

## REVIEW ARTICLE

## THE MOST COMMON UROLOGICAL CONDITIONS IN POSTMENOPAUSAL WOMEN

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### ABSTRACT

**The aim:** To analyze the available literature on the most common daily urological problems in menopausal women and to evaluate the use of hormone replacement therapy for troublesome urological symptoms.

**Materials and methods:** Analysis of publications from PubMed databases on the most common disorders during menopause was performed and the most common urogynaecological problems in postmenopausal women were selected according to literature data. Different available methods of treatment of these disorders were compared.

**Conclusions:** During menopause, women struggle with many unpleasant symptoms from the genitourinary system. For most women, this is a very embarrassing topic and, although bothersome, underestimated. The urinary tract infections, urinary incontinence or kidney stones can lead to serious complications, if left untreated. We should strive to make women more aware of possible methods of prevention and treatment of the menopausal symptoms in the context of urological disorders.

**KEY WORDS:** urology, menopause, urinary tract infections, Urinary incontinence, nephrolithiasis

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### INTRODUCTION

Menopause, as defined by the WHO, is the period in a woman's life when her last menstrual period occurs with a subsequent 12-month break in menstruation. It is a natural process marking the end of the female reproductive capacity and results from the hormonal changes taking place. The end of menopause most commonly affects women between the ages of 45 and 55 and is often associated with reduced quality of life. The most common symptoms include sudden hot flashes and increased sweating, resulting from hypoestrogenism, leading to impaired thermoregulation. In addition, loss of bone mass leads to osteoporosis and increases the risk of low-energy fractures. Equally troublesome are sleep and memory disorders, mood swings and uncontrolled weight gain. It is worth noting that the postmenopausal complaints concerning the genitourinary system are often underestimated.

They are very often embarrassing and shameful for the patients while the symptoms resulting from urogynaecological disorders can be very distressing and require spe-

cialist help. The most common perimenopausal conditions include genitourinary atrophy, recurrent urinary tract infections, urinary incontinence and sexual dysfunctions. The symptoms experienced by the postmenopausal women vary and depend on genetics, race, cultural behavior and ethnicity. In addition, the prevalence of particular symptoms depends on the time and stage of menopause[1, 2]. Menopause is an interdisciplinary problem and it is important to stress the importance of collaboration between many specialists including gynecologists and urologists in order to achieve the best possible results in alleviating these disorders.

### THE AIM

In this paper, we analyze the literature and collect information on the most common urological problems in menopausal women. Much has been said about the main complaints associated with this period and methods of managing them. Problems, such as urinary incontinence

or recurrent urinary tract infections, are often underestimated. In addition, the occurrence of urolithiasis is often not associated with hormonal changes occurring during menopause associated with the use of hormone replacement therapy (HRT). In the event of urogenital symptoms, women should be immediately referred to a urologist.

## MATERIALS AND METHODS

The aim of this study was to review the literature from PubMed databases published between 1992 and 2022, regarding the urological disorders and complaints of the menopausal women. The literature data were analyzed to identify the most common urological disorders in postmenopausal women. Publications on the three interdisciplinary urological problems, most frequently encountered in everyday practice, were selected for analysis: urinary incontinence, recurrent urinary tract infections and the occurrence of kidney stones.

## REVIEW AND DISCUSSION

The data point to the postmenopausal period accounting for an average of 1/3 of a woman's life. Decreased estrogen concentrations, characteristic of menopause, not only cause the typical vasomotor symptoms, such as hot flashes and night sweats but also induce urogenital atrophy. This results from the presence of estrogen and progesterone receptors in the vagina, urethra, bladder and pelvic floor muscles [3]. The estrogens are responsible for promoting the contractility of the bladder, increasing the integrity of the urothelial epithelium and for the synthesis of glycogen, which is a substrate for *Lactobacilli*. Estrogens have been shown to affect the smooth muscle function by modifying muscarinic receptors and inhibiting calcium ion flow to muscle cells. They also increase the sensory threshold of the bladder, increase the pressure closing the urethra, favorably affect the pressure in the proximal part of the urethra and have a positive effect on the blood supply to the pelvic organs [4]. As a result of reduced estrogen levels, women experience vaginal dryness and pruritus. The vaginal epithelium thins, the natural vaginal microbiome is disturbed and the pH increases, which results in an increased susceptibility to infections and mechanical injuries.

