

The Efficacy of the Antimuscarinic Drug Oxybutynin in the Treatment Women with Overactive Bladder (OAB) Symptoms

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ABSTRACT:

BACKGROUND:

Overactive bladder (OAB) is a symptom based syndrome. These symptoms include: urgency, with or without urgency incontinence, usually with frequency and nocturia with no proven infection or other pathology. It is encountered in women visiting urodynamic units as part of mixed urinary incontinence (MUI). It greatly affects physical and social activities. Incontinence is often the key symptom for the assessment of OAB symptoms and the decision to treat patients. Antimuscarinic drugs are the main agents used to treat this condition. Oxybutynin (immediate-release) 5 mg orally is the main available form in our clinical practice.

OBJECTIVE:

The objective of this study is to assess the efficacy of Oxybutynin immediate-release (OXY-IR) 5 mg oral tablets, in the treatment of women with overactive bladder, i.e. reduction in episodes of urge incontinence, total incontinence, and micturition frequency.

MATERIALS AND METHODS:

Twenty-five patients, age range from 18-75 years, diagnosed as having overactive bladder symptoms were treated with Oxybutynin immediate-release (IR) 5 mg tablets 2-3 times daily for 8 weeks period. Homma OAB symptom score system was used for assessment of treatment efficacy. Cystometry was done in all patients to look for detrusor overactivity.

RESULTS:

After Oxybutynin treatments, all the parameters in micturition patterns improved significantly: frequency, nocturia, urgency (p value < 0.005). Homma overactive bladder symptoms scores also improved following the treatment (p value < 0.001). Cystometric examination revealed the presence of detrusor overactivity in 20 of the 25 (80%) patients at presentation. This was reduced to 4/25 (16%) following treatment. About two-thirds (64%) of the patients reported good to great benefit from the treatment and had a positive effect on their life concerning physical and social activity, sleep and feeling of well-being.

CONCLUSION:

The selective antimuscarinic agent Oxybutynin (OXY-IR) 5 mg 2-3 times orally is effective in treating overactive bladder symptoms in these women by reducing incontinence attacks, urgency, micturition times and nocturia; consequently, it improves their life quality. We recommend devising a score system for OAB suiting Iraqi patients.

KEYWORDS: overactive bladder, OAB, urgency, incontinence, urodynamic study, oxybutynin.

INTRODUCTION:

Overactive bladder is a symptom based syndrome and defined by the International Continence Society (ICS) as urgency, with or without urgency incontinence, usually with frequency and nocturia, if there is no proven infection or other obvious pathology⁽¹⁾.

The term OAB was coined by the pharmaceutical industry during the development and promotion of new oral medications to treat these symptoms.

Urgency with at least one other symptom is essential to diagnose OAB. Thus urgency is the pivotal symptom, defined by the ICS as the complaint of a sudden compelling desire to void that is difficult to defer⁽¹⁾.

In many OAB patients, urgency incontinence occurs, defined as involuntary leakage of urine,

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accompanied or immediately preceded by urgency. This distinguishes it from stress incontinence ⁽¹⁾.

OAB is a chronic condition that affects people of all ages ⁽²⁾. However, it is more prevalent in adult female patients. The prevalence of OAB in adult males varies from 10.2% to 17.4% and in females from 7.7% to 31.3% ⁽³⁾.

A higher percentage of women report urge incontinence (UI) with OAB (9%) compared with men (3%) ⁽⁴⁾.

There is a conflicting data about the relation of OAB with the increase of age especially in the type of OAB without incontinence (dry type) ⁽³⁾. Studies have suggested that there could be 17.5 million women in the United States who suffer from the condition. ⁽⁵⁾

OAB greatly affects physical and social functioning, including work, sleep, sexual relationships and interpersonal relationships ⁽⁴⁾. Incontinence is often the key symptom associated with the assessment of OAB symptom severity and the decision to pharmacologically treat patients ⁽⁶⁾.

A wide variety of pharmacologic therapy is employed in OAB. The antimuscarinic agent Oxybutynin is on the head of the list and has been available for many years. It works by reducing intra-vesical pressure, increasing compliance, raising the volume threshold for micturition and reducing uninhibited detrusor contractions ⁽⁷⁾. Oxybutynin is a tertiary amine compound. It is metabolized by the liver, specifically the cytochrome P450 (CYP 450) 3A4 system, and is eliminated in the feces and urine ⁽⁸⁾.

It competitively antagonizes the M1, M2, and M3 subtypes of the muscarinic acetylcholine receptor ⁽⁹⁾.

