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Epidemiological Features and Resistance Pattern in Uropathogens Isolated from Chronic Bacterial Prostatitis

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Chronic bacterial prostatitis (CBP) is, usually, caused by uropathogens, especially gram-negative bacilli, although infection is sometimes due to Gram-positive and atypical microorganisms. A recent increasing in prevalence of Gram-positive strains has been reported. The aim of this study was to explore the epidemiological features and resistance rates in uropathogens isolated from CBP outpatients in last 10 years. All consecutive outpatients with demonstrated CBP attending a single Sexually Transmitted Disease centre from January 1997 and December 2008, were enrolled and underwent microbiological cultures in first void early morning urine, midstream urine, expressed prostatic secretion, and post prostate massage urine. Prevalence of different bacterial strains was stratified in four different periods: 1997-1999, 2000-2002, 2003-2005, 2006-2008. Any changes observed in epidemiological features and resistance rates in uropathogens over the whole study period have been analyzed. The present study has been planned, thus, as in vitro study. From 6,221 patients, 4,601 Gram-positive and 1,620 Gram-negative bacterial strains have been isolated. *Enterococcus faecalis* and *Escherichia coli* strains are the first and second frequent pathogens found, respectively. Significant differences between *E. faecalis* prevalence in the 1997-1999 and 2006-2008 periods were found. *E. coli* showed a significant difference between prevalence in 1997-1999 and 2006-2008 periods. Gram-positive organisms showed a decreasing of susceptibility to ciprofloxacin as well as Gram-negative strains, while a good susceptibility to the levofloxacin was evidenced. *E. faecalis* prevalence seemed to be raised in 2006-2008 periods. Moreover, a decreasing of activity of ciprofloxacin and a good activity profile of levofloxacin have been reported.

***Keywords*:** bacterial prostatitis, Gram-positive, Gram-negative, antibacterial agents, antibiotic susceptibility

Chronic prostatitis still represents an enigmatic and poorly understood entity (Krieger *et al.*, 2003; Krieger, 2004; Walz *et al*., 2007). Several clinical researches and trials have been encouraged by the latest classification of the National Institutes of Health (NIH) (Krieger *et al*., 1999) that stimulated a different approach to the disease as well as prevalence studies determining information on epidemiology, morbidity and social-economic weight of this condition (Krieger *et al*., 2008). The term "prostatitis" suggests its inflammatory origin, probably related to infective agents or microrganisms although chronic bacterial prostatitis (CBP) account approximately only 5% to 10% of all cases clinically found (Naber *et al*., 2001; McNaughton-Collins *et al*., 2007). Most of the infectious agents are from the Enterobacteriaceae family (Naber *et al*., 2001; Mazzoli, 2007; Krieger *et al*., 2008). These bacteria reflect the spectrum of organisms known to cause urethritis, urinary tract infection, or deeper genital infections. Other causative agents include Enterococcus, Pseudomonas, Staphylococcus species, Gonococcal organisms (Potts and Panye, 2007) or other atypical organisms (Krieger and Riley, 2004; Motrich *et al*., 2006; Mazzoli *et al*., 2007; Türk *et al*., 2007; Nickel and Xiang, 2008). However, the probable low prevalence of diagnosed CBP should be due either to the difficulty in new organisms identification or due to a substantial lack in microbiological methods used for the diagnosis (Weidner *et al*., 2002). Another point to consider in treating CBP patients is the increasing rate of antibiotic resistance. Current problems in treating CBP, therefore, include the emergence of extended spectrum beta-lactamase-producing *Escherichia coli*, the tendency of fluoroquinolones both to select for resistant strains of major CBP pathogens and to induce cross-resistance among different drug classes, and beta-lactam and vancomycin resistance of enterococci and coagulase-negative staphylococci (Ena *et al*., 2006; Wagenlehner *et al*., 2008b). The aim of this study was to explore the epidemiological features and resistance rates in uropathogens isolated from a large CBP outpatient in last 10 years.

Materials and Methods

Study design

The present study has been planned to evaluate the epidemiological features and resistance rates in bacteria isolated from prostatitis outpatients in a period of 10 years. In the present study no information about therapy, clinical outcome or follow-up data have been reported.

