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Efficacy of Mirabegron Add-on Therapy to Oxybutynin for BPH Patients with Persistent Urgency on Oxybutynin Alone

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Abstract--- Aims: *To compare the efficacy of mirabegron add-on therapy for persistent overactive bladder (OAB) symptoms despite oxybutynin monotherapy in men with irritative lower urinary tract symptoms suggestive of benign prostatic hyperplasia*

Methods: *50 patients with persistent irritative lower urinary tract symptoms despite Ditropan monotherapy were randomized to receive add-on therapy with mirabegron (50 mg/day) for 3 months. Improvement in IPSS score and QOL were assessed in patients before and after addition of mirabegron at 3 months*

Result: *From September 2018 to December 2019, 50 patients were enrolled in this study. 38 out of 50 patient got improvement in quality of life (QOL) score. The IPSS score had a mean improvement from 16.6 before addition of mirabegron to 12.68 after 12 weeks of mirabegrone addition.*

Conclusions: *In our study, we noticed that the add-on mirabegron to patients already on anticholinergic drugs but still with persistent irritative LUTS had get good imapact on IPSS score and QOL.*

Keywords--- *Mirabegron, Therapy, Oxybutynin, BPH.*

I. INTRODUCTION

Overactive bladder (OAB) is a common condition, with symptoms affecting up to 35.6% of men and women ≥40 years of age, and prevalence increasing with age. Characterized by urinary urgency, with or without urinary incontinence, nocturia, and urinary frequency, OAB often negatively impacts sleep, mental health, and work productivity of affected individuals OAB can have a profound impact on quality of life. It has been estimated that up to 50% of people with OAB experience depression and anxiety OAB can also negatively impact the ability to participate in physical activity, sleep, sexual activity, and work or employment and is associated with fatigue, erectile dysfunction, and falls. The breadth of adverse impacts associated with OAB contributes to the considerable economic impact of the condition Behavioral therapies and lifestyle changes are initial treatments for OAB; if such interventions insufficiently manage symptoms, pharmacotherapy may be prescribed.

Although the American Urological Association recommends that antimuscarinics and mirabegron as first-line pharmacotherapy options for OAB, there is evidence that in clinical practice mirabegron may only be offered after treatment failure with antimuscarinics.

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Add-on of an anticholinergic agent to α1-blocker therapy effectively improves OAB symptoms. As for β3-AR agonists, mirabegron has been shown to effectively improve subjective symptoms and bladder storage functions, without deteriorating voiding functions. Recently, several studies demonstrated that add-on treatment with mirabegron for patients with residual OAB symptoms despite α1-blocker monotherapy was more effective and safer than continuing α1-blocker monotherapy.

To the best of our knowledge, no randomized controlled studies have compared the improvements in LUTS when we add B3 agonist for anticholinergics for patients with persistent irritative .Therefore, the aim of the present study was to compare the efficacy of add-on B3, for anticholinergic agent in persistent irritative LUTS.

II. MATERIALS AND METHODS

This was a single-center, comparative study. All participants provided written informed consent before enrollment.

The study included men who had persistent OAB symptoms despite anticholinergic treatment for12-24 weeks. The inclusion criteria were as follows: total International Prostate Symptom Score (IPSS) ≥8; IPSS-QOL ≥3; one or more urinary urgency episodes per week; and residual urine <150 mL. Patients were excluded if they had previously received 5-α reductase inhibitors, antidepressants, anti-anxiety agents, or sex hormonal agents; had neurogenic bladder dysfunction, bladder calculi, or an active urinary tract infection; and/or had severe cardiac disease, renal dysfunction (serum creatinine level ≥3 mg/dL), and hepatic dysfunction.

Patients who satisfied all inclusion and exclusion criteria were assessed before and 3 months after addition of B3 agonist for the anticholinergic agent in regard to IPSS and QOL score. To evaluate changes in subjective symptoms, the total IPSS, as well as QOL scores, were assessed before and at 12 weeks after initiating add-on treatment

The primary endpoint was the change from baseline to 3 months in the IPSS score of ≥3points, because a change of >3 points in the IPSS was reported to be a clinically significant or beneficial improvement for patients with irritative LUTS. The 2nd endpoint was determined by direct answer for improvement in quality in life before and after add-on therapy.

