Methods and Findings in Experimental and Clinical Pharmacology 2010, 32(1): 39-45

CCC: 0379-0355/2010
DOI: 10.1358/mf.2010.32.1.1423885

ORIGINAL ARTICLE

CLINICAL AND MICROBIOLOGICAL EFFICACY OF PRULIFLOXACIN FOR THE TREATMENT OF CHRONIC BACTERIAL PROSTATITIS DUE TO *CHLAMYDIA TRACHOMATIS* INFECTION: RESULTS FROM A PROSPECTIVE, RANDOMIZED AND OPEN-LABEL STUDY

T. Cai[1,2], S. Mazzoli[3], P. Addonisio[3], V. Boddi[4], P. Geppetti[1] and R. Bartoletti[2]

[1]Department of Preclinical and Clinical Pharmacology, University of Florence, Florence, Italy; [2]Department of Critical Care Medicine and Surgery, Urology Unit, University of Florence, Florence, Italy; [3]STD Centre, Santa Maria Annunziata Hospital, Florence, Italy; [4]Department of Public Health, University of Florence, Florence, Italy

SUMMARY

The purpose of this study was to compare the efficacy of a 14-day course of prulifloxacin 600 mg with standard antibiotic therapy for the treatment of chronic prostatitis due to Chlamydia trachomatis (Ct) infection. All patients with clinical and instrumental diagnosis of bacterial chronic prostatitis (CP) due to Ct infection were enrolled. After randomization, all patients were administered oral prulifloxacin 600 mg once daily for 14 days or doxycycline 100 mg orally twice daily for 21 days. At enrollment and 30 days after beginning treatment, all patients underwent microbiological cultures for uropathogens bacteria and yeasts, DNA extraction and mucosal IgA evaluation for Ct diagnosis, seminal plasma IL-8 evaluation and serum IgA and IgG anti-Ct analysis. The National Institutes of Health - Chronic Prostatitis Symptom Index (NIH-CPSI) was given to each patient. A total of 109 patients received prulifloxacin and 102 received standard therapy. Prulifloxacin had clinical efficacy rates equivalent to standard therapy (82.5% vs. 79.9%) (P = 0.08) and showed superior microbiological efficacy rates compared to standard therapy, in terms of decreasing mucosal IgA (P < 0.001) and IL-8 levels (P < 0.001). Prulifloxacin was also equivalent to standard therapy for clinical success, as demonstrated by a decrease in the number of patients affected by CP due to Ct infection.

INTRODUCTION

Chronic prostatitis (CP) is an important socio-economical problem and is a very common health condition that affects patients' quality of life (QoL) (1, 2). We have recently observed an overall prevalence of chronic prostatitis patients in Italy (13.7%), particularly in young males (mean age 34.9 years) (3). Moreover, recent reports have shown that *Chlamydia trachomatis* (Ct) can cause symptomatic infection in the lower genital tract of males and could have a possible role in CP pathogenesis (4, 5). However, it is still debatable whether Ct can cause prostatitis because of the technical difficulties in localizing the pathogen to the prostate (6). The incidence of Ct infections in everyday clinical practice is increasing due to the fact that they are the most prevalent sexually transmitted bacterial infections worldwide, affecting couple's reproductive health (7, 8). For the management and treatment of patients with Ct infections, the following factors should be taken into account: a) *Chlamydia* are only metabolically active in the host cell and therefore only targeted intracellularly by antibiotics and b) intracellularly accumulated antibiotics are tetracyclines, macrolides and quinolones (9, 10). Doxycycline and azithromycin are the most widely prescribed drugs for the treatment of Ct infections, although other fluoroquinolones such as ofloxacin and levofloxacin are suggested as alternative drugs (10). Although little is known about Ct survival in the presence of fluoroquinolones in patients with prostatitis, it is well known that after multiple cultivation passages resistant mutants for some fluoroquinolones have been described (11). In a recent report, Smelov et al. suggested that ofloxacin can be recommended as the primary

Correspondence: Tommaso Cai, MD, Department of Urology, University of Florence, via dell'Antella 58, 50011 Florence, Italy. E-mail: ktommy@libero.it.

drug in the treatment of *Chlamydia*-infected patients with CP because of its pharmacokinetic profile (11). Moreover, the same authors stated that the decision to prescribe pefloxacin or lomefloxacin should be made on an individual basis. They concluded that the conditions of in vitro susceptibility studies are incompatible with in vivo studies so it would be useful to investigate antibiotic susceptibility in patients with CP and Ct prior to treatment (11).