Currently, there are three forms of the drug: immediate-release (OXY-IR), extended-release (OXY-ER) and transdermal patch (OXY-TSD). However, in our clinical practice, the main available form is OXY-IR 5 mg tablet taken

orally. It is empirically used by the physician, surgeons, gynecologists and even GPs to relieve the LUTS associated with lower urinary tract infection like other anticholinergics as hyoscine butylbromide and Clinidium bromide. However, it can be used specifically to treat the overactive bladder symptoms especially by urologists.

The objective of this study is to assess the efficacy of Oxybutynin (OXY-IR) in the treatment of women with overactive bladder, i.e. reduction in episodes of urge incontinence, total incontinence, and micturition frequency.

PATIENTS AND METHODS:

From January 2010 to February 2012, women visiting the urodynamic unit of Al-Karama Teaching Hospital were diagnosed as having OAB from a total of 44 women referred to this unit complaining of incontinence and/or urgency, nocturia or severe frequency for urodynamic assessment.

The 32 women were included in the study based on the following inclusion criteria:

- Involuntary leak of urine preceded or associated with urgency of twice or more times per day and/or
- Daytime frequency (eight micturitions or more), and/or
- Waking up at least twice each night to urinate, and/or
- Urgency (sudden feeling of a full bladder and the immediate need to urinate to avoid accidental loss of urine) of twice or more times per day.

Twelve patients were excluded. Six of the excluded patients were shown by cystometry to have 'pure' stress incontinence and the cause of referral was to exclude mixed urinary incontinence (MUI). Other six patients had pyuria on urinalysis. Each of the 32 patients was interviewed at presentation using an Arabic translation of the Homma Overactive Bladder Symptoms Score ⁽¹⁰⁾ (OABSS), shown in Table 1, as a measure of the severity of OAB.

OVERACTIVE BLADDER

Table 1: Homma Overactive Bladder Symptoms Score (OABSS).

Question	Frequency	Score
How many times do you typically urinate from waking in the morning until sleeping at night?	≤7	0
	8-14	1
	≥15	2
How many times do you typically wake up to urinate from sleeping at night until waking in the morning?	0	0
	1	1
	2	2
	≥3	3
How often do you have a sudden desire to urinate, which is difficult to defer?	Not at all	0
	Less than once a week	1
	Once a week or more	2
	About Once a day	3
	2-4 times a day	4
	5 times a day or more	5
How often do you leak urine because you cannot defer the sudden desire to urinate?	Not at all	0
	Less than once a week	1
	Once a week or more	2
	About Once a day	3
	2-4 times a day	4
	5 times a day or more	5

The Homma OAB symptoms score ranges from 0-15, scores are given based on subjective basis by the patient herself; with frequency ranging from 0-2, nocturia from 0-3, and urgency from 0-5, and urge incontinence from 0-5.

Cystometric examination was done in all patients using a double-lumen vesical catheter and rectal catheter with sticker-electrode EMG recording when appropriate with the patient in lithotomy position in an air-conditioned quiet room. Oxybutynin 5 mg orally, 2-3 times daily was given for an 8 weeks period. The patients were asked to record the micturition numbers per day, nocturia episodes, urge incontinence episodes and side effects (such as dry mouth, constipation and blurred vision) during the 8 weeks period. In

addition, patients were given instructions to make treatment more effective as: lifestyle modification (fluid restriction, avoidance of caffeine) and bladder retraining. Only 25 patients completed the 8-week follow-up period. At the end of 8-week, patient-reported outcomes (PROs) ⁽¹¹⁾ were used to assess treatment efficacy. Homma OABSS was applied again and recorded for each patient. In addition, Cystometry was repeated for each patient and results recorded graphically. A simple interview questionnaire of how much benefit the patient got from treatment and how her life affected was devised and delivered verbally to patients (Table 2).

Table 2: Assessment of patient's satisfaction with treatment.

1- I had no benefit from treatment, I still suffer
2- The treatment gave me some benefit but I am not satisfied with it
3- The treatment gave me good benefit and this affected my life in a positive way
4- The treatment gave me great benefit and my life changed completely

Statistical Analysis

Descriptive statistics such as mean, standard deviation were used to describe the summary measures. For continuous data paired *t*-tests were applied to compare before and after treatment and categorical data using marginal chi-square tests. A p-value of less than 0.05 was considered to indicate statistical significance. Microsoft Office Excel 2010 was used for data analysis and double checked by SPSS.

RESULTS:

Incontinence was the main cause of referral to the urodynamic unit. Twenty-two patients (88%) had varying (moderate to severe) degrees of incontinence for more than one month duration (1-36 months), with an average of 13 months Table 3.

Table 3: Patients Characteristics.

	Mean ± SD	Range
Age	43.3 ± 12.5	18.0-75.0
Duration of OAB (months)	13.0 ± 8.4	1.0-36.0

After oxybutynin treatments, all the parameter in micturition patterns improved significantly (Table 4). The mean ± SD of the micturition reduction was 58.8 ± 12.7% (p value < 0.005).

