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IMIDAFENACIN, A NOVEL ANTICHOLINERGIC AGENT WITH LOW SIDE EFFECTS, SHOWS EQUIVALENT EFFICACY TO SOLIFENACIN IN OVERACTIVE BLADDER PATIENTS – GAP (GLOBAL ASSESSMENT STUDY OF ANTICHOLINERGICS ON EFFICACY AND TOLERABILITY FOR PATIENTS WITH OAB) STUDY IN JAPAN

Hypothesis / aims of study

Overactive bladder (OAB) is a symptom syndrome characterized by urgency with or without urgent incontinence, which affects 12.4% in population >/=40 years old in Japan. OAB is a bothersome condition affecting the quality of life (QOL) of the patients. Recently, pharmacological treatment for OAB is centered on anticholinergic agents. However, it is well known that anticholinergic agents can deteriorate the QOL of the OAB patients due to adverse effects such as dry mouth and constipation. Unwillingness and inability of OAB patients to continue oral therapy with anticholinergic agents due to these adverse effects have been the clinical problem especially in the long term therapy.

The purpose of this study is to assess the efficacy and tolerability of imidafenacin and solifenacin in Japanese OAB patients, by evaluating the clinical efficacy, dry mouth, and constipation with Overactive bladder symptom score (OABSS), Dry mouth scale (DMS), and Constipation assessment scale (CAS), respectively.

Study design, materials and methods

Patients >/= 20 years old with OAB (n=341) enrolled into this multi-centre, open label, randomized study. Patients were diagnosed as OAB if they scored 3 or more points in the OABSS, and answered “more than once a week” regarding the sub-score of urgency in OABSS. Patients were randomized to imidafenacin (0.1 mg, twice a day, daily, 12 weeks) or solifenacin (5 mg, once a day, daily, 12 weeks). OABSS was used to evaluate the clinical efficacy, DMS, CAS and satisfaction questionnaire were used to evaluate the tolerability. Subjects answered OABSS, DMS and CAS at 0 (baseline), 4, 8 and 12 weeks, and satisfaction questionnaire at 12 weeks. The dry mouth symptoms, accompanying symptoms and QOL were asked on the basis of face scale in DMS. In addition, onset and duration of dry mouth after the medication were asked. CAS includes 8 items to ask the defecation status which was validated in Japanese and is a reliable tool to assess the constipation in Japanese population. Patients answer on three points scale, 0 (none, rarely), 1(mild, sometimes), and 2 (never, always). Satisfaction questionnaire is consisted with three questions, satisfaction with the prescribed medications, bothersome by adverse effects and hope to continue the treatment, on the basis of VAS. For statistical analysis, repeated measures ANOVA and Dunnett’s test were used and p value <0.05 was considered statistically significant.

Results

Total 341 subjects were enrolled (imidafenacin n=171, solifenacin n=170) in the study. The 297 subjects (imidafenacin, n=150 male n=66, female n=84, solifenacin, n=147 male n=49, female n=98) were eligible for the efficacy and tolerability assessment in this study. Their average age was 66.7 years old in imidafenacin group, and 66.4 years old in solifenacin group.

- Efficacy

There were significant improvements in total score and four sub-scores (daytime frequency, night time frequency, urgency, urge incontinence) of OABSS in both groups at 4, 8 and 12 weeks (Figure. 1). There was no significant difference in the changes of total score of OABSS at 12 weeks.

- Adverse effects

37 cases in imidafenacin group and 52 cases in solifenacin group were reported. The cases which needed to cease medication due to adverse effects were 8 cases in imidafenacin and 14 in solifenacin.

