

Women with OAB may benefit from initial treatment with monotherapy compared with combination therapy, because both have similar therapeutic efficacy and effects on the autonomic nervous system but less dry mouth in the monotherapy group.

Objectives: To compare the efficacy of mirabegron or tolterodine, alone or in combination, and their effects on symptoms and the autonomic nervous system and bladder blood flow.

Methods: Consecutive women with overactive bladder syndrome (OAB) were randomly assigned to receive mirabegron 25 mg, tolterodine, or the combined treatment (mirabegron plus tolterodine) for 12 weeks

Results: A total of 130 women were enrolled in this study. Forty-seven women received mirabegron 25 mg daily, 40 women received tolterodine daily, and 43 women received mirabegron combined with tolterodine daily. However, after 4 weeks, only 32 women who received mirabegron, 32 who received tolterodine, and 38 who received mirabegron plus tolterodine remained in the study.

After 4 weeks of treatment, no differences in efficacy were observed among the three groups, as assessed by Global Response Assessment (GRA), Urgency Severity Score (USS), Overactive Bladder Symptoms Score (OABSS), and bladder diary (Analysis of heart rate variability (including low-frequency, high-frequency, and low-frequency/high-frequency ratio) also revealed no differences between the groups (Table 1). However, the incidence of dry mouth was significantly higher in the combined treatment group than in the mirabegron monotherapy group (Table 1).

After 12 weeks of treatment, efficacy was assessed using GRA, USS, OABSS, and bladder diary, showing no statistically significant differences among the three groups (Table 2). Analysis of heart rate variability, including low-frequency and high-frequency, and the low-frequency/high-frequency ratio, also showed no statistically significant differences among the three groups (Table 2). However, the change in the vascularization index was significantly greater in the mirabegron monotherapy group than in the tolterodine monotherapy group (p = 0.045).

Table 1. Comparison of changes at 4 weeks after OAB treatment

Variables	Mirabegron (a, n=32)	Tolterodine (b, n=32)	Combined (c, n=38)	P ^a	Post hoc analysis ^b
GRA	1.0 (1.0, 3.0)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)	0.774	
USS	-1.0 (-1.0, 0.0)	0.0 (-1.0, 0.0)	0.0 (-1.0, 0.0)	0.942	
OABSS	0.0 (-3.0, 0.0)	-1.0 (-5.0, 0.0)	-1.0 (-4.0, 0.0)	0.628	
Bladder diary					
Frequency, 72h	-2.0 (-6.0, 0.0)	-4.0 (-8.0, 0.0)	-4.0 (-6.3, 0.3)	0.643	
Nocturia, 72h	0.0 (-1.0, 0.0)	0.0 (-3.0, 1.0)	0.0 (-2.0, 2.0)	0.537	
Urgency, 72h	-1.0 (-5.0, 0.0)	-2.0 (-6.0, 0.0)	-2.0 (-7.3, 2.0)	0.530	
Incontinence, 72h	0.0 (0.0, 0.0)	0.0 (-1.0, 0.0)	0.0 (-0.3, 0.0)	0.506	
Voided volume, 72h	85 (-860, 1720)	-340 (-1610, 70)	-40 (-940, 1235)	0.172	
Fluid intake, 72h	-30 (-1470, 940)	-175 (-998, 1100)	180 (-635, 750)	0.792	
Heart rate (per min)	4.5 (-4.5, 8.0)	3.3 (-0.8, 10.3)	5.5 (1.0, 10.0)	0.487	
LF	-29 (-173, 23)	-17 (-144, 5)	-2.0 (-62, 69)	0.128	
HF	17 (-266, 119)	-0.5 (-60, 122)	3.5 (-48, 57)	0.847	
LF/HF ratio	-0.01 (-0.97, 0.43)	-0.14 (-0.92, 0.22)	-0.18 (-0.89, 1.25)	0.236	
Dry mouth	8 (25)	14 (44)	20 (54)	0.011	a vs c, p=0.019
Constipation	7 (22)	3 (9)	9 (24)	0.311	
Palpitation	1 (3)	0 (0)	0 (0)	0.634	
Voiding difficulty	0 (0)	0 (0)	2 (5)	0.328	

Data were expressed as median (25-75 interquartile range) or number (percentage). The abbreviations are as in Table 1.

^aANOVA test

^bChi-square test

Table 2. Comparison of changes at 12 weeks after OAB treatment

Variables	Mirabegron (a, n=26)	Tolterodine (b, n=23)	Combined (c, n=29)	P ^a	Post hoc analysis ^a
GRA	2.0 (1.8, 3.0)	2.0 (1.0, 2.0)	2.0 (1.0, 3.0)	0.308	
USS	-1.0 (-2.0, 0.0)	-1.0 (-1.0, 0.0)	0.0 (-2.0, 0.0)	0.278	
OABSS	-2.0 (-4.0, -0.5)	-2.0 (-5.5, -0.8)	-2.5 (-5.5, -1.0)	0.973	
Bladder diary					
Frequency, 72h	-4.5 (-10.8, 1.0)	-1.0 (-5.0, 1.0)	-7.5 (-12.3, 2.8)	0.296	
Nocturia, 72h	-2.5 (-5.3, 0.0)	0.0 (-2.0, 1.0)	-1.0 (-1.5, 0.5)	0.091	
Urgency, 72h	-2.0 (-5.3, 0.0)	0.0 (-9.0, 0.0)	-4.0 (-10.5, 0.5)	0.488	
Incontinence, 72h	0.0 (0.0, 0.0)	0.0 (0.0, -2.0)	0.0 (0.0, 0.0)	0.188	
Voided volume, 72h	-489 (-2348, 490)	-440 (-900, 160)	-540 (-1575, 1563)	0.582	
Fluid intake, 72h	320 (-595, 975)	270 (-625, 1763)	750 (-310, 1495)	0.357	
Heart rate	1.0 (-5.9, 15.3)	9.3 (-3.9, 13.0)	10.0 (2.1, 19.0)	0.365	
LF	-89.3 (-219.1, 328.3)	-2.8 (-126.5, 94.0)	6.0 (-134.5, 45.0)	0.622	
HF	-48.5 (-116.3, 276.5)	14.0 (-86.3, 125.6)	-21.0 (-126.5, 3.5)	0.407	
LF/HF ratio	0.04 (-0.41, 0.48)	-0.10 (-0.79, 1.67)	0.78 (-0.27, 4.00)	0.436	
Dry mouth	9 (35)	10 (43)	11 (38)	0.804	
Constipation	6 (23)	1 (4)	6 (21)	0.163	
Palpitation	0 (0)	0 (0)	0 (0)	-	
Voiding difficulty	1 (4)	1 (4)	2 (7)	1.000	
VI	-4.2 (-12.5, 0.5)	-0.1 (-4.5, 2.0)	0.26 (-2.7, 5.2)	0.049	a vs b, p=0.045
FI	-1.6 (-8.3, 9.9)	2.0 (-0.8, 6.9)	0.80 (-1.6, 4.2)	0.896	
VFI	-1.3 (-4.2, 0.1)	-0.0 (-1.3, 1.2)	0.1 (-0.8, 1.5)	0.065	

Data were expressed as median (25-75 interquartile range) or number (percentage). The abbreviations are as in Table 1.

^aANOVA test with Bonferroni correction

