

INTERMEDIATE RELEASE OXYBUTYNIN IN SYMPTOMATIC OVERACTIVE BLADDER

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Abstract

Background : Anticholinergic drugs are recommended as first line with Oxybutynin (IR) being one of the most commonly recommended drug. Older pharmacological agent such as propanthelene, dicyclomine and tricyclic antidepressant like imipramine have been used but have become alternative due to poor patient tolerability and lack of strong evidence from clinical trials. A combination of behavioral therapy and drug therapy has been shown to be more effective than either drug therapy or behavioral therapy alone. To assess the efficacy of Oxybutynin (IR) on number of micturition per day, episodes of incontinence per day and voided urinary volume along with the adverse effects of Oxybutynin (IR) and safety of the drug. **Materials and methods:** This study was conducted at the Department of Urology, Chittagong Medical College Hospital, Chittagong, from July, 2012 to June, 2013. Purposive sampling was done. Bladder diary was used for evaluating the symptoms of the patient during baseline and 08 weeks follow up. Perceived level of benefit of the patients was assessed and graded using Likert scale. Data analysis was conducted by SPSS version-21. **Results:** Out of 84 patients, 25 (29.8%) were male and 59 (70.2%) were female. Male female ratio was 1:2.4. The study revealed that the most of the patients, 49 (58.33%) were subjected to much benefit

followed by 26 (30.95%) patients experienced little benefit and 09 (10.71%) patients were not benefited from the treatment. **Conclusion:** Oxybutynin showed a significant level of efficacy on overactive bladder with an acceptable level of side effects.

Key words

Overactive bladder; Bladder diary; Oxybutynin.

Introduction

Overactive Bladder (OAB) is a chronic, more prevalent and often significantly debilitating disorder. It is a distressing condition for its sufferers¹. This condition limits and disrupts sufferers' everyday lives and cause intense feelings of embarrassment, anxiety, fear, humiliation, anger, frustration and depression².

The international Continence Society produced its revised definition in 2002 as follows : The overactive bladder is defined as urgency, with or without urge incontinence, usually with frequency (>8 micturition / 24 hours) and nocturia³. Another definition of overactive bladder is a debilitating medical condition having the symptoms of urinary frequency and urgency with or without urge incontinence in the absence of local pathologic or metabolic factors that would account for these symptoms⁴. Though no data is available in Bangladesh but the prevalence of the OAB is increasing gradually. Studies on OAB show that approximately 33 million US adults of all ages are affected⁵.

Upon patient complaint of urinary urgency, frequency with or without urge incontinence and involuntary loss of urine a thorough history taking and physical examination is carried out in order to determine which type of incontinence is present and to rule –out any underlying conditions. OAB is suspected when a patient complains of dysuria, nocturia, more than 8 micturition per 24 hours and often leaks after a preceding urge to void. In contrast, stress incontinence is the involuntary loss of urine during an increase in intra-abdominal pressure from activities such as laughing, coughing, sneezing or exercising. Diagnostic tests such as

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Received on : 17.03.2018

Accepted on : 24.03.2018

urinalysis, post-void residual urine volume and uroflowmetry for obstructing bladder can help categorizing the specific type of urinary incontinence. Treatment begins with using one of a number of different modalities tailored to the diagnosed type of urinary incontinence^{5,6,7}.

Anticholinergic drugs are recommended as first line with Oxybutynin (IR) being one of the most commonly recommended drug. Older pharmacological agent such as propanthelene, dicyclomine and tricyclic antidepressant like imipramine have been used but have become alternative due to poor patient tolerability and lack of strong evidence from clinical trials^{7,8,9}. A combination of behavioral therapy and drug therapy has been shown to be more effective than either drug therapy or behavioral therapy alone.

Antimuscarinic agents inhibit the binding of acetylcholine to muscarinic receptors and suppress the involuntary detrusor contraction¹⁰. Oxybutynin (IR) was the gold standard in the pharmacologic treatment of OAB for almost three decades. Its antimuscarinic (M_3) activity is nonselective for the urinary bladder, resulting in significant systemic side effects, particularly dry mouth, limits its clinical utility^{11,12}.

This current study has been conducted to find out efficacy of Oxybutynin (IR) to allay symptoms of overactive bladder and their tolerability. And the result was focused on the objective evidence of efficacy of Oxybutynin (IR) to increase function, decrease symptoms and also observed the subjective sense of improvement of clinical symptoms in the management of symptomatic overactive bladder. This study also evaluated the tolerability of the drug with the foci on the number and degree of severity of adverse effects.

Materials and methods

It was an observational study to explore the efficacy and safety of intermediate release Oxybutynin (IR) in patients with symptomatic overactive bladder. The place of study was Department of Urology, Chittagong Medical College Hospital (CMCH) and Chittagong from July 2012 to June 2013. 93 patients diagnosed with symptomatic overactive bladder were selected consecutively according to selection criteria from the patients attending Urology OPD of Chittagong Medical College Hospital with symptomatic overactive bladder with 09 lost patients to follow up.

