	0	-	
5 times a day or more	1	2.0	0	-	
Score 4					0.001^{**S}
Less than once a week	17	34.0	27	54.0	
Once a week or more	17	34.0	23	46.0	
About once a day	11	22.0	0	-	
2-4 times a day	4	8.0	0	-	
5 times a day or more	1	2.0	0	-	

**Chi square test, **Fishers exact test, S=Significant, NS=Not significant.*

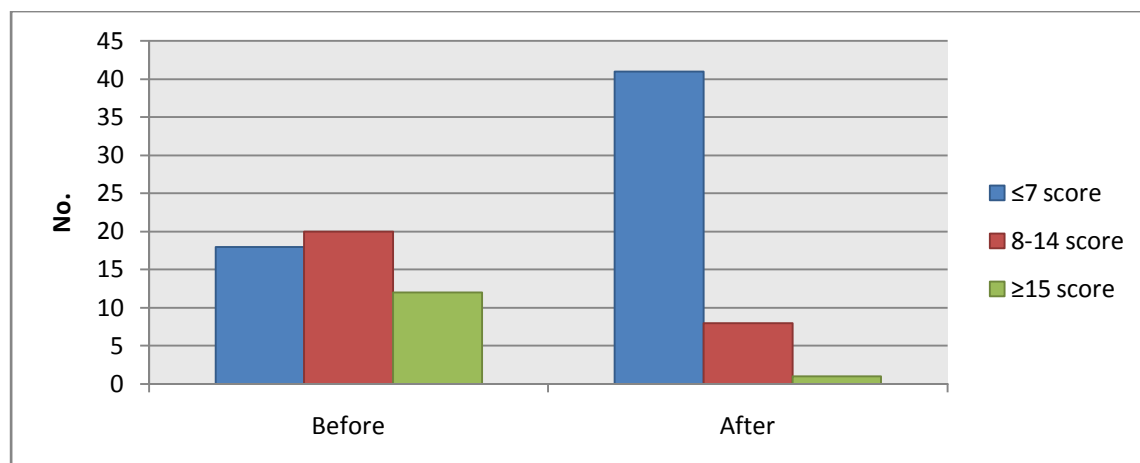


Figure 1: Distribution of score before and after treatment.

No significant differences were observed in women with OAB before and after Solifenacin treatment regarding question 5 ($p=0.2$) and question 6 ($p=0.1$). There was a highly significant increase in control of urination after treatment with Solifenacin for women with OAB ($p<0.001$). All these findings were shown in table 7 and figure 2.

Table (7): Distribution of OAB questions before and after Solifenacin treatment.

Variable	Before		After		P
	No.	%	No.	%	
Q5					0.2* ^{NS}
Because I have mild urge	15	30.0	21	42.0	
Because I have moderate urge or desire	19	38.0	25	50.0	
Because I have severe urge or desire	14	28.0	4	8.0	
Because I have desperate urge or desire	2	4.0	0	-	
Q6					0.1* ^{NS}
No more often than one in	9	18.0	15	30.0	
About 30-60 minutes	22	44.0	27	54.0	
About 10-30 minutes	13	26.0	7	14.0	
A few minutes (less than	5	10.0	1	2.0	

Must go immediately	1	2.0	0	-	
Q7					<0.001**^S
Poor	31	62.0	49	98.0	
No control at all	19	38.0	1	2.0	

*Fishers exact test, **Chi square test, S=Significant, NS=Not significant.

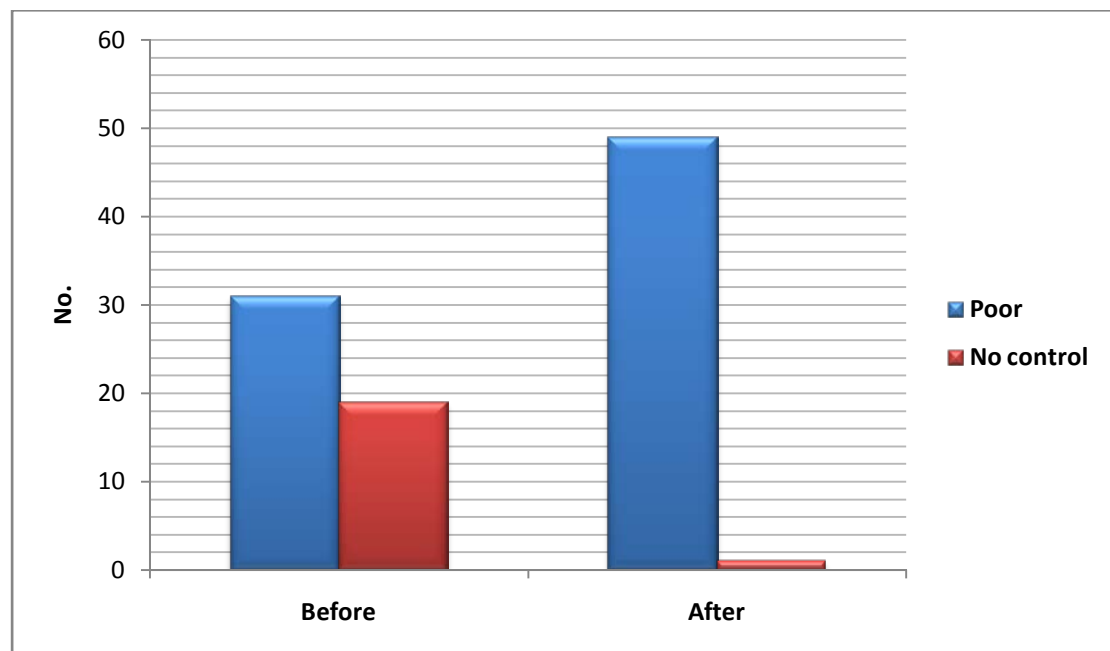


Figure 2: Distribution of control before and after treatment.