Atrophy of the mucous membrane of the urethra, causes dilatation of its lumen, which consequently leads to increased migration of bacteria from the vagina to the bladder. This is also one of the main causes of urinary incontinence, as the reduced resistance to urine flow caused by widening of the urethral lumen requires increased muscle tone to control micturition. In menopausal women, the pelvic floor muscles weaken, resulting in urinary incontinence [5, 6]. Genitourinary symptoms occur several years after the last menstrual period. This is thought to be due to the fact that estrogen levels during the transition period are already too low to stimulate endometrial proliferation, but high enough to prevent the development of urogenital complaints during this period [7]. With these data, effec-

tive pharmacological treatment is possible, allowing the maintenance of such a concentration of estrogens which can reduce urogenital symptoms and cause no endometrial proliferation.

## UTI (URINARY TRACT INFECTION)

As the estrogen levels decrease during the perimenopausal period, the risk of UTIs increases. This is associated with impaired bladder emptying, dilatation of the urethra, decreased integrity of the urothelial epithelium and disruption of the vaginal microbiome. Deteriorated bladder emptying causes urine retention, which then leads to bacterial proliferation and impaired bladder clearance. Estrogen deficiency results in disruption of the integrity of the urothelium by reducing the amount of E-cadherin linking proteins. In addition, a decrease in estrogen levels causes a decrease in the level of glycogen, which is a substrate for lactic acid bacteria. The disruption of the natural bacterial flora of the vagina, causes increased frequency of infection, and because the urethra is atrophied and dilated, it is much easier for infection from the vagina to spread to the urinary tract [4]. UTI can involve the lower or upper urinary tract, and can be uncomplicated or complicated. Uncomplicated UTIs occur in healthy individuals with no significant urinary tract changes, whereas complicated UTIs occur in patients with urinary tract abnormalities. Recurrent UTI (RUTI) is defined as  $\geq 3$  uncomplicated UTIs within 12 months or 2 uncomplicated, symptomatic UTIs within 6 months. One of the main risk factors for RUTI, in addition to previous infection, is age, and an increase in incidence with age has been observed. The most common causative agent of UTI is *Escherichia coli*, as well as *Klebsiella pneumoniae*, *Staphylococcus spp*, *Enterococcus faecalis*, *Group B Streptococcus*, *Proteus mirabilis*, *Pseudomonas aeruginosa* and *Candida spp* [8]. The main symptoms of UTI include tachycardia, pain during micturition, frequent passing of small portions of urine, urgency, and hematuria. The mainstay of treatment is antibiotic therapy. In a population of menopausal women struggling with RUTI, many studies were conducted to show whether estrogen supplementation would be able to prevent recurrence.

Raz and Stamm conducted a study on 93 postmenopausal women with recurrent urinary tract infections. 50 women received estradiol vaginally and the remaining 43 women received placebo vaginally. The incidence of urinary tract infections was significantly lower in the estrogen-treated group compared with the placebo group. In addition, the number of lactobacilli in the vaginal swab increased in estrogen-treated women, the pH decreased and the vaginal colonization with *Enterobacteriaceae* was reduced. The authors demonstrated that vaginal administration of estrogen prevented recurrent urinary tract infections in postmenopausal women, suggesting that this was influenced by modification of the vaginal flora [9]. Ferrante and co-authors conducted a 6-month study involving the use in postmenopausal women with documented UTIs of estrogen in the form of a cream, a vaginal ring and

a placebo group. In women using estrogen, there was a significant reduction in the recurrence of urinary tract infections. This confirms that commonly prescribed forms of vaginal estrogen with contemporary dosing regimens prevent UTIs in postmenopausal women with an active diagnosis of UTI [10].

It is known that while estrogens administered vaginally significantly reduce the incidence of UTIs, as for oral estrogen therapy, studies have not fully confirmed the positive effects of the therapy. Cardozo et al. conducted a study evaluating the efficacy of oral estriol in preventing recurrent urinary tract infections in elderly women. Women were given oral estriol or placebo for six months. The researchers found no positive effect of oral estriol over placebo in preventing recurrent urinary tract infections [11].

