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THE ZUIDEX™ SYSTEM FOR THE TREATMENT OF STRESS URINARY INCONTINENCE: 24-MONTH FOLLOW-UP

Hypothesis / aims of study

The Zuidex™ system (Q-Med AB, Uppsala, Sweden) is a new treatment for stress urinary incontinence (SUI). It consists of four pre-filled syringes containing non-animal stabilised hyaluronic acid/dextranomer (NASHA/Dx) copolymer and the Implacer™ device. NASHA/Dx copolymer is a biocompatible and biodegradable material used for many years in the treatment of vesicoureteral reflux (VUR) without any safety concerns, while the Implacer is a novel guiding instrument that facilitates reproducible and standardised transurethral injection of the NASHA/Dx copolymer into the mid-urethra. The treatment procedure is performed without the need for surgical facilities. NASHA/Dx copolymer has gained European approval in the treatment of SUI, and is the only injectable agent approved by the US Food and Drug Administration for endoscopic treatment of VUR in children.

Previous studies have indicated that long-term efficacy following Zuidex treatment is likely. Treatment using NASHA/Dx copolymer produced long-term efficacy over a 6.5-year follow-up period in older women (median age 74.5 years) who had failed both previous and subsequent treatments for SUI (1). Moreover, in an open, prospective, multicentre study, significant improvements in efficacy were sustained for at least 12 months (2). Here we report the efficacy data at 24 months' follow-up.

Study design, materials and methods

An open, multicentre study was approved by independent ethics committees, and performed in accordance with the principles of the Declaration of Helsinki. Female patients 18 years of age or older were recruited with SUI verified by demonstrable leakage on coughing or Valsalva manoeuvre. Patients had a history of SUI for at least 12 months, had failed prior non-invasive treatment (e.g. behaviour modification, pelvic floor exercises, drug therapy) and were invasive therapy-naïve. Exclusion criteria included: mean volume voided <200 ml; post-void residual urine (PVRU) >100 ml; urge incontinence; detrusor overactivity; medication for SUI; recurrent urinary tract infection; and anticoagulant or immunosuppressive therapy. The pathophysiology of SUI (i.e. hypermobility and/or intrinsic sphincter deficiency) was not determined.

Four sequential injections of NASHA/Dx copolymer were administered into the mid-urethra using the Implacer, at approximately the 2, 4, 8 and 10 o'clock positions. Two different injection volumes were studied: 4 x 1.0 ml (n=32) and 4 x 0.7 ml (n=10). The two volumes showed very similar efficacy results, and are therefore considered as one group in the efficacy evaluation. Patients non-responsive to the first treatment were offered one re-treatment, 1–2 months after the initial procedure.

Treatment efficacy parameters, urine leakage by provocation test, the number of incontinence episodes/24 hours and patients' perception of bladder condition (i.e. bothersomeness graded on a six-point scale as: no, some very minor, some minor, some, some severe, and many severe problems) were assessed at baseline and 1, 3, 6, 12 and 24 months' follow-up.

Results

A total of 20 patients were assessed at the 24-month follow-up visit. For this population, a significant reduction in urine leakage by provocation test was observed within 1 month of treatment, sustained at 24 months (Figure 1; $p<0.0001$ *vs* baseline). No statistically significant differences were observed between the values at 3, 12 and 24 months. The percentage of patients with a ≥50% reduction in urine leakage remained at 85–90% between 3 and 24 months.

Significant reductions in the median number of incontinence episodes/24 hours were observed, also sustained at 24 months (Figure 2). In terms of patients' perception of bladder condition, the percentage improved by at least one category on the six-point patient perception scale was 70–90% at 3, 12 and 24 months.

Figure 1. Median urine leakage by provocation test following Zuidex treatment.

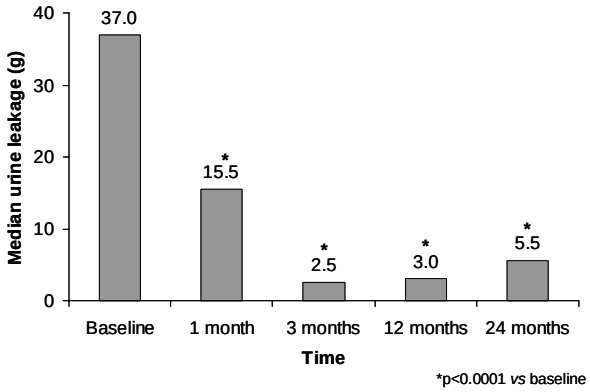
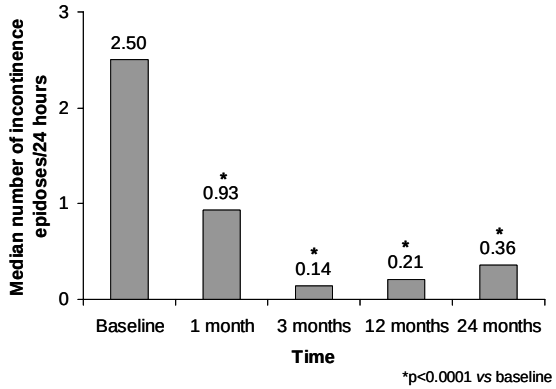


Figure 2. Median number of incontinence episodes/24 hours following Zuidex treatment.



For the total study population (n=42), 15 patients reported treatment-related adverse events, which were transient and of an expected nature, with the majority of mild (70%) or moderate (26%) intensity. No serious treatment-related adverse events were observed. Three patients required temporary catheterisation, with a mean duration of 4 days. No further treatment-related adverse events or complications occurred during the 24-month follow-up.

Interpretation of results

Zuidex treatment was well tolerated. Efficacy, in terms of provocation test urine leakage, the number of incontinence episodes/24 hours and patients' perception of bladder condition, was sustained for at least 24 months.

Concluding message

The lack of both durability and established safety has limited the widespread acceptance of urethral injection. Therefore, the fact that Zuidex treatment is well tolerated and remains effective for at least 24 months is extremely encouraging.

References

1. Urethral injection for stress urinary incontinence: long-term results with dextranomer/hyaluronic acid copolymer. *Int Urogynecol J Pelvic Floor Dysfunct* 2003; **14**: 335–8.

2. Efficacy and safety of a novel system (NASHA/Dx copolymer via the Implacer device) for the treatment of SUI. *Urology*: In press.

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