We focused our attention on a new fluoroquinolone antibacterial agent: prulifloxacin. Although no pharmacological or pharmacodynamic data on the activity of prulifloxacin against Ct have been reported in the literature, it is known that prulifloxacin has a long elimination half-life, allowing once-daily administration, and is generally more active in vitro than other fluoroquinolones against a variety of clinical isolates of Gram-negative bacteria (12, 13). Prulifloxacin has been shown to be generally well tolerated and had good efficacy in the treatment of urinary tract infections in comparison with the most widely used drugs, in particular in the management of CP due to uropathogens and in the prophylaxis for transrectal prostate biopsy (14-16). The principal aim of the present study was to compare the efficacy of a 14-day course of once-daily orally administered prulifloxacin 600 mg with standard antibiotic therapy (doxycycline 100 mg p.o. twice daily for 21 days) for the treatment of chronic prostatitis CP due to Ct infection.

MATERIALS AND METHODS

Study design

All patients with clinical and instrumental diagnosis of bacterial CP due to Ct infection, attending the same Sexually Transmitted Disease (STD) Centre from March 2007 to May 2008, were eligible for the study. This was a prospective, randomized, open-label study of two parallel treatment arms of patients with CP due to Ct, that included a selection visit and one follow-up visit, as described below. Inclusion criteria were the presence of bacterial CP (National Institute of Health classification, class IIb (17). In accordance with EAU guidelines, all patients underwent total PSA determination, digital rectal examination (DRE), transrectal ultrasonography (TRUS) and Meares-Stamey 4-glass test with total ejaculate collection, to define site and etiology of the infection (9). Genital samples were collected from each patient in accordance with indications described in our previous report: first void early morning urine (VB1), mid-stream urine (VB2), expressed prostatic secretion (EPS), post-prostate massage urine (VB3) and total ejaculate (TE) (18). In order to exclude patients with urethritis due to Ct infections, an urethral swab was taken from all patients. The 4-glass test indicates bacterial prostatitis only if the bacterial load in EPS or in VB3 is at least 1000 colony-forming units (CFU)/mL and at least 10 times higher than in VB1 and VB2. Moreover, we used the term "positive M&S test" for all tests where the presence of a significant number of bacteria in EPS and/or VB3 was found. Moreover, only patients with VB3 and/or EPS positive to Ct infection were enrolled (9). The symptoms related to prostatitis were measured by using the Italian version of the National Institutes of Health - Chronic Prostatitis Symptom Index (NIH-CPSI) (19). In accordance with Nickel et al. prostatitis-like symptoms were considered significant by a pain score of ≥ 4 (20). The NIH-CPSI was also used to determine clinical therapy efficacy (21). Patients under 18 and over 45 years of age affected by major concomitant diseases or known anatomical abnormalities of the genital and urinary tract, those who had previously undergone prostate surgery, patients allergic to fluoroquinolones, patients who had recently (< 4 weeks) been treated with oral or parenteral antimicrobial agents or who were currently using prophylactic antibiotic drugs, as well as patients with urinary or total ejaculated cultures positive for uropathogens were excluded from the study. All patients with a history of liver and/or renal failure were also excluded. We enrolled only patients at their first diagnosis of bacterial CP due to Ct infection in order to obtain a homogeneous cohort of patients to treat. We used the term CP due to Ct for all patients where the presence of mucosal anti-Ct IgA and/or Ct plasmid DNA had been found by using the same methods and criteria described in our previous paper (22). Moreover, all patients positive to urethral swab for Ct, uropathogens bacteria, fungi or other pathogens, were also excluded. The study was approved by a local research ethical committee. Written informed consent was obtained from all patients before treatment. The study was conducted in line with Good Clinical Practice guidelines, with the ethical principles laid down in the latest version of the Declaration of Helsinki and with the applicable laws and regulations of Italy, where the study was conducted.

Sample collection and laboratory procedures

Each patient underwent microbiological cultures for uropathogens bacteria and yeasts, DNA extraction and mucosal IgA evaluation for Ct diagnosis. All samples were collected and immediately taken to the laboratory under refrigerated conditions and analyzed for cultures and aliquot for DNA extraction and polymerase chain reaction (PCR) as described previously (22, 23). Moreover, natural human-produced IL-8 concentration was determined in TE of all subjects by the solid-phase enzyme-linked immunosorbent assay (ELISA) Quantikine IL-8 Immunoassay (R&D Systems, Minneapolis, MN, USA) (22). All samples were tested in duplicate in agreement with the manufacturer's recommendations. The medium minimal detectable dose (MDD) of the IL-8 assay was 3.5 pg/mL. Normal value was considered < 31.2 pg/ml (22). In accordance with Nickel et al. the white cell counts in all biological samples were obtained but not considered in this study (24). All patients also underwent serum IgA and IgG anti-Ct analysis. Blood sample collection was performed upon arrival at the STD Centre. Serum IgA, IgG and genital secretion IgA analyses were performed by using the same methods described in our previous paper (22). In brief, mucosal IgA was detected by IPAzyme Chlamydia IgG/IgA by Savyon Diagnostics (Ashdod, Israel), an immune-peroxidase test, with a modification of the original method by overnight incubation and, thereafter, processing the samples in agreement with the manufacturer's recommendations (22). In accordance with a previous study, we assigned a value in "plus" (i.e., from 1+, 2+, to 20+) in order to quantitatively define the level of mucosal IgA found in all samples (22). The "plus" value was dependent on the color intensity of intracellular inclusion caused by Ct present in the infected fibroblasts used as antigen in the method and evaluated by microscopic reading (400X) (22). Anti-Ct mucosal IgA level evaluation was carried out in all genital collected samples.

