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DURATION OF DRY MOUTH INDUCED BY ANTICHOLINERGIC AGENTS VARIES WIDELY: RESULTS OF CLINICAL PROSPECTIVE STUDY

Hypothesis / aims of study

Anticholinergic agents are in the mainstream of treatment for overactive bladder (OAB). However, a major problem with the use of anticholinergics is dry mouth as a dose-limiting factor. While the incidence of dry mouth has received attention in the past, there has not been any research about its duration with respect to the type of anticholinergics used. In this study, therefore, we investigated the profile of dry mouth as perceived by the patients.

Study design, materials and methods

A prospective questionnaire survey was conducted from October 2008 to June 2009 in OAB patients being treated at 18 urology clinics in Tokyo, Japan. Each patient received one of the following anticholinergics, propiverine at 10 or 20 mg QD, tolterodine at 4 mg QD, solifenacin at 5 mg QD, or imidafenacin at 0.1 mg BID. The efficacy of each anticholinergic as well as the patients' perception of the general condition were assessed 3times, at baseline, the initial 3 days after treatment initiation (early phase), and after 1 month of treatment (late phase). 1) Overactive Bladder Symptom Score (OABSS) as a measure of OAB severity (0-15 range scale: the severer, the higher the score), and 2) the mood of daily life index as a measure of the patient's perception of the general condition were evaluated at each point. The OABSS is a survey form comprising 4 questions about the symptoms of OAB, and is widely used in Japan as a concise, standard index that makes it possible both to diagnose OAB and to assess its severity [1]. The mood of daily life index is used as a simple assessment tool in the clinical setting (the patients were asked to describe their "perception of the general condition" on a 5-level scale, from "Cheerful" to "I feel like crying"). In addition to these measures, at the early phase time point, a "24-hour clock table scale" that we originally prepared (Table 1) was used to assess the duration of dry mouth when it occurred. Finally, dry mouth was assessed again using a 3-level scale (disappear, no change, worsened) at the late phase.

Results

A total of 126 OAB patients (with a mean age of 68.24 ± 12.28) participated in the study. 1) The usage of an anticholinergic significantly reduced the total score of OABSS from 8.65 ± 2.62 to 5.67 ± 3.04 and no significant differences were seen among the different anticholinergics. 2) Improvement on the mood of daily life index was seen with all anticholinergics, except for propiverine. 3) At the early phase, the incidence of dry mouth was from 80% to 91.7%; no significant differences were seen among the drugs. However, the study of the 24-hour clock table scale showed that the mean duration of dry mouth in the imidafenacin group was significantly shorter than in either propiverine group or tolterodine group ($p = 0.0013$, 0.0299, respectively, Figure 1). 4) At the late phase time point, the disappearance of anticholinergic-associated dry mouth was observed in some patients. The proportion of patients in whom dry mouth disappeared was significantly higher with imidafenacin than with solifenacin ($p = 0.021$, Figure 2).

Interpretation of results

This study provides the first results of assessments of anticholinergics from the standpoint of the duration of dry mouth. Although the incidence of dry mouth was 80% to 91.7%, which seems enormously high, this is attributed to the fact that patients were proactively surveyed specifically about dry mouth. The apparent lack of improvement on the mood of daily life index with propiverine alone is possibly explained by the fact that there were a lot of patients who responded that their dry mouth lasted for 8 hours or more. When a patient experiences dry mouth, the patient may be able to endure it for a few hours. However, if it continues for a long time, the patient's satisfaction with the treatment would be decline. It was also demonstrated that dry mouth disappeared in some patients when they continued taking antichorinergics for one month. The reason why imidafenacin showed a significantly higher disappearance rate of dry mouth than solifenacin in the late phase may be due to the differences in the pharmacokinetic characteristics of the two drugs: in repeated-dosing, the Cmax and T1/2 of imidafenacin remain unchanged, but both the Cmax and the T1/2 of solifenacin increase. Imidafenacin is the newest anticholinergic; its superiority to placebo and noninferiority to propiverine have been demonstrated in placebo- and propiverine-controlled clinical studies, and it was marketed in Japan in 2007[2]. Imidafenacin has a short blood half-life – 2.9 hours – but preclinical research that looked at binding to tissue receptors has shown that the duration of receptor binding is longer in the bladder than in the salivary glands, and that imidafenacin thus has high bladder selectivity [3]. It is assumed that the present study also confirmed the pharmacokinetic characteristics of imidafenacin in the clinical setting.

Concluding message

This study clearly demonstrated that there are considerable differences among anticholinergics in terms of the dry mouth profile over time. Since dry mouth is a major adverse reaction of anticholinergics, its incidence should be minimal in order to continue the treatment. In this aspect, we concluded that imidafenacin would be an extremely beneficial anticholinergics for OAB patients.

Table.1 24-hour clock table scale

Date: ( )		
Time of drug-taking behavior	first time :	second time :

Please draw circles around a times you experienced "dry mouth" (you may draw as many circle as you like).

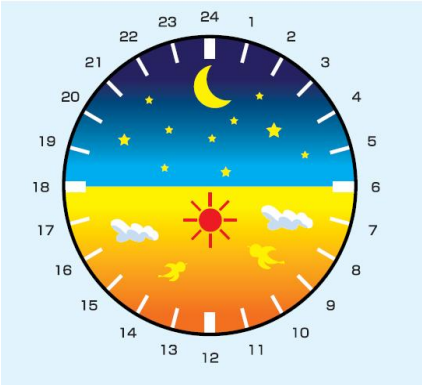
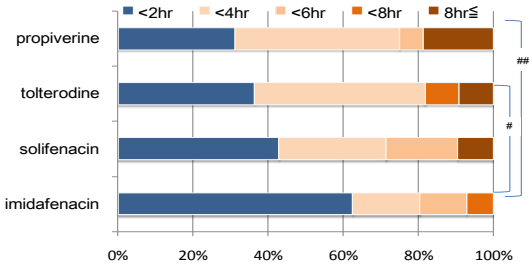
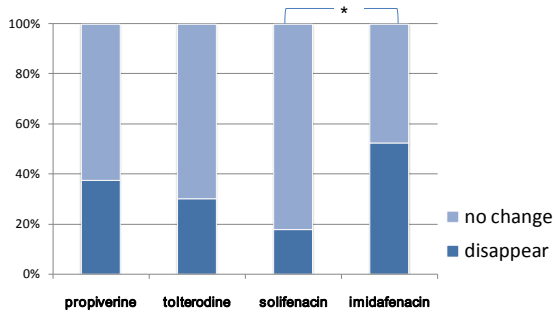


Figure.1 Percentage of the duration of dry mouth caused by antichorinergic medication



•p<0.05 : Mann-Whitney U test vs. imidafenacin
#p<0.05 ##p<0.01 : χ2 test vs. imidafenacin

Figure. 2 State of the dry mouth after one month anticholinergic medication



•p<0.05 : Mann-Whitney U test vs. imidafenacin

References

1) Urology. 68(2):318-23, 2006
2) Int J Urol. 16, 499-506, 2009
3) ICS 2009 abstract No.502

References

1. Urology. 68(2):318-23, 2006
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3. ICS 2009 abstract No.502

Specify source of funding or grant	**none**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**No**
Is this a Randomised Controlled Trial (RCT)?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**No**
This study did not require ethics committee approval because	**It was held under daily clinical practice**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**