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Impact of body mass index on treatment efficacy of mirabegron for overactive bladder in females

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ABSTRACT

Objective: Conclusive data comparing treatment efficacy of OAB pharmacotherapy in normal weight versus obese patients are not available. Obesity represents a risk factor for OAB/LUTS. We hypothesized that the effect of treatment with mirabegron might be diminished in obese patients.
Study design: One hundred sixty nine women were prescribed mirabegron, 50 mg/day. Subjective and objective parameters were compared prior to and following three months of treatment. The study population was stratified into three groups according to a patients' BMI (A-normal weight, B-overweight, C-obese). We compared the change in parameters before and after treatment within each group. Subsequently the differences between groups were correlated. The same analysis was performed separately in patients who failed anticholinergic therapy ($n = 85$). A paired t-test was used to compare the parameters before and after the procedure within groups, and a two-sample t-test was applied to conduct a comparison between groups. A p value of <0.05 was considered statistically significant.
Results: Significant improvement ($p < 0.001$) within all groups was observed in all parameters, with an exception in the number of severe urgency episodes per 24 h ($p = 0.291$) in Group B. We did not observe any statistically significant difference between groups A, B and C. The same trend has been observed in subgroup of patients, who did not respond previous antimuscarinic treatment.
Conclusions: This study provides evidence in support of previously documented data indicating good efficacy of mirabegron in the treatment of OAB. The data obtained do not confirm our hypothesis that the body weight influences the treatment outcome of mirabegron.

Introduction

The term overactive bladder (OAB) was introduced to describe the clinical problem of urgency (sudden compelling desire to urinate) and urge incontinence (involuntary leakage accompanied by or immediately preceded by urgency), from a symptomatic prospective [1]. OAB is not a life threatening disease; however, it is a debilitating condition affecting the quality of life of many patients [2]. The prevalence of OAB in the adult population is estimated to be 10–12% [3].

Anticholinergics are considered to be the first-line pharmacological treatment for OAB. The effectiveness and safety of anticholinergics have been confirmed in numerous clinical trials and meta-analyses [4].

Beta-3-adrenergic agonist mirabegron represents a novel class of compounds which has been recently introduced as a new oral treatment for OAB. Because of its different mechanism of action when compared to anticholinergics, mirabegron has the same efficacy with an improved side effect profile [5].

Metabolic syndrome and obesity have been shown to be independent risk factors for urinary incontinence and OAB [6]. Weight reduction in overweight and obese women with urinary incontinence has been documented to be effective in

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reducing urine leak and other lower urinary tract symptoms (LUTS). It has also been documented that weight loss leads to a significant reduction of the frequency and severity of urge incontinence episodes [7]. Conclusive data comparing treatment efficacy of OAB pharmacotherapy in normal weight versus an obese patient population are not currently available. The aim of this study was to evaluate the impact of Body Mass Index (BMI) on the treatment efficacy of mirabegron for OAB in adult women.

Material and methods

A total of 169 women (age 62.7 ± 12.31), with OAB symptoms lasting a minimum of 3 months, were included in the multicentre study. IRB approval was waived, as the study was considered a non-interventional clinical follow-up without any alteration of the routine clinical practice. Patients with the following conditions were excluded from enrollment in the study: symptomatic urinary tract infection, significant stress or mixed urinary incontinence where stress was the predominant factor, clean intermittent catheterization, indwelling catheter, post-void residual of more than 200 mL, clinically significant pelvic organ prolaps, diabetic neuropathy, neurogenic bladder, clinically significant bladder outlet obstruction (BOO), history of previous malignant disease in the pelvic area or previous irradiation to the pelvis. Of the total 169 patients, 150 had previously used at least one anticholinergic.

All patients were prescribed 50 mg/day of mirabegron. One hundred sixty five patients completed the three month treatment period and were included in the final analysis. Subjective and objective parameters were compared prior to and following three months of uninterrupted treatment. Patients' Perception of Intensity of Urgency Scale (PPIUS), OAB questionnaire, short form (OAB-q SF), and the visual analog scale for urgency bother (VAS-UB) were used to evaluate the subjective perception of the treatment efficacy. PPIUS is a validated 5-point scale ranging from 0 (no urgency at all, patient felt no need to empty the bladder, but did so for other reasons) to 4 (urge incontinence, urine leakage before arriving at the bathroom) [8]. OAB-q SF is a validated questionnaire consisting of 13 items related to the severity of OAB symptoms. An additional six items on this questionnaire were designed to quantify the impact of OAB on a patients' quality of life; the higher the score, the higher the impact of OAB [9]. The severity of bother associated with urgency was monitored using a VAS-UB, where 0 represented no bother and 100 signified the most severe bother. Data from the voiding diaries were used to assess the number of nocturia episodes as well as the number of voids and the severity of each urgency episode over a 24 h period.

