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INITIAL CLINICAL RESULTS FROM COAPTITE® INJECTION FOR STRESS URINARY INCONTINENCE COMPARATIVE CLINICAL STUDY

Aims of Study

In the last decade, significant clinical experience has shown the potential of bulking agents for treatment of urinary stress incontinence due to intrinsic sphincteric deficiency. The ideal bulking agent for the endoscopic treatment of stress incontinence is emerging. Optimal characteristics for these agents include: biocompatibility, non-antigenicity, durability, migration resistance, easy injectability without leakage, and off-the-shelf use.

Methods

Coaptite is a cohesive implant created from the combination of spherical particles of synthetic calcium hydroxylapatite (CaHA) and an aqueous carrier gel. Its components have extensive history of safe pharmaceutical and medical device use.

A comprehensive assessment program was instituted to assess biological, functional, and clinical performance. *In vivo and in vitro* biocompatibility assessments were conducted according to ISO 10993. A three-year canine safety study with transurethral injections in the proximal urethra was performed with evaluation of ease of injection as well as local gross and histopathological responses. Functional assessments, including shelf life testing and injectability with various needles, were performed. Subsequent initial clinical evaluations were conducted in the U.S. and U.K. for the treatment of stress incontinence, with a primary endpoint evaluation at one year. Some patients were followed up after more than five years.

A prospective, randomized comparative parallel group study is being conducted at multiple centers for women with urinary stress incontinence due to intrinsic sphincteric deficiency (leak point pressure less than 100 cm of water) without associated hypermobility (less than 35 degrees). Women are randomized to receive either Coaptite or bovine collagen. Follow-up includes symptom analysis, pad use, and Stamey grade change, as well as complications after injection. The first forty women have completed 6-month evaluation at the time of this analysis.

Results

The pre-clinical testing demonstrated Coaptite is non-antigenic and non-toxic with no mutagenic response. Functional testing demonstrated Coaptite is easily injected with injection catheters as small as 3.7 Fr. The animal implant study demonstrated acceptable hematology, clinical chemistry and urinalysis results. There was no gross or microscopic inflammatory tissue response. Gross and microscopic evaluation of the three-year animal implants revealed persistent pliability without evidence of ossification. The CaHA particles were infiltrated with fibrous tissue, were durable, and remained at the injection site with no evidence of migration and with no reaction of surrounding tissue.

An initial interim assessment of the first group of patients, 22 women having received Coaptite and 18 women, bovine collagen, has been performed. The average number of injections was 2.0 for Coaptite patients and 2.3 for collagen patients, and the mean total volume injected was 3.7 cc for Coaptite and 7.4 cc for collagen.

The mean starting Stamey grade for the Coaptite patients was 2.7 and there was significant mean decrease of 59% to a mean Stamey Grade of 1.1. The patients in the collagen side of the study had a mean starting grade of 2.4 and 50% reduction to 1.2. 86 % of the Coaptite patients improved by at least one Stamey grade, 67% improved by 2 grades, and 38 % were completely continent as compared to women who received collagen with 66%, 55%, and 44% comparable changes. While 33% of the collagen patients had no change in Stamey grade, only 14 % of the Coaptite patients had no change. Overall pad weight reduction of 90% was observed in 46% of the patients, 75% reduction in 77% of the patients, and 50% reduction in 82% of the patients randomized to Coaptite. For the collagen patients, the same pad weight reductions were observed respectively in 33%, 55%, and 77% of patients. No prolonged retention, urgency, or periurethral erosion or abscess was seen in either group.

This clinical study is verifying the results from the pilot study. These results, although interim, demonstrate Coaptite is easy to inject with standard cystoscopic instrumentation without a device to enhance mechanical

leverage, does not cause pain at the injection site, remains at the injection site, is durable, and has shown no evidence of migration.

Conclusions

The pre-clinical, laboratory and pilot clinical assessments demonstrate that Coaptite meets all of the desired requirements for a bulking agent and is a biocompatible, easy-to-use, and durable treatment for incontinence. Expanded clinical studies continue to demonstrate that Coaptite requires less volume for results, and a general trend toward greater improvement in patients with severe incontinence is seen with Coaptite as compared to collagen. The full study follow-up is ongoing.