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The present study has been planned, thus, as in vitro study. All consecutive patients with symptoms and signs suggestive of chronic prostatitis attending the same Sexually Transmitted Disease Centre from January 1997 and December 2008, were eligible for this study. The analysis has been restricted only to patients with laboratory-confirmed diagnosis of CBP [Category II - National Institute of Health (NIH) classification] (Krieger *et al*., 1999). Inclusion criteria were the presence of symptoms related chronic prostatitis for at least 3 months, according to the NIH classification guidelines (Krieger *et al*., 1999), and a positive Meares-Stamey (M&S) 4-glass test. We used the term positive M&S test for all tests in which bacterial load in expressed prostatic secretion (EPS), or in post prostate massage urine (VB3) is at least 1,000 colony forming units per millilitre and at least 10 times higher than in first void early morning urine (VB1) and midstream urine (VB 2). All patients were symptomatic according to the Italian version of the NIH-Chronic Prostatitis Symptom Index (CPSI) (Giubilei *et al*., 2005) with cut-off for symptomatic CBP of 15. Patients under 18 years of age, affected by major concomitant diseases, with urethral strictures, acute urethritis with urethral discharge or neurological bladder voiding disturbances were excluded. Furthermore, all patients positive to cytological urine analysis or who had previously undergone prostate surgery or who had undergo antibiotics for 4 weeks prior to the study were also excluded. All patients with more than one isolated bacteria or positive to tests for *Chlamydia trachomatis*, Trichomonas vaginalis, Urogenital Mycoplasmata, *Neisseria gonorrhoeae*, HSV and HPV were also excluded. Moreover, in order to exclude also all patients with urethritis resulting from *Chlamydia trachomatis* infections, each patient underwent urethral swab. The present study has been planned as retrospective observational study in a specific patients population and has been approved by the local research ethical committee. Data from each patient have been obtained from our prostatitis database (Advanced PROSTATitis DataBase, Microsoft Access format).

Microbiological procedures

From each patient, four biological samples were collected: VB1, VB 2, EPS, VB3. VB1, VB2 samples were collected and immediately taken to the laboratory under refrigerate conditions. Each patient at the arrival at our STD Centre underwent prostatic massage and EPS and VB3 samples collection. Then, each sample underwent microbiological cultures for common bacteria and yeasts, DNA extraction, polymerase chain reaction (PCR), and mucosal IgA evaluation for Ct diagnosis as described in our previous studies (Mazzoli, 2007; Mazzoli *et al*., 2007). Moreover, all samples were cultured 48 h at 37°C for urogenital mycoplasma on Urèe-Arginine Lyo 2 broth (bioMérieux, Switzerland), and positive samples were subjected to identification and drug susceptibility test by Mycoplasma IST (bioMérieux). In accordance with Nickel the white blood cell (WBC) counts in all biological samples were obtained due to the fact that the combination of high bacterial counts and lacking WBC in VB1, VB2, and VB3 is a strong sign for contamination or normal colonization of the anterior urethra (Nickel *et al*., 2003). All collected samples were cultured at 37°C in a 5% CO_2 enriched atmosphere on Columbia agar with 5% sheep blood, on the same medium supplemented with colistin and nalidixic acid, on ThayereMartin agar, on vaginalis agar and on MacConkey agar without CO_2 (bioMérieux) for the detection of *Gardnerella vaginalis*, *Neisseria gonorrhoeae*, and other Gram-negative and Gram-positive bacteria as well as trichomonas and yeast-like fungi (*Candida* spp.). Roiron broth and Sabouraud agar were used for the cultivation of *Trichomonas vaginalis* and *Candida* spp., respectively. The antimicrobial susceptibility testing, moreover, has been performed according to standard methods guidelines of Clinical and Laboratory Standards Institute (CLSI) (http://www.clsi.org). Mucosal secretion IgA analyses were performed by using the same methods described in our previous paper (Mazzoli *et al*., 2007).

