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COMPARATIVE STUDY BETWEEN DIFFERENT COMBINATION OF MIRABEGRON (25 OR 50 MG) AND ANTIMUSCARINICS IN TREATMENT OF OAB PATIENTS

Hypothesis / aims of study

Mirabegron, a beta-3 agonist, and antimuscarinic drugs are currently the mainstay of pharmacological treatment for overactive bladder (OAB) syndrome. If a patient experiences inadequate symptom control and/or unacceptable adverse events (AEs) with one medication, then a dose modification or a different medication may be tried. So far there is no suggestion regarding which kind of medication should be given first. We compared the therapeutic effects and AEs in OAB patients receiving different combination of mirabegron and antimuscarinics.

Study design, materials and methods

Men or women aged 18 or above with OAB symptoms lasting for at least 3 months were enrolled in this prospective randomized study. All the patients received mirabegron 25 mg (M25) daily first for one month (1M) and then were randomized as (1) Group 1 to continue M25, (2) Group 2 to receive mirabegron 50 mg (M50), (3) Group 3 to shift to solifenacin 5 mg (S5) and (4) Group 4 to combine M25 and S5 daily for further 2 months (totally 3 months, 3M, Fig. 1). The International Prostate Symptom Score total (IPSS-T), voiding and storage subscores (IPSS-V and IPSS-S), quality of life (QoL), Overactive Bladder Symptom Score (OABSS), Urgency Severity Scale (USS), Patient's Perception of Bladder Condition (PPBC), Global Response Assessment (GRA) and uroflowmetry parameters, e.g. maximum flow rate (Qmax), voided volume (Vol) and postvoid residual (PVR) were evaluated at baseline, 1M and 3M after treatment. AEs were also recorded. At the end of 3M, the future management was provided according to the preference of the individual patient.

Results

A total of 168 patients (112 males and 56 females, median age 70) were included in this study. Among them, one hundred completed the 3 months' treatment. At 1M after treatment with M25 daily, significant improvements in mean IPSS-S, QoL and PPBC could be observed in all the four groups. At 3M, the mean QoL and PPBC decreased, and Vol increased significantly in group 1; the mean OABSS increased significantly in group 2; the mean PVR increased and GRA decreased significantly in group 3; the mean OABSS decreased and GRA increased significantly in group 4, when compared with those at 1M (Table 1). There were significant differences in changes of OABSS and GRA from1M to 3M between the four groups. When comparing the AEs occurred at 1M with those at 3M, there was no significant difference in all the four groups. However, there was significant difference in AEs between the four groups at 3M (Table 2). At the end of 3M, 64%, 68%, 50% and 75% of the patients in group 1, 2, 3 and 4 experienced a successful outcome (by GRA $\geqq$ 1) (Table 3). Among them, the preferred options for further treatment are shown in Table 3.

Interpretation of results

Treating OAB with M25 daily for one month could lead to significant symptom improvement. If the treatment extended to 3 months, the symptoms continued improving (group 1). If the dose was escalated to 50 mg for 2 months, no further benefit was noted (group 2). If M25 was substituted by S5 for 2 months, the mean PVR increased and GRA decreased significantly (group 3). And if S5 was added on to M25 mg as combination therapy for 2 more months, further improvement of symptoms could be achieved (group 4). Nevertheless, only 38.1% in group 4 were willing to continue combination therapy thereafter. The incidence of AEs increased significantly in groups using S5.

Concluding message

Mirabegron 25 mg daily is effective and safe in treating OAB. Dose escalation to 50 mg or shifting to antimuscarinics may not further increase the therapeutic benefit. Combined mirabegron 25 mg and antimuscarinics may provide better treatment efficacy than mirabegron 25 mg alone at the expense of significantly increased AEs and should be used carefully.

Table 1. Comparison of the changes in each parameter from one month to 3 months after treatment among the four groups of OAB patients

Change of 1M-3M	Group 1 (n=25)	Group 2 (n=25)	Group 3 (n=22)	Group 4 (n=28)	P value*
IPSS–V	0.80±4.88	0.20±4.33	0.52±4.07	-1.93±5.06	0.132
IPSS–S	-0.44±1.94	0.72±2.59	-0.19±1.44	1.04±2.84	0.075
IPSS–T	0.36±4.74	0.92±5.53	0.33±4.39	-0.89±6.05	0.640
QoL	0.48±0.96[#]	-0.08±1.29	-0.24±0.99	0.18±1.42	0.188
Qmax (mL/s)	-1.52±7.94	0.286±7.25	3.33±8.09	1.96±12.76	0.381
Vol (mL)	-50.96±112.45[#]	14.48±109.67	2.11±102.12	32.25±150.10	0.119
PVR (mL)	-3.38±36.88	-3.58±76.59	-26.10±38.54[#]	-35.33±137.41	0.463
Nocturia	-0.24±0.93	0.08±0.86	-0.23±1.19	0.33±1.30	0.190
OABSS	-0.08±2.33	-0.76±1.62[#]	0.38±3.2	1.61±3.97[#]	0.032
USS	0.16±1.70	-0.32±2.02	0.52±2.32	0.29±1.68	0.490
PPBC	0.72±1.40[#]	-0.16±2.25	-0.43±1.29	0.25±2.07	0.157
GRA	-0.08±1.71	-0.04±1.59	0.67±1.49[#]	-0.79±1.79[#]	0.031

[#]Significant difference when compared between 1M and 3M in each group. Wilcoxon signed ranks test was used. *Compared between groups with ANOVA.

