NEW ADVANCES IN THE NONSURGICAL MANAGEMENT OF STRESS URINARY INCONTINENCE*  

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ABSTRACT

Most patients with stress urinary incontinence (SUI) warrant a trial of nonsurgical therapy before considering surgery. Pelvic muscle exercises and improved management of fluid intake and voiding habits can reduce the frequency of urine loss for many patients. Weight loss and smoking cessation can address factors that contribute to SUI in some women, as can appropriate management of pulmonary conditions and allergies that can cause coughing and sneezing, 2 common contributors to SUI-related urine leakage. Several adjuvant therapies are available for use by themselves or in combination with behavioral therapies and include vaginal cones, biofeedback, and electrical stimulation. Some evidence suggests, however, that currently available adjuvant therapies are no more effective than pelvic muscle exercises and might be less effective. Devices for management of SUI include tampons, continence rings, pessaries, and occlusive/obstructive devices that block inadvertent urine flow from the urethra. Although the devices can reduce episodes of urine leakage, patient adherence is problematic, particularly over the long term, and some of the more invasive devices have a fairly high risk of complications. The dual neurotransmitter reuptake inhibitor duloxetine is expected to become the first medical therapy approved by the US Food and Drug Administration for SUI, which would have a major impact on nonsurgical management of the condition.

NONSURGICAL treatment remains a major component of the therapeutic options for stress urinary incontinence (SUI). Nonsurgical therapy has several advantages that are appealing and applicable to a substantial number of women affected by SUI. The current array of options has a number of common features, beginning with the most obvious: Nonsurgical approaches are less invasive compared with surgery. Cure rates with nonsurgical therapy are low, typically in the range of 10% to 15%; however, they can achieve substantial improvement in symptoms, depending on a patient's compliance with the therapy. Childbearing introduces an important consideration for many women who are evaluating treatment options for SUI, and nonsurgical approaches can be used safely by women who plan to have children in the future or who have not yet decided whether they have completed their childbearing.

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Aside from the low cure rates, the primary obstacle to treatment success and patient satisfaction with nonsurgical therapy for SUI relates to the need for ongoing adherence to the treatment. Response and patient satisfaction with results are highly dependent on the patient’s willingness to remain compliant with the treatment regimen.

In contrast, surgery offers high cure rates compared with less invasive strategies, and response and outcomes are less dependent on patient compliance. Surgery is not recommended, however, for women who anticipate having children after the operation. Moreover, surgery has risks of intraoperative and postoperative complications that can lead to new types of urinary problems, such as voiding dysfunction and urge incontinence.

With thoughtful review, explanation, and encouragement by physicians, noninvasive treatment options for SUI can provide symptom relief that satisfies a considerable proportion of patients. Availability of an effective oral medication for treatment of SUI will expand the nonsurgical options and perhaps improve patient satisfaction with noninvasive therapy.

**Current Nonsurgical Options for SUI**

Nonsurgical treatment of SUI spans a wide spectrum with respect to simplicity. Perhaps the simplest approach is to educate the patient about factors that can alter the magnitude of intra-abdominal pressure, or stress, on the bladder. Other traditional approaches include behavioral therapy, pelvic muscle rehabilitation, biofeedback training, and various types of devices. No US Food and Drug Administration (FDA)-approved medication for SUI is currently available.

**Altering Intra-abdominal Pressure**

One of the simplest ways to manage intra-abdominal pressure on the bladder is to change habits related to fluid intake and voiding. Its simplicity might be one reason this strategy is often overlooked in the management of urine leakage related to SUI. When asked about fluid intake, many women respond, “Not enough,” mistakenly believing that consuming large quantities of fluid is beneficial for their “bladder problem.” In reality, heavy fluid intake is counterproductive to effective management of SUI symptoms. Specifically, no data support a physiologic basis for the advice that adults should consume 8 glasses of water daily—in addition to any other fluid intake—to maintain good health. Appropriate fluid intake of 6 to 8 glasses daily is advisable for good bladder health and overall health. Patients also should be advised not to allow their bladders to become overdistended but instead to void at regular intervals.

