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Etiology of Chronic Prostatitis Syndrome in Patients Treated at the University Hospital for Infectious Diseases »Dr. Fran Mihaljević« from 2003 to 2005

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A B S T R A C T

A total of 835 patients with symptoms of chronic prostatitis syndrome and no evidence of structural or functional lower genitourinary tract abnormalities were examined in a three year period at the Outpatient Department for Urogenital Infections, University Hospital for Infectious Diseases »Dr Fran Mihaljević« Zagreb, Croatia. Disease etiology was determined in 482 (57.72%) patients. Chlamydia trachomatis *was proved to be the causative pathogen in 161 patients,* Trichomonas vaginalis *in 85,* Escherichia coli *in 68,* Enterococcus *in 51,* Proteus mirabilis *in 20,* Klebsiella pneumoniae *in 9,* Streptococcus agalactiae *in 15,* Ureaplasma urealyticum *in 49 patients with chronic prostatitis. Other patients had mixed infection. In 257 (53.32%) of 482 patients, the inflammatory finding (>10 WBCs/hpf) was found in EPS or* VB_3*. Normal WBCs/hpf (<10) was found in 103 (63.98%) of 161 patients with symptoms of chronic prostatitis in whom* C. trachomatis *was detected in EPS or* VB_3*, in 50 (58.82%) of 85 patients in whom* Trichomonas vaginalis *was isolated, and in 23 (46.94%) of 49 patients in whom* Ureaplasma urealyticum *was isolated.*

Key words: *chronic prostatitis syndrome, etiology,* Chlamydia trachomatis

Introduction

The term prostatitis syndrome refers to a number of conditions affecting the prostate and is clinically presented with:

1. urethral symptoms (frequency, difficult and urgent urination, burning in the urethra during voiding, thin interrupted voided urine, urethral discharge, prostatorrhea, leukocytospermia),

2. prostatic symptoms (pressure, tension or pain in perineum, groins, lower abdomen and back, testes and epididymes),

3. sexual dysfunction (erectile dysfunction, ejaculatory dysfunction, loss of libido),

4. other symptoms (fatigue, myalgia, headache etc.)[1,2].

Basic factors for the classification of prostatitis syndrome are clinical symptoms and signs and the presence of bacteria and leukocytes in selectively collected urine samples (first voided urine – VB_1, midstream urine – VB_2, urine collected immediately after prostatic massage – VB_3) and in expressed prostatic secretion (EPS) by Meares and Stamey localization technique[3]. Generally accepted classification of prostatitis syndrome differentiates between:

1. acute bacterial prostatitis,
2. chronic bacterial prostatitis,
3. nonbacterial prostatitis,
4. prostatodynia[4]

In December 1995, a new classification system of prostatitis syndrome has been introduced in the USA:

1. acute bacterial prostatitis (ABP) – acute infection of the prostate,

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2. chronic bacterial prostatitis (CBP) – recurrent infection of the prostate,

3. chronic pelvic pain syndrome (CPPS) – no demonstrable infection,

3a. inflammatory CPPS – chronic abacterial prostatitis – white cells in expressed prostatic secretions / voided bladder urine$_3$ (VB_3),

3b. non-inflammatory CPPS – no white cells in EPS /VB_3,

4. asymptomatic inflammatory prostatitis (AIP) – no subjective symptoms detected either by prostate biopsy or the presence of white blood cells (WBC) in prostate secretions during evaluation for other disorders[5].

Symptoms, clinical signs and microscopic finding of expressed prostatic secretion during inflammatory chronic pelvic pain syndrome with no demonstrable infection and chronic bacterial prostatitis are not different[6]. Chronic bacterial prostatitis is the most common cause of relapsing urinary tract infection in men. It is manifested by longer asymptomatic period between episodes of recurrent bacteriuria. Pathogens of chronic bacterial prostatitis are also causing other urinary tract infections. Patients with inflammatory chronic pelvic pain syndrome – no demonstrable infection – have no history of previously diagnosed urinary infection, and bacteriological analysis of urine sample and EPS by standard methods cannot prove the infectious nature of the disease. Controversy regarding the role of chlamydia, ureaplasma, and mycoplasma in the pathogenesis of prostatitis continues[7–10]. Therefore, *Chlamydia trachomatis*, *Ureaplasma urealyticum*, *Mycoplasma hominis* and *Trichomonas vaginalis* findings in EPS of some patients cannot be ignored[11–18].

