

## THE INFLUENCE OF ADMINISTRATION OF $\alpha$ 1-ADRENERGIC RECEPTOR ANTAGONIST (URAPIDIL) ON ORAL DRYNESS IN FEMALE PATIENTS WITH URINARY DISORDERS

### Hypothesis / aims of study

Anticholinergic agents are commonly used for treating urinary disorders such as overactive bladder. It is clinically well-known that such agents can cause dry mouth as a side effect by blocking the muscarinic receptor in salivary glands. In addition to the muscarinic receptor, the  $\alpha$ 1-adrenergic receptor is also known to mediate saliva production by human salivary glands. [1] In general, the common adverse events associated with  $\alpha$ 1-adrenergic receptor antagonists include orthostatic hypotension and dizziness. To our knowledge, few clinical studies have focused on the relationship between  $\alpha$ 1-adrenergic receptor antagonists and oral dryness. We therefore conducted a cross-sectional study using a questionnaire on the subjective symptoms of dry mouth or oral dryness in female patients receiving urapidil for urinary disorders.

### Study design, materials and methods

Subjects were selected from among patients being followed regularly at our hospital. The patient group (urapidil group) consisted of female patients receiving the  $\alpha$ 1-adrenergic receptor antagonist urapidil (30 mg/day) for urinary disorders. The control group consisted of age-matched patients. We conducted a questionnaire survey on subjective symptoms of dry mouth for patients who agreed to study participation and gave informed consent. The questionnaire (Dry Mouth Scale, DMS) consisted of 9 questions with the face scale (1 to 7 points), the reliability and validity of which have been confirmed.[2] We also included a question about the influence of dry mouth on quality of life with the Visual Analogue Scale (VAS, 0 to 10 points). Excluded subjects had underlying diseases that can cause dry mouth (diabetes mellitus, Sjögren syndrome, head and neck tumors, etc.), had previously received radiation therapy for head and neck cancer, or were taking medications that can cause dry mouth. Statistical analysis was performed using the *t*-test, with a *P* value < 0.05 considered to be significant.

### Results

Patient characteristics are shown in Table 1. The urapidil group had significantly higher scores than the control group for both the International Prostate Symptom Score and Overactive Bladder Symptom Score. The results obtained from the questionnaire are shown in Table 2. The urapidil group had a significantly higher total and all three subscale scores (dry mouth symptoms, accompanying symptoms, and other symptoms) than the control group on DMS. With regard to each question, the urapidil group had significantly higher scores on all questions except for Q6 (tongue pain). The scores for the quality of life question were  $2.0 \pm 1.6$  in the control group and  $4.4 \pm 2.2$  in the urapidil group, showing that the urapidil group had a poorer quality of life than the control group.

### Interpretation of results

Previous studies found that  $\alpha$ 1-adrenergic receptors as well as muscarinic receptors mediate saliva production in rat and human salivary glands. While it was reported that  $\alpha$ 1-adrenergic receptor antagonists decreased saliva production in a basic study in rats, [1] no clinical studies have been conducted in human subjects.

The present clinical results demonstrated that the urapidil group had more symptoms of oral dryness than the control group. Furthermore, a more significant effect on quality of life was observed in the urapidil group. These results suggest that urapidil affects the salivary glands as well as the urethra and can cause oral dryness by inhibiting saliva secretion.

Oral dryness is a common problem for elderly people. The complaint of oral dryness is expected to increase as one ages. It is also expected that dental complications will increase with such changes. In clinical practice,  $\alpha$ 1-adrenergic receptor antagonists are frequently used in combination with anticholinergic agents for the treatment of overactive bladder. Clinicians should be aware that  $\alpha$ 1-adrenergic receptor antagonists can cause oral dryness, as well as orthostatic hypotension and dizziness, when treating patients with urinary disorders or overactive bladder.

### Concluding message

The present results suggest that not only anticholinergic agents but also  $\alpha$ 1-adrenergic receptor antagonists (urapidil) can cause oral dryness.

Table 1 Patient backgrounds

	Control group	Urapidil group	P value
Age	70.8±6.8	71.7±10.7	0.6141
IPSS total score	3.2±2.0	7.3±3.9	<0.0001
OABSS total score	2.1±1.6	5.7±2.4	0.0002

IPSS: International Prostate Symptom Score, OABSS: Overactive Bladder Symptom Score

Table 2 Results obtained from the questionnaire (DMS)

	Control group	Urapidil group	P value
Q1(Oral dryness)	1.95±1.40	3.19±1.38	<0.0001
Q2 (Oral dryness when wake up)	2.00±1.27	2.98±1.44	0.0001
Q3 (Throat dryness)	2.35±1.35	3.23±1.51	0.0002
Q4 (Difficulty in speaking due to dryness)	1.34±1.01	1.90±1.27	0.0073
Q5 (Sticky feeling)	1.66±1.13	2.13±1.25	0.0342
Q6 (Pain of tongue)	1.15±0.58	1.41±1.09	0.1154
Q7 (Bad breath)	1.31±0.77	2.00±0.89	<0.0001
Q8 (Taste impairment)	1.10±0.44	1.30±0.55	0.0339
Q9 (Difficulty in eating due to dryness)	1.17±0.53	1.61±1.12	0.0070
Total scores	13.9±6.83	19.7±8.66	0.0001
Subscale scores			
Dry mouth symptoms(Q1+2+3)	6.20±3.78	9.38±4.18	<0.0001
Accompanying symptoms(Q4+5+9)	4.17±2.48	5.64±3.36	0.0070
Other symptoms(Q6+7+8)	3.56±1.34	4.69±1.75	0.0001
Influence on Quality of Life	2.0±1.6	4.4±2.2	<0.0001

#### References

1. Eur J Pharmacol 2012;679:127-131.
2. Jpn J Urol Surg 2011;24:1489-1500.

#### Disclosures

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