Cough is another major contributor to intraabdominal pressure on the bladder. To a large extent, better cough control can be achieved through recommendations that fall within the realm of good primary care practice. Every patient who smokes should be advised to stop and to seek professional smoking cessation assistance if needed. Appropriate treatment of underlying pulmonary conditions and allergies also can improve cough control.

Though often difficult to achieve, weight loss in overweight and obese patients clearly relieves pressure on the bladder. In a randomized clinical trial of women who had a baseline body mass index (BMI) that averaged 35 kg/m², weight loss that resulted in a BMI reduction of 5 kg/m² was associated with a 60% decrease in the frequency of weekly incontinence episodes. Importantly, a number of patients reported complete cures, or no episodes of incontinence. The difference was highly significant compared with a control group (43% reduction in episodes; P < .001) that had no decrease from baseline in BMI.

Among women who exercise regularly, SUI represents more than a minor annoyance. Modification of exercise routines can help minimize urine leakage attributable to intra-abdominal pressure on the bladder. For example, a woman who normally performs high-impact aerobics might want to consider swimming or bicycling as an alternative that maintains physical fitness but causes fewer problems with urine leakage.

Avoiding heavy lifting or other activities that increase stress on the bladder is another commonsense approach to management of SUI-associated urine leakage. Similarly, good bowel function can minimize bladder pressure—specifically, avoidance of constipation and chronic straining with bowel movements.

**Pelvic Muscle Rehabilitation**

One of the most widely used noninvasive therapies for SUI, pelvic muscle training (ie, Kegel exercises) can improve muscle tone but rarely provides a cure. Clinical studies of pelvic muscle training have
not employed a consistent technique, making evaluation of effectiveness problematic. Moreover, results with pelvic muscle training correlate directly with the patient's ability to contract the muscles, motivation, and commitment to performing the exercises regularly.

For pelvic muscle training to be successful, a patient must be able to contract the muscles and to contract them correctly, a prerequisite that should not be taken for granted. Verbal instruction is not sufficient; patients must demonstrate the ability to contract muscles during a pelvic examination. Having demonstrated that ability, patients should be instructed to perform the exercises in sets of 10, repeated 2 or 3 times daily. Once good muscle tone has been attained, the exercises should be continued, but daily practice is not necessary.

Improving muscle strength is just one issue addressed by Kegel exercises. The other is muscle recruitment. The adage "use it when you're going to lose it" captures the essence of muscle recruitment. Patients should learn to perform pelvic muscle contraction when possible in situations associated with urine leakage, such as coughing or sneezing.

Adjuvant Therapies

Several adjuvant therapies can be used in association with pelvic muscle training, including vaginal cones, biofeedback, electrical stimulation, and extracorporeal magnetic innervation (Figure 1). Some of these adjuvants have been reported to improve muscle development or results achieved with pelvic muscle training; however, the data are not entirely clear. For example, a study that compared pelvic muscle exercises alone with muscle training plus biofeedback demonstrated a higher objective cure rate for SUI with combined therapy, although the difference was not statistically significant. Moreover, pelvic muscle strength improved to a similar degree in both treatment groups.

Results of another study suggested that some adjuvants are no better than pelvic muscle training when used alone and might be less effective. The randomized controlled study compared pelvic muscle training, electrical stimulation, and vaginal cones. Compared with an untreated control group, pelvic muscle training led to greater improvement in muscle tone and higher cure rate, as defined by pad usage, than either of the adjuvants.

Extracorporeal magnetic innervation is one of the newest adjuvant therapies for SUI. The therapy makes use of a special chair to stimulate pelvic muscles with magnetic energy. In a preliminary study, 97 women with SUI received 20-minute treatments twice per week for 6 weeks. Among patients followed up for 6 months, 28% reported being completely dry, and 70% reduced pad use from a median of 2.16 per day to 1 per day. Fewer than half of the patients (n = 47), however, completed the 6-month follow up, reflecting a problem with compliance that frequently complicates nonsurgical therapies for SUI.

