Ureaplasma male genital infections in an ambulatory urology ward

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Abstract

Introduction: Ureaplasma urealyticum is a member of the normal genital flora in both men and women. In some cases, e.g. mechanical lesions, increased sexual activity, immune deficiency, subnutrition, immune depleting therapy, anticonceptional medication and hperoestrogenemia these infections become symptomatic, causing pelvic inflammatory disease and acute or chronic prostatitis. They can also serve as sources of infections for their partner. Our aim was to analyse the factors that lead to Ureaplasma prostatitis and to follow-up the antibiotic sensitivity changes of the Ureaplasma isolates during a 3 year period.

Material and methods: In the 2010-2013 June period 256 patients were diagnosed with prostatitis in the Marmed Urology Ward, and were tested for Ureaplasma sp. infection. Culturing of urethral swabs were performed on Mycoplasma IST2 medium. Identification and antibiotic susceptibility testing were done and results were read after 48 hours. A growth count greater than 10⁴ colony forming units per mL (CFU/ml) was considered positive. We used 9 used antibiotics, as following: doxycycline (DOT), josamycin (JOS), ofloxacin (OFL), erythromycin (ERY), tetracycline (TET), ciprofloxacin (CIP), azithromycin (AZI), clarithromycin (CLA), and pristinamycin (PRI). The full urological investigation consisted of IPSS, abdominal ultrasound, postmictional residual urine determination, digital rectal examination and uroflowmetry.

Results: 52 of the tested patients presented Ureaplasma sp. infection. Their age ranged from 19 to 69 years, the mean age was 37,62 year; 50,98 % of the patients had ages between 30 and 39 years, 64,71 % living in urban area. In 82,35 % of the cases the leading symptom was dysuria, associated with minimal residual urine, in 23,53 %, while in 19,61 % of the patients - a decreased urine flow. In 78,43 % of the cases the ultrasound examination was normal. Regarding the antibiotic sensitivity, tetracyclines represented the first line of treatment, although, resistance against them is increasing. The isolates presented an increased resistance against fluoroquinolones,thus they could not be used without testing.

Conclusions: The prostatitis caused by Ureaplasma sp. affects mainly middle aged patients and shows an increasing tendency. It is very important to detect and treat correctly all patients in order to prevent the appearence of complications such as infertility.

Key words: antimicrobial therapy, non-gonococcal prostatitis, Ureaplasma infections

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**Introduction, objectives**

Prostatitis appears in approximately 25% of male patients aged 18-55 with lower urogenital symptoms. Almost 35% of male patients develop at least once in their life signs for this disease. Incidence of prostatitis is 6%, prevalence 9% and may have different causes.[1]

The *Ureaplasma* species and *Mycoplasma hominis* are part of the male and female normal genital flora. In some circumstances (immune depletion, changes in local pH, sexual behavior- multiple sexual partners, mechanical lesions) these bacteria become pathogenic. In male patients they cause: non-gonococcal urethritis (NGU), prostatitis, chronic pelvic inflammation, infertility. Transmission is sexual, so it is necessary to treat the sexual partner too, in order to avoid recurrence of the infection. [2]

Prostatitis caused by *Ureaplasma spp.* was enrolled in the year 1998 by the „International prostatitis collaborative network“ in the group of symptomatic prostatitis, more precisely in the group of „Inflammatory pelvic disease, IPD“. [3][4]

Infection caused by *Ureaplasma spp.* has special features that render diagnosis by routine biological methods more difficult. Special culture media and molecular biological methods are needed to identify the isolates. [5]

In our study we examined: the incidence of prostatitis caused by *Ureaplasma urealyticum* infections: investigation of the 269 samples confirmed in 52 cases, 19.33%, the presence of a *Ureaplasma* infection. The 52 positive patients belonged to the five age-groups shown in figure 3.

**Materials and methods**

The investigated group of 269 patients were diagnosed with prostatitis at the „Marmed“ Urological Ambulatory ward between October 2010 and June 2013. Urethral secretions obtained via prostatic massage, Stamey probe, [1][3] were collected on swabs and placed in a special culture medium which favors growth of *Ureaplasma sp.* Gram and Giemsa stained smears were also performed (Fig. 1).