Data from all patients who completed three months of mirabegron treatment were included in the final analysis. The total study population was stratified according to a patients' body mass index (BMI). Group A: Normal BMI (BMI 18.5–24.9, $n = 59$), Group B: Overweight (BMI 25–29.9, $n = 61$), Group C: Obese (BMI $\geq$30, $n = 45$). We compared the change in parameters before and after treatment within the groups, and subsequently the differences between groups. The same analysis was performed in a sub-group of patients who failed anticholinergic therapy in the past due to low treatment efficacy ($n = 85$). Good treatment efficacy of anticholinergic treatment was defined by a decrease in the number of urgency episodes (grades III and IV) by at least 50% over a period of 3 months of anticholinergic treatment. Patients who discontinued previous anticholinergic treatment due to poor tolerability (unacceptable side-effects) were not included in this sub-group.

Statistical analysis: Data were processed and statistical analysis was performed using the IBM SPSS, v 20. Data are expressed as means ± standard error of the mean (SEM). A paired *t*-test was used to compare numeric values of parameters before and after the procedure within groups, and a two-sample *t*-test was applied to compare the differences between groups. Categorical data were tested for differences between groups using *z*-test and chi-square test. A p value of <0.05 was considered statistically significant.

Results

When the entire study population was analyzed as a whole ($n = 165$), comparison of treatment outcomes showed a significant improvement ($p < 0.05$) within individual groups (A, B, C) in all parameters except the number of grade IV urgency episodes per 24 h ($p = 0.291$) in Group B. When comparing the differences before and after the treatment, we did not observe any statistically significant difference between groups A, B, and C, suggesting that the degree of improvement is not dependent on the BMI. These data are summarized in Tables 1 and 2.

Subsequently, the same analysis was performed in patients whose symptoms did not improve when treated by antimuscarinics

Table 1
Baseline characteristics of the entire study population.

	Group A Normal weight ($n = 59$)	Group B Overweight ($n = 61$)	Group C Obesity ($n = 45$)	Difference between groups	
				p	
Age	61.7 ± 12.74	64.1 ± 13.07	62.1 ± 10.67	>0.05	
Body mass index	22.8 ± 1.52	27.3 ± 1.52	34.0 ± 3.93	<0.05	C > B > A
Weight (cm)	62.6 ± 5.61	73.4 ± 6.99	91.4 ± 10.97	<0.05	C > B > A
Height (kg)	165.5 ± 5.70	163.9 ± 6.50	164.0 ± 5.76	>0.05	
Type of OAB					
OAB dry	23 (39.0%)	15 (24.6%)	6 (13.3%)	<0.05	A > B > C
OAB wet	31 (52.5%)	40 (65.6%)	35 (77.8%)	<0.05	B > A
Mixed incontinence with predominant OAB	5 (8.5%)	6 (9.8%)	4 (8.9%)	>0.05	
Previous OAB therapy with anticholinergics					
No	7 (11.9%)	6 (9.8%)	1 (2.2%)	>0.05	
Yes	52 (88.1%)	55 (90.2%)	44 (97.8%)	>0.05	
Total micturitions/24 h	12.1 ± 2.82	12.5 ± 4.29	12.8 ± 2.96	>0.05	
Total urgency episodes/24 h	4.6 ± 3.87	5.4 ± 4.78	7.2 ± 4.09	<0.05	
Total urgency grade III episodes/24 h	3.7 ± 3.25	4.0 ± 3.87	5.0 ± 3.46	>0.05	
Total urgency grade IV episodes/24 h	0.9 ± 1.51	1.4 ± 2.33	2.2 ± 2.74	<0.05	C > A
Total number of nocturia/24 h	2.0 ± 1.02	2.2 ± 1.25	2.6 ± 2.99	>0.05	
OABq-SF total score	50.1 ± 19.83	48.4 ± 17.78	43.5 ± 22.50	>0.05	
PPIUS score	3.6 ± 1.04	3.6 ± 0.83	3.8 ± 0.96	>0.05	
VAS-UB score	72.6 ± 18.43	71.6 ± 18.76	73.4 ± 19.64	>0.05	