Qualitative control for PCR procedure

This STD Laboratory is registered for the UK national external quality assessment (NEQUAS) for microbiology for the molecular detection of Ct (Quality Assurance Laboratory. Health Protection Agency Centre for Infection, 61 Colindale Avenue, London NW 95HT, UK).

Study and treatment schedule

Patients who met the inclusion criteria were treated with oral prulifloxacin 600 mg once daily for 14 days or doxycycline 100 mg orally twice daily for 21 days, according to a 1:1 randomization (Fig. 1). In accordance with Bjerklund Johansen et al., who stated that the minimum duration of antibiotic treatment should be 2-4 weeks, we decided to use a 14-day treatment course in order to decrease adverse effects related to a long treatment course with fluoroquinolones (25). All patients were contacted by telephone on day 14 of therapy to be sure about the correct timing and dose treatment. All patients were scheduled for follow-up visits at 30 days after the end of therapy. At the follow-up visit a questionnaire, VB1, VB2, EPS, VB3, TE cultures and serum were collected. The main outcome measure was the clinical and microbiological cure rate at the end of the entire study period. Treatment efficacy was evaluated by means of the NIH-CPSI. A decrease of 4 points in the NIH-CPSI was considered as significant. Patients were considered microbiologically cured if they were negative for all tested Ct-related laboratory parameters. Clinical failure was defined as the persistence of clinical symptoms after treatment or discontinuation of treatment due to significant reported adverse effects. Moreover, microbiological failure was defined as persistence of one or more tested Ct-related laboratory parameters after treatment. The sexual partners of all patients were treated at the same time according to with their gynecologists' suggestions. Efficacy data regarding sexual partners are not shown in this paper since it was not one of the study aims. Moreover, in order to avoid a new infection after treatment, patients were asked to use sexual abstinence or condoms up to the follow-up visit.

Statistical analysis

Two-sided 95% confidence intervals of the differences between the success rates (prulifloxacin minus doxycycline) were calculated by using Mantel-Haenszel weighting (26). For prulifloxacin to be considered less effective than the comparator drug, the lower limit of each one of these confidence intervals had to be greater than –10%. The two tailed t-test for independent samples was used to compare QoL by outcome and adverse events. Chi-square test was used to evaluate the relationship between the QoL questionnaire and the other parameters. Fischer's exact test was also used to assess the significance of other statistical analyses. $P < 0.05$ was considered to be statistically significant . All reported P values are two-sided. All statistical analyses were performed by using SPSS 11.0 for Apple-Macintosh (SPSS, Inc., Chicago, IL, USA).

RESULTS

From a total population of 343 patients affected by bacterial CP due to Ct infection, 221 patients were finally enrolled and randomized. Among 122 patients excluded from the study, 31 refused to be enrolled, 31 reported adverse effects to quinolones, 37 chose to be treated in another center and 23 reported a previous tendon pain or rupture (Fig. 2). All anamnestic and clinical data at enrollment time are shown in Table I. No statistically significant differences between the groups were reported.

Clinical presentation

All clinical findings are shown in detail in Table I. However, all patients had had dysuria and/or pain for at least 3 months. Moreover, no patients had hematuria, hemospermia or fever.

Laboratory and questionnaire results at baseline

All patients were negative for uropathogens bacteria and yeast in all tested samples. A total of 173 of 211 patients (81.9%) were positive for mucosal IgA anti-Ct and negative for Ct-DNA amplifications, and 38