- Tolerability

(DMS) In imidafenacin group, there was a significant increase in dry mouth symptom score of DMS at 4 week in comparison to 0 week. The dry mouth symptom score at 8 and 12 weeks in imidafenacin group returned to the same level as 0 week. However,in solifenacin group, there was significant increase in dry mouth symptom score at 4, 8 and 12 weeks in comparison to 0 week (Figure.2). There were no significant changes in dry mouth accompanying score, QOL score in both groups 4,8 and 12 weeks. Total number of the dry mouth in both group were decreased at 8 and 12 weeks in both group in comparison to 4 week. The onset and duration of the dry mouth showed no significant difference in both group at any time.

(CAS) No significant change in CAS was observed in both groups at any time.

(Satisfaction questionnaire) There was no significant difference in both groups about the effect of the prescribed medications, bothersome by adverse events and hope to continue the treatment.

Interpretation of results

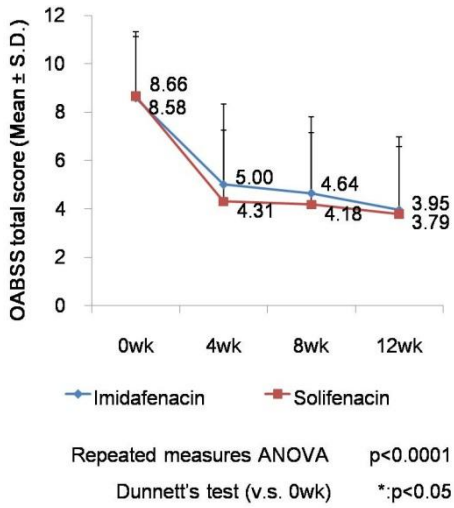
In OAB patients, significant improvements in OABSS were observed by the administration of imidafenacin and solifenacin. Imidafenacin revealed equivalent efficacy to solifenacin.

DMS showed low adverse effects in imidafenacin group. OAB patients were satisfied with the treatment of imidafenacin and solifenacin.

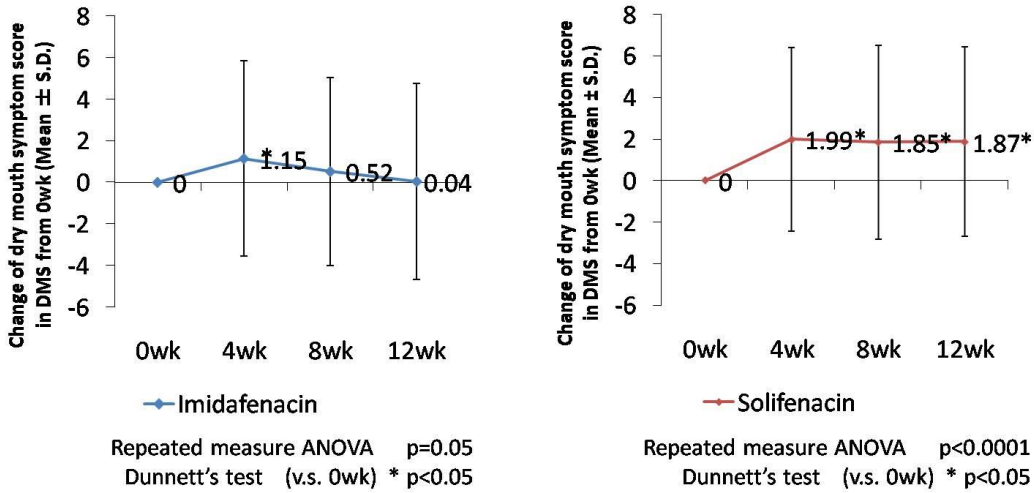
Concluding message

This study indicated that imidafenacin to be well tolerated and show satisfactory effects in OAB patients.

(Figure.1) The changes of total score of OABSS



(Figure.2) The changes of dry mouth symptom score in DMS



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Specify source of funding or grant	**none**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**Yes**
Specify Name of Public Registry, Registration Number	**UMIN000003033**
Is this a Randomised Controlled Trial (RCT)?	**Yes**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**University of Occupational and Environmental Health, Japan, Ethics Committee**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**