Supportive and Occlusive Devices

Several types of supportive and occlusive devices can be offered to minimize urine leakage due to SUI. Intravaginal devices provide support for a hypermobile urethra and partly compress the urethra. These include tampons and tampon-like devices, continence rings, and pessaries. Tampons are simple but can offer an effective solution to urine leakage for some women. The most effective type is the short OB® brand, which seems to provide better urethral compression and support than other brands that have longer profiles.

Pessaries and occlusive rings are additional nonsurgical options for SUI patients. Pessaries have been studied fairly extensively, and the 2 following examples are representative of the data. A study of 55 women with a mix of incontinence diagnoses resulted in a cure rate of 38%, and 40% of the women said the devices improved their symptoms. Two
thirds of the cohort continued to use pessaries long term. In contrast, a study of 38 women with urodynamic SUI showed a 24% cure rate with pessaries, and only 16% of the patients continued to use the devices long term.6

Urethral occlusive and obstructive devices prevent urine from exiting the urethra and include the urethral patch and intraurethral plug. Studies of devices inserted into the urethra have demonstrated high rates of negative pad results—more than 90% of patients in some instances. These devices tend to be poorly tolerated, however, and are associated with significant complication rates that include urinary tract infection, hematuria, and irritation.7-9 Some evidence has suggested that if patients can tolerate an intraurethral device for 6 months, complications decrease substantially during long-term use.

**Medical Therapy for SUI**

No FDA-approved drug for SUI currently exists, but several types of agents have been used off label, including alpha-adrenergic agonists, estrogen, and tricyclic antidepressants. In general, the experience with medical therapies has been problematic, complicated by questionable effectiveness and side effects.

Alpha-agonists (such as pseudoephedrine) increase urethral tone and closure pressure by direct stimulation of alpha-1 adrenergic receptors. As a class, however, the alpha-agonists result in side effects that many patients find intolerable.

A considerable theoretical basis supports the use of estrogen in the treatment of SUI. Estrogen, either vaginal or oral, thickens the urethral mucosa, which results in a better seal. Estrogen also has direct effects on lower urinary tract tissues and might increase the sensory threshold of the bladder and increase bladder relaxation. Data on estrogen's ability to improve SUI symptoms has been variable, however. Most studies have involved too few patients to achieve adequate statistical power to demonstrate a clear effect on SUI symptoms.

Tricyclic antidepressants have anticholinergic properties, directly induce smooth muscle relaxation, and inhibit norepinephrine reuptake, all of which might be beneficial to SUI. However, side effects with agents in this class create problems with tolerance, particularly among older patients.

**Duloxetine: A Potential New Option for SUI**

Recent advances in understanding the neurobiology of bladder function and dysfunction have provided the impetus for a new approach to investigation of pharmacologic therapies for SUI. The research suggests that inhibition of the reuptake of serotonin and norepinephrine at the level of Onuf's nucleus can increase signal transmission through the pudendal nerve to the urethral sphincter.10 The observations have led to the development of duloxetine, a dual-reuptake inhibitor that has demonstrated efficacy in the treatment of SUI. Though still an investigational agent, duloxetine could become the first approved medical therapy for SUI.

Dual-neurotransmitter reuptake inhibitors already exist and are commercially available. Duloxetine differs from other dual-reuptake inhibitors by providing a more balanced and potent inhibition of reuptake, resulting in a more favorable ratio between norepinephrine and serotonin.11,12

Duloxetine has been evaluated in a randomized, placebo-controlled phase 3 clinical trial involving almost 700 women with stress-predominant urinary incontinence.13 Patients enrolled in the study had a minimum of 7 SUI episodes weekly. Urinary frequency was normal, and urgency was not a predominant

Figure 2. Patient Global Impression of Improvement*

*This information concerns a use that has not been approved by the US Food and Drug Administration. Data from Zinner et al.44
symptom. The patients also had normal bladder capacity. Each patient had a positive cough stress test for SUI, and stress pad test yielded a weight exceeding 2 g.

