



URINARY INCONTINENCE – FROM CHILDHOOD ONWARDS

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SUMMARY – Urinary incontinence (UI) is a condition that affects patients of all ages, starting with childhood. There are two peaks in its incidence, i.e., in childhood and another one in patients over 40 years of age, which increases continuously with patient age. It is a condition recognized by the World Health Organization as a set of diseases (International Classification of Diseases, ICD-10), and the International Classification of Functionality recognizes the associated extreme disablement. UI is a major health problem affecting the lives of an estimated 400 million persons worldwide. The global aging of the population will cause rise in the incidence of UI in the future. It is expected that UI itself will become a serious health and social burden for both patients and health service providers. UI can be an isolated problem, or it can be associated and/or aggravated by any associated disorder affecting the nervous system such as myelomeningoceles, Parkinson's disease or stroke. UI often affects the patient daily life, and it can have repercussions on their physical, financial, social, and emotional well-being. At last, it has a negative influence on their sexual health.

Key words: Urinary incontinence; Stress urinary incontinence; Mixed urinary incontinence; Dysfunctional voiding

Introduction

Urinary incontinence (UI) is a condition that affects patients of all ages, starting with childhood. There are two peaks in its incidence, i.e., in childhood when different types of incontinence are diagnosed and may resolve with growth of the child, and another one in patients over 40 years of age that increases continuously with patient age. It is a condition recognized by

the World Health Organization as a set of diseases (International Classification of Diseases, ICD-10), while the International Classification of Functionality recognizes the associated extreme disablement¹. UI is a major health problem affecting the lives of an estimated 400 million patients worldwide¹⁻³. It is believed that the global aging of the population will cause a rise in the incidence of UI in the future. It is expected that UI itself will become a serious health and social burden for both patients and health service providers¹.

Urinary incontinence can be an isolated problem, or it can be associated with and/or aggravated by any associated disorder affecting the nervous system such as myelomeningoceles, Parkinson's disease, stroke, multiple sclerosis, or neuropathies.

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Urinary incontinence often significantly affects the patient daily living and can have repercussions on their physical, financial, social, and emotional well-being⁴. And the last but not the least, it has a negative influence on their sexual health⁵.

Incontinence in Children

The International Children's Continence Society (ICCS) defines UI as an involuntary leakage of urine that can be continuous or intermittent⁶. When a child has a constant loss of urine, it is usually associated with certain congenital malformations (ectopic ureteric orifice below the sphincter, functional loss of the external urethral sphincter [as in bladder exstrophy]), or is iatrogenic. Intermittent incontinence is occasional leakage of urine in either small or large amounts that can occur during the day (daytime incontinence) or sleeping periods (enuresis)⁶. Intermittent UI is the most common form of incontinence in children, and below in the text, UI in children refers to intermittent incontinence.

Urinary incontinence in children can be a symptom of several non-neurological voiding disorders. The most common ones are dysfunctional voiding, detrusor overactivity disorder, and giggle incontinence⁶.

In neonates, micturition occurs every time the bladder is filled with urine. It is a process that does not involve cortical interference. With maturation of the child, voiding slowly goes under voluntary control. First awareness of the bladder function occurs around the age of 1-2 years. That is the time when toilet training is attempted.

Toilet training of a child is one of the most challenging developmental milestones. There are several approaches to toilet training in children, but the one that is recommended by the American Academy of Pediatrics for children suggests the beginning of toilet training process only when the children show signs of readiness⁷. It is believed that the appearance of the readiness sign suggests that the child is physiologically mature, but is also motivated both from outside (by the parents) and from the inside (by himself/herself)⁷. As every child is unique, it is expected that the child should achieve adult voiding pattern somewhere between the age of 3 and 5 years⁷. Any form of lower urinary tract dysfunction is therefore considered physiological in children up to 5 years of age. After that age, any symptom, including recurrent urinary tract infections (UTIs), incontinence, frequency, hesitancy and holding maneuvers, should be evaluated.

