

## DIFFERENTIAL PHARMACOKINETICS BETWEEN SALIVARY GLANDS AND BLADDER DETRUSOR MUSCLE WITH PROPIVERINE HYDROCHLORIDE ON OVER ACTIVE BLADDER PATIENTS

### Aims of Study

Many over active bladder patients (OAB) usually have been treated with anti-cholinergic drugs. Propiverine hydrochloride which is one of the anti-cholinergic drugs has been commonly used for OAB, and the effective results are reported [1]. However, it is occasionally difficult to maintain the therapy with anti-cholinergic drugs because of the thirst which is one of the side effects. It is reported that the incidence of thirst is 5 % with Propiverine hydrochloride. However, the clinical course of the thirst with this drug is unknown. In this study, we investigated about the thirst and effects of the bladder function by Propiverine hydrochloride on patients with OAB.

### Methods

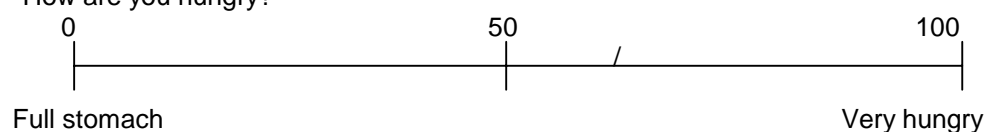
Fifty-six OAB patients, 25 males and 31 females, who were treated with Propiverine hydrochloride were investigated. The range of their age was from 13-year-old to 90-year-old (mean: 68.9 year). They were newly patients, and have not yet been treated with anti-cholinergic drugs. Each patient was administered 20 mg of Propiverine hydrochloride once daily for 4 weeks. For control, 49 healthy volunteers, 41 males and 8 females, were investigated. Their age was from 23-year-old to 90-year-old (mean: 64.3 year). OAB patients were surveyed of thirst at the institution of therapy with Propiverine hydrochloride, at the 2 weeks later and at the 4 weeks later. Survey of healthy volunteers as for thirst is the same way as patients group. To survey of thirst, visual analog scale [2] was used with each same paper for 3 times [figure 1]. Visual analog scale was measured from zero to 100 scales. When the visual analog scale was up more than ten points after 2 or 4 weeks later, patients were judged to feel thirsty. Furthermore, voiding function was evaluated by the frequency and volume chart of voiding on OAB patients. Student's t-test was used in statistical comparisons.

[Figure 1]

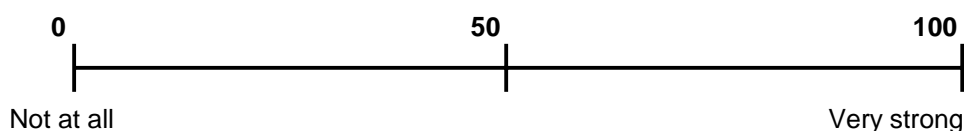
Would you like mark on the line with your condition about the thirst?

For example;

How are you hungry?