Table 2. Adverse events at one month and three months after treatment

1M	Group 1 (n=44)	Group 2 (n=39)	Group 3 (n=44)	Group 4 (n=41)	P value*
Dry mouth		2(5.2%)		2(4.9%)	
Constipation	1(2.3%)		1(2.3%)	2(4.9%)	
Dizziness	1(2.3%)		2(4.6%)		
Blurred vision	1(2.3%)				
Hypertension		1(2.6%)			
dysuria		1(2.6%)		2(4.9%)	
Slow stream			1(2.3%)		0.683
3M	Group 1 (n=25)	Group 2 (n=25)	Group 3 (n=22)	Group 4 (n=28)	P value*
Dry mouth			1(4.5%)	4(14.2%)	
Constipation		1(4.0%)	2(9.0%)	2(7.1%)	
Dizziness			1(4.5%)		
Blurred vision			1(4.5%)	1(3.6%)	
dysuria		1(4.0%)	1(4.5%)		
P value#	0.182	0.763	0.052	0.280	0.017

*Compared between groups with Fisher's exact test. #Compared between 1M and 3M in each group with Fisher's exact test.

Table 3. Patient's preference for future treatment after 3 months' study.

	Group 1 (n=25) M25-M25	Group 2 (n=25) M25-M50	Group 3 (n=22) M25-S5	Group 4 (n=28) M25-M25+S5
GRA≧1 at 3M	16(64%)	17(68%)	11(50%)	21(75%)
Continue M25	15(93.8%)	15(88.2%)	3(27.3%)	10(47.6%)
Shift to S5	1(6.3%)	1(5.9%)	5(45.5%)	3(14.3%)
Shift to others	----	----	1(9.1%)	----
M25+S5	----	----	2(18.2%)	8(38.1%)
Lost follow-up	----	1(5.9%)	----	----

M25: Mirabegron 25 mg. M50: Mirabegron 50 mg. S5: solifenacin 5 mg. GRA: Global response assessment.

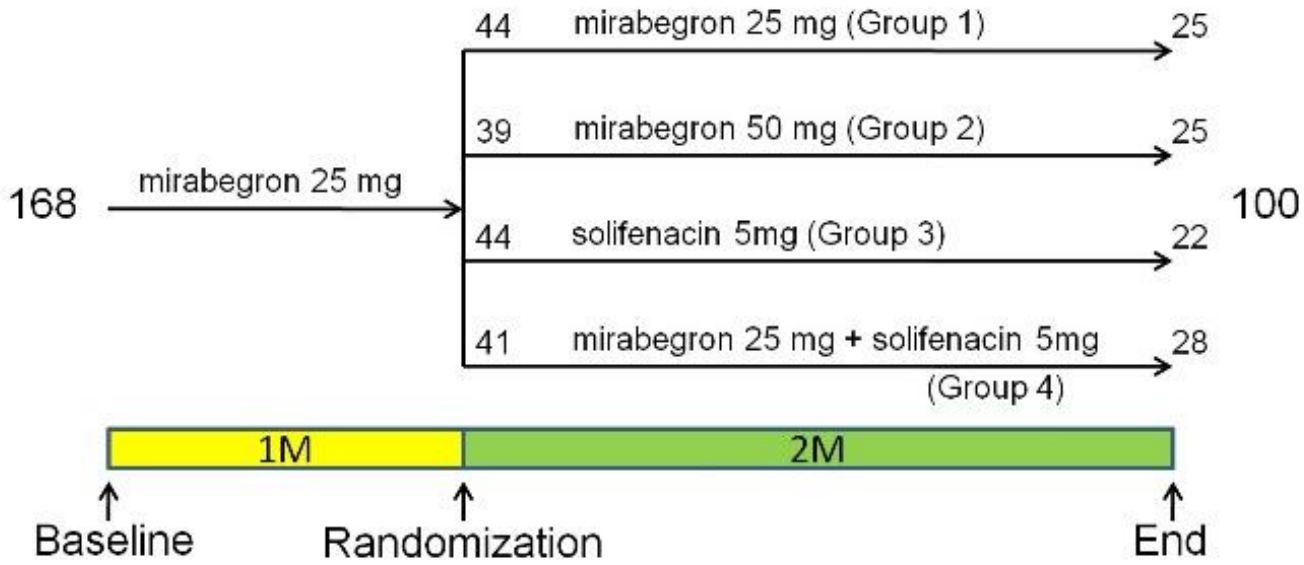

Fig. 1. Randomization of the study.

Disclosures
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