

Digestive symptoms associated with α 1-adrenoceptor antagonists (α 1-blockers) therapy in patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH)

[Hypothesis / aims of study]

The objective of this study was to evaluate the short-term efficacy and safety, focused digestive symptoms, of two alpha 1-adrenoceptor antagonists (α 1-blockers), Silodosin (S) and Tamsulosin (T), in patients with untreated LUTS/BPH.

[Study design, materials and methods]

Drug S or T was administered to patients with untreated BPH, and their efficacy and safety in the early stage of treatment were compared using the questionnaire of International Prostate Symptom Score (IPSS)/quality of life (QOL), the Japanese version of the Gastrointestinal Symptom Rating Scale (GSRs) <#1>, and the Bristol Stool Form Scale questionnaire <#2>.

- T group; tamsulosin 0.2mg once daily (Japanese standard dose)
- S group; silodosin 4 mg twice a day

	Pre	1 week	2 weeks	4 weeks
<i>Pts' characteristics</i>	○	○	○	○
IPSS/QOL	○	○	○	○
GSRs	○	○	○	○
Bristol Stool Form Scale	○	○	○	○
Adverse Event	○	○	○	○

This study was approved by the Asahikawa Medical University Ethical Committee (No. 862) and registered at the Japan Primary Registries Network (JPRN-UMIN000005151).

Statistical Analysis

All values were expressed as the mean \pm SEM. Statistical analyses were performed using ANOVA. Differences were considered to be significant at a P-value < 0.05.

<#1> Gastrointestinal Symptom Rating Scale (GSRs)

The GSRs [1] is a disease-specific instrument of 15 items combined into five symptom clusters. The GSRs has a seven-point graded Likert-type scale where 1 represents absence of troublesome symptoms and 7 represents very troublesome symptoms. The reliability and validity of the GSRs are well-documented [2], and norm values for a general population are available [3].

<#15 items> 1. Abdominal pains. 2. Heartburn. 3. Acid regurgitation.

4. Sucking sensations in the epigastrium. 5. Nausea and vomiting. 6. Borborygmus.

7. Abdominal distension. 8. Eructation. 9. Increased flatus.

10. Decreased passage of stools. 11. Increased passage of stools. 12. Loose stools.

13. Hard Stools. 14. Urgent need for defecation. 15. Feeling of incomplete evacuation.

<#5 symptom clusters> Regurgitation (2+3), Pain (1+4+5), Dyspepsia (6+7+8),

Diarrhea (11+12+14), Constipation (10+13+15)

[1] Dimenäs E, et al. Scand J Gastroenterol. 1993;28:681-7.

[2] Dimenäs E, et al. Scand J Gastroenterol. 1995;30:1046-52.

[3] Dimenäs E, et al. Scand J Gastroenterol. 1996;221:8-13.

<#2> The Bristol Stool Form Scale questionnaire

Irritable Bowel Syndrome in Adults: Diagnosis and Management of Irritable Bowel Syndrome in Primary Care [Internet]. National Collaborating Centre for Nursing and Supportive Care (UK). London: Royal College of Nursing (UK); 2008 Feb.

Type	Description	Image
Type 1	Separate hard lumps, like nuts	
Type 2	Sausage-shaped but lumpy	
Type 3	Like a sausage or snake but with cracks on its surface	
Type 4	Like a sausage or snake, smooth and soft	
Type 5	Soft blobs with clear-cut edges	
Type 6	Fluffy pieces with ragged edges, a moaty stool	
Type 7	Watery, no solid pieces	

[Results-1]

The per protocol set consisted of 20 patients in the S group (mean age, 73.00 \pm 6.48 yrs) and 22 patients in the T group (70.15 \pm 5.70 yrs) (Fig. 1 and Table 1).

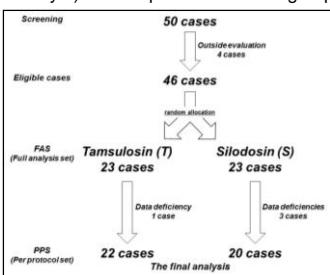


Figure 1. Patient enrollment.

Table 1. Pts' characteristics.