Evaluation of a child with voiding disorders should include thorough history, including past medical/surgical history, use of medications, any previous workup, and/or therapies or interventions. Special focus should be given to voiding and stooling habits. Complete voiding history includes questions about the frequency of voids, sensation of urgency, hesitancy, sensation of complete/incomplete emptying, daytime and/or night-time incontinence, and quality of the urinary stream. In addition, for all patients, detailed history of bowel habits is very important as the connection between voiding disorders and inadequate bowel habits is well established⁸. Physical examination of the abdomen, lower back, and external genitalia should be performed. While the majority of physical examinations are normal, detailed physical examination could reveal either a distended bladder, full rectal ampulla, signs suggestive of an occult spinal dysraphism, or other genital malformations such as phimosis, meatal stenosis or labial fusion. The initial evaluation should also include obtaining the patient voiding and stooling diaries. Those could be done on paper charts or on various smart device applications, with measured voided volumes⁶. Most of the physicians dealing with voiding disorders insist on incontinence questionnaires⁹. Over the past couple of decades, several voiding and elimination questionnaires have been developed for use in children with voiding disorders. The ICCS recommends that one questionnaire be fulfilled at the initial visit to evaluate the initial severity of symptoms; the same should be repeated at all subsequent visits to monitor treatment response^{6,10}.

Once the full voiding history has been obtained, further diagnosis is indicated. First, urine studies (i.e., urinalysis, and urine culture when indicated) are performed to exclude the presence of UTI as a possible cause of symptoms. Once UTI has been excluded, uroflowmetry ± simultaneous electromyography, coupled with evaluation of the presence of post-void residual urine should be done. Renal and bladder ultrasound is usually performed to exclude any form of anatomical malformations^{6,11}.

In all children with any type of voiding dysfunction, standard urotherapy (SU) should be advised at the first visit, even before any of the diagnostic procedures have been done. Despite different definitions, the most comprehensive one identifies five key aspects of SU: (1) demystification of the disorder, i.e., explaining the child the parts and function of the urinary tract

system, and problems related to it; (2) instructions regarding optimal micturition behavior (timed voiding); (3) guidelines for drinking and eating (adequate fluid intake with avoidance of carbonated fluids, timed fluid intake, and food with adequate fiber content enabling regular stool); (4) exact documentation of the symptoms (realization of a problem occasionally results in an immediate cure); and (5) continuous and supportive contact with the therapeutic team, as well as fellow patients with similar problems⁶.

Standard urotherapy is a useful treatment option, being a purely behavioral intervention with no side effects, practically free, and sometimes resulting in spontaneous resolution of the symptoms⁶. SU can be done at home as an individual program, or it can be performed as an inpatient program, either individually, or as part of a group of patients with a similar disorder. In contrast to all other treatment options, SU is well accepted by the patients in general. Biofeedback may be added to SU for patients with detrusor-sphincter dyssynergia. In animated biofeedback, video computerized systems obtain information regarding the activity of the pelvic floor muscles and allow the children to see, learn about, and control them, i.e., contract or relax them¹².

In patients with hyperactive bladder, treatment usually includes antimuscarinic agents. Oxybutynin has been identified as the drug of choice in children. It is approved for use in children, and has already been on the market for 20 years. Newer generation antimuscarinics such as propiverine, tolterodine, and solifenacin have recently also been approved for use in children, but they are still not as widely used as oxybutynin. Although all antimuscarinics are generally safe and well tolerated, some issues affect their use in children¹³. First of all, almost all antimuscarinics are in tablet form and children are sometimes reluctant to swallow them. Only oxybutynin is available in both syrup and patch forms, but their use has not shown to be a great success¹⁴. Typical side effects such as dryness of the mouth, dizziness, headache, and constipation sometimes hinder the use of antimuscarinics in children. The chance of having these side effects is reported to be 3%-23%¹⁵, and these side effects will make either children or their parents stop the treatment.