Statistical analysis

As null hypotheses we assume that: 1) No differences between bacteria isolated prevalence in the last 10 years have been found, 2) No difference between Gram-negative and Gram-positive strains prevalence in study period have been found, 3) No difference in antibiotic susceptibility over the entire study period have been reported. The difference between strains prevalence per year has been evaluated by using T-test or chi square test when appropriate. ANOVA test has been used for evaluating significant differences between means of each isolated bacteria. Moreover, the Mann-Whitney test was also used to compare different parameter mean values. Statistical significance was achieved if p was <0.05. All reported p-values are two-sides. All statistical analyses were performed by using SPSS 11.0 for Apple-Macintosh (SPSS, Inc., USA).

Results

15,930 were considered for this study. 673 patients were excluded for lack of data collection and 15,257 consecutive patients were analyzed. Then, 6,221 patients (mean age 37.3,

Table 1. Patient anamnestic and clinical characteristics at enrolment time

No. of total patients	15,257	
Median age (±SD*) (range)	37.3±7.9	(18-44)
Sexually active (past month)	13,568	(88.9)
Clinical data		
Clinical presentation		
Dysuria	7,524	(49.3)
Urgency	7,689	(50.3)
Dysuria+Frequency	5,497	(36.0)
Burning	2,123	(13.9)
Pain		
Yes	13,564	(89.4)
No	1,693	(10.6)
Perineal	7,023	(51.6)
Scrotal	3,452	(25.3)
Suprapubic	2,414	(17.6)
Lower Abdominal	765	(5.5)
Pain frequency		
Daily frequency	12,815	(83.9)
Weekly frequency	749	(16.1)
Sexual symptoms		
ED	5,332	(34.9)
PE	5,578	(36.5)
ED+PE	784	(5.1)
Sexual desire abnormalities	687	(4.5)
Start of CBP history (months)	7.8±9.2	
Symptoms Score at baseline (mean) (range)		
NIH-CSPI	18.62	(15-28)

SD, Standard Deviation; ED, Erectile dysfunction; PE, Premature ejaculation; CBP, chronic bacterial prostatitis; NIH-CSPI, National Institutes of Health-Chronic Prostatitis Symptom Index

Table 2. Microbiological culture results and organism identification over the all study period

Enrolled patients	15,257	
Positive patients	6,221	
Gram-positive	4,601	
Gram-negative	1,620	
	Number of positive patients	Percentage
Isolated bacteria		
Enterococcus faecalis	2,745	44.0
Enterococcus faecium	101	1.4
Staphylococcus aureus	280	4.4
Staphylococcus haemolyticus	640	10.1
Staphylococcus epidermidis	327	5.2
CONS	154	2.4
Streptococcus agalactiae	267	4.2
Other Streptococci	87	1.2
Acinetobacter spp.	8	0.1
Citrobacter spp.	80	1.2
Enterobacter spp.	78	1.2
Escherichia coli	698	11.1
Proteus mirabilis	142	2.2
Klebsiella oxitoca	144	2.3
Klebsiella pneumoniae	100	1.5
Morganella morgani	120	1.7
Proteus mirabilis	142	2.2
Pseudomonas aeruginosa	44	0.6
Pseudomonas putida	16	0.1
Serratia marcescens	190	2.9

ranging from 18 to 44) meet all the inclusion and exclusion criteria were finally considered for this study. All patients attended our centre coming from the all Italian regions. All anamnestic and clinical data at enrolment are shown in Table 1.

Table 3. Microbiological culture results and organism identification stratified per year collection

	Study period (years)				*p*
	'97-'99	*'00-'02*	*'03-'05*	*'06-'08*	
Total cultured bacteria	1092	1138	1281	2710	
Isolated bacteria					
Enterococcus faecalis	360	389	746	1250	<0.001 (I)
Enterococcus faecium	40	41	8	12	<0.001 (D)
Staphylococcus aureus	131	132	9	8	<0.001 (D)
Staphylococcus haemolyticus	150	150	39	301	<0.001 (I)
Staphylococcus epidermidis	30	30	9	258	<0.001 (I)
CONS	12	12	40	90	<0.001 (I)
Streptococcus agalactiae	77	80	23	87	n.s.
Other Streptococci	13	13	18	43	n.s.
Acinetobacter spp.	1	1	2	4	n.s.
Citrobacter spp.	10	10	29	31	n.s.
Enterobacter spp.	11	11	28	28	n.s.
Escherichia coli	110	118	149	321	0.0095 (I)
Klebsiella oxitocia	12	13	39	80	<0.001 (I)
Klebsiella pneumoniae	15	15	22	48	n.s.
Morganella morgani	11	11	31	67	0.0006 (I)
Proteus mirabilis	20	23	54	45	n.s.
Pseudomonas aeruginosa	8	8	18	10	n.s.
Pseudomonas putida	1	1	6	8	n.s.
Serratia marcescens	80	80	11	19	<0.001 (D)

