

Nonsurgical treatment methods in urinary incontinence

Abstract

While the young patients are predominant affected by stress urinary incontinence, on as you age, the causes of urinary incontinence include-menopausal hypoestrogenism and any vegetative and neuro-psychiatric disorders, generating a new pathologic entity - overactive bladder. Diagnosis urinary dyssynergia component (urodynamic studies, cystomanometrie, cystoscopy, etc.) can avoid surgery that would enhance urinary incontinence. Treatment options for this disease are non-surgical and are designed to prevent involuntary loss of urine. The non-surgical treatment is perfectly indicated and effective on overactive bladder. The aim of this study is to analyze the importance and effectiveness of non-surgical methods of treatment of urinary incontinence caused by overactive bladder. We considered the following entities: behavioral changes, Kegel perineal exercises, biofeedback, electrical stimulation, bladder exercise (bladder "re-education"), vaginal cones, devices to maintain continence and pharmacological therapy, including treatment with botulinum toxin A and injection agencies for volume effect. Both micturition behavior modification with bladder "re-education" and Kegel exercises combined with bio-feedback, behavior changes and vaginal cones reported less incontinence and improved quality of life. Postmenopausal women should not receive oral hormonal therapy because it worsens symptoms in women with incontinence and in those initial continent, increases the risk of this condition. But topical administration of estrogen has improved UI symptoms.

Keywords: urinary incontinence, overactive bladder, non-surgical methods, menopause

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Introduction

It is said: 'every day we live; we grow old'. Women aging brings menopause, physiological phenomenon that includes multiple aspects of the urogynecology antiaging: labia minor atrophy, vaginal atrophy, dyspareunia, uterine volume reduction, breast adipose tissue involution and endometrial atrophy. Urinary incontinence (UI) is also counted among antiaging phenomenon with numerous and unpleasant physical and psychological consequences^(1,2).

UI defines inability to control the micturition act, manifested by involuntary urine loss. The prevalence of urinary incontinence ranges between 20 and 50%⁽³⁻⁵⁾, being difficult to quantify because, for socio-cultural reasons, a large part of the affected population does not report affection⁽⁶⁾.

UI etiopathogeny includes many factors, the age being one of the most important. Beside pelvic structure disorders, continent mechanisms are also affected by changes in trophic and neurological urinary tract caused by postmenopausal estrogen deficiency. In menopause, the tophficity of bladder trigon and urethra descreases, urethral submucosal vascularity decreases, urethral tone and elasticity descrease, also collagen and elastin of musculo-aponeurotic structures of support (especially pelviperineal floor) are reduced. Menopause, having hormone deficiency associated hypoestrogenism, causes overactive bladder incontinence, while at the young patients prevail stress UI. Race, parity,

genetic factors, chronic diseases and lifestyle are other factors influencing urinary incontinence⁽⁷⁾. UI due to overactive bladder occurs due to uninhibited detrusor contractions. In this way, micturition necessity is the sudden need impossible to postponed to urinate, associated or not with symptoms of incontinence. However overactive bladder syndrome can have cases such as: local factors (strip eroded into the bladder), cystitis or may be idiopathic. UI can also be transient, caused by diuretics, psychiatric disorders, urinary infections, excessive fluid intake, constipation or genitourinary fistula⁽⁸⁾.

For the treatment of incontinence symptoms, it tried to find effective solutions, cheap and simple, non-surgical methods⁽⁹⁾.

The choice of efficient method or methods in a patient depends on local circumstances of perineal muscles, depending on their tone, the control that the patient has on the muscles and the situation of the pelvic organs. You can choose between methods as: changes in behavior, Kegel perineal exercises, biofeedback, electrical stimulation, bladder training (bladder "re-education"), vaginal cones, maintaining continence devices and pharmacologic therapy⁽¹⁰⁾.

Nonsurgical treatment method

Behavior changes include:

- frequently urinary to reduce the likelihood of leakage of urine;
- reduction of excess fluid intake;

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- avoidance of alcohol, tea, caffeine, which can overstimulate bladder or foods that can irritate, such as spices, carbonated beverages, citrus;
- a fall in weight (for obese patients);
- maintaining blood sugar within normal limits for people with diabetes;
- quitting smoking, preventing irritation of the bladder and bladder cancer;
- avoidance of constipation, aggravating UI.