The aim of this prospective study was to investigate the etiology and the role of unusual pathogens in chronic prostatitis syndrome (bacterial prostatitis, inflammatory as well as noninflammatory chronic pelvic pain syndrome).

Patients and Methods

The study was conducted at the Outpatient Department for Urogenital Infections, University Hospital for Infectious Diseases »Dr Fran Mihaljević« Zagreb, Croatia, between January 1, 2003 and December 31, 2005. The Ethics Committee of the hospital approved the study.

Patients

We examined a total of 835 patients, older than 18 years of age, with symptoms of chronic prostatitis syndrome (bacterial prostatitis, inflammatory as well as noninflammatory chronic pelvic pain syndrome) and no evidence of structural or functional lower genitourinary tract abnormalities, of urethritis or urethral pathogens by culture.

Diagnostic criteria

The inclusion criteria for *chronic prostatitis syndrome* was the duration of symptoms for at least three months.

The inclusion criteria for *chronic bacterial prostatitis* were:

- presence of clinical symptoms
- a bacterial count of 10^3 cfu/ml or more (if only Gram-positive cocci are found in EPS, a bacterial count of 10^4 cfu/ml or more is required), and 10 or more WBC_s/hpf (including macrophages) in EPS or VB_3, or
- finding of 10 or many times greater number of bacteria in EPS and urine bladder sample collected immediately after prostatic massage, than in first voided urine or midstream urine, and
- presence of 10 or more WBC_s/hpf in EPS or VB_3.

The inclusion criteria for *chronic prostatitis caused by C. trachomatis* were:

- presence of clinical symptoms,
- presence of *C. trachomatis* in EPS or VB_3
- absence of *C. trachomatis* in urethral swabs
- absence of other possible pathogens of chronic prostatitis in urethral swabs, EPS or VB_3.

The inclusion criteria for *chronic prostatitis caused by Ureaplasma urealyticum or Mycoplasma hominis* were:

- presence of clinical symptoms
- presence of *U. urealyticum* or *M. hominis* in EPS or VB_3,
- absence of *U. urealyticum* or *M. hominis* in urethral swabs
- absence of other possible pathogens of chronic prostatitis in urethral swabs, EPS or VB_3.

The inclusion criteria *for chronic prostatitis caused by T. vaginalis* were

- presence of clinical symptoms
- presence of *T. vaginalis* in EPS or VB_3
- absence of *T. vaginalis* in urethral swabs
- absence of other possible pathogens of chronic prostatitis in urethral swabs, EPS or VB_3.

The inclusion criteria for *nonbacterial prostatitis or inflammatory chronic pelvic pain syndrome* were

- presence of clinical symptoms
- presence of ten or more WBC/hpf in EPS or VB_3
- presence of other possible nonbacterial pathogens in EPS or VB_3
- absence of possible bacterial pathogens of chronic prostatitis in urethral swabs, EPS or VB_3.

The inclusion criteria for *non-inflammatory chronic pelvic pain syndrome* were

- presence of clinical symptoms of prostatitis syndrome
- no white cells in EPS or VB_3
- absence of possible pathogens of chronic prostatitis in urethral swabs, EPS or VB_3.

Methods

The following data were obtained for each patient: anamnesis, clinical status including digitorectal prostatic examination, urethral swab specimen and selective samples of urine and EPS, according to the 4-glass localization test.

Urethral swab specimens were analyzed for *Chlamydia trachomatis, Trichomonas vaginalis, Ureaplasma urealyticum* and *Mycoplasma hominis*. In segmented samples of urine (VB_1, VB_2, VB_3) and EPS we determined the number of leukocytes and the number of Gram-positive and Gram-negative bacteria in 1 ml of sample.

EPS and urine sample collected immediately after prostatic massage were analyzed for the presence of *Chlamydia trachomatis, Ureaplasma urealyticum, Mycoplasma hominis* and *Trichomonas vaginalis*.

Quantitative segmented cultures and bacterial identification in three voided urine samples and EPS as well as bacteriological analysis of urethral swabs were performed at the Laboratory for Clinical Microbiology of the University Hospital for Infectious Diseases »Dr. Fran Mihaljević«, Zagreb, Croatia, with standard microbiological methods. The diagnosis of urogenital mycoplasma was confirmed by semiquantitative culturing and antimicrobial susceptibility test Mycoplasma duo and S.I.R Mycoplasma test (Bio Rad Laboratories). The diagnosis of *Trichomonas vaginalis* was confirmed by culturing on DIAMOND modified medium. *Chlamydia trachomatis* was proved in urethral swabs / EPS / urine sample collected immediately after prostatic massage, by isolation on McCoy cells and immunofluorescent typing with monoclonal antibodies (Croatian Institute for Public Health, Zagreb, Croatia) or by DNA/RNA hybridization method (hospital's laboratory).