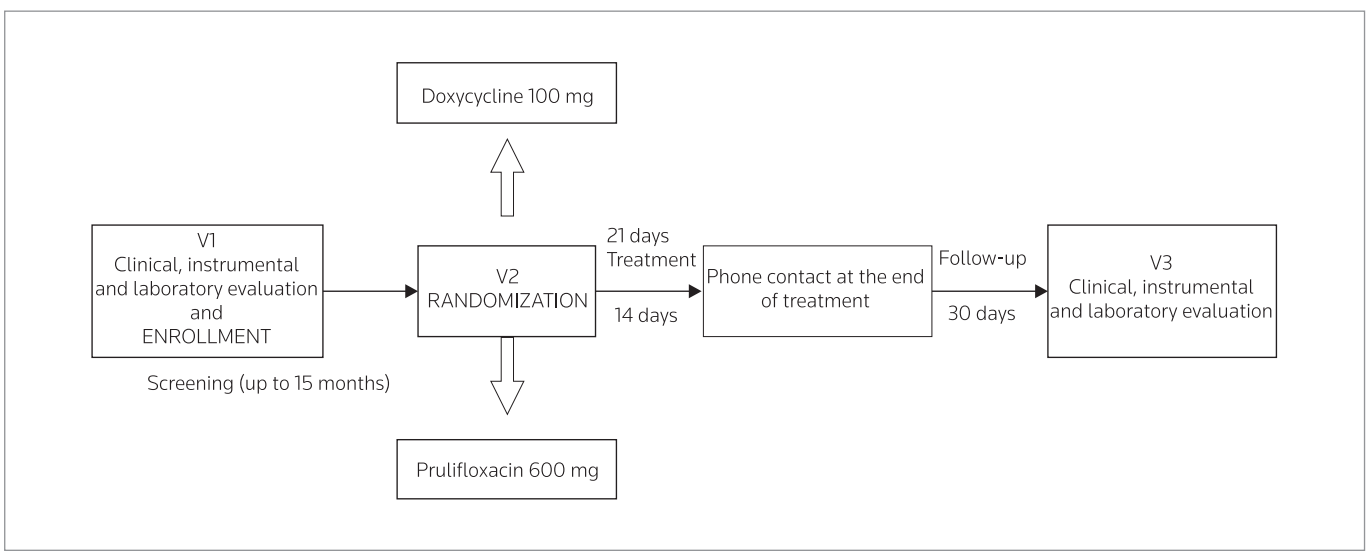

Figure 1. Study design and treatment schedule.

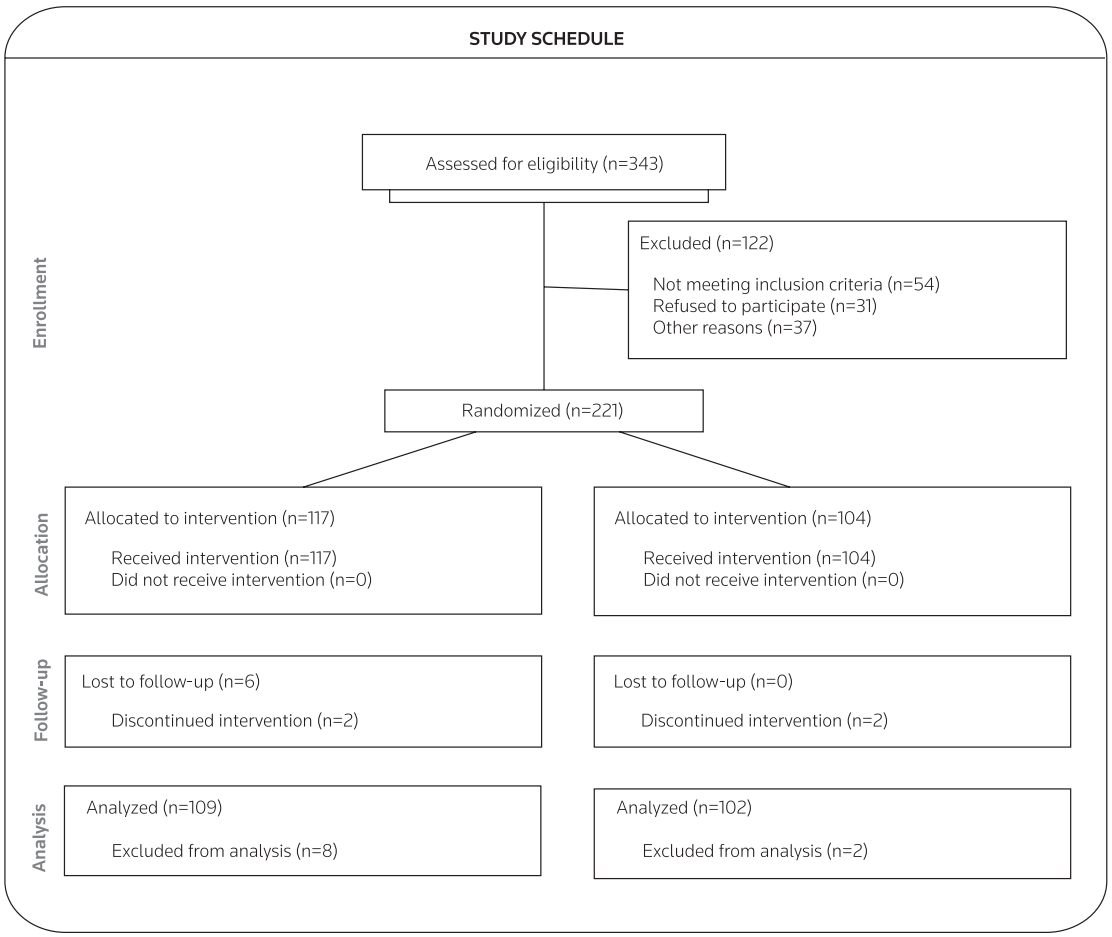

Figure 2. The flow of participants through each stage of the study, in accordance with CONSORT guidelines.