An additional benefit is the interval between urination, the aim being to increase the interval between two micturition. Initially, the patient is advised to empty the bladder at a time and once you manage to do this easily, the interval between urination will progressively increase adding all the 15 minute, until it manages to empty the bladder 2-4 hours (bladder "re-education")⁽¹⁰⁾.

Looking to behavioral changes, Fante and contributors⁽¹¹⁻¹⁴⁾ showed a 57% reduction in episodes of urinary incontinence and 54% in amount of urine of patients who have "re-educated" bladder.

Behavioural changes can be a cheap way, simple and without side effects of treatment of urinary incontinence, which may be combined with other methods⁽¹⁵⁾.

Kegel exercises

Since gynecologist Arnold Kegel, studying pelvic muscles, described for the first time 50 years ago, the exercises that bears his name, numerous studies have evaluated their effectiveness, with conflicting results^(16,17).

Kegel exercises focus on pubococci geni muscles that make up the pelvic floor, supporting the urethra, bladder, uterus and rectum. The effect of these exercise on urine loss are not fully understood^(18,19).

Kegel exercises can be incorporated in other methods such as bio-feedback for identification of pelvic muscles or electrostimulation. Bio-feedback is a complementary or alternative medicine technique with which a person is training to improve health via motor control and alter the body's physiological reactions by changing behavior⁽²⁰⁻²⁶⁾.

These methods can be beneficial for patients who have difficulty in identifying the correct muscles. For electrical stimulation, the electrodes can be placed on the surface, the vagina or anal level to measure contractions.

We have analyzed the studies that have investigated the effectiveness of Kegel exercises with biofeedback therapy or not. Some studies have shown significant improvements in patients who adhered to a strict program of behavioral changes and Kegel exercises^(3,19). Motivation and patient compliance are essential.

A recent study⁽²⁶⁾ studied 204 women comparing UI per treatment, physiotherapy exercises and bladder Kegel exercises or biofeedback assisted by the combination of the two. At the end of three months of study, the group subjected to combined techniques have reported a marked decrease in incontinence episodes and improved quality of life.

Even if behavioral changes including Kegel exercises are effective in the treatment IU, patient compliance and motivation are essential for success⁽²⁶⁾.

Studies on the benefits of pelvic floor exercises reduce episodes of UI report over 50%. Berghmans et al.⁽²⁾ concluded that the benefit of these exercises to reduce UI. But they did not establish how important is whether adding strength exercises or biofeedback performing or electrostimulation bring any benefit over just performing exercises⁽²⁾.

In contradiction, Weatherall⁽²⁴⁾ showed that the addition of biofeedback at Kegel exercises gives remarkable results compared to only practicing exercises⁽²⁷⁾.

Goad et al.⁽¹²⁾, in a study of 200 patients with UI concluded that there are not significant differences between the group performing only exercises and the group receiving electrostimulation associated.

A systematically review of the clinical trials of electrostimulation in women with UI have demonstrated that electrostimulation is effective in the treatment of UI, but it requires methodological studies as to achieve a high level of the scientific evidence and also to examine the optimal parameters IU currently used⁽¹⁵⁾.

Kegel exercises or biofeedback associated with electrostimulation, appropriate techniques that help patients identify the pelvic floor muscles, along with performing exercises technique, reduces IU.

Vaginal cones

By introducing vaginal cones (i.e. devices of different sizes) in the vagina, pelvic area muscles contract and will gather around them, keeping them in one place, strengthening the pelvic floor muscles and helping to combat IU. Patients are instructed to enter their vagina cones with different weights and try to keep the vaginal canal. The sensation of sliding cone vagina causes contraction of the pelvic floor muscles to keep the cone in place.

Wilson et al.⁽²⁵⁾ concluded that the vaginal cones can benefit in some patients, but most likely have no additional benefit to patients practicing Kegel exercises.

In their study Bo et al.⁽⁴⁾ wanted to highlight the benefit of using 107 IU women with four methods: Kegel exercises, electrical stimulation, vaginal cones or no therapy.

The conclusions were:

- bio-feedback-assisted exercises are more useful than practiced alone;

- insufficient evidence were to conclude whether electrical stimulation is more beneficial than not using any treatment. Some protocols electrostimulation can do better than others, and some patients may be more effective than others.