p, difference between prevalence in 1997-1999 and 2006-2008 years period. (I), increasing; (D), decreasing; n.s., no statistically significant

Microbiological results

From 15,257 analyzed patients, 45,871 genitourinary samples have been collected and analyzed. 9,036 patients have been excluded due to: a) 4,013 positive to Chlamydia trachomatis, b) 3,558 positive to more than one isolated bacteria, c) 1,010 positive to Urogenital Mycoplasmata and/or *Neisseria gonorrhoeae* and/or genitourinary viruses. 6,221 bacterial strains have been, finally, isolated from all biological samples. 1,092 bacterial strains have been isolated in the 1997-1999 period, while 1138, 1281, and 2710 in the 2000-2002, 2003-2005, 2006-2008 period, respectively. 4,601 Gram-positive (73.9%) and 1,620 Gram-negative (26.1%) strains have been isolated in the all study period. Gram-positive strains are the most common isolated bacteria, with a prevalence statistically higher than Gram-negative prevalence ($p<0.001$). *Enterococcus faecalis* is the most frequent pathogen with prevalence per study period of 32.9%, 34.1%, 58.2%, and 46.1% respectively. Moreover, *E. coli* is the second most frequent pathogen with a prevalence of 10%, 10.3%, 11.6%, and 11.8%, respectively. Table 2 shows all microbiological findings over the all study period while Table 3 all microbiological results stratified by collection years. From all patients, 4,601 Gram-positive strains have been isolated. Among all Gram-positive bacteria, *E. faecalis* is the most frequently isolated strain, with isolation prevalence per year of 44.2%, 45.9%, 83.6%, and 61.0%, respectively. Therefore, we found a statistically significant difference between the *E. faecalis* prevalence in the 1997-1999 and 2006-2008 year period (44.2% sd=0.49 *vs* 61.0% sd=0.48; t-value of difference: -8.165; df-t: 1466; $p<0.001$). In the last years we noted an increasing prevalence of *Staphylococcus epidermidis* from 3.6% in 1997-1999 to 12.5%, with a statistically significance difference ($p<0.001$ - t-value of difference: -9.018; df-t: 2523). In the last years we found a decreasing prevalence of *Enterococcus faecium* from 4.9% (sd= 0.216) in the 1997-1999 year to 0.5% (sd=0.076) in the 2006-2008 years (t-value of difference: 5.578; df-t: 893; $p<0.001$). *Staphylococcus aureus* strains showed the same decreasing prevalence [from 16.1% (sd=0.368) in the 1997-1999 year to 0.4% (sd=0.062) in the 2006-2008 years (t-value of difference: 12.125; df-t: 830; $p<0.001$)]. On the other hand, coagulase-negative staphylococci (CoNS) showed a slight prevalence increasing from 1.5% (sd=0.121) to 4.4% (sd=0.205) in the last years (t-value of difference: -4.707; df-t: 2458; $p<0.001$). 1,620 Gram-negative strains have been isolated. *E. coli* is the most frequently isolated strain, with an isolation prevalence per year of 39.4%, 40.5%, 38.3%, 48.5% respectively. We found a statistically significant difference between the *E. coli* prevalence in the 1997-1999 and 2006-2008 year period (39.4% sd=0.489 *vs* 48.5% sd=0.5; t-value of difference: -2.601; df-t: 533 $p=0.0095$). A decreasing prevalence of *Serratia* spp. from 28.6% (sd=0.452) in the 1997-1999 years to 2.8% (sd=0.167) in the 2006-2008 years has been found (t-value of difference: 9.266; df-t: 310 $p<0.001$). Moreover, increases of *Klebsiella oxitoca* and *Morganella morgani* prevalence have been found from the 1997-1999 to 2006-2008 years [from 4.3% (sd=0.203) to 12.1% (sd=0.326) ($p<0.001$) and from 3.9% (sd=0.195) to 10.1% (sd=0.302) ($p<0.001$) respectively].