(18.1%) were positive for both mucosal IgA anti-Ct and Ct-DNA amplifications. Mucosal IgA levels ranged from 3+ to 20+ with a mean value of 10.5+. Significant levels of IL-8 were found in TE from 160 of 211 patients (75.8%). Serum IgA anti-Ct were found in 69 of 211 (32.7%), and serum IgG anti-Ct were found in 48 (22.7%). Moreover, serum IgA and IgG were found in 26 (12.3%) patients. IL-8 values ranged from 568 to 1200 pg/ml (mean, 728 pg/ml). Total NIH-CPSI score was 15.61 (range: 13-26) for all patients (all groups). In Table II, all laboratory findings at baseline evaluation are shown according to the groups.

Randomization

A total of 117 patients received prulifloxacin and 104 received standard therapy. Treatment arms were comparable for all variables at both enrollment and randomization visit.

Adherence to treatment schedule and adverse effects

A total of 109 patients were evaluated (93.1%) in the prulifloxacin arm (6 lost at follow-up, 2 discontinued intervention for gastroenterical adverse effects) and 102 patients in the doxycycline arm (98%) (2 discontinued intervention for gastroenterical adverse effects). Compliance to this study protocol was, therefore, good. Antibiotics were well tolerated in all evaluated patients and there were no significant drug-related side effects. In the prulifloxacin arm, 3 of 109 (2.8%) patients had mild adverse effects which, however, did not require treatment suspension (1 of 3 had nausea and 2 back pain). In the doxycycline arm 2 of 102 patients (1.9%) reported nausea.

Clinical and laboratory results at follow-up examination

In the prulifloxacin arm at 30 days after the end of treatment, 38 of 109 patients (34.9%) showed statistically significant changes in questionnaire results [at baseline, NIH-CPSI 15.61 (range: 13-26); at the follow-up visit, NIH-CPSI 6.5 (0-12)] ($P < 0.001$), although presenting detectable mucosal IgA anti-Ct. However, mucosal IgA anti-Ct levels were lower than those found at baseline evaluation ($P = 0.031$). IL-8 levels were statistically significantly lower than those found at baseline (IL-8 312 ng/mL) ($P < 0.001$). In addition, 52 of 109 (47.7%) showed both statistically significant reduction in NIH-CPSI

Table I. *Patient anamnestic and clinical characteristics at enrollment time.*

Total no. of patients	211	
	Prulifloxacin	Doxycycline
No. of patients	109	102
Median age (± SD*)	35.2 ±7.8	33.1 ±6.9
Sexually active (past month)	107 (98.2)	101(99.0)
Sexual behavior		
1 partner	68/107 (63.5)	62/102 (60.7)
> 1 partners	39/107 (36.5)	60/102 (39.3)
Contraceptive use	37/107 (34.5)	40/102 (39.2)
Condom	27/37 (72.9)	30/40 (75.0)
Coitus interruptus	10/37 (27.1)	10/30 (25.0)
	Clinical data	
Clinical presentation		
Dysuria	53 (48.6)	47 (46.0)
Urgency	68 (62.3)	63 (61.7)
Dysuria + frequency	31 (28.4)	28 (27.4)
Burning	23 (21.1)	24 (23.5)
Pain		
Perineal	57 (52.3)	56 (54.9)
Scrotal	36 (33.0)	33 (32.3)
Suprapubic	9 (8.2)	7 (6.8)
Lower abdominal	7 (6.5)	6 (5.8)
Start of CP# history (months)	6.8 ±7.1	6.3 ±6.9
Symptom score at baseline (mean) (range) NIH-CSPI§	15.61 (13-26)	14.91 (13-26)

SD*, standard deviation; CP#, chronic prostatitis; NIH-CPSI§, Italian version of National Institute of Health - Chronic Prostatitis Symptom Index.