- vaginal cones are beneficial, but lose their usefulness when introducing the practice of Kegel exercised.

Keeping continence device

There are several types: occlusion (extraurethral, intra-urethrally) and pessaries.

Occlusive devices

Extraurethrale occlusive devices are applied into the external urethral meatus and removed when emptying the bladder.

Studies have shown significant improvement in terms of disposable devices, the very common side effects such

as urinary tract infections, vaginal or lower urinary tract irritation⁽²⁵⁾.

Intraurethral occlusive devices are disposable devices, thin and flexible that are inserted into urethra to obstruct urinary flow in the proximal urethra and which is removed for urination. Of the many available on the market traversing, only FemSoft proved efficiency for these devices include, among adverse reactions: hematuria, urinary infection and discomfort⁽²⁵⁾.

Pessaries

Although it is mainly used for the symptoms of genital prolapse, Davila et al.⁽⁷⁾ have shown in their study of 70 patients with IU a significant reduction of IU, improving the quality of life. Urodynamic studies in patients with pessaries showed no obstruction. About 23 patients reported vaginal irritation and pain, 10 patients presented urinary infection during the study.

Although intravaginal support multiple devices have been developed (e.g. Coloplast Corporation, Marietta, Ga), they have not been studied extensively and is not tradable.

Pharmacological treatment

1. α -adrenergic agonists

The bladder and urethra contain a large number of α 1-adrenergic receptor which when are stimulated cause muscle contractions. Many α -adrenergic agents, including phenylpropanolamine were studied in patients with UI⁽⁶⁾, noting reduction of symptoms by 19% to 60%, 5-33% of adverse effects and drop between 0% and 4.3%.

Another study⁽¹⁶⁾ suggested an increased risk of hemorrhagic stroke with the use of the appetite suppressant phenylpropanolamine. Thus phenylpropanolamine was withdrawn from the market and other drugs like ephedrine or pseudoephedrine, and took place with excellent results in patients with UI. Among the adverse effects of α -adrenergic agonists include: high blood pressure, anxiety, headache, tremor, palpitations, arrhythmias and difficulty breathing.

Usually, α -adrenergic agonists can produce spectacular results in patients with minimal or moderate UI, not in the severe, but should be used with caution in patients with hypertension, cardiac disease or hyperthyroidism (Table 1).

2. Imipramine

It is part of tricyclic antidepressants which many clinicians believe that reduce bladder contractility. These drugs have anticholinergic effect through their influence on a neurotransmitter, acetylcholine, inhibiting effect on serotonin-norepinephrine reuptake and sedative effect probably due to the antihistaminic properties. Some adverse effects include: postural hypotension, constipation, dry mouth and eye accommodation disorders, nightmares, appetite disorders, endocrine disorders and sexual. Avoid to be prescribed if delusional or hallucinatory state of cardiac disorders or glaucoma.

Gilje et al.⁽¹¹⁾ reported a study of 30 women with UI who received imipramine 75 mg on day 4 weeks and concluded that 22 of the patients have noticed the disappearance of incontinence.

The same result had Lin and his colleagues⁽¹⁷⁾ in the study: 40 females UI Imipramine treated with 25 mg 3 times a day for 3 months. Many clinicians have proven IU reduce symptoms in patients treated with Imipramine.

3. Duloxetine

It is a serotonin-norepinephrine reuptake inhibitor. The US has not received approval to treat UI because of liver toxicity and suicidal events and the UK is still used.

In the randomized study of Norton and his colleagues⁽²¹⁾, there were examined 553 patients with UI who were treated with duloxetine and placebo in various concentrations. It was thus observed that the frequency of episodes of UI decreases as Duloxetine dose administered was higher (i.e. 20 mg per day, 40 mg and 80 mg).

The result obtained by Dmochowski and his colleagues⁽⁹⁾, in their study were almost the same. Adverse drug effects like nausea, fatigue, dry mouth, insomnia, made 24% of participants undergo treatment discontinuously and 6.4% withdrew from the study due to gastrointestinal symptoms.

The frequency of UI episodes decreases as administered Duloxetine dose is higher.

It is contraindicated in severe hepatic or renal impairment.

4. Anticholinergic medication

Anticholinergic drug therapy reduces micturition necessity and increase bladder capacity, proven in multiple clinical studies. Included side effects: inhibition of saliva, constipation, inhibition of ocular lodgings close by blocking the ciliary muscles, tachycardia and decreased cognitive function.