The design of the study included a 2-week screening period followed by 2 weeks of observation and a 2-week placebo run-in phase. Upon completion of that 6-week introductory phase, patients were randomized to duloxetine 40 mg twice daily or matching placebo and followed up for 12 weeks. The primary efficacy variables were weekly incontinence episode frequency and the change in scores on the Incontinence Quality of Life (I-QOL) questionnaire from the beginning to end of the treatment period. Secondary efficacy variables consisted of the Patient Global Impression of Improvement (PGI-I), mean time between voids in minutes, and scores on the I-QOL domains (avoidance and limitation of behavior, psychosocial impact, and social embarrassment).

At baseline, the patients averaged 18 to 19 incontinence episodes per week, and about two thirds had at least 14 episodes of urine leakage each week. The average I-QOL score at baseline was approximately 63 (on a scale of 0-100), and almost 70% of patients in each group had moderate or severe SUI symptoms, as assessed by the PGI-I severity.

At the end of the treatment period, 62% of patients taking duloxetine said they had improved, as indicated by PGI-I scores, compared with 39.6% of patients taking placebo ($P < .001$). Moreover, fewer than 2% of patients reported worsening of SUI during treatment with duloxetine, more than a 3-fold reduction compared with placebo (Figure 2).

With respect to the other primary efficacy endpoint, duloxetine treatment was associated with a 50% reduction in weekly incontinence episode frequency, compared with a 27% reduction in the placebo group ($P < .001$). Overall, 85% of patients treated with duloxetine had a reduction in urine leakage, and half of the patients had at least a 50% decrease in the number of incontinence episodes.

The mean I-QOL score increased by 11.0 in the patients taking duloxetine and 6.8 with placebo ($P < .001$). Patients treated with duloxetine also had a statistically significant 20-minute increase in the time between voids, whereas patients taking placebo reported a 2-minute increase ($P < .001$; Table 1).

Duloxetine was associated with more adverse events than placebo, the most common being nausea. In most instances, however, nausea was mild or moderate in severity (87.2%) and resolved within 1 week in more than half of the affected patients. More than 80% of patients had resolution of nausea within 1 month. Only 1 patient reported worsening of nausea, and 7 patients discontinued treatment because of nausea (Table 3).

### Table 1. Summary of Efficacy

<table>
<thead>
<tr>
<th></th>
<th>IEF % Decrease</th>
<th>I-QOL Increase</th>
<th>PGI-I % Better</th>
<th>MTBV Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duloxetine</td>
<td>-50</td>
<td>+11.0</td>
<td>62</td>
<td>+20.0</td>
</tr>
<tr>
<td>Placebo</td>
<td>-27</td>
<td>+6.8</td>
<td>40</td>
<td>+2.0</td>
</tr>
</tbody>
</table>

All $P$ values <.001.

- 85% of the patients experienced a reduction in leakage.
- Half of the patients experienced at least a 50% reduction in the number of leakages.
- 30% of the patients experienced improvement in quality of life.

IEF = incontinence episode frequency; I-QOL = Incontinence Quality of Life; PGI-I = Patient Global Impression of Improvement; MTBV = mean time between voids.

Data from Zinner et al.