For cultivation of *Ureaplasma sp.* a commercial culture medium – *Mycoplasma IST2*, BioMerieux, France, was used. This enables identification and, simultaneously, antimicrobial susceptibility testing for nine antibiotics: doxycycline- DOT (4 and 8 mg/l), josamycin- JOS (2 and 8 mg/l), ofloxacin- OFL (1 and 4 mg/l), erythromycin- ERY (1 and 4 mg/l), tetracycline- TET (4 and 8 mg/l), ciprofloxacin- CIP (1 and 2 mg/l), azithromycin- AZI (0.12 and 4 mg/l), clarithromycin- CLA (1 and 4 mg/l), pristinamycin- PRI (2 mg/l). (Fig. 2).

After inoculation, the culture media were place in an incubator set to 37°C for 48 hours. The appearance of a pink color in the medium of the cell showing $10^4$ Uu/ml was interpreted as positive result for *Ureaplasma* infection.

**Results**

Incidence of prostatitis caused by *Ureaplasma urealyticum* infections: investigation of the 269 samples confirmed in 52 cases, 19.33%, the presence of a *Ureaplasma* infection.

The 52 positive patients belonged to the five age-groups shown in figure 3.
A correlation between age and frequency of infection was calculated, and the results were the following. For linear correlation (the older the patient, the more likely he/she is to be infected with *Ureaplasma*): \( p=0.27 \) – not significant.

Statistically the most probable age for developing the aforementioned infection was 28.9 years. (for this value, \( p < 0.0001 \) – very significant).

**Distribution of patients by provenience:** from the 52 positive results, 34, respectively 65.38%, lived in urban area, figure 4.

**Distribution of patients by variability of symptoms.**
The symptomatic patients were enrolled in two groups: one with patients having only dysuria and another with patients presenting more than one symptoms (sexual malfunction, pain in the groin, hypogaster and scrotum). A number of 43 cases (82.69%) were associated with lower urinary tract symptoms, and only nine, 17.3%, with multiple symptoms.

**Distribution of patients by the results of ultrasonography** is shown in table 1.

**Table 1. Distribution of patients by ultrasonography**

<table>
<thead>
<tr>
<th>Ultrasound</th>
<th>Number of cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Image without modifications</td>
<td>41</td>
<td>78.85</td>
</tr>
<tr>
<td>Hyperechogenic image</td>
<td>9</td>
<td>17.31</td>
</tr>
<tr>
<td>Hyperechogenic image with conical shadow</td>
<td>2</td>
<td>3.85</td>
</tr>
<tr>
<td>Total number</td>
<td>52</td>
<td>100</td>
</tr>
</tbody>
</table>

A statistical correlation between the number of symptoms and the ultrasonography results was calculated, which resulted in \( p=0.00001 \) – high probability of correlation.

**Distribution of patients by presence of postmictional reziduum:** only 12 patients showed a minimal postmictional residual urine.

**Distribution of patients by Uroflowmetry.** Based on the value of Qmax. we divided patients in 2 groups, one with lower Qmax than 1.5 ml/sec, and the other greater. (fig. 5).

**Antimicrobial susceptibility over the tested years, 2011-2013.** In 2010, we could only identify *Ureaplasma* infections but had no possibilities to test their antibiotic susceptibility, so we ruled out said year from our study. Between 2011-2013 we investigated 30 *Ureaplasma* infections; table 2 illustrates the sensitivity of the *Ureaplasma sp.* isolates, to the nine tested antibiotics, and figure six shows the trend of resistance of *Ureaplasma sp.* isolated from the patients of the Urology ward of Marmed in Târgu- Mureș.

**Table 2. Distribution of the Ureaplasma isolates regarding the antibiotic susceptibility between 2011-2013**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Year 2011</th>
<th>Susceptibility</th>
<th>Year 2012</th>
<th>Susceptibility</th>
<th>Year 2013</th>
<th>Susceptibility</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOT</td>
<td>11</td>
<td>100</td>
<td>9</td>
<td>81.81</td>
<td>6</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>JOS</td>
<td>11</td>
<td>100</td>
<td>11</td>
<td>100</td>
<td>8</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>OFL</td>
<td>6</td>
<td>54.54</td>
<td>6</td>
<td>54.54</td>
<td>6</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>ERY</td>
<td>7</td>
<td>63.63</td>
<td>8</td>
<td>72.72</td>
<td>6</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>TET</td>
<td>11</td>
<td>100</td>
<td>9</td>
<td>81.81</td>
<td>6</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>CIP</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>AZI</td>
<td>9</td>
<td>81.81</td>
<td>9</td>
<td>81.81</td>
<td>7</td>
<td>85.7</td>
<td></td>
</tr>
<tr>
<td>CLA</td>
<td>11</td>
<td>100</td>
<td>10</td>
<td>90.90</td>
<td>8</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>PRI</td>
<td>11</td>
<td>100</td>
<td>11</td>
<td>100</td>
<td>8</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