		Tamsulosin (T)		Silodosin (S)		p-value		
		Mean	SD	Mean	SD			
IPSS	Age (yrs)	73.00	6.48	70.15	5.70	0.140		
	1. Incomplete Rmpting	1.45	1.50	1.90	1.65	0.400		
	2. Frequency	2.00	1.63	2.20	1.54	0.681		
	3. Intermittency	2.32	1.64	1.50	1.19	0.084		
	4. Urgency	1.23	1.41	1.35	1.66	0.802		
	5. Weak Stream	3.27	1.64	3.85	1.39	0.316		
	6. Straining	2.00	1.77	2.10	1.97	0.949		
	7. Nocturia	2.50	1.30	2.25	1.37	0.407		
	Total	14.77	7.25	15.15	5.91	0.487		
	QOL	4.09	0.92	4.50	1.24	0.228		
		GSRs	1. Abdominal pains	1.32	0.95	1.10	0.31	0.670
			2. Heartburn	1.32	0.78	1.25	0.55	0.971
			3. Acid regurgitation	1.41	1.05	1.20	0.52	0.741
			4. Sucking sensations in the epigastrium	1.27	0.70	1.05	0.22	0.194
			5. Nausea and vomiting	1.27	0.88	1.00	0.00	0.096
6. Borborygmus			1.32	0.48	1.30	0.66	0.544	
7. Abdominal distension			1.14	0.35	1.11	0.46	0.431	
8. Eructation			1.32	0.57	1.10	0.31	0.155	
9. Increased flatus			1.82	0.85	1.70	0.86	0.594	
10. Decreased passage of stools			1.86	1.25	2.35	1.63	0.279	
11. Increased passage of stools			1.36	0.58	1.40	0.82	0.659	
12. Loose stools			1.27	0.55	1.50	0.83	0.462	
13. Hard Stools			2.14	1.25	2.30	1.38	0.767	
14. Urgent need for defecation			1.50	0.67	1.40	0.68	0.542	
15. Feeling of incomplete evacuation	1.59		0.91	1.55	0.76	0.954		
subscale	Regurgitation (2+3)	2.73	1.55	2.45	1.05	0.589		
	Pain (1+4+5)	3.86	2.49	3.15	0.37	0.669		
	Dyspepsia (6+7+8)	3.77	1.15	3.45	1.00	0.282		
	Diarrhea (11+12+14)	4.14	1.39	4.30	1.92	0.924		
	Constipation (10+13+15)	5.59	3.10	6.20	2.84	0.299		
Total	21.91	7.60	21.25	5.15	0.970			
Bristol Stool Form Scale		4.00	1.02	3.65	0.99	0.196		

[Results-2]

The IPSS and QOL score improved at week 1 in both groups as compared to the baseline (Fig. 2). Although the overall GSRs score showed no significant change in either group. But, the GSRs score for "13. hard stools" was significantly decreased at week 4 in both groups (Fig. 3A). The GSRs subscale score for "constipation" was significantly decreased only in S group at week 4 (Fig. 3B). The Bristol Stool Scale score was significantly increased at week 4 only in the S group (Fig. 4).

Figure 2. Changes of IPSS total score (A) and QOL score (B).

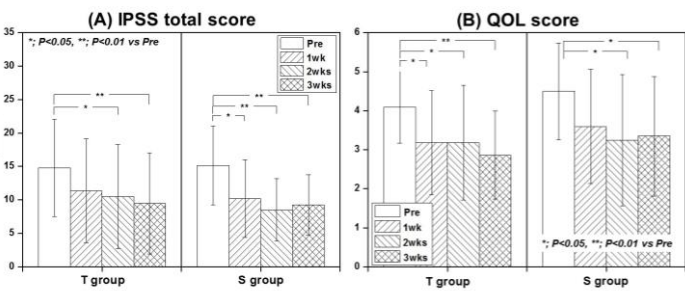


Figure 3. Changes of GSRs score for "13. hard stools" (A) and GSRs subscale score for "constipation" (B).

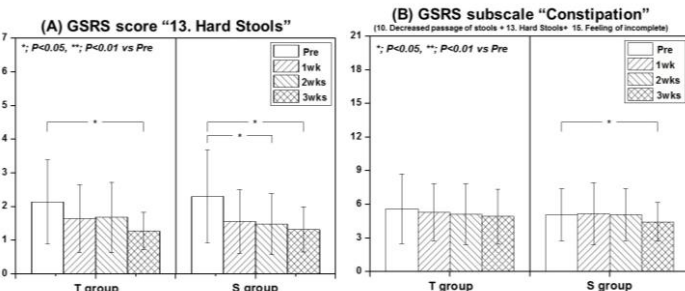
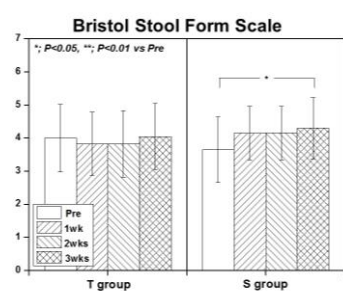


Figure 4. Changes of Bristol Stool Scale score.



[Interpretation of results]

The GSRs score for "13. hard stools" was significantly decreased at week 4 in both groups. In S group, the GSRs subscale score for "constipation" and the Bristol Stool Scale score were significantly changed at week 4.

[Limitation]

The limitation of this study includes a very small number of the pts.

[Conclusions]

Alpha 1 blockers, which are major therapeutic agents for the treatment of LUTS/BPH, were effective from the early stage of treatment as often reported in the past. Regarding digestive symptoms related to safety, there was "loose stools" trend in both groups, especially "hard stools" in GSRs score showed improvement in S group. This study revealed that the selectivity of alpha-1 adrenergic receptors is associated with digestive symptoms such as diarrhea and loose stools. Therefore, oral drugs for BPH need to be selected by taking into consideration the digestive symptoms, including with the state and type of stool.

[Disclosures Statement]

The authors declare no conflicts of interest associated with this paper.