
Transurethral Collagen Injection in Neuropathic Sphincter Deficiency

Leila Tabibian and David A. Ginsberg

A small but significant subset of patients with lower urinary tract dysfunction secondary to neurogenic etiology develop intrinsic sphincter deficiency (ISD). This is manifested clinically as stress urinary incontinence. We sought to evaluate the efficacy of transurethral collagen injections in the management of ISD of neuropathic origin in the male patient. A retrospective chart review over a 3-year period revealed 11 patients who underwent between one and three collagen injections for ISD. Follow-up data were available for 9 patients. Preoperative symptoms and urodynamic studies as well as postoperative symptoms were recorded. The majority of our patients (67%) had symptomatic improvement of their urinary incontinence. Although more long-term data are needed, this method appears to be a viable alternative for the male patient with neurogenic ISD. *Key words: collagen, intrinsic sphincter deficiency, neurogenic bladder, urinary incontinence*

Most patients with spinal injury develop a certain degree of neurourologic dysfunction. Depending on the level of injury, bladder dysfunction can range from detrusor areflexia to detrusor hyperreflexia, with or without external sphincter dyssynergia. A subset of these patients also develops intrinsic sphincter deficiency (ISD), manifested as stress urinary incontinence. Even though there has been much recent advancement in the medical management of neurogenic bladder, the management of ISD can be challenging and minimally responsive to pharmacotherapy. Surgical options for ISD include bladder neck closure, sling procedures, and artificial urinary sphincters. We evaluated our success with a less invasive form of therapy with the use of transurethral collagen.

The use of injectable bulking agents is a minimally invasive alternative to the treatment of ISD. Periurethral injection was first described in 1938 by Murless¹ who used a sclerosing agent to cause scarring around the

urethra to improve continence. Later polytetrafluoroethylene (PTFE) was introduced by Politano²; however, it was discontinued due to particle migration and granuloma formation. GAX-collagen was approved in 1993 and has rapidly gained popularity. The bulking agent consists of a highly purified bovine dermal collagen that is cross-linked with glutaraldehyde and suspended in a buffered physiologic saline.^{3,4} Advantages include lack of foreign body

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reaction, lack of particle migration, and biodegradability. We sought to evaluate the clinical efficacy of transurethral collagen injection in nine male patients with neuropathic intrinsic sphincter deficiency secondary to spinal cord injury (SCI) or myelomeningocele.

Materials and Method

Between October 1998 and September 2001, 11 male patients who had undergone transurethral collagen injections at Rancho Los Amigos National Rehabilitation Hospital were identified. One chart was not retrievable, and one patient was excluded from the study due to a prior external sphincterotomy. Retrospective chart review and telephone interviews by an independent third party were performed. All of the patients had a neurogenic bladder secondary to traumatic myelopathy except for one patient with spina bifida. Patient age range was from 23 to 49 years with a mean of 35 years. SCI levels ranged from T4 to L5. Charts were reviewed for preoperative symptoms including number of pads required, urodynamics findings, number of collagen injections, and postoperative subjective outcomes.

Seven of the patients managed their bladders with intermittent catheterization and two by Crede maneuver. Two patients had previously undergone bladder augmentation. All patients had classic symptoms of ISD manifested by leakage with Valsalva maneuvers such as wheelchair transfers, coughing, and sneezing. One patient previously had an artificial urinary sphincter, which was removed secondary to an infection.

Objective findings of ISD were demonstrated by multichannel urodynamics, with or without video monitoring. The abdominal

leak point pressure (LPP) was recorded as the minimum amount of abdominal pressure required to produce urinary leakage. In our group, the LPP ranged from 20 to 80 cm H₂O with a mean of 42.6 cm. All of the patients had stable bladders without evidence of detrusor hyperreflexia or loss of compliance.

All patients had a negative skin test at least 1 month prior to receiving their first transurethral injection. Transurethral collagen injection was then administered via a cystoscope under general or monitored anesthesia. A 21 French (F) cystoscope and a 30 degree lens was used to inject one syringe (2.5 cc) of collagen into each lateral lobe of the prostate at the level of the prostatic urethra (**Fig. 1**). Patients received two syringes (2.5 cc/syringe) per each injection. Care was taken not to reenter the bladder with the cystoscope after the injections were complete, and the bladder was emptied using a 14 F red robinson catheter. Patients were discharged home the same day and were instructed to resume their regular bladder management.

