

Treatment efficacy of chronic urethral syndrome with Doxycycline in females

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KEY WORDS

urethral syndrome ▶ urethral pain ▶ dysuria ▶ chronic infections ▶ doxycycline

ABSTRACT

Introduction and objectives. Urethral syndrome (US) is a term for a complex of symptoms including urinary urgency and frequency as well as urethral and bladder pain. The genesis of US often relates to young woman and their sexual activities. Examinations such as urethral or vaginal swabs and urinary cultures do not lead to the identification of an infectious organism. Sometimes leukocyturia occurs. Cystourethroscopy reveals increased vascularization and hyperemia of the urethra as well as pseudopapillary papillomas at the bladder neck, all of which we consider to be signs of chronic infections. Sometimes microbiological urinalysis and urethral swabs show *Escherichia coli*, *Enterococcus*, *Chlamydia trachomatis*, *Mycoplasma hominis*, or *Ureaplasma urealyticum*. Doxycycline is a broad-spectrum antibiotic that is effective against microorganisms that are not detected by routine urinary cultures. The aim of the study was evaluation of the results of treatment with doxycycline in females with urethral syndrome.

Materials and methods. Between the years 2000 and 2008, after initial examination included urethral swabs, urine examination, and culture, 156 (100%) women with US were treated with doxycycline (and their sexual partners, too) 100 mg twice a day for 10 days and for the next 10 days 100 mg per day. The average age of the 156 women was 32 years old (ranging from 16 to 80) and the average symptoms history was 11 months (ranging from 3 to 96). Until now all the women had been repeatedly treated without long-term improvement in symptoms. The search for the infectious agent in 118 (75.6%) patients proved futile, but in the other 38 (24.4%) an infectious organism was identified (32 – *E. coli*; 3 – *Staphylococcus*; 3 – *Enterococcus*), and 79 (51%) had leukocyturia.

Results. After the treatment with doxycycline, 118 (75.6%) of the women were symptom-free or had a considerable decrease in symptoms for a period of up to 3 months. Amongst the 32 women with infections with *E. coli*, no recurrent infections were confirmed in 25 (16%). Altogether an effective treatment with doxycycline in 143 (91.6%) women was confirmed.

Conclusions. 1. Treatment with doxycycline is effective in 75% of patients with chronic urethral syndrome. 2. We confirmed no recurrent US symptoms up to 3 months after the treatment. 3. This high rate of effectiveness, 91.6%, may also be the result of the simultaneous treatment of the sexual partner.

INTRODUCTION

Urethral syndrome (US) is a term for a complex of symptoms including urethral and bladder pain as well as urinary urgency and frequency and whose diagnosis decision is based on clinical symptoms only. After having seen the internist and gynecologist without effect, the women turned to the urologist. Many women have been complaining about the symptoms for at least months and very often for years. Many of the patients had been repeatedly treated with antibiotics for empirically recurrent urinary infections often with short-term relief, but without any long-term improvement in symptoms. Various studies including bacteriological urinary cultures and urethral swabs do not frequently lead to the identification of the cause of infections. Diagnostic procedures also include ultrasonography (USG) and urodynamics. Sometimes cystourethroscopy reveals increased vascularization and hyperemia of the urethra as well as pseudopapillary papillomas at the bladder neck, all of which we consider to be signs of chronic infections [1]. Doxycycline is a broad-spectrum tetracycline antibiotic that is very effective against many microorganisms, in particular *Chlamydia trachomatis*, *Ureaplasma urealyticum*, and *Mycoplasma genitalium*, which are the most common sexually transmitted diseases [2, 3, 4] that are not detected by routine urinary cultures.

This research presents women with US, without conventional urinary tract infections, who were treated with doxycycline and an antimycotic agent also. The aim of the study was the evaluation of the results of treatment with doxycycline in females with urethral syndrome.

MATERIAL AND METHODS

Between the years 2000 and 2008, in the Outpatients Urological Clinics in Warsaw 156 (100%) women with chronic urethral syndrome were treated with doxycycline. The average age of the women taking part in the study was 32 years old (ranging from 16 to 80). All 156 (100%) patients, with nearly all their sexual partners (some patients were incidentally having sexual intercourse with many partners), were treated with doxycycline; 100 mg twice a day for 10 days and 100 mg per day for the next 10 days. These patients were directed to the urologist after having seen their internist, general practitioner, or gynecologist and after treatment provided only short-term relief, but without any long-term improvement in symptoms. The pain remained in the ostium and/or female urethra, especially during micturition, along with urgent pressures with polyuria and oliguria. No infections were found in cultures and swabs. All patients were sexually active. These conditions constituted the criteria of including doxycycline to the treatment. The exclusive criteria for the study were: acute urinary tract infection, residual urine (greater than 50 ml), a history of oncological therapy, and intermittent or long-term catheterization. All patients suffered from long-term symptoms and the average symptom history was 11 months (ranging from 3 to 96). The examination entailed ultrasound and cytology as well as microbiological urinalysis and urethral and vaginal swabs, which were performed before and one

and three months after the treatment. The condition of the patients was considered to be improved if they reported no pain symptoms, far less urinary frequency and urgency, no dysuria or suprapubic discomfort, or any pain at least three months after the treatment.