Giggle incontinence is a specific condition in children when they have incontinence episodes only while laughing. There are two different approaches in the treatment of giggle incontinence, depending on the as-

sumed etiology. One approach is to treat it as a voiding dysfunction, with prolonged biofeedback treatment. Another one is to treat giggle incontinence as a neurological disorder, using methylphenidate as the drug of choice¹⁶.

Urinary Incontinence in Women

It is considered that UI affects mostly women. The prevalence of UI in women increases with age and parity, from 19% at age younger than 45 to 29% in women 80 years or older¹⁷. Current US national estimates are that more than 20 million women have UI or have had an episode or episodes of UI at some point in their lives¹⁸. There are several types of UI affecting women, i.e., stress, urge, and mixed incontinence. Stress UI is the inability to hold urine during coughing, sneezing, or other activities that increase intra-abdominal pressure. Urge UI is the involuntary loss of urine associated with the sensation of a sudden, strong urge to void that is difficult to postpone. Urge incontinence can also be manifested as nocturia¹⁹. Mixed UI occurs when both symptoms of stress and urge UI are present¹⁹.

Stress urinary incontinence

Stress urinary incontinence (SUI) is incontinence occurring under conditions of increased intra-abdominal pressure coupled with a weakened sphincteric mechanism, resulting in urine leakage.

There are established risk factors for SUI such as pregnancy and childbirth²⁰. Hysterectomy has been associated with the development of SUI due to damage to the pelvic floor muscles²¹. Other risk factors for SUI are increased weight (body mass index >25), heavy physical work, and connective tissue weakness. SUI could also be associated with either vaginal wall or pelvic organ prolapse, including cystocele (prolapse of the bladder), rectocele (prolapse of the rectum), and uterine prolapse.

Diagnosis of UI is based on patient complaints, bladder diary, clinical and gynecological examination, urine analysis, cough and pad test, as well as data provided from a variety of questionnaires available, such as the International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form (ICIQ-UI-SF)), Urinary Incontinence Severity Score (UISS), Incontinence Severity Index (ISI), and Stress and Urge Incontinence and Quality of life Questionnaire (SUIQQ)²².

Physical examination identifies the presence of associated pelvic organ prolapses, as well as a woman's ability to initiate voluntary contraction of the pelvic floor muscles (the pelvic floor muscle exercise). The cough stress test with a full bladder identifies the presence of SUI in most cases. The stress test is performed by coughing in either the supine or lithotomy position. The test is positive if urine leakage is observed. Cystometry is not required in patients with uncomplicated SUI.

The treatment of UI should start with behavioral/lifestyle interventions. Women with all types of incontinence can be advised to decrease their intake of caffeinated and/or carbonated drinks, stop smoking, cease intake of alcoholic beverages, as well as reduce their body weight if indicated²³. Constipation often complicates UI, therefore managing those problems might alleviate problems with involuntary urine loss as well.

Pelvic floor muscle exercise is considered the first-line treatment according to most of the accepted continence guidelines (ICS, AUA, EUA, ACOG, NICE)^{24,25}. Those exercises should be repeated several times a day over a period of several months in order to achieve improvement of the symptoms²⁶. In women who are motivated for such a treatment, clinical improvement can be sustained for years. Those exercises could be performed by the patients on their own, or they can be performed with the help of a trained urotherapist or pelvic floor trainer, with or without the use of a biofeedback. When pelvic floor muscle exercise and lifestyle changes do not achieve a desirable effect, surgery should be suggested. Five procedures are endorsed by the American Urological Association, i.e., the use of injectable bulking agent, laparoscopic colposuspension, midurethral sling, pubovaginal sling, and open retropubic suspension²⁷. Today, midurethral sling is by far the most popular sling owing to its good long-term efficacy and minimally invasive approach^{25,27}.