A case record form was completed for each patient that included in the study containing particulars of the patients, history, results of physical examination and relevant baseline investigations. During evaluation of urogenital system presence of pain, haematuria, renal stone, urethral stricture, meatal stenosis or urinary tract infection was excluded. After completion of baseline clinical evaluation and investigations, Oxybutynin (IR) 05 mg twice daily was given orally for 08 weeks. Patients were explained well about the possible side effects of the drugs and precaution was taken. If there are any intolerable adverse effects, patients were requested to report to urology OPD.

Clinical safety was evaluated in terms of adverse effects that were reported or directly observed during the 8 weeks of treatment. During follow up visit at 8 week patients were again underwent physical examination and bladder urinary variables like number of micturations per day, episodes of incontinence per day and amount of voided volume per micturition (ml) were assessed and the side effects of the drugs were recorded. On 2nd visit, patient's perception of treatment benefit was also evaluated.

Inclusion criteria:

Symptomatic OAB having

- i) Adults aging 18 years or more
- ii) Urinary frequency (At least 8 voids / 24 hours).

Exclusion criteria:

- i) Require intermittent catheterization or an indwelling catheter
- ii) Recurrent or acute UTI
- iii) Patients with congestive cardiac failure, severe liver and renal diseases
- iv) Presence of contraindications for antimuscarinic agents
- v) Pregnant or lactating women.

Results

Table 1 : Age distribution of the patients based on sex (n=84)

	Sex	N	Group Statistics		
			Mean	Std. Deviation	p value
Age of the patients	Male	25	48.64	8.49	0.101
	Female	59	51.83	7.87	

*p value calculated by t-test

Table II: Findings on clinical examination of patients.

Clinical Examinations	n=84 Mean ± SD
Heart Rate (Per minute)	85 ± 12.35
Systolic BP (mmHg)	131.4 ± 15.25
Diastolic BP (mmHg)	82.10 ± 11.52
BMI (Kg/m ²)	25.66 ± 2.71

Table III: Number of micturition/day, incontinence/day and urinary volume/micturition at baseline and at 08 weeks.

Name of condition	Before drug n (84) Mean ± SD	After drug n (84) Mean ± SD	Mean difference n (84) Mean ± SD	p value
No. of micturition/day	11.85±1.83	9.04± 1.33	2.81± 1.55	0.001*
Incontinence/ day	1.69± 0.47	0.77 ± 0.79	0.39± 0.83	0.001*
Urinary voided Volume/micturition (ml)	164.09± 8.32	210.45±10.78	46.36±13.17	0.001*

* p value calculated by t-test

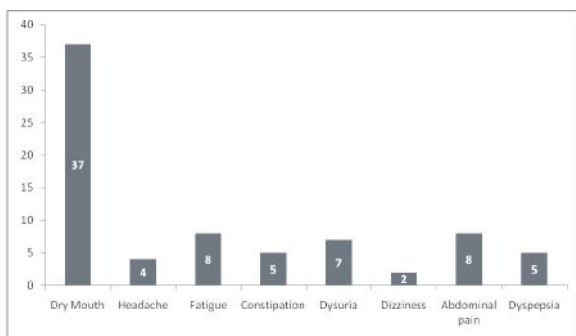


Fig 1 : Frequency of side effects with Oxybutynin (n=84)

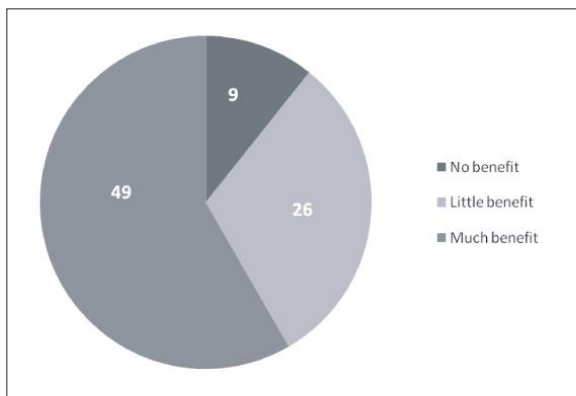


Fig 2 : Perception on treatment benefit of the patients with Oxybutynin (n=84)

Out of 84 patients, 25 (29.8%) were male and 59 (70.2%) were female. Male female ratio was 1:2.4. The age of males were (Mean- 48.64 ± SD- 8.49) and age of females were (Mean- 51.83 ± SD- 7.87) with an overall value as (Mean- 50.88 ± SD- 8.14) with no statistically significant difference (Table I).

On clinical examination mean heart rate was found 85 beats/ minute and SD was 12.35 beats/ minute.

Systolic blood pressure found to be (Mean- 131.4 mm of Hg ± SD- 15.25 mm of Hg) diastolic blood pressure was (Mean- 82.10 mm of Hg ± SD- 11.52 mm of Hg) and mean BMI was found to be 25.66 ± SD- 2.71 (Table II).