Anticholinergic medication is contraindicated in patients with narrow-angle glaucoma or gastric retention, myasthenia gravis, ulcerative colitis. The maximum effect of anticholinergics appears in 2-4 weeks, therefore the patient should be advised to be patient and to follow the treatment, even if immediate improvement could not be seen.

Of 905 eligible references⁽²²⁾, has shown that continence was achieved in 1 in 8 women treated with Fesoterodin, 1 of 12 with Tolterodin, 1 of 9 with Oxybutynin, 1 of 9 with Solifenancin, 1 of 9 with Trospium. Discontinuation was achieved due to adverse effects manifested most often in those treated with Oxybutynin and Fesoterodin than in those treated with Tolterodine.

5. β -adrenergic antagonists

β -adrenergic antagonists would be useful for UI patients due to the fact that the β -adrenergic receptor blocking effect would increase norepinephrine and α -adrenergic receptors in the urethra. It was shown that propranolol, a β -adrenergic antagonist may be beneficial in a small number of patients with UI.

Studies have not yet demonstrated with certainty the effectiveness of this class of drugs⁽¹⁾, which have as contraindications: heart failure uncontrolled, cardiogenic shock, atrioventricular block (i.e. without pacemaker electronic), Raynaud's phenomenon, bradycardia, asthma, spastic bronchitis, hypoglycemia, metabolic acidosis (i.e. such as diabetics).

Table 1 Summary of outcome of nonsurgical treatment.

Study	No	Method of treatment	Dose	Adverse effects	Contraindications	Results
Vasile ⁽²³⁾	17	Injectable volume effect agents	Suburethral injected in symmetrical places (hours 3,6,9,12)	Irritative symptoms at one patient. Minor incontinence episodes 2 weeks post intervention in a patient.	Allergy to one of the components.	94.11% of the patients with decreased symptoms.
Denys et. al. ⁽⁸⁾	99	Treatment with botulinum toxin A	100 U and 150 U	Urinary retention at 6.8% of patients.	In people with hypersensitivity to Clostridium botulinum type A neurotoxin complex or any of the excipients. Patients with myasthenia gravis.	55% of patients treated with 100U and 65% treated with 150U were complete continence.
Nitti et. al. ⁽²⁰⁾	557		100U	Retention and urinary infection in 5.4% of patients	In people with hypersensitivity to Clostridium botulinum type A neurotoxin complex or any of the excipients. Patients with myasthenia gravis.	60.8% of patients reported treatment benefit.
Yasuda et. al. ⁽²⁷⁾	165	β -adrenergic agonists	Clenbuterol 20 mg 3 times per day	Dizziness, nervousness, heart pain, increased sweating, muscle cramps, tremors of the hands, which manifests itself differently from individual to individual.	Thyrotoxicosis, tachycardia, acute phase of myocardial infarction, pregnancy, hypersensitivity to Clenbuterol.	64.3% of patients with symptomatic improvement.
Andersson et. al. ⁽¹⁾	Not specified the numbers of patients included	β -adrenergic antagonists	Not specified the dose.	Insuficiente cardiaca, bloc atrioventricular, bronhospasm, bradicardie, hipotensiune, tulburari gastrointestinale, depresie.	Uncontrolled heart failure, cardiogenic shock, atrioventricular block (without pacemaker electronic), Raynaud's phenomenon, bradycardia, asthma, spastic bronchitis, hypoglycemia, metabolic acidosis (eg diabetics).	It has not been demonstrated with certainty, the efficacy of this class of drugs.
Shamliyan et. al. ⁽²²⁾	905 eligible references	Anticholinergic medication	They used different anticholinergic: fesoterodine, trospium, tolterodine, oxybutynin, solifenacin.	Inhibition of saliva, constipation, inhibition of ocular lodgings close by blocking the ciliary muscles, tachycardia and decreased function cognitive. Stop treatment due to adverse effects manifested most often in those treated with fesoterotin and oxibutin than in those treated with tolterodin.	Patients with narrow angle glaucoma or gastric retention, myasthenia gravis, ulcerative colitis.	Continence was achieved in 1 in 8 women treated with fesoterotin, 1 of 12 with tolterodine, 1 of 9 with oxybutynin, 1 of 9 with silifenancin, 1 of 9 with trospium.