Results

Six patients underwent one injection only; one patient underwent two, and two had three total collagen injections. Outcome was gauged by overall patient satisfaction and pad use. Two patients (22.2%) reported near complete resolution of symptoms, and two patients (22.2%) reported over 50% improvement. Two patients (22.2%) reported moderate improvement but still required protection with pads, and three patients (33.3%) reported no change. Of the patients with near complete resolution, one underwent one injection only, while the other required three injections over a 1-year period. One had a history of bladder augmentation. Of those

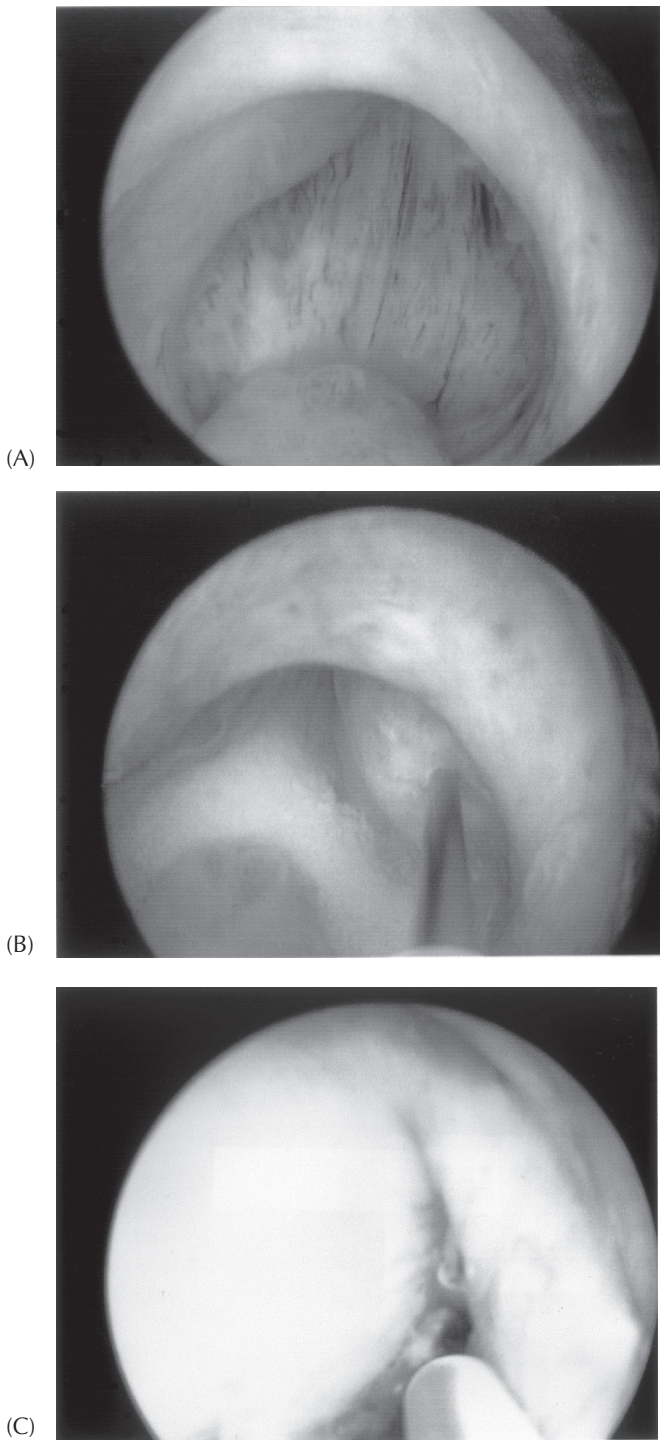


Figure 1. (A) Prostatic urethra prior to collagen injection. (B) Collagen injection along left lateral aspect of prostatic urethra. (C) Prostatic urethra after collagen injection.

with no improvement, all received one injection only and did not present for repeat injections. There was no correlation between the number of injections and outcome.

There were no adverse effects after injections, such as significant hematuria or urinary tract infections. Preoperative bladder management was resumed in all cases, and no patient had difficulty in subsequent catheterizations. There were no long-term complications attributable to collagen injections.

Discussion

The majority of our patients with neuropathic ISD demonstrated improvement in their continence after transurethral collagen injection. Between one and three injections were necessary to optimize results, and treatments were well tolerated.