The numbers of micturition per day were (Mean- 11.85± SD- 1.83) during baseline in comparison to (Mean- 9.04 ± SD- 1.33) after 08 weeks with drug and mean decrease of micturition per day was 2.81± 1.55. During baseline, numbers of episodes of incontinence per day were (Mean- 1.69± SD- 0.47) and after 08 weeks with drug were (Mean- 0.77 ± SD- 0.79) with a mean decrease of (0.39± 0.83) episodes of incontinence per day. There was mean increase of urine voided /micturition (ml) (46.36±13.17) considering the baseline amount of urine voided /micturition as (Mean- 164.09 ± SD- 8.32) ml and amount of urine voided /micturition after 08 weeks of treatment was (Mean- 210.45 ± SD- 10.78) ml. Baseline values for numbers of micturition per day, numbers of episodes of incontinence per day and amount of urine voided /micturition (ml) were significantly different when compared to findings on 08 weeks follow up (Table III).

In our study there were no moderate or severe level side effects had been reported by the patients. A total of 76 patients experienced mild form of side effects (Fig 1). Percentage of patients experienced different side effects were included dry mouth (44.5%) headache (4.76%), fatigue (9.52%) constipation (5.95%) dysuria (8.33%) dizziness (2.38%) abdominal pain (9.52%) and dyspepsia (5.95%).

In response to commenting on perceived benefit of the treatment 09 (10.71%) patients reported that they were not benefited from treatment, while 26 (30.95%) patients experienced little benefit and most of the patients, 49 (58.33%) were subjected to much benefit (Fig 2).

Discussion

This observational study was carried out with an aim to evaluate the efficacy and safety of intermediate release Oxybutynin (IR) to assess the extent of symptoms in 84 patients under evaluation based on bladder diary, to determine the changes of symptoms after 08 weeks with Oxybutynin (IR) and to note any adverse effect associated with the drug.

The age range for the patients was 39 to 65 years with a male female ration being 1: 2.36 as comparable to other studies it is seen that symptoms of overactive bladder are more prevalent in female^{13,14}. The mean age for male and female were 48.64±8.49 and 51.83 ± 7.87 respectively. In another study the mean age was 57.9 ± 12.5 years and 63.1 ±12.0¹⁵.

The patients complaining urinary frequency of at least 08 voids / 24 hours were evaluated considering the selection criteria. mean heart rate was found 85 beats/ minute and SD was 12.35 beats/minute. Systolic blood pressure found to be (Mean- 131.4 mm of Hg ± SD- 15.25 mm of Hg) diastolic blood pressure was (Mean- 82.10 mm of Hg ± SD- 11.52 mm of Hg) and mean BMI was found to be 25.66 ± SD- 2.71.

There was an average episode of incontinence more than once a day with an average volume of 164.09 ml of urine per day. The findings were altered with administration of Oxybutynin (IR) for following 08 weeks. On a follow up after 08 weeks the mean values for no. of micturition/day, incontinence/ day and urinary voided volume/ micturition (ml) were 9.04, 0.77 and 210.45 respectively. Findings from randomized double –blind trial were closely resemble with the present study^{16,17}.

Fig 1 showed mild form of side effects experienced by 76 patients including dry mouth (44.5%) headache (4.76%) fatigue (9.52%) constipation (5.95%) dysuria (8.33%) dizziness (2.38%) abdominal pain (9.52%) and dyspepsia (5.95%). No moderate or severe level side effects had been reported by the patients. Adverse effects of Oxybutynin in earlier studies included dizziness, headache, dysuria, dyspepsia, fatigue, visual disturbance ,abdominal pain, constipation and were 2.9%, 5.9%, 11.8%, 5.9%, 11.8%, 2.9%, 8.8%, 8.8 %^{15,16,17}.

The study revealed that the most of the patients, 49 (58.33%) were subjected to much benefit followed by 26 (30.95%) patients experienced little benefit and 09 (10.71%) patients were not benefited from the treatment.

Limitations

The study was done on a small number of patients in a single center within a short period of time without urodynamic study. Any conclusion regarding efficacy and safety may be seriously biased by the patients of investigator's knowledge of which treatment was given (Open label).

Contribution of authors

MR - Conception, desing, acquisition of data, drafting the article and final approval.

MMUH - Data analysis, drafting critical revision and final approval.

AKMAI - Interpretation of data, critical revision and final approval.

Acknowledgements

The authors gratefully acknowledge the support of all duty doctors and staffs working in the Department of Urology, Chittagong Medical College Hospital, Chittagong. We are also appreciating the kind contributions of our colleagues working in the Department of Urology of CMCH, Chittagong and Bangabandhu Sheikh Mujib Medical University, Dhaka on their valuable suggestion on successful completion of the study.

Conclusion

Intermediate Release Oxybutynin (IR) therapy in overactive bladder patients showed improvement in reduced number of micturition per day, decreased number of incontinence per day and increased amount of urine voided in each micturition. It was also found to be well tolerated with few and milder side effects with a satisfactory level of patients compliant.

Disclosure

All authors hereby declare no competing interest.

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