A study by Brown also demonstrated no effect of oral hormone therapy on reducing the incidence of urinary tract infections in this study group [12]. These studies suggest that postmenopausal women should use vaginal estrogens because they significantly reduce urological symptoms and prevent recurrence of urinary tract infections. Women should definitely visit a gynaecologist or urologist and should not underestimate the symptoms or be ashamed to talk about them.

### UI (URINARY INCONTINENCE)

Another significant and distressing problem faced by menopausal women is urinary incontinence. Urinary incontinence (UI) is defined as involuntary leakage of urine. There are three types of UI: stress, urgency and overflow. Stress UI is the involuntary leakage of urine when intra-abdominal pressure increases and is not preceded by urination. It usually occurs during coughing, sneezing and laughing. It is the most common type of incontinence in young women. In contrast, involuntary urine leakage with a sudden feeling of urge is referred to as urge incontinence and is the most common type of incontinence in elderly women. Risk factors for incontinence include obesity, multiple births, heavy physical work and menopause. There are a comparable number of estrogen receptors in the urethra as in the vagina. During menopause the decreased concentration of estrogen, is responsible, among other causes, for the proper functioning of the epithelium of the inner surface of the urethra and the bladder. The urethra becomes dilated, resulting in involuntary urine leakage due to decreased resistance and the need for increased tension of the sphincters, whose tension decreases during menopause. In addition, the bladder capacity decreases, which is also one of the causes of urinary incontinence. Maintaining urine is therefore an increasing problem. Many women avoid a doctor's appointment because of embarrassment, lack of knowledge about the available treatment options and fear of possible surgery [13]. Women with urinary incontinence should seek specialist consultation so that optimal treatment can be implemented. The substitutive administration of estrogens is the subject of much debate, and to date there is much conflicting information regarding the efficacy of estrogens in urinary incontinence.

Rud conducted a study to evaluate the urodynamic effects of hormone therapy on the lower urinary tract in women. During the study, in one group of women with urinary incontinence, oral estradiol (E2) and estriol (E3) were administered for a period of 3 weeks, while the other group of women studied received a single intramuscular injection of gestagen. The author demonstrated that estradiol 4 mg daily and estriol 8 mg daily given for a sufficiently long period (3 weeks) could improve the course of stress urinary incontinence in women, mainly by improving the intra-abdominal pressure transmission to the urethra [14].

Similar conclusions were reached by Dessole et al. In their study, they evaluated the efficacy and safety of vaginal administration of estriol for urinary incontinence, urogenital atrophy and recurrent urinary tract infections in postmenopausal women. They demonstrated that vaginal administration of estriol can be a satisfactory therapeutic choice for postmenopausal women with genitourinary disorders [15].

A different conclusion was reached by Jackson et al., who evaluated the effect of hormone replacement therapy on stress urinary incontinence in postmenopausal women, but showed no improvement in the study group after six months of estradiol therapy. The researchers consider it unlikely that estrogen plays an important role in this condition [16].

The literature suggests that the use of certain antidepressants during menopause may reduce UI. Van Kerrebroeck et al. evaluated the effect of duloxetine in women with stress urinary incontinence. The frequency of incontinence episodes was found to be significantly reduced after duloxetine compared with placebo, which may lead to future consideration of duloxetine as a potential treatment for women with stress urinary incontinence [17].

Despite various attempts, it is believed that surgical treatment is the only effective treatment for urinary incontinence in women. The most effective treatment is the placement of transobturator tapes, regardless of age and hormonal status.

Sahin et al. evaluated the effect of menopause on the long-term 5-year outcomes of transobturator tape (TOT) surgery. Both post- and pre-menopausal patients were included in the study. Significant improvement was found as early as 1 year follow-up. There were no significant differences between pre- and post-menopausal patients in terms of TOT efficacy at both 1 and 5 years of follow-up, suggesting that transobturator tape surgery is an effective treatment for UI regardless of pre- or post-menopausal status [18].