ISD is characterized by a poorly functioning proximal urethra that leaks urine at relatively low intra-abdominal pressures. In the neuropathic urethra, sphincter deficiency is caused by denervation of muscle fibers responsible for the continence mechanism. The identification of ISD is often difficult in the neurogenic population. Investigations tend to focus on the evaluation of detrusor hyperreflexia and can often overlook concomitant stress urinary incontinence (SUI) secondary to ISD. Patients with neuropathic ISD complain of leakage with wheelchair transfers, bending, coughing, or other Valsalva maneuvers, and this can be documented on urodynamic evaluation. The combination of video monitoring with urodynamic studies is especially helpful in identifying an open bladder neck and leakage with Valsalva, and these studies are an integral adjunct to the diagnosis of ISD in the spinal cord-injured patient.

Treatment of urethral incompetence is mainly surgical and includes bladder neck closure, fascial slings, and placement of artificial urinary sphincters. The use of fascial slings has shown long-term durability and success in the treatment of women with stress incontinence; however, its role in men has been limited. Daneshmand et al.⁵ reviewed 12 male patients with neurogenic urethral sphincter incompetence who underwent puboprostatic slings with an overall success rate of 83%. This procedure may be appropriate in the patient already committed to an open surgical procedure, namely those undergoing augmentation cystoplasty. For those who do not require abdominal surgery, the perineal male sling may be an option. In a 12-month follow-up on 21 patients, Comiter⁶ reported a cure rate in 76% and improvement in 14% of men who had a perineal polypropylene mesh sling. Artificial urinary sphincters (AUS) have been commonly used for sphincteric incompetence and have been very successful in the postprostatectomy patients. Known complications of this procedure are infection, urethral cuff erosion, and mechanical failure requiring revision. Because patients with SCI tend to be younger, placement of an AUS has a higher likelihood of needing revisions in the future. In addition, Petrou et al.⁷ demonstrated that prosthetic infection and erosion rates were in fact higher in the neurogenic population.

Injectable agents such as GAX collagen enhance the apposition of the urethral walls and increase the efficiency of compression in the sphincter mechanism. Most initial experience with transurethral collagen injection has been in women, with an increasing role in men. Cross et al.⁸ conducted a review of 139 women who received collagen injections for

SUI with a median follow-up of 18 months. Of those, 74% were substantially improved and 20% had some improvement. Tchetgen et al.⁹ treated three women who had developed stress incontinence after radical cystectomy and orthotopic neobladder reconstruction. At 7 to 8 months after the last injection, one woman was dry, one used one or no pads daily, and one reported no significant improvement. Transurethral collagen injections in men have been studied in those with ISD secondary to various forms of therapy for both benign and malignant prostate disease. Tiguert et al.¹⁰ treated 21 men with post prostatectomy incontinence, including those with prior radiation or transurethral resection of the prostate (TURP). Fifty-seven percent had significant improvement and 5% became completely dry. Smith et al.¹¹ had a median follow-up of 29 months on 62 men who had previously undergone radical prostatectomy or transurethral resection of the prostate. Initial social continence rate (less than one pad a day) was 38.7%, and at 2-year follow-up only 42.8% maintained their status. Only a few studies have evaluated the use of collagen in the neuropathic sphincter. Herschorn et al.¹² evaluated 41 patients, including 4 male patients with neuropathic ISD. All of those with a neuropathic sphincter showed some improvement. Bennett et al.¹³ evaluated nine male and two female patients with ISD secondary to SCI or myelomeningocele. Seven patients were either cured or improved with an average rise of 57 cm H₂O in their Valsalva leak point pressure.

In the neurologically intact population, transurethral collagen injections have demonstrated good results in women with somewhat disappointing results in men. Treatment of men may be less successful partially because of the etiology of their incontinence. Endoscopic and pelvic prostatic surgery are both associated with significant scarring periurethrally that can impede the efficacy of collagen. The absence of preexisting fibrosis in the neuropathic sphincter allows for a better response to collagen injection and is likely to produce better results.

Conclusion

In the 9 years since GAX-collagen was first approved by the Food and Drug Administration, its role in ISD of neurogenic etiology has been limited. To our knowledge, this is the first study to look at transurethral collagen injection in this population of males only. Although our group is small and objective follow-up is limited, our initial outcome is promising. The majority of our patients (67%) had symptomatic improvement without any adverse affect on their bladder management. Our study does not predict who fails treatment or which patients require repeat injections. In addition, long-term follow-up is needed to evaluate persistence of symptomatic and urodynamic improvement. However, its ease in administration, patient tolerability, and low risk of complications make transurethral collagen injection an attractive first-line treatment for patients with neuropathic ISD.

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