Antibiotic susceptibility

The mean susceptibility rates for the antibacterial studied, over the all study period, are summarized in Table 4. Levofloxacin, lomefloxacin and tetracycline were tested from 2002, 2001 and 200, respectively. In particular, we noted that norfloxacin showed a substantial invariant activity rates in the all study period against the major of Gram-positive strains, such as *E. faecalis*, while showed a increasing resistance rate against

Table 4. Mean susceptibility rates (%) for the all antibacterial studied over all study period

	Antimicrobial agents tested								
	Norfl	Cipro	Levo	Lome	Tetra	Pip/Taz	Trim/Sulf	Genta	Nitro
Isolated bacteria									
E. faecalis	88.5	96.7	99.5	80	15.6	100	99.5	88	99.75
E. faecium	65.75	68.75	85	70	18.33	99.5	99.5	89	99.5
S. aureus	65.75	70.75	70	67	50	nt	91.7	90.5	89
S. haemolyticus	63.5	66	65	60	57.3	nt	91.5	81	84.2
S. epidermidis	68	61.2	73	66	51.6	nt	75	97.2	72.2
CONS	67.5	61.2	73	66	51.6	nt	75	97.2	72.2
Str. agalactiae	72.2	71.5	83.5	66	74	nt	83.2	91	76.7
Other Streptococci	71.7	78	79	65	74	nt	87	89.5	70.5
Acinetobacter spp.	83.2	83.5	90	78	64.6	100	83.7	90.7	70
Citrobacter spp.	88.7	89.5	93	80	65	96.7	90.5	92.5	70.2
Enterobacter spp.	89	90.7	96.5	80	59.3	99.5	99	91.2	79
E. coli	82	90.7	88.5	80	55	68.5	77.5	85.5	86.2
K. oxytoca	91.5	91.7	96.5	89	69.6	98.2	92.7	89.5	78.5
K. pneumoniae	90.7	91.5	96.5	89	66.6	98.2	90.7	90.7	81
M. morganii	91.7	95	96.5	80	69.3	98.2	91.2	91.2	90.2
P. mirabilis	90.7	91.5	97.5	90	66.6	99.7	89.5	82.5	81.5
P. aeruginosa	73.2	69.5	89.5	88	nt	89.5	nt	nt	nt
P. putida	73.2	70.2	88	89	nt	89.2	nt	nt	nt
S. marcescens	74.2	72.2	80.5	70	66.6	89	nt	nt	nt

nt, not tested.

Table 5. Mean susceptibility rates (%) for the all antibacterial studied stratified by each study period

	Isolated bacteria (Gram-positive)							
Antimicrobial agents tested	*E. faecalis*	*E. faecium*	*S. aureus*	*S. haemoliticus*	*S. epidermidis*	*CONS*	*Str. agalactiae*	Other Streptococci
Norfloxacin								
1997-1999	89	66	66	70	70	70	71	73
2000-2002	90	67	66	62	66	67	70	70
2003-2005	85	63	65	60	70	66	78	74
2006-2008	90	67	66	62	66	67	70	70
Ciprofloxacin								
1997-1999	99	75	72	68	68	60	74	78
2000-2002	97	66	70	65	67	60	70	77
2003-2005	94	68	71	66	68	65	72	80
2006-2008	97	66	70	65	67	60	70	77
Levofloxacin								
2003-2005	100	85	65	60	78	71	79	78
2006-2008	99	85	75	70	80	75	88	80
Nitrofurantoin								
1997-1999	100	99	87	88	96	74	74	72
2000-2002	100	99	89	80	99	70	70	70
2003-2005	99	100	90	89	90	75	75	70
2006-2008	100	100	90	80	100	70	88	70
Gentamicin								
1997-1999	90	90	92	85	95	100	98	90
2000-2002	86	88	90	81	90	100	88	89
2003-2005	90	90	90	77	90	89	90	90
2006-2008	86	88	90	81	90	100	88	89
Trimet-sulfam								
1997-1999	100	100	95	95	95	85	85	90
2000-2002	100	100	90	91	90	70	80	80
2003-2005	98	98	92	89	89	75	88	98
2006-2008	100	100	90	91	90	70	80	80
Tetracycline								
2000-2002	11	15	45	56	65	50	75	75
2003-2005	25	25	60	60	71	55	72	72
2006-2008	11	15	45	56	65	50	75	75