Results

In our study an infectious etiology in patients with chronic prostatitis syndrome was determined in 482 (57.72%) patients (Table 1.). The analysis of the etiology of chronic prostatitis syndrome in 835 patients showed that *Chlamydia trachomatis*, *Trichomonas vaginalis* and *Ureaplasma urealyticum* were the causative pathogens in one third (295/835 – 35.33%) of our patients with chronic prostatitis syndrome. In 257 (53.32%) of 482 patients, the inflammatory finding (>10 WBCs/hpf) was found in EPS or VB_3. Normal WBCs/hpf (<10) was found in 103 (63,98%) of 161 patients with symptoms of chronic prostatitis in whom *C. trachomatis* was detected in EPS or VB3, in 50 (58,82%) of 85 patients in whom *Trichomonas vaginalis* was isolated, and in 23 (46,94%) of 49 patients in whom *Ureaplasma urealyticum* was isolated.

In 113 (76.35%) of 148 patients in whom *E.coli, Enterococcus, P. mirabilis or Klebsiella pneumoniae* were detected in EPS or VB_3, the inflammatory finding (>10 WBCs/hpf) was found in EPS or VB_3.

In 10 (66.67%) of 15 patients in whom *Streptococcus agalactiae* was isolated in EPS or VB_3, the inflammatory finding (>10 WBCs/hpf) was found in EPS or VB_3.

Discussion and Conclusion

Pathogens of bacterial prostatits also cause urinary infections[1,2]. These are *Escherichia coli, Klebsiella pneumoniae, Morganella* spp, *Enterococcus* spp and significantly rare *Pseudomonas aeruginosa*. Prostatitis pathogens are bacteria capable of replicating in prostate, causing relapsing urinary tract infections and can be detected in expressed prostatic excretion. Therefore, it is questionable whether coagulase negative staphylococci, *Staphylococcus aureus*, micrococci, streptococcus outside group D and diphtheroids, can be considered pathogens of bacterial prostatitis[1,2,6]. Of special interest is to clarify the etiological meaning of group B streptococcus[19]. *Streptococcus agalactiae* often colonizes vagina, and causes urinary tract infections and perinatal complications. Men can acquire *Streptococcus agalactiae* from their partners and vice versa. *Staphylococcus aureus* is also described as pathogen causing hospital acquired prostatitis in patients with permanent urinary catheter[20]. Several patients with prostatitis were described in whom *Staphylococcus epidermidis* eradication from EPS was accompanied by significantly reduced clinical symptoms and with disappearance of polimorphonuclear leukocytes from EPS[21].

In the 835 analyzed patients with etiologically proved chronic prostatitis, *Escherichia coli* was detected in 68 (8.14%) of patients, *Enterococcus* in 51 (6.11%) *Proteus mirabilis* or *Klebsiella pneumoniae* in 29 (3.48%), and *Streptococcus agalactiae* in 15 (1.80%), while 23 (2.75%) patients had mixed infection.

Chlamydia trachomatis is a Gram-negative intracellular bacterium with special lifecycle of development and growth. It is the most common bacterial pathogen causing sexually transmitted diseases and the most frequent cause of epididymitis in patients up to 35 years of age[22,23]. More than half of the infected persons have asymptomatic form of infection or very mild clinical course, which is one of the reasons for its non recognition and untreatment thus leading *Chlamydia trachomatis* to be the constant source of infection among general population[25].

Chlamydia trachomatis was proved to be the only causative agent of prostatitis syndrome in 161 (19.38%) patients with etiologically proved chronic prostatitis syndrome. We believe that the role of *Chlamydia trachomatis* in chronic prostatitis has been underestimated so far. Since *Chlamydia trachomatis* is a bacterium, chlamydial prostatitis should be classified as chronic bacterial prostatitis as was suggested by other authors as well[26].