As shown in table 8; mean OAB score before Solifenacin treatment (7.6) was reduced after treatment with Solifenacin to (5.6) with a significant difference ($p < 0.001$).

Table (8): Distribution of OAB score before and after Solifenacin treatment.

Variable	Before	After	P
	Mean \pm SD	Mean \pm SD	
OAB score	7.6 \pm 2	5.6 \pm 1	<0.001*^S

*Paired t-test, S=Significant.

Discussion:

The overactive bladder syndrome is a chronic medical disorder affecting women's quality of life⁽⁹⁾. Nowadays, many anti-muscarinic agents are selected in treatment of overactive bladder syndrome^(10, 11). as acetylcholine stimulates muscarinic receptors of detrusor muscle which in turn stimulates involuntary bladder contraction⁽¹²⁾.

Current study revealed that included women with overactive bladder syndrome were characterized by increased age, multi-parity and vaginal delivery. These findings are consistent with results of Shaker *etal.*,⁽¹³⁾. study in Iraq on 34 women with urinary incontinence and found that age, parity and body mass index were the main risk factors for incontinence. However, Chae *etal.*,⁽¹⁴⁾. study in South Korea found that age, current smoking, hyperlipidemia, cardiovascular and renal disease were the common risk factors for OAB among Korean women. Handa *etal.*,⁽¹⁵⁾. study in USA reported that spontaneous and operative vaginal delivery was associated with higher risk of urinary incontinence and prolapse. It was shown that vaginal birth is accompanied with higher incidence of pelvic floor diseases⁽¹⁶⁾.

Present study revealed a significant decline in overactive bladder syndrome score (OABSS) after treatment with Solifenacin ($p < 0.001$). This finding is similar to results of Kwon *etal.*,⁽¹⁷⁾. twelve weeks prospective, open-label, multicenter, randomized study in South Korea on 127 patients with OAB and found that mean OABSS was significantly reduced after 12 weeks treatment with Solifenacin regardless of medication timing. This finding is also consistent with results of Cardozo *etal.*,⁽¹⁸⁾. randomized, placebo-controlled, double-blind, efficacy trial in 105 centers in 14 European countries which found that the solifenacin efficiently decreased attacks of urgency and extent of bothering in addition to safety and effectiveness within three days of treatment. It was also

found that OABSS is highly recommended for assessing women with overactive bladder and to evaluate the effectiveness of anticholinergic drugs *etal.*,⁽¹⁹⁾. However, another study carried out by Yoo *etal.*,⁽²⁰⁾. study in South Korea reported that use of solifenacin alone had less effectiveness in reduction of OABSS mean that combination of solifenacin and tamsulocin therapy among women with overactive bladder. Hsiao *etal.*,⁽²¹⁾. study in Taiwan found that female gender, high urgency severity scale score, high maximum flow rate and low postvoid residual volume were the common risk factors for better therapeutic efficacy⁽²⁰⁾. The solifenacin is M3 anti-muscarinic agent with higher plasma levels 3–8 hours after oral administration. It has 98% plasma protein binding and is highly distributed to peripheral tissues with 90% bioavailability and a long half-life of 45–68 hours⁽²²⁾. Many clinical trials proved the effectiveness of solifenacin in treatment of overactive bladder syndrome in women following delivery such as Chapple *etal.*,⁽²³⁾. clinical trial in Spain which found a profound decline in the mean number of voids per 24 hours and elevation in mean volume voided per void for patients taking 5 mg, 10 mg, and 20 gram of solifenacin and they found also that the effectiveness and tolerability was dose dependent. Another clinical trial by Cardozo et al⁽²⁴⁾. in UK on 12 weeks duration found a significant decline in number of nocturia, micturition and urgency after taking 10 mg of solifenacin⁽²⁴⁾.

In current study, number of micturition from waking to sleeping was significantly decreased after taking solifenacin by women ($p < 0.001$). This finding coincides with results of Govier *etal.*,⁽²⁵⁾ multicenter, randomized, double-blind, parallel-group, Phase III, pivotal trial in USA on 634 patients with OAB and found that once daily of 10 mg solifenacin was effective in treating OAB symptoms mainly frequency, incontinence and

urgency. Our study found also a significant decline in number of nocturia attacks after taking solifenacin by women ($p=0.01$). This finding is consistent with results of Yokoyama *et al.*,⁽²⁶⁾.subgroup analysis study in Japan which found that use of 10 mg solifenacin by patients with overactive bladder decreases the nocturia episodes.

Conclusion:

- 1) The solifenacin anti-muscarinic agent is effective and safe drug in treatment of women with overactive bladder syndrome.
- 2) The solifenacin drug is effective in reduction of overactive bladder syndrome score three months after treatment.

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