**Fig. 6. Fluctuation of antibiotic susceptibility of Ureaplasma sp. isolates between 2011-2013.**
Statistical analysis of a correlation between the passage of time (years) and susceptibility of Ureaplasma showed the following results:

- since there are less than 5 values, the value of $p$ will always show a value above 0.05, but we can calculate the coefficient of correlation ($r$):

1. DOT: $r = -0.957$; $r < 0$ – there is a reverse proportionality between the passage of time and susceptibility, the pathogen presented a significant decrease in susceptibility over the years.
2. OFL: $r = 0.866$
3. ERY: $r = 0.957$
4. TET: $r = 0.957$
5. AZI: $r = 0.866$

For antibiotics 2-5 $r > 0$ – there is a direct proportionality between the passage of time and susceptibility, over the years the pathogen presented a significant increase in susceptibility for the 4 antibiotics mentioned above.

6. CLA: $r=0$ there was no correlation between time and susceptibility.

For the remaining antibiotics (JOS, AZI, PRI) the afore mentioned value could not be calculated.

**Discussion**

Prostatitis caused by *Ureaplasma sp.* is difficult to diagnose because in most of the cases symptoms are poor, and identification in the laboratory needs special culture media. Our results show that *Ureaplasma sp.* is not the main cause of prostatitis in the „Marmed“ Urology Ward, the incidence of 19.33% is similar with the one obtained by another study performed in Brescia, Italy, where the incidence was 18.6%.[6]

Patients ranging between 30-39 years (50%) and 19-29 years (25%) of age were the most, while the over 50 years group was the least affected (5.77%). Because this infection spreads via sexual route, the higher incidence in sexually active persons is understandable.

Dysuria was the leading and sometimes the only symptom, present in 82.69% of the cases.

Paraclinical findings, such as ultrasound tests were not relevant for the diagnosis of the disease.

*Ureaplasma sp.* lack cell wall and cannot be destroyed by medicines targeting this area such as penicillin. This is the reason why protein synthesis inhibitors, e.g. tetracyclines, macrolides or DNA replication inhibitors, e.g. fluoroquinolones are primary agents of treatment. Our results show that fluoroquinoline resistance is very elevated; they cannot be used without antibiotic susceptibility testing. Resistance was investigated by a series of authors and results confirm that point mutations of the DNA topoisomerase IV are responsible for this effect. In the literature no plasmid mediated fluoroquinolone resistance was described for *Ureaplasma sp.* [7][8][9][10] Thus the first line of treatment remain the tetracyclines. Our results show that resistance against these agents is significantly decreasing over the years included in our study, possibly due to a tetM gene located in the bacterial chromosome. Ureaplasma strains are constantly reducing their genomic size which leads to recombinations and developing of mosaic tetM gene structures.[11] There were no major changes in macrolide susceptibility in our study, although authors describe mutations harbored in the V domain of the 23S rRNS gene, leading to loss of macrolide activity.[12]

**Conclusions**

*Ureaplasma sp.* infects mainly sexually active people living in urban areas. Periodical screening is very important in order to detect and apply early treatment in these infections. Ultrasound test, uroflowmetry were performed; modifications in the investigated cases were minor and rare. Urethral swabs collected by Stamey method represent a sure diagnostic method for detecting *Ureaplasma* infections. Cultivation identifies bacteria and detects susceptibility to nine antimicrobial drugs. This ensures an adequate treatment. The frequency of fluoroquinolone resistant *Ureaplasma* strains was high. Macrolides and tetracyclines can be used as first intention therapy; the resistance against tetracyclines remained low throughout the investigated period, although it showed a statistically significant decreasing tendency. Our work underlines the importance of antibiotic susceptibility testing in order to apply an adequate treatment. Because *Ureaplasma* infections are sexually transmitted, simultaneous treatment of the sexual partner is compulsory.

**Bibliography**