Serratia spp., *Pseudomonas* spp. or *Morganella* spp. Moreover, susceptibility of *E. faecium* to ciprofloxacin decreased from 75% to 66%, while susceptibility of *E. faecalis* and *E. coli* remained invariant. In addition, *Serratia* spp., *Pseudomonas* spp., *Morganella* spp., and *Klebsiella* spp. susceptibility to ciprofloxacin showed the same decreasing. On the other hand, levofloxacin activity against *E. faecalis* and *E. faecium* remains high while, in the last period (2006-2008), is higher than the other study periods against *Staphylococcus aureus*, *Staphylococcus haemolyticus*, *Streptococcus agalactiae*, *Enterobacter* spp., *E. coli*, *Morganella morgani*, and *Proteus mirabilis*. However, all susceptibility rates for the antibacterial studied, stratified by each study period, are summarized in Table 5 and Table 6.

Discussion

CBP patients management has been recently described by Murphy by focusing several key-points (Murphy *et al*., 2009): 1) the first therapeutic approach is a 4- to 6-week course of a fluoroquinolone, which provides relief in 50% of men and is more efficacious if prescribed soon after symptoms begin, 2) patients with chronic bacterial prostatitis experience recurrent episodes of bacterial urinary tract infection caused by the same organism, usually *E. coli* or other Gram-negative organisms. Thus, the questions are: Why has fluoroquinolone treatment other than another compound been chosen? Are still *E. coli* or other Gram-negative organisms the most common isolated bacteria from CBP patients? These questions stimulated our microbiological survey on prostatitis patients. Several authors highlighted that CBP was mainly caused by Gram-negative uropathogens and the role of Gram-positives, atypicals, and anaerobes was still debatable (Schaeffer, 2006; Naber, 2008). Clinical series of patients used to support approval of antibiotics for treatment of CBP have reported a predominance of Gram-positive cocci (Wagenlehner *et al*., 2008a). In our large outpatient study population, we found a higher prevalence of Gram-positive other than Gram-negative bacteria. The difference becomes more evident during the last study years. This finding is particularly significant foregrounding the importance of a correct microbiological evaluation of each CBP patient to plan a correct treatment strategy schedule. Moreover, Wagenlehner indicated that the increasing trend of Gram-positive infections should be justified with the improved clinical use of fluoroquinolones for CBP patients treat-

Table 6. Mean susceptibility rates (%) for the all antibacterial studied stratified by each study period