Surgery may not be necessary in numerous women, including those without remarkable changes after behavioral treatment or with the lack of motivation for such a treatment; those with little or no pelvic organ prolapse; and those with slight to moderate SUI. For those women, in the last 10 years, laser treatment has been introduced as a potentially good option. Currently, the vaginal erbium laser (VEL) and CO₂ laser are used for the treatment of SUI. The procedure is performed in an outpatient clinical setting. Neither anesthesia nor post treatment medications are necessary.

Non-ablative Er:YAG SMOOTH laser pulses are delivered to the intravaginal mucous tissue in order to achieve controlled heating of the collagen in the deeper mucosa layers (lamina propria), without ablation and over-heating of the mucosa surface, thus avoiding the risk of perforation with accidental lesions of the urethra, bladder or rectum.

The first pilot study started in September 2009²⁸, and it clearly showed improvement at the first follow-up (1 month after the intervention) in 17/52 women (42.3% were continent; ICIQ-UI-SF score=0) and at the second follow-up (2-6 months after the intervention) in 18/47 women (38.3% were continent). Another study showed impressive 77% of ICIQ-UI-SF score reduction in patients with SUI²⁹. Recently, the first randomized placebo-controlled clinical trial with VEL and sham as a placebo showed statistically significant improvement in the VEL group 3 months after the treatment (ICISQ-UISF $p < 0.001$; PISQ ($p = 0.014$)³⁰.

So far, just a few studies have been published using CO₂ laser in treating SUI. The most recent one showed the baseline ICIQ-UI SF score (14.34 ± 2.65) to have decreased significantly at 12 months (7.09 ± 1.1 , $p < 0.001$), 24 months (7.49 ± 0.94 , $p < 0.001$) and 36 months (6.76 ± 0.82 , $p < 0.001$)³¹.

Estrogen substitution therapy is another treatment option for postmenopausal women. Vaginal atrophy may aggravate SUI in these women, and estrogen substitution therapy resolves vaginal atrophy and reduces the number of incontinence episodes³².

Women with SUI who are reluctant to undergo surgery and/or are unable or unwilling to try laser therapy, can use vaginal continence pessaries. These devices aim to compress the urethra, and they show the greatest benefit in those patients with severe SUI³³.

Urge urinary incontinence and overactive bladder

Overactive bladder (OAB) is a disorder caused by uninhibited detrusor contractions. It can be idiopathic, or secondary to various other diseases such as polyneuropathy, diabetes, neurological disturbances, etc. The symptoms of OAB may include any or all of the following: urinary urgency (sudden urge) to void that is difficult to postpone, frequency, nocturia, and incontinence¹⁹. The initial management of OAB is conservative, which includes managing oral fluid intake; timed voiding – the patient voids regularly at 3-4 hour or shorter intervals to minimize urgency and urge leak-

age; bladder training techniques that postpone voiding for progressively longer time intervals; reduction of excessive body weight if indicated; and smoking cessation²⁶. If the suggested lifestyle changes do not relieve the symptoms, further evaluation and therapy is needed. It is a matter of debate whether or not to perform urodynamic examination in a patient with clear symptoms of OAB. According to the International Continence Society recommendation, it is unnecessary in uncomplicated patients with urge urinary incontinence (UUI).

Overactive bladder irresponsive to the abovementioned lifestyle changes is treated with antimuscarinic administered *per os*. Antimuscarinics block muscarinic receptors³³. Thereby, they decrease the ability of the bladder to contract. Antimuscarinic drugs act mainly during the storage phase, inhibiting detrusor contractions and increasing bladder capacity. They do not interfere with the voiding itself³⁴. Most antimuscarinics have a similar side effect profile, which includes dryness of the mouth and eyes, and constipation. Second- and third-generation selective antimuscarinics have relatively more affinity for M2 and M3 receptors, which are most prevalent in the bladder, reducing side effects in other systems³⁵.

