Injected Carbon Beads May Curb Fecal Incontinence

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FORT LAUDERDALE, Fla.—Injecting the anal sphincter with microscopic carbon beads led to a promising degree of improvement in fecal incontinence, based on interim results from a phase II study. Several major procedures have been tested for fecal incontinence caused by abnormality of the internal anal sphincter. Injection with Duraphase FL beads is one of the treatments that is most advanced in clinical development. It appears that this approach may relieve symptoms for some patients, but so far no injectables have been approved for this condition, in the United States, Dr. Eric G. Weiss said at an international colorectal disease symposium sponsored by the Cleveland Clinic Florida. Data were gathered in patients who received intraperineural injections with microscopic, pyrolytic carbon beads in a suspension gel; each bead is 212-500 mcm in diameter. The introduced material is designed to passively close the anal canal and distal rectum and also improve symmetry.

Most patients were enrolled in 40 patients, and 79% were women. By 1 month after treatment, the average CCIS score was 8.3 (the average CCIS baseline for this subgroup was 12.4).

This degree of improvement is an important finding because a CCIS of less than 8.5 indicates “significant improvement in quality of life,” said Dr. Weiss, a colorectal surgeon at Cleveland Clinic Florida, West Palm Beach.

Self-assessments by the 49 patients followed for 6 months showed that 41% said their status was much better, compared with baseline, “and an additional 20% said they felt a little better. Another 22% rated themselves as the same, 2% said they were a little worse, and 6% self-rated as much worse.”

Of the 77 actively treated patients, 24 had a mild sparse event, and 7 patients had a moderate adverse event. No patients had a severe adverse event. The most common adverse events were rectal pain or irritation in 10 patients, an abscess in 10 patients, and bead leakage in 7 patients. Two patients had rectal bleeding, and one patient had an allergic reaction and anal stiffness.

Patients were injected with the carbon beads during an outpatient, ambulatory procedure using local anesthesia. In the initial, phase I study, some patients received the beads in the anal submucosal space, but during the study this approach was replaced by injections into the intersphincteric space using ultrasonographic guidance, which appeared to have better efficacy. The beads were injected at six locations set 60 degrees apart.

Duraphase beads were approved by the Food and Drug Administration in 1999 for treatment of women with urinary incontinence. The beads are approved for the fecal incontinence indication in Europe. The manufacturer is also developing the beads for treatment of gastrointestinal reflux.

Several other injectable materials have been clinically tested for treating fecal incontinence in phase II studies, and these substances have been reported from studies that used polytetrafluoroethylene (PTFE); autologous fat; Contigen, a collagen implant; Bioplastique, a silicone polymer; Solera, a hyaluronan matrix; and microbubbles. Bioplastique was also tested in a phase II study with 82 patients, Dr. Weiss said.

Carcinogened, Mutagenesis, Impairment of Fertility—A 104-week carcinogenicity study of BYETTA (exenatide) was conducted in Sprague-Dawley rats and CD rats. No evidence of a carcinogenic effect was observed in female rats at all xenon-dosed doses. The incidences in female rats were 8% and 7% in a bone, lymph, thymus, kidney, adrenal, ovary, and thyroid. In males, the incidence was 1% to 3% in 25% of the male doses with systemic exposures of 5.22, and 170, respectively, the human exposure resulting from the maximum recommended dose of 20 mcg/day. In a 104-week colorectal disease study in mice, no evidence of tumors was observed at doses up to 10 to 40 the human exposure resulting from the maximum recommended dose of 20 mcg/day.

Pregnancy—Pregnancy Category C—Exenatide has been shown to cause reduced fetal and neonatal growth, and showed effects in mice of systemic exposure 5.5 times the human exposure resulting from the maximum recommended dose of 20 mcg/day. Exenatide has shown to cause a decrease in maternal weights, and in rabbits systemic exposure 5 times the human exposure resulting from the maximum recommended dose of 20 mcg/day. Exenatide has not been shown to cause birth defects when administered to pregnant rats and rabbits.

Nursing Mothers—Exenatide is not excreted in human milk. Caution should be advised when BYETTA is administered to a nursing woman.