	Isolated bacteria (Gram-negative)										
	Citrobacter spp.	*Enterobacter.* spp.	*Acinetobacter.* spp.	*E. coli*	*K. oxytoca*	*K. pneumoniae*	*M. morganii*	*P. mirabilis*	*P. aeruginosa*	*P. putida*	*S. marcescens*
Norfloxacin											
1997-1999	85	88	89	87	91	91	95	95	80	80	85
2000-2002	80	89	89	80	90	90	90	90	70	70	70
2003-2005	88	89	89	81	95	92	92	88	73	73	72
2006-2008	80	89	89	80	90	90	90	90	70	70	70
Ciprofloxacin											
1997-1999	86	90	90	90	95	95	95	95	70	75	78
2000-2002	80	89	90	89	90	90	95	90	69	68	70
2003-2005	88	90	93	95	92	91	95	91	70	70	71
2006-2008	80	89	90	89	90	90	95	90	69	68	70
Levofloxacin											
2003-2005	90	93	96	87	95	95	95	95	90	87	81
2006-2008	90	93	97	90	98	98	98	100	89	89	80
Nitrofurantoin											
1997-1999	70	71	74	77	78	79	82	85	nt	nt	nt
2000-2002	67	71	80	89	78	80	89	80	nt	nt	nt
2003-2005	70	68	82	90	80	85	90	81	nt	nt	nt
2006-2008	73	71	80	89	78	80	100	80	nt	nt	nt
Gentamicin											
1997-1999	95	95	95	84	90	90	95	93	nt	nt	nt
2000-2002	89	90	90	84	89	89	90	80	nt	nt	nt
2003-2005	90	95	90	90	90	95	90	77	nt	nt	nt
2006-2008	89	90	90	84	89	89	90	80	nt	nt	nt
Trimet-sulfam											
1997-1999	90	90	100	78	93	93	95	90	nt	nt	nt
2000-2002	80	90	98	76	90	90	90	89	nt	nt	nt
2003-2005	85	92	100	80	98	90	90	90	nt	nt	nt
2006-2008	80	90	98	76	90	90	90	89	nt	nt	nt
Tetracycline											
2000-2002	65	66	60	55	70	65	70	65	nt	nt	65
2003-2005	64	63	58	55	69	70	68	70	nt	nt	70
2006-2008	65	66	60	55	70	65	70	65	nt	nt	65

ment (Wagenlehner *et al*., 2008b). On the other hand the fluoroquinolone treatment choice was often oriented by the need of antimicrobial agents with optimal pharmacokinetic properties, properly indicated to easily reach both prostatic secretion and prostate tissue (Schaeffer, 2006). Fluoroquinolones are mainly indicated in CBP treatment because of recent evidences showed surviving bacteria in prostate tissue due to a biofilm protected milieu (Mazzoli, 2010) and fluoroquinolones seemed to be more active in biofilm than other antimicrobials such as beta-lactamases or aminoglycosides (Bundrick *et al*., 2003). In our series we found a high prevalence of *E. faecalis* and *E. coli* that have been reported as strong biofilms producers (Mazzoli, 2010). We found that levofloxacin activity against both Gram positive and negative strains is very high, if compared with the other fluoroquinolones such as ciprofloxacin or norfloxacin. Levofloxacin has been, then, reported as an agent that has good microbiological activity against the pathogens that cause the vast majority of infections of the prostate, due to its excellent penetration properties into extracellular fluid as well as into cells (Drusano *et al*., 2000; Bundrick *et al.*, 2003; Arslan *et al*., 2005). On the other hand, the recent increasing resistance to ciprofloxacin, found in the all strong biofilms producers, have been reported also in other studies and it should be taken into account when the CBP patient treatment will be planned (Arslan *et al*., 2005). In this sense, should be discussed also the recent increasing of Nitrofurantoin activity against *E. faecalis*, *E. faecium*, *S. agalactiae*, *E. coli*, and *M. morgani*. This finding is probably due to the decreasing in nitrofurantoin prescription observed in the last years. However, nitrofurantoin demonstrated poor penetration properties into prostate cells and should not be indicated for prostatitis patient management (Fowler, 2002). Moreover increased bacteria isolated resistance to trimethoprim-sulfamethoxazole, probably due to the discriminated used of this drug in CBP patients have been recently evidenced (Fowler, 2002). In conclusion antimicrobial susceptibility testing of such bacterial strains should be interpreted as initial indication for appropriate antibiotic treatment, taking into account pharmacological and pharmacokinetical proprieties of each drug. The our study, however, shows few limitations that should be taken into account in findings interpretation: 1) the methods used in our clinical laboratory for selecting particular bacterial col-

onies for antimicrobial susceptibility testing changed in the last years; 2) the our study population is a population of patients attending an Sexually Transmitted Diseases clinic; 3) no data about the our prostatitis patient management have been reported. Significant increasing prevalence of *E. faecalis* strains in the last years compared with a lower incidence of gram negative strains in CBP patients biological fluids indicated that appropriate and personalized antibiotics treatment should be chosen for each patient. Levofloxacin seemed to be more indicated than ciprofloxacin in the treatment of Gram positive bacteria. Due to these reasons microbiological evaluation of each CBP patients is essential to plain a correct treatment schedule.

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