Besides antimuscarinics, β_3 -adrenergic receptor agonists are currently evaluated for the treatment of OAB. Currently, mirabegron is the only one registered for the treatment of OAB. It causes relaxation of the detrusor muscle during bladder filling and inhibits detrusor contractions³⁶. The result of its action is an increased bladder capacity with no change in micturition pressure or residual volume³⁷.

Desmopressin acetate is a synthetic form of the antidiuretic hormone vasopressin, the main action of which is decrease of overnight urine production. It has been used for the treatment of nocturia and nocturnal enuresis in both children and adults under the age of 65³⁸.

Intradetrusor injection of botulinum toxin is a Food and Drug Administration approved treatment option for patients with idiopathic and neurogenic OAB refractory to antimuscarinic or β_3 -adrenergic receptor agonist therapy³⁹. The effect of botulinum toxin injection is relaxation of the detrusor muscle that might require either permanent or temporary self-catheterization after the intervention.

The last option for treating non-responsive OAB could be permanent sacral neuromodulation of the

nerves involved in the micturition process. The first step is placement of the electrodes in the sacral foramen, then the electrodes are tested for 21 days, and finally either the electrodes are removed if no response was observed during the test period, or the neurostimulator is permanently inserted⁴⁰. The efficacy of sacral neuromodulation in OAB is 70%, but there are some obstacles preventing sacral modulation from becoming a primary treatment option, such as high price, displacement of the electrodes, wound infection, and pain⁴⁰.

Mixed urinary incontinence

Approximately 1/3 of women with UI have mixed urinary incontinence (MUI). They have episodes of incontinence associated with both increased intra-abdominal pressure and urinary urgency¹⁹. The etiology of MUI may be due to two independent pathologies (OAB and weakened pelvic floor muscles), or primarily due to one or the other⁴¹.

Appropriate therapy for MUI should combine the abovementioned therapeutic options for SUI and UUI, with accentuation on the ones for the more prominent symptomatology.

Male Urinary Incontinence

Even though UI is traditionally considered a condition affecting women mostly, there is a significant number of males also affected by it. It is believed that 12%-17% of males are affected by UI, and this prevalence increases with age⁴². It interferes with their social, professional and sexual activities. It can be caused by bladder or sphincter dysfunction, or both. UI in males is very similar to UI in females. There are two main types of UI, i.e., stress incontinence (involuntary leakage on effort, sneezing or coughing) and urge incontinence caused by detrusor overactivity. There are, however, some specific situations in males, such as UI after radical prostatectomy, transurethral resection of the prostate, and/or radiation therapy for prostatic cancer. The incidence of post prostatectomy incontinence ranges from 1% to 40% and it depends on the criteria used for the definition of UI, as well as the length of the follow-up^{43,44}. The risk factors for UI after prostatectomy are advanced age, obesity, associated bladder dysfunction, increased prostate volume, previous transurethral resection of the prostate, and traumatic injuries of the urethra and/or sphincter⁴⁵.

Similar to making a diagnosis in women, in males, detailed history and physical examination are the starting point of evaluation of a patient with UI. History should focus on voiding habits, including the frequency of the voids, quality of the stream, presence of hesitancy, and sensation of complete/incomplete emptying. Duration of the symptoms is also of importance, as well as the presence of other urinary symptoms, history of infections, degree and subjective estimate regarding the level of bother caused by incontinence. Prior procedures and other risk factors such as significant comorbidities should be evaluated as well. Physical examination should detect any significant urine leakage on effort, sneezing or coughing^{45,46}. A bladder diary is helpful and consists of day and night time frequency of micturition, number of incontinence episodes, voided volumes, and 24-hour urinary output⁴⁷. Urine analysis is a simple and reliable test aimed at excluding the urinary tract infection, while urine culture should be done only when indicated. Ultrasound is used to evaluate the presence of residual urine. Urodynamic examination is both invasive and uncomfortable for patients and should be done in selected cases⁴⁸. Cystourethroscopy is useful to exclude urethral strictures and bladder neck abnormalities, and to assess bladder status.

