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SAFETY AND EFFICACY OF EXTENDED-RELEASE TOLTERODINE FOR NON-NEUROGENIC OVERACTIVE BLADDER IN JAPANESE ELDERS >/=75 YEARS

Hypothesis / aims of study
Overactive bladder syndrome (OAB) affects millions of elderly people in Japan as well as in other countries, and is equally prevalent in men and women. Its impact on quality of life can be devastating, especially to elderly patients with other medical comorbidities. Elders, especially in elders >/=75 years are known to have more and greater adverse events (AEs) potential compared with young and adults. For the elders, safety and tolerability are key factors, even during the treatment of OAB. There is uncertainty about the role, AES and efficacy of anticholinergic drugs in the elderly, especially elders >/=75 years. We evaluate the tolerability and efficacy of Tolterodine extended release (ER) once daily in elders >/=75 years with non-neurogenic OAB.

Study design, materials and methods
A total of 130 healthy Japanese subjects >/=75 years diagnosed as having non-neurogenic OAB were enrolled into the study. All patients had evidence of urgency (>/=1 episode per week) and >/=8 voids per 24h at baseline and had completed at least the 8 weeks study. All patients were given 4.0 mg Tolterodine ER once daily. Before and at week 8, patient perception of treatment benefit (PPTB) and overactive bladder symptom score (OABSS; consisting of four questions about number of daytime frequency, night-time frequency, presence and degree of urgency and presence and degree of urge incontinence) were examined. The primary end point was to assess the PPTB and I-PSS QOL, and safety and tolerability of 4.0 mg Tolterodine ER for treating elderly subjects with OAB. And secondary end point was the proportion of subjects who became continent and had no urgency episodes, and the mean change from baseline of number of micturitions/24 hours at 8 weeks. Safety and efficacy were evaluated according to two age cohorts; elders (>/=75, < 80 years; old group) and more elders (>/= 80 years; old-old group).

Results
A total of 130 Japanese patients were enrolled (aged 75 to 88 years, mean 79.1 years old). Mean age in the old and old-old group was 77.0 (75-79) and 82.4 (80-88) years, respectively. Forty six percent of patients reported >/=1 AE during the study. The most frequent AEs were dry mouth (21.2%), constipation (11.5%), difficult voiding (5.3%), urinary tract infections (3.5%) and abdominal pain (3%) (**Table 1**). Most AEs reported in our study were mild in intensity. Seven patients (6.2 %) experienced moderate to serious AEs and withdrew due to the AEs. During the study, no cases of significant residual urine were detected. No central nervous system and cardiac safety were noted. There was no difference in occurrence rate of AEs between old group and old-old group and there was no significant difference of withdrawal rates due to the AEs between the two groups. After 8 weeks' Tolterodine ER treatment, 79.1% of patients considered their treatment beneficial (much benefit + little benefit). There was no significant difference of PPTB (much benefit + little benefit) between the two groups (Table 2). After 8 weeks' treatment, the mean reduction number of micturitions during 24 hours were -1.9 +/- 1.9 times in old group times and -1.6 +/- 1.6 times/24h in old-old group, respectively. The restoration rate of daytime increased frequency, nocturia, urgency and urge incontinence was shown in Table 3. Of the elderly patients suffering OAB symptoms, a significantly great proportion of old group had resolution of urgency and urge incontinence than old-old group (Table 3). However, Tolterodine treatment resulted in statistically significant improvements in OAB-SS scores at week 8 in both groups.

Interpretation of results

Concluding message
Within 8 weeks Tolterodine ER 4mg was statistically significant in improving PPTB and OAB-SS in both groups. And this clinical trial showed good safety tolerability of 4.0 mg Tolterodine ER once daily for the treatment of elders (>/=75, < 80 years) and more elders (>/= 80 years) suffering from OAB. Our data suggest that Tolterodine ER could be a safe and effective potential therapeutic drug even in healthy elders, especially >/= 80 years old with non-neurogenic OAB.

Table 1

Patient perception of treatment benefit of 4.0 mg Tolterodine ER at week 8

group	n	age (years)	much benefit (%)	little benefit (%)	no benefit (%)
old group	36	77.0+/-1.4	47.2	19.4	33.3
old–old group	58	82.3+/-2.6	32.8	22.4	44.8
total	94	40.4	38.3	21.3	40.4

Table 2

Most common adverse events caused by Tolterodine ER treatment

group	total (%)	dry mouth (%)	Constipations (%)	difficult voiding (%)	UTIs* (%)
old group	43.3	20.9	10.4	10.4	3.0
old–old group	50.0	21.7	13.0	8.7	4.3
total	46.0	21.2	11.5	5.3	3.5

UTIs*; urinary tract infections

Table 3

The restoration rate of each overactive bladder symptoms after Tolterodine ER 8weeks' treatment

group	frequency (%)	nocturia (%)	urgency (%)	urge incontinence (%)
old group	37.9	9.1	22.4	68.8
old–old group	25.0	8.6	11.1	36.7
total	33.0	8.9	18.1	53.2

Specify source of funding or grant	**no**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**No**
This study did not require eithics committee approval because	**Tolterodine ER 4.0 mg treatment for OAB has benn approved in Japan.**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**