RESULTS

Gynecological consultations in all patients did not demonstrate any changes within the genitalia (past history of exudates, infections of the vaginal mucosa or cervix of uterus, although blisters on the mucosa were periodically reported) before the addition of doxycycline. A slight degree of leukocyturia and microhematuria were identified in 79 (51%) women before the treatment with doxycycline. Amongst 118 (75.6%) of the patients no pathogen was detected, but in the other 38 (24.4%) an infectious organism from urethral swabs was identified (in 32 women – *E. coli*; in three – Staphylococci; and in three women – Enterococcus). After the treatment with doxycycline, 118 (75.6%) patients reported subjective improvement or were symptom-free for not shorter than three months. Along with the 32 women with *E. coli* infections, no recurrent infections were confirmed in 25 (16%) of all the patients with US. Altogether the effectiveness of treatment with doxycycline in women with US was confirmed in 143 (91.6%) patients.

DISCUSSION

All the women presented in the study had urinary tract symptoms; like urethral syndrome. Diagnostic testing (ultrasonography, cytology, cultures, and smears) did not show any deterioration or pathology. Amongst these patients the search for an infectious agent often proved futile. After a number of ineffective treatment regimens, patients can be classified as those with cystitis or they may be diagnosed with another ailment and eventually sent, for instance, to a psychiatrist. Often, as a result, young and sexually active women were unable to continue normal lives. Their symptoms incited dyspareunia and neurasthenia, among others. Amongst the treated patients only the following symptoms were stated: a pain located in the female urethra and its ostium that increased during micturition, urgent pressure of urine, frequent urination as well as infrequent urination, and pains in the suprapubic area. Therefore the diagnostics were based on the exclusion of known causes of dysuria – diagnosis of exclusion (infections, tumors, iatrogenic changes, and, in some patients, prior to the exclusion of interstitial inflammation of the bladder during the cystoscopic evaluation).

Sometimes a meticulous examination leads to the identification of an infectious organism. A high percentage of chlamydial infections are asymptomatic (80% in women and 50% in men). In the remaining, the progress manifests itself with ailments of acute urethral syndrome (dysuria, leukocyturia, axenic urine culture, or insignificant bacteriuria) [5]. Infections with Chlamydia are linked to sexual activity and multiple sexual partners. Another study showed that *E. coli* infections can be transmitted by sexual contact [6, 7]. Other infectious factors may be the cause of ailments in the female urethra (*Trichomonas vaginalis* as well as viruses and numerous bacteria). Bacteriuria in women is preceded by colonization of the vagina by Enterobacteriaceae, which are later found in urine [8]. All of these facts confirm the postulation that treatment of the sexual partners is important. The authors have also found out that nearly 48% of women complaining of chronic voiding symptoms had infections with *Ureaplasma urealyticum* or *Mycoplasma hominis* [4]. The detection of chlamydial infections, the most common bacterial cause of sexually transmitted diseases, is difficult [9]. Many tests, including polymerase chain reaction (PCR), are technically demanding and expensive. Serological tests require a high level

of technical expertise. Another dilemma is the high probability of false-negative results. Therefore treatment with doxycycline seems to be an appropriate approach owing to this antibiotics' effectiveness against the common bacterial causes of sexually transmitted diseases, including chlamydial infections [10, 11]. Treatment with doxycycline was introduced due to a number of factors, including: the significant proportion of asymptomatic infections, the general inability to identify Chlamydia with typical methods (they live intracellularly and do not grow on acellular medium), the presence of leukocyturia in urine tests of the patients and their partners, as well as previous history of treatment due to cervical or adnexal infections. Moreover, this decision was based on the fact that ailments of the urinary tract are caused by the same pathogens in both men and women. The treatment regimen in men adheres to the same doses and schedule as for women; not to mention the fact that they were based on experiences thus far of the author of this paper. However, long-term antibiotic treatment can cause side effects such as nausea, vomiting, diarrhea, and fungal infections (treated with antimycotic agent); but considering the 90% chance of cure or improvement, it is considered an acceptable option.

CONCLUSIONS

1. Treatment with doxycycline was effective in 75% of patients with chronic urethral syndrome (US) and 16% of patients with concurrent *E. coli* infection. 2. No recurrent US symptoms, for up to 3 months after treatment, amongst 91.6% of patients were diagnosed. 3. This high success rate circa 91.6% may also be due to the simultaneous treatment of the patients' sexual partner.

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