In patients who have had their prostate surgically removed, improvement in incontinence can be expected over a period of up to 12 months⁴⁹. Conservative management such as physical therapy in the form of pelvic floor muscle exercises may be offered for periods of up to 6-12 months⁵⁰.

The injectable bulking agents present a minimally invasive treatment option for SUI. Submucosal injection of bulking agents in the urethra should be able to overcome the intravesical pressure. However, the initial success rate of 43% reported by some authors tends to deteriorate over time, resulting in 32% success six months after the procedure⁵¹. The treatment of male incontinence using bulking agent can be recommended only in patients not willing or not fit enough for the standard surgical treatment.

The male sling procedure is an alternative therapeutic approach for patients with UI and intact pelvic floor. Three subtypes of the male sling procedures include the bone-anchored sling, retro-urethral trans-obturator sling, and adjustable retropubic sling⁴⁷. All of them should either elevate or compress the urethra in order to prevent urine leakage under the conditions of elevated intra-abdominal pressure. The male

sling placement is an attractive treatment option in patients with low-to-moderate SUI owing to a lower risk of urethral erosion and atrophy compared to the artificial urinary sphincter (AUS). Despite the growing popularity of male sling procedures, the AUS is still considered the gold standard in the treatment of male incontinence. The most commonly implanted AUS is the AMS 800 (AMS, Minnetonka, Minnesota, USA)⁴⁶. It enables patients to open or close their sphincter as needed. The AUS is the most successful surgical treatment for sphincteric insufficiency in patients with high-degree incontinence. The reported rates of success for the AUS are 59%-91%⁴⁷. The potential drawbacks of the AUS are the need for revision in some patients due to malfunction, infection, later urethral atrophy, and erosion⁴⁶.

Therapeutic options for urge incontinence in males are equal to those in female patients.

Conclusion

Urinary incontinence is a distressing condition that affects patients of all ages and both sexes, and it has a devastating effect on patient social, professional and sexual activities. However, a carefully tailored approach can reduce, or completely cure incontinence, resulting in significant improvement in the patient quality of life.

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Sažetak

INKONTINENCIJA MOKRAĆE – OD DJETINJSTVA DO STAROSTI

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Inkontinencija mokraće (IM) je stanje koje pogađa osobe svih dobnih skupina počevši od djetinjstva. Postoje dva vrhunca incidencije i to u djetinjstvu, a drugi u bolesnika starijih od 40 godina, koji se stalno povećava s dobi bolesnika. To je stanje koje Svjetska zdravstvena organizacija prepoznaje kao skup bolesti (Međunarodna klasifikacija bolesti, MKB-10), a Međunarodna klasifikacija funkcionalnosti prepoznaje pridruženu ekstremnu onesposobljenost. IM glavni je zdravstveni problem koji utječe na živote oko 400 milijuna ljudi širom svijeta. Globalno starenje stanovništva uzrokovat će porast učestalosti IM u budućnosti. Očekuje se da će i sama IM postati ozbiljno zdravstveno i socijalno opterećenje za bolesnike i pružatelje zdravstvenih usluga. IM može biti izolirani problem ili može biti povezana s i/ili pogoršana bilo kojim povezanim poremećajem koji pogađa živčani sustav, kao što su mijelomeningocele, Parkinsonova bolest, moždani udar itd. IM često utječe na svakodnevni život bolesnika i može imati posljedice na njihovo fizičko, financijsko, socijalno i emocionalno stanje. Napokon ima negativan utjecaj na njihovo seksualno zdravlje.

Ključne riječi: *Inkontinencija mokraće; Stresna inkontinencija mokraće; Miješana inkontinencija mokraće; Disfunkcionalno mokrenje*