III. RESULTS

In total of 50 patients with irritative LUTS of BPH who complained of poor response of anticholinergic agents when added to alpha blocker as monotherapy, the patients were discussed for addition of another drug category to reduce the OAB symptoms without cessation of the previous anticholinergic drug. This include B3 agonist drug (e.g. mirabegron 50 mg) From September 2018 to December 2019, 50 patients were enrolled in this study.

All patients were assessed before add-on treatment by IPSS score, all patients informed as for poor QOL before enrollment in the study. All patients were reassessed 12 weeks later by reassessment of IPSS score and also QOL assessment. The IPSS score for all patients was between 10 as minimum score recorded to 23 as maximum score recorded with a mean of 16.6 before starting the study.

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Report		
IPSS before add- on mirabegrone		
Mean	N	Std. Deviation
16.6600	50	3.70113

12 weeks later, all patients were re-evaluated again with IPSS score and asking specifically for QOL improvement. 38 patient out of 50 (76 %) show good improvement in QOL,12 patients out of 50 (24 %) show no significant improvement in QOL.

QOL					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	no improvent in QOL	12	24.0	24.0	24.0
	improved QOL	38	76.0	76.0	100.0
	Total	50	100.0	100.0	

The IPSS score 12 weeks later, when we add the mirabegrone for the anticholinergic agents was between 5 as minimum score recorded and 20 as maximum score recorded with a mean of 12.68

Report		
IPSS with mirabegrone 12 weeks later		
Mean	N	Std. Deviation
12.6800	50	3.34078

When we compare the results before and after mirabegrone for the management, there was significant improvement for both IPSS and QOL

Descriptive Statistics					
	N	Minimum	Maximum	Mean	Std. Deviation
IPSS1	50	10.00	23.00	16.6600	3.70113
IPSS2	50	5.00	20.00	12.6800	3.34078
Valid N (listwise)	50				

IV. DISCUSSION

This trial is focused to compare the add-on effects of mirabegron on lower urinary tract functions and symptoms in LUTS/BPH male patients with persistent OAB symptoms despite receiving anicholinergic treatment to theα1-blocker. Adding mirabegron to antichlinergic therapy significantly improved patients' storage symptoms and functions, and their QOL, without deteriorating voiding symptoms and BOO.

Comparisons between the IPSS score and QOL before and after addition revealed that the combination therapy yielded significantly greater improvements in patients' storage symptoms and functions.

In our study, we examined the changes in IPSS score and QOL imprompment that were induced by adding miraegrone to the anticholinergic agent. We found that 38 patient out of 50 (76 %) show good improvement in QOL, while 12 patients out of 50 (24 %) show no significant improvement in QOL. Also the mean IPSS score before add-on treatment was 16.6.The mean IPSS score was significantly reduced to 12.68 when assessing the score 12 weeks after mirabegrone addition.

The detailed mechanisms underlying the better efficacy of mirabegron add-on therapy in terms of the improvement in storage symptoms and function remains not fully understood. Many theories exist. For one, regarding the effects of these drugs on detrusor smooth muscle, mirabegron and anticholinergics have different

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mechanism of action in inhibiting detrosur over activity. Mirabegron relaxes the detrusor smooth muscle during the storage phase and promote the bladder distension by activation of β3-adrenergic receptors, and it is thought to have little effect on the suppression of the strong detrusor involuntary contraction that occurs in the storage phase, causing OAB symptoms.

While anticholinergic drugs, inhibits detrusor contraction by inhibition of muscarinic receptors which may play an important role to suppress detrusor overactivity. This difference in the action mechanisms between the two drugs may explain the synergistic affect on detrosur muscle.

One limitation of this study is that the follow-up period was only 3 months. Drugs managements for irritative BPH symptoms need to be continued for a longer time, long-term studies of add-on therapies need to be performed in the future.

V. CONCLUSION

In our study, we noticed that the add-on mirabegron to patients already on anticholinergic drugs but still with persistent irritative LUTS had get good imapact on IPSS score and QOL . More than 3 quarters of the patients feeling pleasant for the results and continue on both agents with significant bother of combined side affect

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