

CURRENT TREATMENT OPTIONS
FOR STRESS URINARY INCONTINENCE*Mike B. Siroky, MD, FACS[†]ABSTRACT

Physicians and their patients have a growing number of therapeutic options for management of stress urinary incontinence (SUI). Patient education and training, including pelvic floor muscle exercises, remain an effective strategy for motivated patients. However, problems with adherence continue to limit the effectiveness of intervention. Pharmacologic therapy has a checkered history, and currently, no medication has been approved by the US Food and Drug Administration for treatment of SUI. Advances in understanding of the neurologic contributions to bladder function and to dysfunction associated with incontinence have led to development of duloxetine, a combined serotonin and norepinephrine reuptake inhibitor. In clinical trials to date, duloxetine has demonstrated significant improvement in incontinence frequency and quality of life. Injection therapy has a history of limited success but remains an option for selected patients. Surgery improves incontinence symptoms in most cases, but patient satisfaction tends to decline over time. Moreover, a substantial number of patients continue to use absorbent pads and take concomitant medication after surgery. The expanding number of treatment options and improved recognition of the episodic nature of SUI provide a mandate for a patient-centered approach to treatment that gives paramount consideration to individual patient characteristics and wishes.

(*Adv Stud Med.* 2003;3(8E):S834-S838)

*Based on a presentation given by Dr Siroky at a symposium preceding the 98th Annual Meeting of the American Urological Association.

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Recent advances in the understanding of the origin and pathophysiology of stress urinary incontinence (SUI) have led to the recognition that SUI is not a binary condition that a patient either “has” or “doesn’t have.” Instead, the most common answer to the question of whether a patient has SUI is “sometimes.” The condition affects patients at certain times in their lives but not others, and the episodic nature of SUI must be taken into account in the development of an effective strategy for clinical management.

As treatment options for SUI expand, the episodic nature of the condition becomes a more prominent issue in the selection of a therapy that meets an individual patient’s characteristics, needs, and preferences. In assessing the appropriateness of therapies, physicians generally follow 1 of 3 approaches: (1) an evidenced-based decision-making process that relies on what the medical literature shows regarding efficacy; (2) an empiric approach based on clinical experience and what has worked well in the past; or (3) a patient-centered approach guided by the wishes and desires of the patient.

Regarding management of SUI, the patient-centered approach should command primary consideration. Most patients have strong preferences toward the various therapeutic options. Some are quite determined in rejecting the prospect of continuing drug therapy, whereas others feel just as strongly about surgery. Some patients do not want estrogen therapy. Others have medical conditions that eliminate certain therapies as treatment options.

Ultimately, the decision-making process should focus on what is the best option for a specific patient. As the number of treatment options for SUI increases, especially with respect to medical therapy, physicians and patients will have more considerations to weigh. Hopefully, the availability of more alternatives will

increase the likelihood that each patient will receive the most appropriate therapy.

CURRENT TREATMENT OPTIONS FOR SUI

Available treatment options for SUI fall into the 4 broad categories of education/training, pharmacologic, injectable, and surgical. The therapeutic categories encompass the entire spectrum from nonpharmacologic and noninvasive to highly invasive. Each category has advantages and disadvantages that will be more or less prominent for a specific patient. The physician faces the challenge of matching what each therapy has to offer with the needs and desires of the patient.

EDUCATION/TRAINING

Pelvic floor reeducation is an effective therapy that has withstood the test of time. The strategy encompasses a variety of reasonably simple but effective interventions to manage SUI. Some of the interventions, such as management of fluid intake and diet, reflect common sense and are often undertaken by patients without a physician's advice.

Voiding diaries are another component of a clinical strategy of education and training. The diaries are a form of biofeedback that offer encouragement and rewards to patients for increasing the interval between voiding and leaking. Timed voiding, or urge inhibition, can be used in conjunction with a voiding diary and involves use of positive reinforcement to teach patients how to stop involuntary bladder contractions.

Pelvic muscle training (Kegel exercises) is another component of education and training.¹ When performed correctly, pelvic muscle training can improve SUI. Unfortunately, the exercises are often performed incorrectly. As originally described by Kegel, pelvic muscle training has 3 key components. The first component is external observation in the lithotomy position. In that position, the patient contracts the perineal floor, and the presence of an intact pubococcygeus muscle is indicated by movement of the anus anteriorly toward the pubic arch. The second component is digital vaginal examination to identify and test the strength of the pelvic floor muscles. The patient squeezes while 1 or 2 fingers are inserted in the vagina. The third component is use of the Kegel perineometer, one of the original biofeedback instruments. The

device was used to measure the strength of vaginal contraction, which was recorded by the patient.

Kegel emphasized the need for a total of 300 contractions daily, divided among three 20-minute sessions, for 6 weeks to achieve adequate muscle tone. Over the decades, clinicians have reduced the exercise requirement to 10 or 20 contractions performed 3 or 4 times daily, or a total of 40 to 80 contractions daily. Kegel also noted that improvement often does not become noticeable until about 4 weeks into the training program, making positive reinforcement essential for a successful outcome.

