400

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EFFICACY AND SAFETY OF DEXTRANOMER/HYALURONIC ACID VIA A NOVEL APPLICATOR (ZUIDEX®) IN THE TREATMENT OF STRESS URINARY INCONTINENCE

Aims of Study

Stress urinary incontinence (SUI) is prevalent in adult women and has a considerable impact on quality of life. Non-invasive treatment is offered in mild cases and may entail physiotherapy, minimally invasive devices or pharmacotherapy. Surgical intervention is widely considered as the only effective option for severe cases. However, these strategies are not adequate or suitable for all patients. Urethral injection with bulking agents has been investigated as an alternative treatment option. The approach had limited success, for reasons such as difficulty with ensuring correct injection technique and shortcomings with the previously available bulking agents in terms of safety and/or efficacy (e.g. lack of biocompatibility, allergenicity, insufficient longevity in the tissue).
Dextranomer/hyaluronic acid (Dx/HA) copolymer is a biocompatible material with excellent properties for submucosal injection, having recently been approved by the FDA for endoscopic treatment of vesico-ureteral reflux in children (Deflux ®, Q-Med, Uppsala, Sweden). Dx/HA copolymer also has European approval for the treatment of SUI (Zuidex™). The Zuidex™ system includes a novel applicator (Implacer™ device) that allows transurethral injection of Dx/HA copolymer as an office procedure, eliminating the need for surgical facilities. We report 12-month results from a pilot study undertaken to investigate the safety and efficacy of this treatment.

Methods

This was an open, prospective, multi-centre study. Female patients 18 years of age or older with urodynamically verified SUI were recruited, regardless of SUI pathophysiology (hypermobility and/or intrinsic sphincter deficiency). All patients had a history of SUI for at least 12 months and had failed prior non-invasive treatment. Exclusion criteria included mean volume voided <200 ml, post-void residual urine (PVRU) >100 ml, patients with urinary incontinence attributable to causes other than SUI, and patients on medication for SUI. Patients with urinary tract infection, or patients receiving anticoagulant or immunosuppressive therapy were also excluded.
Following administration of local anaesthetic, Dx/HA copolymer injections were administered at the mid-urethra using the Implacer™ device. The device facilitates sequential injection of four injections at the 12, 3, 6 and 9 o'clock positions. Two different injection volumes were investigated: 4 x 1.0 ml and 4 x 0.7 ml. No clinically relevant differences were observed between the two groups, therefore pooled data are presented.
Clinical parameters were measured at baseline, and at 3, 6 and 12 months. The measurements included provocation test, micturition chart assessment and safety analyses including adverse events (AEs), urinalysis and urine culture. Patients not responding to treatment were offered one re-treatment with Zuidex™, using identical methodology to the first procedure.

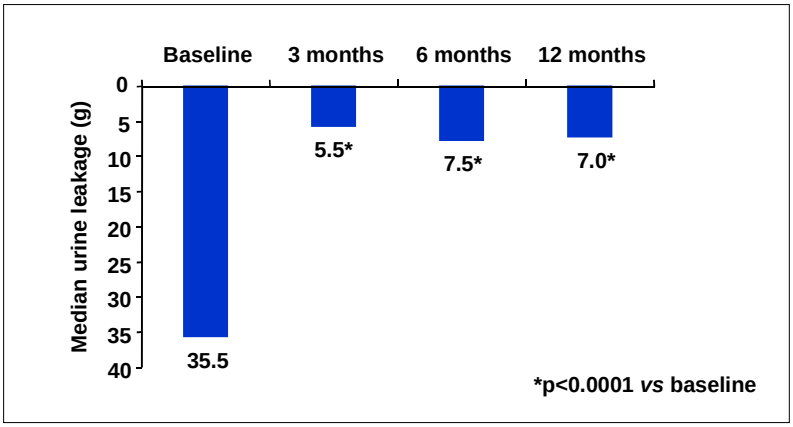
Results

A total of 42 patients were recruited into the study (Table 1).
Table 1. Patient characteristics.

Age in years (range)	52.8 (30.5–77.9)
Menopause n (%)	22 (52.4%)
Duration of symptoms >5 years	33 (78.6%)
Severe problems (patient perception)	22 (52.4%)
Previous non-drug therapy for SUI	42 (100.0%)

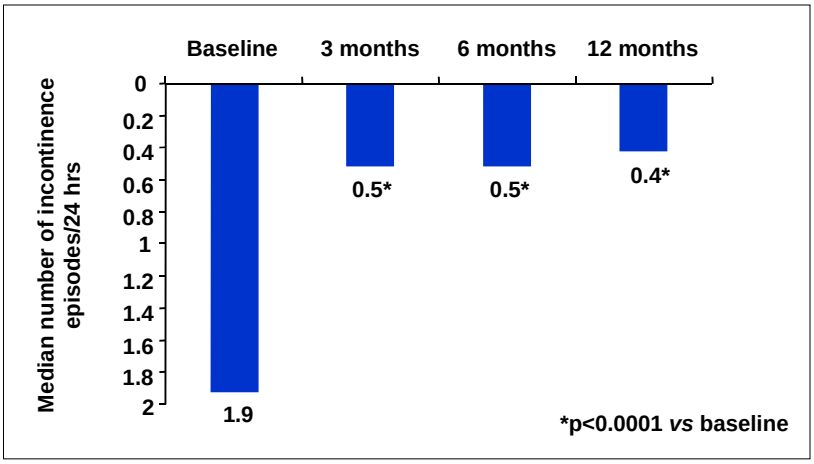
The procedure proved simple to perform and there were no complications associated with the use of the Implacer™ device. Eighteen patients received one re-treatment due to an initial lack of improvement. Five patients were withdrawn between baseline and the 3-month follow-up visit, due to lack of efficacy (n=3), loss from follow-up (n=1) and withdrawn consent (n=1). There were 11 dropouts between 3 and 12 months' follow-up, the reasons for withdrawal being lack of efficacy (n=7) and loss from follow-up (n=4).

Figure 1. Provocation test results following treatment with Zuidex™ (n=42).



A large reduction in median urine leakage was observed during the first 3 months after treatment, from 35.5 g at baseline to 5.5 g at the first follow-up visit (Figure 1). This reduction was maintained between months 3 and 12 with little change over this period. Moreover, the reduction from baseline was statistically significant at month 12 ($p<0.0001$). Reductions in the median number of incontinence episodes per 24 hours were of a similar magnitude and also sustained from months 3 to 12 (Figure 2).

Figure 2. Incontinence episodes/24 hours following treatment with Zuidex™ (n=42).



Treatment-related AEs affected 15 patients. The most common of these were pain/discomfort in the treatment area, decreased urinary flow, urinary retention, haematuria and urinary tract infection. Almost all treatment-related AEs were of mild (70%) or moderate (26%) intensity. Three patients had AEs leading to temporary catheterisation lasting for 2–8 days.

Conclusions

This study indicates promising sustained efficacy with a novel means of treating SUI patients. Injection of Dx/HA copolymer using the Implacer™ device was simple to perform, well tolerated by patients and offered reproducible results. Owing to the lack of requirement for surgical facilities and the established safety profile of Dx/HA copolymer, Zuidex® may represent a major advancement in the treatment of SUI.