Table II. *Clinical and laboratory data at enrollment and follow-up (all enrolled patients).*

	Prulifloxacin		Doxycycline	
	V1*	V3#	V1*	V3#
Patients with symptoms	109 (100)	19 (17.4)	102 (100)	21 (20.4)
Symptom score (mean) (range) NIH-CPSI§	15.61 (13-26)	6.1 (0-12)	14.91 (13-26)	6.6 (0-12)
Ct† markers - No. (%)				
Urine and seminal plasma				
Ct† plasmidic DNA-positive only	–	–	–	–
Ct† secretory IgA-positive only	89 (81.7)	57 (52.3)	84 (82.3)	60 (58.8)
Both Ct† plasmidic DNA and secretory IgA-positive	20 (18.3)	–	18 (17.6)	2 (1.9)
Ct† secretory IgA levels (mean)	10.4	6.5	10.6	8.9
Serum				
Ct† serum IgA-positive only	35 (32.1)	28 (25.6)	34 (33.3)	27 (26.4)
Ct† serum IgG-positive only	27 (24.7)	28 (25.6)	21 (20.5)	21 (20.5)
Both Ct† serum IgA and IgG-positive	14 (12.8)	10 (9.1)	12 (11.7)	9 (8.8)
IL-8° (seminal plasma) (pg/mL)				
Patients with IL-8 > 31.2 pg/mL	81 (74.3)	57 (52.2)	79 (77.4)	62 (60.7)
Mean levels (range)	712 (568-1200)	312 (132-680)	738 (568-1200)	512 (132-680)

V1*, enrollment visit; V3#, follow-up visit; NIH-CPSI§, Italian version of National Institute of Health - Chronic Prostatitis Symptom Index; Ct†, *Chlamydia trachomatis*; IL-8°, interleukin-8.

scores (NIH-CPSI 5.3 (0-12) and undetectable levels of mucosal IgA anti-Ct and IL-8. At follow-up evaluation, a strong correlation was found between IL-8 and NIH-CPSI decreases (r = 0.73, $P < 0.001$). A good correlation was also found between mucosal IgA levels and NIH-CPSI decreases (r = 0.68, $P < 0.001$). However, 19 patients of 109 (17.4%) had no clinical improvement, with microbiological persistence of Ct infection markers.

In the doxycyline arm at 30 days after the end of treatment, 41 of 102 patients (40.2%) had statistically significant changes in questionnaire results ($P < 0.001$), although presenting detectable mucosal IgA anti-Ct. However, mucosal IgA anti-Ct levels were lower than those found at baseline ($P = 0.06$). IL-8 levels were statistically significantly lower than those found at baseline (IL-8 512 ng/ml) ($P < 0.001$). Moreover, 40 of 102 (39.2%) showed both statistically significant reductions in NIH-CPSI scores (NIH CPSI 6.1 (0 12) and undetectable levels of mucosal IgA anti-Ct and IL-8. At follow-up evaluation, a strong correlation was found between IL-8 and NIH-CPSI decreases found (r = 0.70, $P < 0.001$). A good correlation was also found between mucosal IgA levels and NIH-CPSI decreases (r = 0.71, $P < 0.001$). However, 21 patients of 102 (20.4%) had no clinical improvement, with microbiological persistence of Ct infection markers. No statistically significant differences were found between the baseline and follow-up evaluation in terms of serum anti-Ct antibodies, as reported in the prulifloxacin arm.

All clinical and microbiological results, as well as NIH-CPSI subscale scores at follow-up visit are shown in Table II.

Prulifloxacin showed equivalent clinical efficacy rates to standard therapy [(90 patients showed clinical efficacy (82.5%) vs. 81 patients in the doxycycline arm (79.9%) ($P = 0.08$)]. On the other hand, prulifloxacin showed superior efficacy rates over standard therapy in terms of mucosal IgA ($P < 0.001$) and IL-8 levels ($P < 0.001$) decreasing. Moreover, 19 of 109 patients (17.4%) in the prulifloxacin group and 21 of 102 (20.4%) in the doxycycline group did not show any clinical improvement, with persistence of Ct infection markers, without any statistically significant differences between the two groups ($P = 0.86$).

DISCUSSION

Several authors have suggested that quinolones could be recommended as the primary drug in the treatment of *Chlamydia*-infected patients with CP because of their pharmacokinetic parameters and higher penetration into prostate tissue (16). In addition, a good prostate tissue diffusion obtained with quinolones (27) would allow using antibiotic therapy for a shorter period of time and with fewer complications. In the preset study we compared the efficacy of a 14-day course of once-daily oral administration of prulifloxacin 600 mg with standard antibiotic therapy (doxycycline 100 mg p.o. twice daily for 21 days) for treatment of patients with chronic prostatitis CP due to Ct infection. The two treatment schedules showed good tolerance, with a good compliance of the patients. Prulifloxacin showed equivalent clinical efficacy rates of standard therapy but superior efficacy rates in terms of mucosal IgA and IL-8 levels decreasing. The good treatment efficacy obtained with this shorter course of prulifloxacin in comparison with the doxycycline schedule may have been due to the fact that a long cycle of therapy with tetracyclines or macrolides is related to the bacteriostatic effect of these drugs. On the other hand, prulifloxacin has a bactericidal effect that permits a shorter course of treatment. This pharmacological property could be the reason for the persistence of patients with Ct-DNA expression in the doxycycline group in contrast with the prulifloxacin group. However, in the prulifloxacin group, 19 of 109 patients (17.4%) showed no improvement after treatment. The reason for treatment failure in these patients is probably due to the recent emergence of Ct resistance to fluoroquinolones and macrolides, as demonstrated by Shkarupeta et al., or a probable need for a longer treatment period (28). Future studies should, however, clarify this aspect.