Kegel's initial reports described response rates on the order of 90%. More contemporary publications suggest response rates of about 60% among women who perform the exercises properly.² Successful results require patient dedication, and a principal drawback of Kegel exercises is low adherence compared with patients whose SUI is treated with drug therapy.³

Some patients with exceptionally weak pelvic muscles require active intervention by a physician or other healthcare provider to teach the patients how to identify and exercise the muscles. The perineal anatomy is more complex than once thought, as 3 muscle layers surround the urethra. Women who are unfamiliar with the anatomy often have difficulty identifying the proper muscles to exercise. Inadequate instruction is probably one of the major reasons for failure of perineal muscle training. Perineal muscle training using externally applied magnetic fields has been developed, but the experience with this technique is too sporadic to permit evaluation at this time.

PHARMACOLOGIC THERAPY

Drugs have been used to treat SUI for the better part of 5 decades. Alpha-adrenergic stimulants have a long history of use, beginning with phenylpropanolamine, which is no longer on the market in the United States. The list of available alpha-agonists includes phenylephrine, ephedrine, and midodrine. All have distinct disadvantages and can be dangerous when used inappropriately. This class of drugs should not be used at all in certain patients, such as those with hypertension or tachycardia, and they should be used cautiously even in patients who have no apparent contraindications. In addition to their risks, alpha-adrenergic stimulants have limited efficacy as monotherapy for SUI, and their stimulant side effects make these agents difficult to tolerate.

Imipramine and other members of the tricyclic antidepressant (TCA) class of drugs also have been used to treat SUI. Similar to the alpha-agonists, TCAs have achieved limited therapeutic efficacy, and the stimulant effects make them contraindicated for some patients and intolerable for others. Additionally, TCAs can be dangerous in overdose.

Estrogens have been used extensively in the treatment of SUI. Unfortunately, little objective data exist to support that use. One particularly comprehensive review of clinical experience with estrogens for SUI included 166 published articles from the English medical literature. Of those, 23 had sufficient objective data, and only 6 controlled trials were found. The authors of the review concluded that estrogen therapy led to subjective improvement in SUI but resulted in no change in fluid loss despite increased urethral pressure.⁴

Most recently, a new class of agent has emerged as potential pharmacologic therapy for SUI, the prototype being duloxetine, a dual reuptake inhibitor of serotonin and norepinephrine. Duloxetine evolved from recent advances in the understanding of lower urinary tract innervation.

Acetylcholine plays an important role by stimulating detrusor contraction. The pudendal nerve stimulates contraction of the perineal floor through nicotinic receptors that originate from an area of the spinal cord known as Onuf's nucleus, which comprises specialized motor neurons that aggregate in the anterior horn and constitute the main motor control of the perineal floor.

Descending neuronal tracts secrete norepinephrine and serotonin, which stimulate neurons in Onuf's nucleus, which in turn stimulates the perineal floor to contract. Preclinical investigations involving electromyography have shown that increased concentrations of norepinephrine and serotonin stimulate muscle activity in the perineal floor.⁵ By inhibiting reuptake of norepinephrine and serotonin, duloxetine would be expected to increase concentrations of both neurotransmitters at the level of Onuf's nucleus.

A recent clinical study showed a 50% reduction in episodes of urinary incontinence among patients with SUI treated with duloxetine.⁶ Patients in the trial reflected a range of incontinence severity, and duloxetine was equally efficacious in patients with mild, moderate, or severe incontinence. The results are particularly noteworthy, given the surprisingly high placebo response of 25% to 30%. Moreover, duloxetine-treated patients

averaged a 20-minute increase in the time between voids compared with 2 minutes in the placebo group. The differences in incontinence frequency and time between voids were significant ($P < .001$).

Data from a validated quality-of-life (QOL) instrument administered to patients in the placebo-controlled duloxetine trial showed substantial improvement in QOL. Overall, patients treated with duloxetine had a greater than 4-point improvement compared with those taking placebo ($P < .001$). Among individuals with severe SUI symptoms, the QOL difference between duloxetine and placebo exceeded 5 points ($P < .001$).

The objective evidence of improvement with duloxetine was accompanied by subjective indications that patients noticed a difference. More than 60% of duloxetine-treated patients reported that they were improved compared with about 40% of patients taking placebo ($P < .001$). Fewer than 5% of patients taking duloxetine felt their condition had worsened versus more than twice as many placebo patients.

Duloxetine is the first of a new class of agents that show promise for being effective pharmacologic therapy for SUI. Clinical trial data indicate that patients treated with duloxetine have significant improvement in incontinence frequency, time between voids, and QOL and significant increases in patient self-reported global impression of improvement.