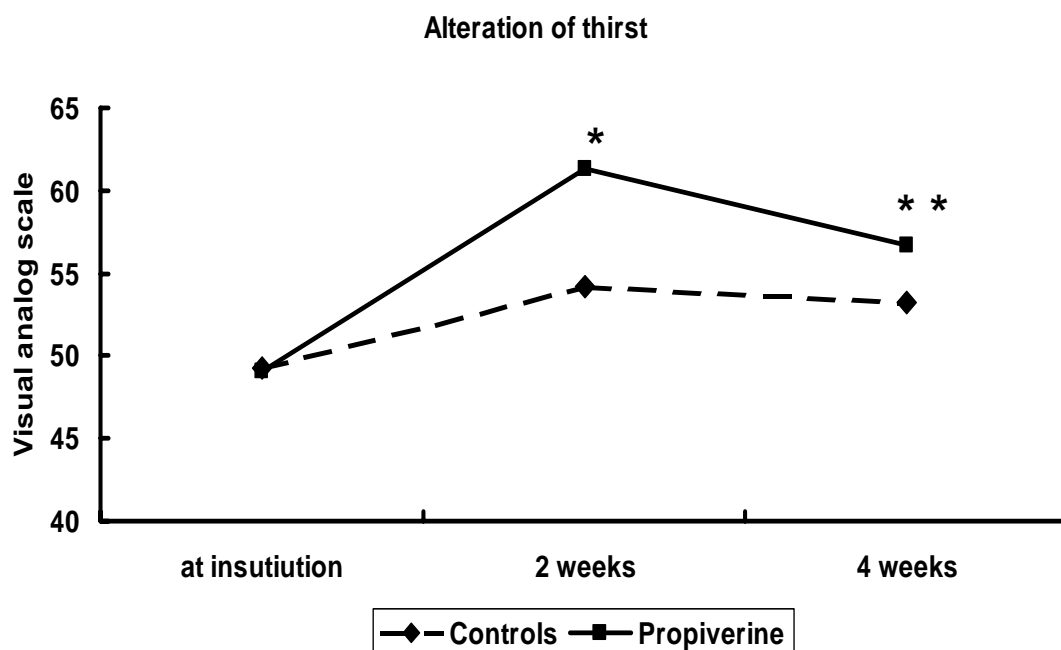
How do you feel thirsty?



### Results

Mean visual analog scale of healthy volunteer was 49.3, and that of OAB patients was 49.1 at the institution of investigation. There was no significant difference between healthy volunteers and OAB patients. There is no significant difference in visual analog scale difference among 3 times surveys of thirst in healthy volunteers. 40 % of OAB patients treated with Propiverine hydrochloride felt the thirst after 2 weeks, mean visual analog scale was significantly up from 49.1 to 61.3 ( $p < 0.01$ ). There is no relationship between thirst and the patients' gender and age. At the 4 weeks later, visual analog scale was down from 61.3 to 56.7, the thirst was significantly diminished compared with the 2 weeks later after the

therapy with Propiverine hydrochloride ( $p < 0.01$ ). In contrast, urinary frequency for a day was from 13 times to 10 times after the therapy with Propiverine hydrochloride ( $p < 0.01$ ). Furthermore, urinary frequency was significantly decreased from 10 times to 9 times at the 4 weeks later ( $p < 0.05$ ). Voided volume was significantly increased from 133.6 ml at the institution to 174.0 ml at the 2 weeks later after therapy ( $p < 0.01$ ) [Figure 2]. Voided volume at the 4 weeks later after therapy was 193ml, it was significantly increased compared at the institution ( $p < 0.01$ ) and at the 2 weeks later ( $p < 0.05$ ).



### **Conclusions**

Propiverine hydrochloride was useful for the improvement of over active bladder and the effect for the bladder function was appeared to persist. In contrast, the thirst was significantly decreased more than for 4 weeks consecutive administration with Propiverine hydrochloride. Different muscarinic receptor subtypes are distributed widely in body [3]. These data suggests that there is different pharmacokinetics in muscarinic receptors between salivary glands and detrusor muscle. It may occur to the dissociation of the thirst and effects of the bladder function for long administration with Propiverine hydrochloride.

### **References**

1. Helmut Madersbacher, Gerd Mürtz Efficacy, tolerability and safety profile of Propiverine in the treatment of the overactive bladder ( non-neurogenic and neurogenic). World J Urol 19; 324-335, 2001.
2. Satischandra Pai, et al. Development of a visual analog scale questionnaire for subjective assessment of salivary dysfunction. Oral Surg Oral Med Pathol Oral Radiol Endod 91: 311-316, 2001.
3. Karl-Erik Andersson Potential benefits of muscarinic  $M_3$  receptor selectivity. European Urology (supplements) 1: 23-28, 2002.