Injectable Bulking Agents and SECCA Radiofrequency Treatment

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13.1 Injectable Bulking Agents

13.1.1 Background

Injectable bulking agents, already used with variable success rates for urinary incontinence (UI) in an outpatient setting without anesthesia and with minimal morbidity [1], have been adopted in the treatment of fecal incontinence (FI). Ideally, the injectable bulking agent should be biocompatible, non-allergenic, non-immunogenic, non-carcinogenic, easy to inject, and should not migrate within the tissues. Technically, the agents are diluted in a carrier: the particles of this solution should have a diameter of no more than 80 μm to avoid a difficult injection. However, agents with an excessively small dimension are at a higher risk for migration from the injection site. This less invasive approach seemed quite attractive, and a variety of agents have been proposed: however, the use of injectables has progressively reduced in popularity, mostly due to inconsistent results and loss of efficacy in the medium-long term.

13.1.2 Early Applications

The first use of injectable bulking agents was due to Shafik [2] who treated, in 1993, 11 patients with injections of polytetrafluoroethylene paste into the anal submucosa. He reported a complete cure in 64% and partial improvement in 36% of them at 18–24 months of follow-up. Thereafter, he injected autologous fat in 14 patients obtaining a 100% success rate at 2–3 months [3]. No complications were observed

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using either agent. However, an analogous approach attempted to treat UI resulted in death from pulmonary fat embolism [4], and autologous fat is currently not used for FI.

Although used in the past, other injectables—including bovine dermal collagen, microballoons, and polyacrylamide hydrogel (Bulkamid)—have not achieved widespread use. Glutaraldehyde cross-linked synthetic bovine dermal collagen (Contigen) was first attempted in 17 patients with FI [5]; in 65% of them a significant improvement of FI was reported at 8-month follow-up. Later, in a larger series of 73 patients [6] receiving three collagen injections just proximally to the anal canal, an improvement was reported in 63% of cases and, in particular, in 49 patients with idiopathic incontinence. However, the allergenic potential and the risk of degradation over time were the major disadvantages of synthetic collagen. Cross-linked silicone microballoons were injected in six patients, obtaining a reduction of FI severity scores [7]. However, this material presented safety problems (sterilization) and was discontinued. A hydrogel of polyvinylpyrrolidone (Bioplastique) was used in pilot studies [8] on ten patients with passive FI: only two patients maintained the improvement at 6 months and, moreover, also anal pain and ulceration were recorded. Despite that, this product was renamed PTQ implant and used in Europe. In a large series of 82 patients with severe FI [9], patients were randomized to receive PTQ implants either with or without endoanal ultrasound (EAUS) guidance for injection. In general, the treatment produced a significant improvement in the patients' FI severity score and quality of life (QoL), significantly better when EAUS was used. Further series using PTQ [10–14] reported significant reduction of the FI severity scores.

The only report of long-term (5-year) results for injectable agents concerned the use of Bioplastique [15] but in only six patients: the median St. Mark's incontinence score remained unchanged. One patient had undergone a colostomy, four of the five remaining patients had subjective improvement of FI and better QoL scores.

Two bulking agents—cross-linked porcine dermal collagen (Permacol) and polyacrylamide hydrogel (Bulkamid)—were studied in a pilot study [16] including only ten patients with passive FI to liquid or solid stool, who were prospectively randomized to receive either of the two injectables. The St. Mark's severity score decreased at 6 months only in the Bulkamid group.

Internal anal sphincter injection of Permacol was used in a nonrandomized retrospective study including 110 patients, 100 of whom followed up for a minimum of 36 months [17]. The Wexner score improved from a median of 14 (range 5–14) to a median of 8 (range 5–14); however, this difference was not statistically significant. A subjective improvement was reported by 68% of patients at 3 years but with further deterioration with time; then, 38% of patients had a second injection and 15% a third one.

Variable results were observed after injection of several other agents. In a randomized controlled trial, 44 patients were treated with injections of polydimethylsiloxane elastomer silicone or saline into the intersphincteric space [18]. There was no difference in success rates, but more discomfort and more frequent adverse effects in the silicone injection group, which was then not recommended.

In one study, calcium hydroxylapatite ceramic microspheres (Coaptite) was injected in ten patients: the mean Fecal Incontinence Scoring System (FISS) score decreased from 85.6 to 28 at 12 months ($p = 0.008$) and three subscales of the Fecal Incontinence Quality of Life (FIQL) scale improved ($p < 0.05$); at anorectal manometry, a better resting pressure (40–47 mmHg, $p = 0.018$) was recorded. Although no complications were observed, a leakage of product from the injection site was reported, requiring another injection [19].

Ethylene vinyl alcohol was injected in 21 patients: at 12-month follow-up, the mean Fecal Incontinence Severity Index score decreased from 32.8 to 22 and the Wexner score from 11 to 6.9, and two subscales of the FIQL scale improved significantly. Some increase in anal canal length and resting pressures was recorded at anorectal manometry [20].

Pyrolytic carbon-coated zirconium oxide beads (Durasphere), a non-reactive and non-biodegradable bulking agent, have been injected in FI patients. Unfortunately, these beads need a large bore needle for injection and can migrate within the tissues. They were first used in 18 patients with an internal anal sphincter defect and injected in the submucosal plane at the site of the sphincter defect in one to four sites [21]. After 12 months, the Wexner score and patients' satisfaction score were both significantly improved; in 15 patients there was also an improvement in their incontinence episodes.