### NEPHROLITHIASIS

Nephrolithiasis is one of the more common conditions of peri-menopausal women. It is the presence in the kidney calyces and pelvis of deposits made up of chemicals that are found in a dissolved form in the urine. A typical symptom of nephrolithiasis is renal colic, which is a sudden, extremely severe pain in the lumbar region.

It is then necessary to consult a urologist. The occurrence of kidney stones is associated with the use of hormone replacement therapy, which on the one hand relieves the unpleasant symptoms of menopause, but on the other, has many side effects.

Maalouf et al. evaluated the relationship between the use of estrogen and the risk of kidney stones in postmenopausal women. The estrogen therapy was associated with a significant increase in the risk of kidney stones from 34-39 cases per 10,000 person-years. The data suggest that estrogen therapy increases the risk of kidney stones in healthy postmenopausal women. These data should be taken into account when deciding about the use of estrogen therapy in postmenopausal women [19].

Mai et al. examined differences in 24-hour urine compositions associated with urolithiasis between pre- and postmenopausal women. Compositions associated with urinary stones were determined in urine samples and compared between pre- and post-menopausal women. It was found that postmenopausal women had lower citrate, magnesium and creatinine excretion, and have significantly lower magnesium concentrations in a 24-hour urine collection than premenopausal women, which may indicate an associated increased risk of urinary stone formation in postmenopausal women [20].

Prochaska et al. have also demonstrated that metabolic changes associated with menopause can affect urine composition and the risk of kidney stones. They investigated the association of menopause with the risk of kidney stones and changes in 24-hour urine composition in the NHS II study. There were 3,456 cases of kidney stones during 22 years of follow-up. Compared with premenopause, urine collections in postmenopausal women showed lower mean calcium, citrate, phosphorus and uric acid content and higher mean volume. Menopause has been found to be associated with a higher risk of kidney stones [21].

It is important to remember that kidney stones are a multifactorial disease. With the onset of menopause, metabolism decreases and the body weight increases, while the physical activity is low or negligible. It is known that obesity is a strong risk factor for kidney stones, but the role of physical activity and the effect of caloric intake on kidney stone formation remains poorly understood. In her study, Sorensen attempted to assess this relationship in 84,225 women with no history of nephrolithiasis. Weekly physical activity, calibrated dietary energy intake and BMI were independently associated with the incidence of kidney stones. As weekly physical activity increased, the risk of kidney stones decreased by 31%.

A higher category of dietary energy intake increased the risk of kidney stones by up to 42%, but low energy intake did not protect against kidney stones. Physical activity may reduce the risk of kidney stones in postmenopausal women. It is a factor independent of dietary calories and BMI, mainly dependent on the amount rather than intensity of physical activity. It is important to note that excessive dietary calories further increase the risk of stone formation [22].

There are many treatment methods. Sometimes observation and lifestyle changes are enough. In the case of a urinary tract infection with ureteral stones, urgent drainage procedures are sometimes necessary. Diastolic drugs, painkillers and alpha blockers are often used, which can facilitate the passage of deposits. Percutaneous nephrolithotripsy, ureteroscopy and laser stone removal are alternative methods of treating kidney stones. Surgical methods are very rarely used [23].

## CONCLUSIONS

Menopause is undoubtedly a difficult yet physiological time for the women. It is important to accept it, but at the same time, try to alleviate its symptoms. The ideal way to prevent menopausal genitourinary syndrome is to maintain stable estrogen levels through HRT. The long-term use of HRTs is associated with multiple risks, which pose some limitations to their use. These include breast, endometrial and colorectal cancer, as well as cardiovascular disease or kidney stones. As long as the therapy and risks are assessed individually and each patient is aware of the risks, postmenopausal women with persistent unpleasant symptoms should not be denied HRT. In many cases, it is sufficient to include drugs in minimal doses, and the comfort of life will be significantly improved. It is also worth mentioning that a proper diet and physical activity play a very important role during the menopause. By following the principles of a healthy lifestyle, many undesirable symptoms of the menopause can be avoided. It should also be emphasized that in the event of signs of infection, urinary incontinence or renal colic, it is important to consult a doctor and not to delay treatment.

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#### Conflict of interest:

*The Authors declare no conflict of interest.*

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