Study	No	Method of treatment	Dose	Adverse effects	Contraindications	Results
Norton et. al. ⁽²¹⁾	553 patients	Duloxetine	20mg per day, 40 mg and 80 mg	Nausea, fatigue, dry mouth, insomnia.	Liver or kidney problems.	Adverse events made 24% of participants undergo treatment discontinuously and 6.4% withdrew from the study due to gastrointestinal symptoms. Frequency of episodes of UI decreases as administered duloxetine is higher.
Gilja et.al. ⁽¹¹⁾	30	Imipramina	75 mg per day, 4 weeks	Some adverse effects are transient, moderate and disappear after a period of time or dose reduction. Ex: neurological or psychological reactions, cardiovascular, digestive, respiratory.	Hypersensitivity to substance, epilepsy, recent myocardial infarction, glaucoma.	22 patients have noticed the disappearance of incontinence.

6. β -adrenergic agonists

Although it seems paradoxical, it suggests that drugs of this class have a beneficial effect in patients with UI.

In their study, Yasuda and his colleagues⁽²⁷⁾ studied the effect of Clenbuterol on 165 women with UI, a β -adrenergic agonist. Compared to placebo, treatment with Clenbuterol was effective.

The most common side effects were: dizziness, nervousness, heart pain, increased sweating, muscle cramps, tremors of the hands, which manifests itself differently from individual to individual.

Although it seems paradoxical, it was suggested that β 2-adrenergic agonist drugs class is beneficial in patients with UI.

7. Hormonal Therapy

Steroid hormones may influence continence control due to the receptors that they have on female urinary tract and thanks areas of the brain that are involved in the initiation and control of urination. Many estrogen receptors are found in the urethra, the detrusor muscle and pubococcygeni. Androgen receptors are expressed in the bladder and urethra but their function has not been fully studied.

The role of estrogen in the urinary tract pathology was postulated based on cytology and clinical changes observed after menopause and increased rate of UI in this age.

Estrogens may be administered as: estradiol implants, oral conjugated estrogen, estriol mono therapy and in

combination with doses of estradiol, estradiol intravaginal cream.

Among estrogen therapy contraindications include: history of breast and endometrial cancer, porphyria, active liver disease, high triglycerides, pulmonary embolism and deep vein thrombosis, dysfunctional vaginal bleeding, endometriosis and uterine fibroids.

Hextall⁽¹³⁾ and Andersonn⁽¹⁾ studying the literature on this subject, concluded that there are no documented evidence about estrogen in women with UI recommendation.

Another study⁽¹⁴⁾ which included 19,313 women with UI has proven that at those who received treatment with oral estrogen, IU symptoms worsened compared with those who received placebo. The situation worsened in those who received estrogen and progesterone compared to patients who received placebo. In patients who received topical estrogen, incontinence symptoms were improved. No other severe adverse effects were reported, except for vaginal bleeding, breast tenderness or nausea in some patients.

Two large studies have examined the effects of hormone therapy in postmenopausal continent women. The first study included 9180 women of childbearing menopause between the ages of 50-79 years. Participants were randomized placebo- or oral conjugated estrogen or a combination of conjugated estrogens with medroxyprogesterone acetate. UI was assessed at baseline and one

year. Hormone therapy increases the incidence of UI in patients who were continent at the beginning. Postmenopausal women should not receive hormonal oral therapy because it worsens symptoms of incontinence in women with incontinence and on those initial continents, increase the risk of this condition. But topical administration of estrogen has improved UI symptoms.

8. Treatment with botulinum toxin A

Treatment with botulinum toxin A (BTX-A) injected in detrusor muscle is used to treat overactive bladder refractory to oral medication. The injection is performed in multiple points cystoscopy intradetrusor dispersed on the internal surface of the bladder (usually 15-30 injections), and therapeutic dose varies depending on the product used and can be increased for the same patient (20-30 ml corresponding to 100- 300 U). The maximum effect of the method is obtained after 7-10 days after injection, and the efficacy was maintained on an average of 6 months, after which the substance is metabolized, requiring reinjection. Among the complications it is mention the pain, urinary tract infection, urinary retention requiring catheterization hematuria and postoperative.