It is significant that *Trichomonas vaginalis* was the causative pathogen in 85 patients, which makes 10.18% of patients with etiologically proved chronic prostatitis, and *Ureaplasma urealyticum* in 49 (5.87%) patients. In 257 (53.32%) of 482 patients, the inflammatory finding

TABLE 1
THE ETIOLOGY OF CHRONIC PROSTATITIS SYNDROME IN PATIENTS TREATED AT THE UNIVERSITY HOSPITAL FOR INFECTIOUS DISEASES »DR. FRAN MIHALJEVIĆ« FROM 2003 TO 2005

Microorganism confirmed in EPS or VB_3	Patients		
	> 10 WBCs/hpf in EPS (no.)	< 10 WBCs/hpf in EPS (no.)	Total no. **(%)**
Chlamydia trachomatis	58	103	161 (19.28)
Trichomonas vaginalis	35	50	85 (10.18)
Ureaplasma urealyticum	26	23	49 (5.87)
Escherichia coli	53	15	68 (8.14)
Enterococcus	38	13	51 (6.11)
Proteus mirabilis	15	5	20 (2.40)
Klebsiella pneumoniae	7	2	9 (1.08)
Streptococcus agalactiae	10	5	15 (1.80)
Pseudomonas aeruginosa	0	1	1 (0.12)
Mixed infection	15	8	23 (2.75)
None	241	112	353 (42.28)
Total	498	337	835 (100)

(>10 WBCs/hpf) was found in EPS or VB_3. Normal WBCs/hpf (<10) was found in 103 (63.98%) of 161 patients with symptoms of chronic prostatitis in whom *C. trachomatis* was detected in EPS or VB_3, in 50 (58.82%) of 85 patients in whom *Trichomonas vaginalis* was isolated, and in 23 (46.94%) of 49 patients in whom *Ureaplasma urealyticum* was isolated.

The authors hope that the results of this study on chronic prostatitis syndrome pathogens as well as the results of our previous studies will contribute to further clarification of etiology of chronic bacterial prostatitis and inflammatory chronic pelvis pain syndrome and help in determining the empirical antimicrobial therapy[27,28].

We believe it would be interesting to investigate the causative pathogens of prostatitis syndrome in HIV/AIDS patients since the causes of urinary tract infections in these patients are different from those in patients who are not infected with HIV.[29]

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REFERENCES

1. KRIEGER, J. N., Prostatitis, epididymitis and orchitis. In: MANDELL, G. L., J. E. BENNETT, R. E. DOLIN (Eds.): Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. (Elsevier Churchill Livingstone, Philadelphia, 2005). — 2. NABER, K. G., W. WEIDNER, Prostatitis, epididymitis and orchitis. In: COHEN, J., W. G. POWDERLY (Eds.): Infectious Diseases. (Mosby, Edinburgh, 2004). — 3. MEARES, E. M., T. A. STAMEY, Invest. Urol., 5 (1968) 492. — 4. DRACH, G. W., E. M. MEARES, W. R. FAIR, T. A. STAMEY, J. Urol., 120 (1978) 266. — 5. NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASE (NICCK): Executive Summary. (Chronic Prostatitis Workshop, Bethesda, 1995). — 6. SCHAEFFER, A. J., Braz. J. Urol., 26 (2000) 122. — 7. BRUNNER, H, W. WEIDNER, H. G. SCHIEFER., J. Infect. Dis., 147 (1983) 807. — 8. POLETTI, F., M. C. MEDICI, A. ALINOVI, M. G. MENOZZI, P. SACCHINI, G. STAGNI, M. TONI, D. BENOLDI., J. Urol., 134 (1985) 691. — 9. DOBLE, A., B. J. THOMAS, M. M. WALKER, J. R. HARRIS, R. O. WITHEROW, D. TAYLOR-ROBINSON, J. Urol., 141 (1989) 332. — 10. EUROPEAN ASSOCIATION OF UROLOGY: Guidelines on urinary and male genital infections. (Drukkerij Gelderland bv, Arnhem, 2002). — 11. SCHAEFFER, A. J., Int. J. Antim. Agents., 11 (1999) 205. — 12. OHKAWA, M., K. YAMAGUCHI, S. TOKUNAGA, T. NAKASHIMA, S. FUJITA, Br. J. Urol., 72 (1993) 918. — 13. CHIARINI, F., A. MANSI, P. TOMAO, V. GENTILE, F. DE MARCO, S. BRUNORI, L. WONGHER, F. DI SILVERIO, J. Chemother., 6 (1994) 238. — 14. SHORTLIFFE, L. M., R. G. SELLERS, J. SCHACHTER, J. Urol., 148 (1992) 1461. — 15. MARUTA, N., Hinyokika. Kiyo., 38 (1992) 297. — 16. GUMUS, B., A. Z. SENGIL, M. SOLAK, T. FISTIK, E. ALIBEY, E. A. CAKMAK, M. YETER, Scand. J. Urol. Nephrol., 31 (1997) 449. — 17. KADAR, A, M. BUCSEK, M. KARDOS, G. CORRADI, Orvosi. Hetilap., 136 (1995) 659. — 18. VERGES, J., J. Urol. Nephrol., 85 (1979) 357. — 19. PROCOPION, M., D. GENNE, P. ABBET, N. DEFABIANI, S. ROHEN, R. AUCKENTHALER., Clin. Infect. Dis., 27 (1998) 403. — 20. MEARES, E. M. Jr., Infect. Dis. Clin. North. Am., 1 (1987) 855. — 21. ARAKAWA, A, S. KAMIDONO, Infection., 20 (1994) S232. — 22. STAMM, W. E., R. B. JONES, B. E. BATTEIGER, Chlamydia trachomatis (trachoma, perinatal