Prulifloxacin superiority in decreasing mucosal IgA and IL-8 levels could be due to the anti-inflammatory effect of quinolones. In fact, the role of proinflammatory cytokines in CP is well established (22, 29). Furthermore, the role of some proinflammatory cytokines in CP due to Ct infection, such as IL-6 or IL-8, is well established and used not only in the diagnosis phase but also in the management and treatment of Ct infections (22, 28, 30). Our results suggest that IL-8 evaluation should be used not only as a Ct infection marker but also as a marker of therapy efficacy. Indeed, a good correlation was found between IL-8 and NIH-CPSI, demonstrating that an improvement in QoL (NIH-CPSI decreases) is related to a decrease in IL-8 levels after therapy. Also, in this study attention was focused on mucosal IgA anti-Ct levels after prulifloxacin treatment. A good correlation was found between mucosal IgA anti-Ct levels and QoL, demonstrating that mucosal IgA anti-Ct levels should also be used as a marker of therapy efficacy. A strong correlation between mucosal IgA levels and IL-8 was also observed, similar to our previous study (22).

Some authors have demonstrated in animal models that a high production of IgA in genital tract secretions seems to be related to the presence, persistence and accumulation of Th2 MoPn cells in the genital tract during chronic infections, with the consequent inability to clear the infection (31). Moreover, in these patients the continued recurrent inflammatory reaction, proven by IL-8 production and determined by the persistent infection (CT-DNA and mucosal IgA), can lead to persistent tissue damage, fibrosis and pelvic pain. Recently it has been shown that increased levels of prostaglandin E_2 (PGE_2), a prostaglandin that is a good inflammatory marker, can be found at increased levels in CP and that PGE_2 can induce IL-8 production by epithelial cells (32, 33). The efficacy of prulifloxacin in the management of CP due to Ct is not only due to an indirect anti-inflammatory effect, mediated by proinflammatory cytokines, on QoL but also to a feasible bactericidal effect on Ct, as demonstrated by the reduction of secretory IgA levels. Our study did not report any correlation between serum IgA or IgG and the other Ct maker of infections, or any significant change before or after therapy, with both prulifloxacin and doxycycline. In fact, the role of serum IgA or IgG anti-Ct in early diagnosis of infection and early treatment has been reported for women's infection, but not yet for males (34).

CONCLUSIONS

In conclusion, the present study demonstrated that prulifloxacin 600 mg once daily for 14 days is equivalent to standard therapy for clinical success and showed superiority over standard therapy in microbiological efficacy rates in terms of decreasing mucosal IgA and IL-8 levels in patients affected by CP due to Ct infection.

ACKNOWLEDGMENTS

We are grateful to all Santa Maria Annunziata Hospital STD members for their technical laboratory assistance, to Professor John Denton for manuscript language revision and to Dr. Laura Piazzini for her help in technical statistics revision.

DISCLOSURES

The authors have no conflict of interest to declare.

