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THE EFFICACY AND SAFETY OF FLEXIBLE DOSE IMIDAFENACIN (0.2MG OR 0.4MG), FOR THE TREATMENT OF OVERACTIVE BLADDER AND NOCTURIA

Hypothesis / aims of study
Imidafenacin is an anticholinergic agent that was approved in Japan for treating overactive bladder (OAB) in 2007. It shows high affinity for M3 and M1 receptors and high organ selectivity for the bladder. In a phase III study performed in Japanese patients with OAB, imidafenacin was shown to be well-tolerated and improved OAB symptoms and nocturia [1,2]. The recommended dose for imidafenacin is 0.1mg twice daily. However, the increased dosage of imidafenacin up to 4mg (0.2mg twice) daily has been approved recently if the results were unsatisfactory. So far the efficacy and safety of increased dose of imidafenacin have not been thoroughly evaluated in the real life practice. The aims of the present study is to evaluate the efficacy of flexible dose imidafenacin (0.2mg or 0.4mg), for the treatment of overactive bladder and nocturia.

Study design, materials and methods
Men and women 20 years, who had OAB symptoms, including urinary incontinence, urinary frequency, and urgency, were eligible for the study. Inclusion criteria were urgency
>1 episode/week (>2/day is recommended) and/or urinary frequency, nocturia or urgency incontinence. Exclusion criteria included clinically significant bladder outlet obstruction and/or postvoid residual volume >100 mL; urodynamic stress incontinence; prostate cancer, bladder cancer. Patients were administered 0.1-mg tablets of imidafenacin twice daily for 4 weeks. If the patients required increase of dosage, they took 0.2-mg tablets of imidafenacin twice daily up to 12 weeks. Subjects completed bladder diaries, the Overactive Bladder Symptom score (OABSS), International Prostate Symptom score (IPSS), Patient Perception of Bladder Condition (PPBC), Urgency Perception Scale (UPS), and nocturnal quality-of-life score (n-QOL) at baseline and weeks 4 and 12. The primary endpoint was change from baseline to week 12 in the total OABSS and n-QOL.

Results
A total of 80 patients were included in the study. Fifteen patients withdrew after the first presentation, nine patients at 4 weeks, 5 patients at 8 weeks. Therefore 51 patients (25 males, 26 females, mean age □SD 70.5□12.9 years old) completed the study. Twenty nine patients increased the dosage up to 0.3mg (n=1) - 0.4mg (n=28) at 4 weeks. Twenty two patients were satisfied with the dosage of 0.2mg or could not increase because of side effects (mostly dry mouth in 5patients). Results on the OABSS, IPSS, and n-QOL at baseline and weeks 4 and 12 were summarized in the table. Postvoid residual (mL) was 9.3□17.9, 15.6□28.9, 7.2□17.0, 18.1□42.6, before, and at 4 and 12 weeks after the therapy.

Interpretation of results
In 22 patients who continued 0.2mg imidafenacin (0.2mg group), OABSS was significantly improved at 4 weeks and the effects were maintained up to 12 weeks. n-QOL score was also significantly increased at 4weeks and further increased at 12 weeks. In 29 patients who increased the dosage of imidafenacin (0.4mg group), the OABSS and n-QOL score were significantly improved at 4weeks and further improved at 12 weeks.

Concluding message
Flexible dose of imidafenacin appeared effective for the treatment of OAB and nocturia.

Table: Results on the OABSS, IPSS, and n-QOL at baseline and weeks 4 and 12

		0.2mg group				(0.3-) 0.4mg group		
		Mean	SD	p-value		Mean	SD	p-value
OABSS	0W	8.59	2.46			9.72	2.45	
	4W	6.14	2.29	<0.0001	8.59	2.23	0.0065	
	8W	6.14	3.28	<0.0001	7.66	2.65	<0.0001	
	12W	6.09	3.68	0.0004		6.97	3.04	<0.0001
IPSS								
	0W	13.73	7.36			16.24	8.66	0.3656
	4W	11.59	7.00	0.0257		13.41	7.94	0.0613
	8W	11.09	7.85	0.0072	12.90	8.27	0.0015	
	12W	10.18	8.18	0.0021		12.69	8.79	0.0039
IPSS-QOL								
	0W	5.82	1.26			6.41	0.84	
	4W	4.68	1.70	0.0165		5.63	1.45	0.0034
	8W	4.91	1.34	0.0282		5.44	1.53	0.0041
	12W	4.59	1.50	0.0043		5.11	1.69	0.0006
IPSS total storage symptom subscores								
	0W	7.73	3.19			9.31	3.45	
	4W	5.95	2.73	0.0107		7.72	3.19	0.0058
	8W	6.00	2.93	0.0127		7.07	3.48	0.0005
	12W	5.36	3.55	0.0013		6.45	3.32	<0.0001
IPSS total voiding symptom subscores								
	0W	4.41	4.52			4.90	4.86	
	4W	4.41	4.47	0.8257	4.38	4.73	0.6859	
	8W	3.91	4.64	0.2441		4.21	4.81	0.3713
	12W	3.59	4.24	0.0957		4.76	5.00	0.9918
IPSS total post-micturition symptom subscores								
	0W	1.59	1.37			2.03	1.94	
	4W	1.23	1.27	0.2964		1.31	1.69	0.0203
	8W	1.18	1.50	0.2246		1.62	1.90	0.1797
	12W	1.23	1.77	0.4367		1.48	1.72	0.0623
N-QOL								
	0W	53.69	20.48			55.17	23.30	.
	4W	65.15	22.64	0.0033		66.02	24.56	0.0006
	8W	69.79	18.95	0.0010		68.53	24.32	0.0016
	12W	71.31	21.95	0.0002		70.33	23.51	0.0002
Sleep/Energy score (N-QOL)								
	0W	57.77	25.04			61.21	25.71	
	4W	69.51	24.24	0.0073		72.13	25.27	0.0028
	8W	68.94	21.31	0.0206		74.14	24.69	0.0019
	12W	70.45	23.64	0.0081		76.01	21.87	0.0002
Bother/Concern score (N-QOL)								
	0W	49.62	21.05			49.14	23.24	
	4W	60.80	25.58	0.0057		59.91	26.03	0.0061
	8W	70.64	21.53	<0.0001	62.93	27.01	0.0087	
	12W	72.16	22.76	0.0003		64.66	26.83	0.0019

References

1. Urology. 2013;82:887-93.
2. Int J Urol. 2009

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