infections, lymphogranuloma venereum and other genital infections). In: MANDELL, G. L., J. E. BENNETT, R. E. DOLIN (Eds.): Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. (Churchill Livingstone, Philadelphia, 2005). — 23. PECHERE, J. C., (Ed.): Intracellular bacterial infections. (Cambridge Medical Publications, Worthing, 1996). — 24. HOOSEN, A. A., N. O'FARRELL, J. VAN DEN ENDE, Genitourin. Med., 69 (1993) 361. — 25. SCHACHTER, J., Chlamydia trachomatis infections: epidemiology and disease spectrum. In: ORIEL, J. D., J. R. W. HARRIS (Eds.): Sexually transmitted diseases. (Churchill-Livingstone, Edinburg, 1986). — 26. BJERKLUND JOHANSEN, T. E., R. N. GRÜNEBERG, J. GUIBERT, A. HOFSTELLER, B. LOBEL, K. G. NABER, J. PALON REDORTA, P. J. VAN CANGH, Eur. Urol., 34 (1998) 457. — 27. SKERK, V., S. SCHONWALD, I. KRHEN, L. MARKOVINOVIC, A. BEUS, N. S. KUZMANOVIC, V. KRUZIC, A. VINCE, Int. J. Antimicrob. Agents., 19 (2002) 471. — 28. SKERK, V., I. KRHEN, S. SCHÖNWALD, V. CAJIC, L. MARKOVINOVIC, S. ROGLIC, S. ZEKAN, A. TAMBIC ANDRASEVIC, V. KRUZIC, Int. J. Antimicrobial. Agents., 24 (2004) S53. — 29. SCHONWALD, S., J. BEGOVAC, V. SKERK, Int. J. Antimicrob. Agents., 11 (1999) 309.

ETIOLOGIJA SINDROMA KRONIČNOG PROSTATITISA U BOLESNIKA LIJEČENIH U KLINICI ZA INFEKTIVNE BOLESTI »DR. FRAN MIHALJEVIĆ«, ZAGREB U RAZDOBLJU OD 2003. DO 2005. GODINE

S A Ž E T A K

Ukupno je 835 bolesnika sa simptomima sindroma kroničnog prostatitisa i bez dokazanih strukturalnih ili funkcionalnih abnormalnosti donjeg genitourinarnog sustava pregledano u trogodišnjem razdoblju u Ambulanti za urogenitalne infekcije Klinike za infektivne bolesti »Dr. Fran Mihaljević«, Zagreb. Etiologija bolesti dokazana je u 482 (57,72%) bolesnika. *Chlamydia trachomatis* je dokazana kao uzročnik bolesti u 161 bolesnika, *Trichomonas vaginalis* u 85, *Escherichia coli* u 68, *Enterococcus* u 51, *Proteus mirabilis* u 20, *Klebsiella pneumoniae* u 9, *Streptococcus agalactiae* u 15, te *Ureaplasma urealyticum* u 49 bolesnika. Ostali bolesnici su imali miješanu infekciju. Ukupno 257 (53,32%) od 482 bolesnika imalo je upalni nalaz u EPS-u ili VB_3. Normalan broj leukocita dokazan je u EPS-u ili VB_3 u 103 (63,98%) od ukupno 161 bolesnika sa simptomima kroničnog prostatitisa u kojih je dokazana *Chlamydia trachomatis*, u 50 (58,82%) od 85 bolesnika s izoliranom *Trichomonas vaginalis*, te u 23 (46,94%) od 49 bolesnika u kojih je izolirana *Ureaplasma urealyticum*.