### Table 2. Adverse Events (>5% with Duloxetine)

<table>
<thead>
<tr>
<th></th>
<th>Duloxetine (%)</th>
<th>Placebo (%)</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least one adverse event</td>
<td>74</td>
<td>50</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Nausea</td>
<td>22.7</td>
<td>2.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Fatigue</td>
<td>14.8</td>
<td>3.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Insomnia</td>
<td>14.2</td>
<td>2.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>12.2</td>
<td>0.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Constipation</td>
<td>9.6</td>
<td>2.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Somnolence</td>
<td>8.7</td>
<td>0.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Dizziness</td>
<td>7.6</td>
<td>2.4</td>
<td>.002</td>
</tr>
<tr>
<td>Headache</td>
<td>7.3</td>
<td>3.5</td>
<td>.04</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>6.1</td>
<td>2.7</td>
<td>.04</td>
</tr>
</tbody>
</table>

Data from Zinner et al.
In the phase 3 trial of duloxetine, 43% of the patients had mixed incontinence symptoms, which were associated with a higher frequency of incontinence episodes and lower I-QOL scores. The dual-neurotransmitter reuptake inhibitor demonstrated similar efficacy in that subgroup of patients, who experienced 60% reduction in the frequency of incontinence episodes.15

Choosing Among the Options

The current array of nonsurgical options for SUI and the likely addition of duloxetine give physicians and patients some flexibility regarding treatment of the condition. To some extent, therapeutic alternatives can be matched to an individual patient’s lifestyle and particular needs. The flexibility remains limited, however, by the absence of an approved medical therapy for SUI (Figure 3).

Every patient has to begin somewhere in the evaluation of therapies, and pelvic muscle exercises are a frequent and reasonable starting point for patients who are willing and able to perform the exercises. If a patient is willing but unable to perform the exercises, consideration turns to the various adjunctive therapies and whether a trial of one of those adjuncts might be worthwhile.

If a patient is unable or unwilling to perform or continue to perform Kegel exercises, the various devices come into play. Many women find devices unacceptable, however, and the impact on incontinence might be fairly modest. For women to use a vaginal device, they must still have some pelvic floor tone, especially for the posterior compartment. Additionally, devices are not without risks, particularly those designed to be inserted into the urethra. Some patients in this category might prefer to dispense with less invasive options altogether and proceed directly to surgery.

When pelvic muscle exercises or adjunctive therapies fail, patients currently have surgery as the only option. The addition of an effective medical therapy, such as duloxetine, could have a major impact in the management of SUI by giving patients an alternative to surgery. Similarly, an effective medical therapy would be a welcome addition for SUI patients who are unwilling or unable to perform pelvic muscle exercises, affording them the opportunity to achieve symptom relief without resorting to surgery.

Summary

Many patients affected by SUI want symptom relief without having to resort to surgery. Physicians have a variety of nonsurgical treatment options at their disposal, covering a wide spectrum with respect to simplicity and invasiveness. Noninvasive therapy does not cure SUI in most instances but can provide symptom relief that many patients find satisfactory. Success of the therapy is directly related to patient motivation and ongoing compliance with interventions that require long-term maintenance. Historically, a major limitation of nonsurgical treatment of SUI has been...

<table>
<thead>
<tr>
<th>Initial Severity</th>
<th>Patients (%)</th>
<th>Worsened (%)</th>
<th>Discontinued Treatment (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>34 (43.6)</td>
<td>1 (2.9)</td>
<td>7 (20.6)</td>
</tr>
<tr>
<td>Moderate</td>
<td>34 (43.6)</td>
<td>0</td>
<td>9 (26.5)</td>
</tr>
<tr>
<td>Severe</td>
<td>10 (12.8)</td>
<td>N/A</td>
<td>4 (40.0)</td>
</tr>
</tbody>
</table>

Data from Zinner et al.14

Figure 3. Nonsurgical Treatment Options for SUI

PME = pelvic muscle exercises.
the absence of an effective FDA-approved medical therapy. The anticipated availability of the dual-neurotransmitter reuptake inhibitor duloxetine has the potential to make a major change in the nonsurgical management of SUI. Patients will have another option to consider and try before resorting to surgery, and the therapy will require less of patients in terms of ongoing maintenance therapy, which should encourage better compliance.

REFERENCES