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HIGHER URGE SEVERITY SCALE PREDICTS THE RECURRENCE OF OVERACTIVE BLADDER SYMPTOMS AFTER DISCONTINUING MIRABEGRON IN PATIENTS WITH OVERACTIVE BLADDER

Hypothesis / aims of study

Previous studies have shown that some patients with overactive bladder (OAB) may discontinue antimuscarinic agent after a period of adequate treatment. Older age and severe urgency urinary incontinence are predictors of re-treatment with antimuscarinic agent. However, limited data show how long a patient should take beta-3 adrenoceptor agonist for OAB and whether OAB will relapse or get worse after discontinuing medication. Thus, we hypothesized that selected OAB patients may discontinue mirabegron and OAB severity plays an important role to decide whether medication can be stopped or not. This study investigated the incidence and predictive factors of symptom recurrence after discontinuation of successful mirabegron therapy in patients with OAB.

Study design, materials and methods

Three hundred seventy-four OAB patients who reported improvement in subjective symptoms after at least 3-month mirabegron treatment were enrolled in this study. One hundred and nine (29.1%) patients who wished to continue medication were excluded from this study. The remaining 265 patients discontinued mirabegron and their recurrence of OAB symptoms was evaluated at baseline, 1, 3, 6, 9, and 12 months. They were requested to record International Prostate Symptom Score (IPSS) questionnaires, Quality of Life index (QoL-I), Overactive Bladder Symptom Score (OABSS), Urgency Severity Scale (USS), Patient's Perception of Bladder Condition (PPBC), Global Response Assessment (GRA), uroflowmetry, and post-void residual (PVR) volume at each visit. When patients' symptoms were recurrent and they wanted to resume medication, administration of mirabegron was refilled. The study protocol was approved by the Institutional Review Board of the hospital and written informed consent was received from all patients.

Results

After discontinuation of mirabegron, 62 (23.4%) patients were excluded due to lost to follow-up. Finally, a total of 203 patients (172 male and 31 female) completed follow-up. Their mean age was 75.3 ± 10.1 (range 45 to 97) years. The mean duration of drug persistence before active discontinuation was 9.2 ± 3.4 (range 3 to 12) months. Ninety-two (45.3%) of 203 patients reported worsening of symptoms after the discontinuation of treatment and they asked to resume treatment. The mean duration from discontinuing to resuming medication was 2.25 ± 1.17 (range 1 to 12) months. Compared with the patients without resuming mirabegron after discontinuation, patients resuming medication had higher USS at baseline. The other parameters were comparable in both groups at baseline (Table 1 and Table 2). Patients resuming mirabegron had significantly worse IPSS, QoL-I, OABSS, USS, PPBC and nocturia episodes at the time point of resuming mirabegron than those at baseline. However, these parameters were similar before and after stopping medication in patients without resuming mirabegron. In addition, the uroflowmetry and PVR were comparable before and after discontinuing mirabegron in both groups. Univariable analysis showed baseline USS was a predictor to resume mirabegron treatment (OR: 1.315, 95% CI: 1.051 – 1.646, p=0.02). The most common reason to resume medication was urge urinary incontinence (50.5%), followed by symptoms of urgency (21.5%) and nocturia (19.4%).

Interpretation of results.

Many patients who are satisfied with the improvement of OAB treatment might wonder how long they should maintain the medication. The study indicates that approximately half of OAB patients may discontinue mirabegron after adequate symptoms control. Although OAB symptoms could only be controlled but not cured, considering the minimal effects of discontinuation of mirabegron, this study suggests that after a priming period, beta-3 agonist might be discontinued in some patients without OAB symptoms relapsed. The clinical information can result in substantial reduction in healthcare expenditure and potential side effects for the patients. On the other hand, patients with higher USS and/or OAB wet should have long-term maintenance of mirabegron treatment to achieve better therapeutic outcomes and quality of life.

Concluding message

About half patients may consider discontinue mirabegron treatment after adequate symptoms control. Higher urgency severity scale may predict re-treatment after discontinuation of mirabegron in OAB patients.

Table 1: Comparison of general characteristics between patients without recurrent overactive symptoms and resuming mirabegron after discontinuing mirabegron.

	No recurrence	Resume mirabegron	p-value
Patient number	111	92	
Gender	M:97 (87.4%)	M:75 (81.5%)	0.247
	F:14 (12.6%)	F:17 (18.5%)	
Comorbidity	86 (77.5%)	74 (80.4%)	0.608
Using antimuscarinic before mirabegron	64 (57.7%)	61 (66.3%)	0.207
Concurrent use of a-blocker/5ARI	77 (69.4%)	62 (67.4%)	0.763
Concurrent use of antimuscarinic	15 (13.5%)	11 (12.0%)	0.741
Only Mirabegron used	49 (44.1%)	44 (47.8%)	0.6

Table 2: Comparison of subjective symptoms and uroflowmetry data between patients without recurrent overactive symptoms and resuming mirabegron after discontinuing mirabegron.

Variables		No recurrent	Resume mirabegron	p-value
Patient number		111	92	
IPSS – V	BL	3.23 ± 4.35	3.75±4.48	0.409
	DC 1M	3.19 ± 3.74	5.27±5.39 *	
IPSS – S	BL	3.85 ± 2.40	4.11±2.05	0.412
	DC 1M	3.77 ± 2.17	5.43±2.82*	
IPSS – T	BL	7.07 ± 5.60	7.85±5.17	0.31
	DC 1M	6.96 ± 4.97	10.71±6.62*	
QOL	BL	1.88 ± 1.00	1.98±0.89	0.583
	DC 1M	1.71 ± 1.10	2.93±1.52*	
Nocturia	BL	2.98 ±1.28	3.13±1.16	0.431
	DC 1M	2.95 ±1.23	3.50±1.27 *	
OABSS	BL	3.94 ±2.75	4.70 ±2.97	0.061
	DC 1M	4.00±2.66	6.36±3.89 *	
USS	BL	0.65±1.33	1.18±1.76	0.017
	DC 1M	0.80±1.43	1.92±1.92 *	
PPBC	BL	1.71 ± 1.32	1.75±1.31	0.871
	DC 1M	1.45 ±0.95 *	2.90±1.95 *	
GRA	BL	1.31 ±1.41	1.30±1.39	0.975
	DC 1M	0.45 ±1.03*	-0.76±1.56*	
Qmax (ml/s)	BL	13.59 ± 6.28	12.29±6.88	0.109
	DC 1M	13.08 ±7.55	12.88 ±6.30	
Vol (ml)	BL	193.17 ±126.91	168.92±123.67	0.23
	DC 1M	184.75 ± 131.77	180.18±117.36	
PVR (ml)	BL	39.71 ± 43.58	37.32±36.03	0.676
	DC 1M	33.46 ± 36.89	47.53±60.24	

BL: baseline (at the time point of discontinuing mirabegron); DC 1M: 1 month after discontinuing mirabegron; * $p<0.05$, significantly difference between BL and DC 1M; p-value: comparison of BL between two groups.

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