620

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AN OPEN, MULTICENTRE STUDY OF NASHA/DX GEL (ZUIDEX™) FOR THE TREATMENT OF STRESS URINARY INCONTINENCE

Hypothesis / aims of study

The Zuidex™ system (Q-Med AB, Uppsala, Sweden) aims to provide reproducible, office-based injection of non-animal stabilised hyaluronic acid/dextranomer (NASHA/Dx) gel into the mid-urethra via the Implacer™ device (1). Here we present results of an open, non-comparative, multicentre study of this treatment over a 12-month follow-up period.

Study design, materials and methods

This study was performed in accordance with Good Clinical Practice and applicable regulatory requirements, as well as the principles of the International Conference on Harmonization. Inclusion criteria were: ≥18 years of age, SUI for ≥1 year, failure of previous non-invasive treatment and no prior invasive therapy. Patients were not sub-divided according to pathophysiology of SUI (hypermobility or intrinsic sphincter deficiency).

Patients were treated with Zuidex (4 x 0.7 ml injections of NASHA/Dx gel via the Implacer); local anaesthetic was administered before treatment. At week 8, all women with persistent leakage, and not improved to their satisfaction, were offered a second treatment. Immediately after treatment, patients were asked to rate the acceptability of the procedure. Follow-up visits were scheduled for 4, 8 and 12 weeks, and 6 and 12 months after initial treatment. The primary efficacy assessment was provocation test urinary leakage, with a positive response defined as ≥50% reduction in leakage *vs* baseline. Secondary efficacy assessments included 24-hour pad-weight test and number of incontinence episodes/24 hours. Quality of life (QoL) was measured by nine domains of the King's Health Questionnaire (KHQ). Patients also provided a global assessment of their incontinence problems on a 4-point scale (none, mild, moderate or severe). Efficacy and QoL were analysed using the intention-to-treat (ITT) population. Missing values for the primary efficacy analysis were derived by multiple imputation (MI), whereby missing values are derived from trends displayed by patients with complete data. Last observation carried forward (LOCF) was used for QoL. Safety was assessed by adverse event monitoring.

Results

A total of 142 patients were enrolled (mean age: 55.7 years). At week 8, 61 patients (43%) underwent re-treatment. Overall, 85% of treatment procedures were rated as acceptable, 10% as unpleasant and 4% as very unpleasant. Thirty-four patients (24%) withdrew from the study prematurely; the most common reason (59% of withdrawals) was lack of efficacy. At 8 weeks, 12 weeks, 6 months and 12 months, 141, 132, 123 and 108 patients remained in the study, respectively (provocation test data were available for 129, 113, 109 and 94 patients).

At 12 months, a positive response was observed in 77% of patients (95% CI 69%, 85%). Similar results were obtained using LOCF (68%; 95% CI 60%, 76%) or per protocol (85%; 95% CI 77%, 92%) analysis. Minimal decrease in response rate was observed between week 12 (78%) and month 12 (77%). A large and highly significant decrease in median provocation test urinary leakage was observed (93%, 12 months *vs* baseline; $p<0.0001$) (Figure 1). Median 24-hour pad-weight leakage and median number of incontinence episodes/24 hours were also reduced at 12 months compared with baseline, by 89% ($p<0.0001$) and 67% ($p<0.001$), respectively. In post-hoc analyses, no correlation was found between treatment response and baseline age, body mass index, maximum urethral closure pressure or menopausal status. However, patients who were re-treated at week 8 had a significantly higher median provocation test urinary leakage at baseline than those treated only once (57.5 *vs* 30.0 g; $p=0.022$). Statistically significant improvements compared with baseline were observed in 8/9 KHQ domains at 6 months ($p\leq0.0025$), and 6/9 domains at 12 months ($p\leq0.0001$), with the greatest improvements observed for incontinence impact, physical limitations, social limitations and personal relationship (Figure 2). At month 12, the proportion of patients reporting global assessment improved by at least one step compared with baseline

was 61%, while the proportion of patients who reported their incontinence problems as mild or absent increased from 12% to 56%.

Figure 1. Median provocation test urinary leakage following Zuidex treatment.

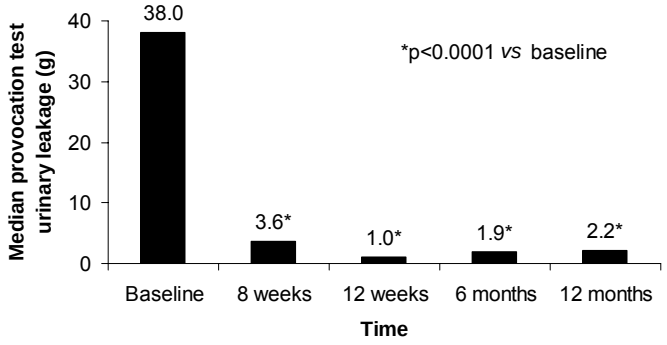
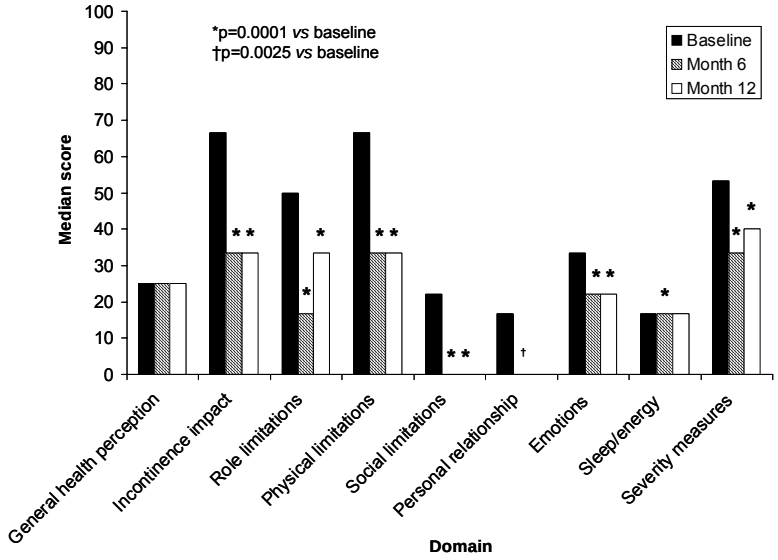


Figure 2. Post-treatment improvements in QoL: change in median KHQ domain scores.



Treatment-related adverse events were reported by 81 patients (57%). Most (83%) were of mild or moderate intensity, and the majority were transient, with a median duration of 7 days. Adverse events were as expected for injection therapy (e.g. urinary tract infection, injection site pain, injection site pseudocyst), with urinary retention (median duration: 2 days) being the most common.

Interpretation of results

This study shows that Zuidex produces significant improvements in both incontinence and QoL, with no long-term side-effects. The results reported here are similar to those of a previous 12-month Zuidex study (1). The lack of apparent effect of baseline MUCP, patient age, menopausal status or body mass index on treatment outcome suggests that the vast majority of patients with SUI may be considered as eligible for Zuidex treatment.

Concluding message

This study has shown that Zuidex is well tolerated, and provides a significant improvement in both incontinence and QoL over 12 months. The results suggest that Zuidex could be considered as an early intervention in treatment-naïve cases of SUI.

1. Efficacy and safety of a novel system (NASHA/Dx copolymer via the Implacer device) for the treatment of SUI. *Urology* 2004; **64**: 276–81.

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