BULKING AGENTS

PTFE. Use of bulking agents has a history of clinical application in SUI dating back about 30 years, when polytetrafluoroethylene (PTFE) was first used. Never approved by the US Food and Drug Administration, PTFE was plagued by numerous complications and was replaced as soon as other candidate bulking agents were available.

Collagen. Collagen was introduced at the end of the 1980s and represented a major improvement over PTFE with respect to biocompatibility. Nevertheless, patients still must undergo skin testing for allergy to the bovine-derived collagen used today to treat incontinence.

Autologous Fat. Use of autologous fat avoids the biocompatibility problems associated with PTFE and collagen. However, success rates have been low, and some cases of fat embolism have been described. Because of its generally favorable safety profile, autologous fat still has a number of advocates.

Carbon-Coated Beads. Carbon-coated beads are nonallergenic and therefore do not require skin testing

prior to use. However, the beads may migrate and are not biodegradable, 2 potential sources of complications.⁷ Silicon beads are not yet available in the United States, but international experience suggests the beads offer results comparable to those achieved with other bulking agents.

SURGERY

Surgical approaches to urinary incontinence are clearly the most numerous and varied. More than 200 different incontinence-related surgical procedures have been described in the literature. Most represent variations on a few common strategies. The large number of modifications reported in the literature suggests that none of the surgical approaches is without problems and complications.

Approaches to SUI surgery include abdominal, vaginal, abdominovaginal, and laparoscopic. Commonly used procedures are colposuspension, vaginal suspension, and the suburethral sling. Colposuspension procedures (eg, Burch, Marshall-Marchetti-Krantz) attempt to elevate and stabilize the urethra by suspending the anterior vaginal wall to the iliopectineal ligaments. Vaginal suspension procedures (eg, Stamey, Raz) stabilize the urethra by supporting the periurethral tissues and anterior vaginal wall. Suburethral slings stabilize the urethra by placement of a suburethral sling attached to the rectus fascia or pubic bone.

Suspension procedures involve suturing tissue onto tissue to provide support for the urethra. Though effective for treatment of SUI, the procedures are susceptible to various forms of erosion and other problems that reflect physiologic wear and tear. Suburethral slings, which have grown in popularity in recent years, obviate some of problems with suspension procedures by substituting the sling for sutures. However, the long-term effects of slings remain under investigation. In particular, it is unclear how long a sling remains in place. Some patients require additional surgery to remove or incise slings to permit voiding. Whether the fascia remains in place or merely acts as scaffolding for ingrowth of patient tissue and scarring is not known.

Slings can be fashioned from autologous or allograft material. A recent review of clinical experience with allograft slings showed success rates of 69% to 98%, depending on the definition of success.⁸ Success rates appear comparable for allograft and autograft slings. Over time, deterioration of slings, and therefore

success rates, is a logical expectation. During the first 3 years after surgery, the overall success rate for surgery typically exceeds 90%, declining to about 85% after 5 years or longer.

Sling failure remains the most common complication of suburethral sling procedures. The most prominent complication after sling failure is hypersuspended urethra and prolonged urinary retention, resulting from improper placement of the sling. Other potential, but less common, problems include pelvic hematoma, incisional hernia, deep venous thrombosis, and pulmonary embolus.

Another recent surgical innovation in SUI therapy is tension-free vaginal tape (TVT). At least 4000 TVT procedures have been performed worldwide. The procedure involves insertion of a piece of mesh-like material through a small vaginal incision and creation of a suburethral sling by anchoring the material to the pubic musculature. Reported cure rates with the procedure are about 90%,⁹ although more long-term follow-up data are needed. The procedure has been associated with a number of complications, including several types of bleeding problems. The most common problem has been postoperative new-onset urge symptoms.

To summarize results with surgical treatment of SUI, the Birch suspension procedure probably remains the gold standard and achieves success rates of 75% to 90%. Suburethral slings achieve comparable results, and the initial clinical experience with TVT suggests that this procedure also will be comparable to surgical suspension. Complication rates vary in different series.

SUMMARY

A key issue in the treatment of SUI relates to the various definitions of success that are used to characterize outcomes. In that respect, QOL has emerged as an important consideration. Some patients do not require a cure or complete dryness to consider their treatment successful. Physicians today must tailor therapy to the patients' wishes, balancing the risks and benefits of available treatment options. Surgery may offer the best chance of success, but the procedures are not without complications, some of them potentially serious. Injection therapy with bulking agents results in lower success rates, but also poses lower risk to the patient. For patients who are poor surgical candidates, the tradeoff of a higher success rate for a lower risk is one that many people are willing to make.

Before offering and explaining therapeutic options to SUI patients, physicians must ask themselves a number of questions. How do we improve the patient's symptoms without taking undue risks and still achieve the patient's wishes? Do we want short-term or long-term results? Which is more important to the patient: objective cure or subjective improvement? These questions all point toward QOL. Only by earnestly and honestly searching for the answers can we arrive at the best treatment option for each patient.

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