

LOW INCIDENCE OF CLEAN INTERMITTENT CATHETERISATION WITH ONABOTULINUMTOXINA IN DIVERSE AGE GROUPS OF OVERACTIVE BLADDER PATIENTS WITH CORRESPONDING IMPROVEMENTS IN URINARY SYMPTOMS, TREATMENT RESPONSE, AND QUALITY OF LIFE

Hypothesis / aims of study

Randomised, placebo-controlled, multicentre trials with onabotulinumtoxinA 100U have demonstrated significant improvements in urinary incontinence (UI) and quality of life in idiopathic overactive bladder (OAB) patients who were inadequately managed by ≥ 1 anticholinergic. Incomplete bladder emptying resulting in the need for clean intermittent catheterisation (CIC) is known to occur in OAB patients who have been treated with onabotulinumtoxinA. However, there is little information on the incidence of CIC in OAB patients according to age following treatment with onabotulinumtoxinA. Thus, this post hoc analysis of the pooled placebo-controlled trials was undertaken to assess the incidence of CIC, and efficacy and quality of life outcomes, in various age groups of OAB patients treated with onabotulinumtoxinA. Quality of life outcomes were also evaluated by patients' urinary tract infection (UTI) status.

Study design, materials and methods

Two phase 3 trials and a post-marketing study enrolled patients with OAB who had experienced ≥ 3 urgency UI episodes over a 3-day period and ≥ 8 micturitions per day. All patients were inadequately managed by ≥ 1 anticholinergic. Patients with a predominance of stress UI were excluded. Pooled data from patients (N=1177) randomised to onabotulinumtoxinA 100U in treatment 1 and patients initially randomised to the placebo group who received open-label onabotulinumtoxinA 100U in treatment 2 were grouped by age: <40, 40–49, 50–59, 60–69, and ≥ 70 years. CIC was initiated during the studies if post-void residual (PVR) urine volume was ≥ 350 mL regardless of symptoms, or was ≥ 200 mL to <350 mL with symptoms of difficult micturition. Assessments at week 12 included incidence and duration of CIC, mean change from baseline in PVR urine volume, mean and percentage change in UI episodes/day, proportions of patients with $\geq 50\%$ and 100% reduction in UI episodes/day, and with a positive response ("improvement" or "great improvement" in their urinary condition) on the Treatment Benefit Scale. The mean change from baseline in King's Health Questionnaire (KHQ) Role Limitations and Social Limitations domain scores and proportions of patients who achieved/exceeded the minimally important difference (-5 points) on the KHQ domains were also evaluated. The KHQ results were also examined in the various age groups by patients' UTI status. Scores on the KHQ range from 0–100 with lower scores (and negative change over time) indicating better quality of life. Adverse events (AEs) were recorded. The incidence of AEs, including use and duration of CIC, was analysed in the safety population (all patients who received treatment), and efficacy and quality of life outcomes were analysed in the intent-to-treat population (all randomised patients).

Results

CIC rates were low in all age groups in the first 12 weeks following treatment with onabotulinumtoxinA. Rates were lowest in the <40 group (1.1%) and increased with age (3.2%, 5.3%, 5.3% and 7.2% in the 40–49, 50–59, 60–69, and ≥ 70 groups, respectively). The mean (median) duration of CIC in the <40 and 40–49 groups was 3 (3) and 44 (26) days and ranged from 78 (68) to 88 (74) days in the other groups. The mean change from baseline in PVR urine volume at week 12 after onabotulinumtoxinA treatment was low overall and showed small increases with age (7.7, 14.1, 20.5, 29.7, and 36.5 mL in the 40–49, 50–59, 60–69, and ≥ 70 groups, respectively). At baseline, the mean numbers of UI episodes/day were 3.9, 4.8, 5.2, 5.7, and 6.0 in the <40, 40–49, 50–59, 60–69 and ≥ 70 y groups, respectively. Substantial reductions in UI episodes/day (-2.4, -2.6, -3.1, -3.6, and -2.9) and percentage change in UI (-60.8%, -50.4%, -62.4%, -64.4%, and -46.8%) were observed. Nearly half (45.6%) of the patients in the <40 group achieved 100% reduction in UI episodes/day, which was the highest among all age groups (28.8%, 34.2%, 31.5%, and 20.3% in the 40-49, 50-59, 60-69, and ≥ 70 groups, respectively). High proportions of patients across all age groups achieved $\geq 50\%$ reduction in daily UI episodes (64.4%, 64.7%, 71.1%, 70.6%, and 58.2%). Likewise, high proportions of patients reported treatment benefit as reflected by a positive response on the TBS (67.8%, 69.9%, 73.8%, 70.9%, and 66.2%) and achieved improvements \geq MID in the KHQ Role Limitations (66.7%, 64.7%, 72.2%, 62.7%, and 58.2%) and Social Limitations domains (54.4%, 57.7%, 63.1%, 55.1%, and 51.7%). Improvements from baseline in the KHQ Role Limitations and Social Limitations domain scores were similar across all age groups and were approximately 5–6 and 3–4 times the MID, respectively. In addition, improvements in the KHQ domain scores were generally similar across all age groups regardless of UTI status, with mean decreases from baseline in patients of all ages either with or without UTI approximately 5 times the MID for Role Limitations and approximately 3 times the MID for Social Limitations. Overall AEs were similar across all age groups. UTI was the most common AE in all groups and showed a trend for increased incidence with age; younger groups reported the lowest rates (10.0% and 8.3% in the <40 and 40-49 groups, respectively) compared with the other groups (range: 11.8-16.8%).

Interpretation of results

In this large cohort of patients with OAB who were inadequately managed by ≥ 1 anticholinergic, the incidence of CIC following treatment with onabotulinumtoxinA was low in all age groups and increased somewhat with age with an acceptable benefit/risk

profile. The <40 group had the lowest rate of CIC (1.1%), with a mean duration of 3 days, and the ≥70 group had a rate of 7.2%, with a mean duration of 86 days. The low incidence of CIC was accompanied by a robust treatment response across all age groups including substantial reductions in UI, clinically meaningful improvements in quality of life, and high proportions of patients reporting treatment benefit. Similar improvements in quality of life were seen following onabotulinumtoxinA treatment regardless of UTI status. OnabotulinumtoxinA treatment results in no unexpected safety signals.

Concluding message

The risk of CIC was low in all age groups, was especially low in the youngest patients, and showed small increases with age. All age groups showed substantial improvements in UI, treatment benefit, and quality of life in this large cohort of OAB patients treated with onabotulinumtoxinA. UTI status did not have an effect on quality of life. OnabotulinumtoxinA was well tolerated in all age groups.

Disclosures

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