Homma overactive bladder symptoms scores also improved following the treatment. The mean ± SD of the OABS score reduction was 4.4 ± 1.3 (p value < 0.001) (Table 5).

Table 4: Micturition variables (before and after Oxybutynin treatment).

Variable	Before Mean ± SD	After Mean ± SD	p-value
Micturition per day (times)	14.3 ± 4.2	5.2± 1.6	<0.05
Nocturia episodes(times)	3.2 ± 2.2	1.1± 1.2	<0.05
	N (%)	N (%)	
Patients with urge incontinence episodes	22/25 (88%)	8/25 (32%)	<0.005
Patients with nocturia	22/25(88%)	3/25(12%)	<0.001

Table 5: OABSS before and after treatment with Oxybutynin.

	Homma OABSS (of 15) Mean ± SD	p-value < 0.001
Before	12.5 ± 2.4	
After	8.1 ± 1.1	

Cystometric examination revealed the presence of detrusor overactivity in 20 of the 25 (80%) patients who completed the study. Detrusor contraction caused a pressure of more than 15 cm water at low volumes (150-200 cc) infused into the bladder of these patients (Figure 1).

Following the 8-week treatment with Oxybutynin, only 4 of 25 (16%) had detrusor overactivity. This marked a statistically significant difference (p<0.001) before and after treatment Table 6.



Figure 1: Detrusor overactivity as shown by cystometry.

Table 6: Effect of Oxybutynin on detrusor overactivity.

Treatment with Oxybutynin	Detrusor overactivity (DO) present	Detrusor overactivity (DO) absent	p-value <0.001
Before	20	5	
After	4	21	

Dry mouth as a side effect of Oxybutynin was reported in 13 (52%) of the 25 patients enrolled in the study.

As for the patient's satisfaction with the treatment, 2 (20%) patients reported no benefit,

7(28%) reported some benefit, 12(48%) reported good benefit and 4(16%) patients reported having great benefit from the treatment (Figure 2).

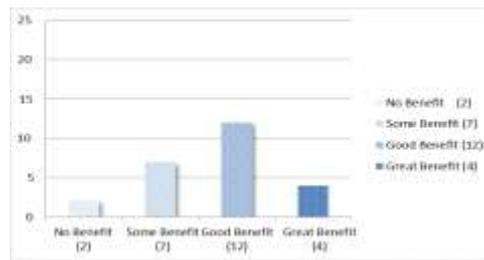


Figure 2: Subjective benefit from treatment as reported by patients.

DISCUSSION:

Overactive bladder (OAB) syndrome is a health problem that challenges every practicing urologist because it should be taken in consideration in every woman presenting with incontinence. It has clinical and social impacts on patient's life. The diagnosis of OAB is subjective depending on a battery of symptoms each patient has. Many score systems have been introduced to quantify the complaint of the patient and reflect the severity of the symptoms and their effects on life quality. Main examples of these score systems are: Homma OABSS⁽¹⁰⁾, Blaivas OABSS⁽¹²⁾, OAB-q by Matza et al⁽¹³⁾, and Patient Perception of Bladder Condition (PPBC) (2006) by Coyne et al⁽¹⁴⁾. We chose the Homma OAB score system because it is simple and can be easily translated and verbally delivered to the patients. Translation of Homma OABSS into other languages was also used by other authors⁽¹⁵⁾. Oxybutynin is a time-tested drug for use in overactive bladder. However, no study was conducted in Iraq to evaluate its efficacy on OAB in women particularly. Our study used the multi-parameter statistical analysis to minimize bias in result, dealing with frequency, nocturia, urgency and urgency incontinence separately than summing them all in Homma scores. Consequently, reduction in episodes of urge incontinence, total incontinence, nocturia and micturition frequency

according to the patient-reported response (PRO) were noticed following the use of OXY-IR and Homma OABSS figures were reduced with a statistical significance. Significant improvement in detrusor overactivity as proved by cystometric study consolidated the efficacy of Oxybutynin as an anti-muscarinic agent. As for life quality, about two-thirds (64%) of the patients reported good to great benefit from the treatment and had a positive effect on their life concerning physical and social activity, sleep and feeling of well-being.

In general, oral Oxybutynin (OXY-IR) was tolerable by most (52%) of the patients and no patients reported dry mouth causing a significant interference with the intake of the drug.

CONCLUSION:

OAB is a chronic condition that should be sought in women presenting with urge incontinence attending the urodynamic units In Iraq. It needs to be properly diagnosed and treated. A national OAB score system suiting the Iraqi patients needs to be formulated. The selective antimuscarinic agent Oxybutynin (OXY-IR) orally is effective in treating this condition by reducing incontinence attacks, urgency, micturition times and nocturia; consequently, it improves the life quality of these patients.

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