In a larger study [22], Durasphere injections were given to 33 patients with minor or intermediate severity FI, who were followed up for a mean period of 21 months. Both the Wexner and American Medical System scores significantly decreased but without relevant changes in the patients' QoL. An improvement of the Wexner score and coping and embarrassment subscales of the FIQL was observed in 11 patients at 6-month follow-up [23]. More recently, Durasphere was used in 23 FI patients, producing a decrease in the Wexner score and an increase in FIQL score, 12 months after injection [24].

Comparison in terms of safety and efficacy between PTQ and Durasphere was attempted in two trials [25, 26]. In the first study [25], 40 patients with FI were randomized: PTQ produced a greater reduction in the Wexner score up to 12 months, no complications, and significant improvements in FIQL and SF-12 scores. The second trial [26] was conducted in Australia in a total of 35 patients who were randomized; however, the trial was closed early due to the removal of PTQ from the Australian Pharmaceutical Benefits scheme. Both Wexner and SF-36 scores did not improve significantly at 12 months.

13.1.3 Recent Applications

More recently, the non-animal stabilized hyaluronic acid/dextranomer (NASHA/Dx) copolymers (Zuidex, Solesta) have been proposed. They consist of dextranomer microspheres suspended in non-animal stabilized hyaluronic acid. In a 2:1 randomized double-blind sham-controlled study including 206 patients, either NASHA Dx or placebo injection was used [27]. In the NASHA Dx group, a 50% or greater

reduction of FI episodes was observed in 52% of patients versus 31% of those randomized to the sham treatment ($p = 0.009$). However, the change in Wexner score due to the two treatments did not differ. Only the coping and behavior subscales of the FIQL were significantly improved in the NASHA Dx group compared to placebo. In both groups, the retreatment rate was high (82% vs. 87%, respectively, in the NASHA Dx patients and controls). Moreover, more adverse events were recorded in the NASHA Dx group.

In another study on 21 patients [28], NASHA Dx injections allowed a significant decrease in incontinence episodes in 56% and 61% of patients at 3 and 22 months of follow-up, respectively. Also the Wexner score decreased and the FIQL score improved but not significantly. In a study on 115 patients subjected to four NASHA Dx injections [29], 83 were followed up for 24 months: 62.7% of them had a significant reduction of FI episodes, a significant increase in the number of incontinence-free days, and a significant reduction in the Wexner and FIQL scores. In another trial [30], 34 patients had NASHA Dx injections; at 24-month follow-up, 26 patients reported a sustained improvement of FI, based on a reduction of the median number of incontinence episodes and Miller score. A significant improvement in QoL at 24 months was demonstrated only in patients with more than a 75% improvement in the number of incontinence episodes. In 2014 the NASHA Dx Study Group reported data from 136 patients at 3-year follow-up [31]. At least a 50% reduction in number of FI episodes was reported by 52% of patients at 6 months, 57% at 12 months, and 52% at 36 months. Also, significant decreases in the mean Wexner score and FIQL scores were recorded at 36-month follow-up.

Finally, the recent use of polyacrylate-polyalcohol [32] would need further confirmation: although injected in a non-consecutive series of 58 patients, only 34 and 22 patients were available at 6- and 36-month follow-up, respectively, and an improvement of at least 50% on the Wexner score was achieved in 60.4% of them.

13.1.4 Conclusions

Studies on injectable bulking agents seem unable to address minimal criteria of sufficient clinical efficacy. Moreover, most frequently they have been planned and carried out on very small patient series followed up for a short time; only very few randomized studies are available. Two systematic reviews [33, 34] and a Cochrane review [35] could not establish evidence to support the efficacy of any of these bulking agents.

Consequently, although the injection of bulking agents would appear very attractive for its methodological simplicity, different technical solutions are desirable in order to maintain a stable position of the agents at the injection site. This is especially important considering that the only mechanism of action (i.e., the bulking effect inside the anal canal) is dependent on the maintenance of the agents in place. It is also fundamental that no degradation should occur and that neither side effects nor severe complications should affect the patients.

13.2 SECCA Procedure

A temperature-controlled radiofrequency procedure (commercially known as SECCA) was first used to treat gastroesophageal reflux disease. Takahashi et al. [36] first used this approach in ten female FI patients observing a significant decrease in the Wexner score at 12-month follow-up. Later, this benefit was confirmed at 2-year follow-up [37], and then at 5-year follow-up in a larger group of 19 patients [38]. A larger multicenter study including 50 patients documented a less significant improvement on the Wexner score [39]. Quite controversial results have been reported in a few other studies with a very limited number of enrolled patients [40–42].

Much less promising were the results of Lam et al.'s study on 31 patients which showed only 6% of them maintaining a 50% reduction in Vaizey score at 3-year follow-up [43]. A very low long-term success rate (22%) of SECCA therapy was also observed by Abbas et al.; at 40-month follow-up, 52% of patients needed additional treatment of FI [44]. Finally, a review of all published studies included 220 patients [45]: the authors concluded that SECCA therapy is associated with moderate clinical benefit. The mechanism of action is thought to be related to scarring or fibrosis of the anal canal which progressively declines over time [46].

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