A double-blind randomized study⁽⁸⁾ identified the full continence in 55% patients treated with 100 U BTX-A and 50% to 150 U BTX-A. The disappearance of urinary must necessity was observed in 65% of patients. After 6 months of treatment, decreased frequency of symptoms and quality of life was significantly improved. As the side effects, the patients showed urinary retention over 200 ml at a dose of 150 U BTX-A.

One of the most recent study⁽²⁰⁾ conducted in 2013 compared the effects of injection of 100 U of BTX-A to placebo in 557 women. Complete continence occurred in 22.9% versus the 6.5% for placebo. Urinary frequency has also been low. The most common side effect was urinary retention and infection in 5.4% of patients. However, 60.8% of the patients have reported the benefit of the treatment⁽²¹⁾. All studies have showed the effectiveness of treatment with BTX-A, improved quality of life and reducing incontinence, urinary frequency, nocturia.

9. Injectable volume effect agents

A useful method in the elderly people with comorbidities in whom surgery is contraindicated, on persons in whom surgical methods are stranded or on younger patients who want pregnancy, is represented by the injectable volume effect agents. There are substances that are injected at the urethro-bladder junction, in submucosa, producing an additional obstacle to the formation of urine evacuation. After 6-12 months after injection, significantly reduces treatment effectiveness, necessitating repetition of the procedure⁽²²⁾.

A study⁽²³⁾ conducted in our country between January - April 2013 period addressed Urodex implant for treating UI. Urodex is sterile gel, viscous, with biocompatible microparticle for tissue stimulation that acts as agent to substitute the volume after simple and safe injections, in urethral submucosa, after local anesthesia. The success of this method is provided by two components: vehicle - hyaluronic acid and the active component - dextranomer

microparticles that stimulates the connective tissue at the injection site. Among the advantages of the procedure are: biocompatible, biodegradable, does not migrate, does not cause erosion, is nonimmunogenic, easy to apply, with the effect lasting, minimally invasive, is performed in safe and ensure continence immediately and the patient can be discharged in same day⁽¹⁶⁾.

Of the 17 cases with urinary incontinence pursued, four of them had an previous anti-incontinence surgery. After Urodex implant, continence can be checked immediately after injection by subjecting the patient to sample the effort. The patients had no complications postimplant, only two of them had irritative symptoms for a week. In the 4-month follow-up of patients, for 16 of them, the degree of continence was significantly improved, only one patient exhibiting a minor incontinence episode in the two weeks postimplant.

Urodex is a viable treatment option in urinary incontinence (i.e. for cases posing serious risks of a laborious intervention) due to safety procedures, risk avoidance and cost efficiency⁽¹⁷⁾.

Conclusions

Behavioral changes may represent an inexpensive method, simple and without any true treatment of UI, which may be compounded with other methods. Even if behavioral changes including Kegel exercises are effective in the treatment UI, patient compliance and motivation are essential for success. Kegel exercises associated with biofeedback or electrostimulation, appropriate techniques that help patients identify the pelvic floor muscles, along with performing exercises technique, reduces UI. Vaginal cones can benefit in some patients, but most likely have no additional benefit to patients practicing Kegel exercises. Although multiple intravaginal support devices have been developed, they have not been studied extensively and is not tradable. α -adrenergic agonists can produce spectacular results in patients with minimal or moderate UI, not in the severe, but should be used with caution in patients with hypertension, cardiac disease or hyperthyroidism. Many clinicians have proven UI reduce symptoms in patients treated with Imipramine. UI episode frequency decreases as administered duloxetine is higher. Studies have not yet demonstrated with certainty β -adrenergic antagonist's efficiency. Anticholinergic drug therapy reduces must necessity micturition and increase bladder capacity, proven in multiple clinical studies. Although it seems paradoxical, it suggests that β 2-adrenergic agonist drug class is beneficial in patients with UI. Postmenopausal women should not receive hormonal oral therapy because it worsens symptoms of incontinence in women with incontinence and on those initial continents, increase the risk of this condition. But topical administration of estrogen has improved UI symptoms. All studies have demonstrated the effectiveness of treatment with BTX-A, improved quality of life and reducing incontinence, urinary frequency, nocturia. Urodex is a viable treatment option in UI (for cases posing serious risks of a laborious intervention) due to safety procedures, risk avoidance and cost efficiency. ■

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