REFERENCES

1. Schaeffer, A.J., Landis, J.R., Knauss, J.S. et al. Chronic Prostatitis Collaborative Research Network Group. *Demographic and clinical characteristics of men with chronic prostatitis: The national institutes of health chronic prostatitis cohort study*. J Urol 2002, 168(2): 593-8.
2. Walz, J., Perrotte, P., Hutterer, G., Suardi, N., Jeldres, C., Bénard, F., Valiquette, L., Karakiewicz, P.I. *Impact of chronic prostatitis-like symptoms on the quality of life in a large group of men.* BJU Int 2007, 100(6): 1307-11.
3. Bartoletti, R., Cai, T., Mondaini, N. et al. Italian Prostatitis Study Group. *Prevalence, incidence estimation, risk factors and characterization of chronic prostatitis/chronic pelvic pain syndrome in urological hospital outpatients in Italy: Results of a multicenter case-control observational study.* J Urol 2007, 178(6): 2411-5.
4. Eley, A., Pacey, A.A., Galdiero, M., Galdiero, M., Galdiero, F. *Can Chlamydia trachomatis directly damage your sperm?* Lancet Infect Dis 2005, 5(1): 53-7.
5. Motrich, R.D., Cuffini, C., Oberti, J.P., Maccioni, M., Rivero, V.E. *Chlamydia trachomatis occurrence and its impact on sperm quality in chronic prostatitis patients*. J Infect 2006, 53(3): 175-83.
6. Wagenlehner, F.M., Naber, K.G., Weidner, W. *Chlamydial infections and prostatitis in men.* BJU Int 2006, 97(4): 687-90.
7. World Health Organization. Global Prevalence and Incidence of Selected Curable Sexually Transmitted Diseases: Overview and Estimates. Geneva, Switzerland: World Health Organizzation 1996.
8. Pacey, A.A., Eley, A. *Chlamydia trachomatis and male fertility*. Hum Fertil (Camb) 2004, 7(4): 271-6.
9. Naber, K.G., Bergman, B., Bishop, M.C. et al. *EAU guidelines for the management of urinary and male genital tract infections*. Urinary Tract Infection (UTI) Working Group of the Health Care Office (HCO) of the European Association of Urology (EAU). Eur Urol 2001, 40(5): 576-88.
10. Centers for Disease Control. Sexually Transmitted Diseases Treatment Guidelines. 2002, 51(RR-6): 32-6.
11. Smelov, V., Perekalina, T., Gorelov, A., Smelova, N., Artemenko, N., Norman, L. *In vitro activity of fluoroquinolones, azithromycin and doxycycline against chlamydia trachomatis cultured from men with chronic lower urinary tract symptoms*. Eur Urol 2004, 46(5): 647-50.
12. Keam, S.J., Perry, C.M. *Prulifloxacin.* Drugs 2004, 64(19): 2221-34; discussion 2235-6.
13. Matera, M.G. *Pharmacologic characteristics of prulifloxacin*. Pulm Pharmacol Ther 2006, 19(Suppl. 1): 20-9.
14. Prats, G., Rossi, V., Salvatori, E., Mirelis, B. *Prulifloxacin: A new antibacterial fluoroquinolone.* Expert Rev Anti Infect Ther 2006, 4(1): 27-41.
15. Giannarini, G., Mogorovich, A., Valent, F. et al. *Prulifloxacin versus levofloxacin in the treatment of chronic bacterial prostatitis: A prospective, randomized, double-blind trial*. J Chemother 2007, 19(3): 304-8.
16. Mari, M. *Single dose versus 5-day course of oral prulifloxacin in antimicrobial prophylaxis for transrectal prostate biopsy*. Minerva Urol Nefrol 2007, 59(1): 1-10.
17. Workshop Committee of the National Institute of Diabetes and Digestive and Kidney Disease (NIDDK). Chronic Prostatitis Workshop. Bethesda, MD, Dec 7-8, 1995.
18. Cai, T., Mazzoli, S., Bechi, A., Addonisio, P., Mondaini, N., Castricchi Pagliaia, R., Bartoletti, R. *Serenoa repens associated with Urtica dioica (ProstaMEV), Curcumin and Quercitin (FlogMEV) extracts are able to improve efficacy of prulifloxacin in bacterial prostatitis patients: Results from a prospective and randomized study*. Int J Antimicrob Agents 2009, 33(6): 549-53.
19. Giubilei, G., Mondaini, N., Crisci, A. et al. *The Italian version of the National Institutes of Health Chronic Prostatitis Symptom Index*. Eur Urol 2005, 47(6): 805-11.
20. Nickel, J.C., Downey, J., Hunter, D., Clark, J. *Prevalence of prostatitis-like symptoms population based study using the National Institutes of Health chronic prostates symptoms index.* J Urol 2001, 165(3): 842-5.
21. Walz, J., Perrotte, P., Hutterer, G. et al. *Impact of chronic prostatitis-like symptoms on the quality of life in a large group of men*. BJU Int 2007, 100(6): 1307-11.
22. Mazzoli, S., Cai, T., Rupealta, V., Gavazzi, A., Castricchi Pagliai, R., Mondaini, N., Bartoletti, R. *Interleukin 8 and anti-Chlamydia trachomatis mucosal IgA as urogenital immunologic markers in patients with C. trachomatis prostatic infection*. Eur Urol 2007, 51(5): 1385-93.
23. Mazzoli, S. *Conventional bacteriology in prostatitis patients: Microbiological bias, problems and epidemiology on 1,686 microbial isolates.* Arch Ital Urol Androl 2007, 79(2): 71-5.
24. Nickel, arsgravisJ.C., Alexander, R.B., Schaeffer, A.J., Landis, J.R., Knauss, J.S., Propert, KJ. *Leukocytes and bacteria in men with chronic prostatitis/chronic pelvic pain syndrome compared to asymptomatic controls*. J Urol 2003, 170: 818-22.
25. Bjerklund Johansen, T.E., Grüneberg, R.N., Guibert, J. et al. *The role of antibiotics in the treatment of chronic prostatitis: A consensus statement.* Eur Urol 1998, 34(6): 457-66.
26. Song, J.X., Wassell, J.T. *Samples size for K 2x2 tables in equivalence studies using Cochran's statistic*. Controlled Clinical Trials 2003, 24(3): 378-89.
27. Mehlhorn, A.J., Brown, D.A. *Safety concerns with fluoroquinolones*. Ann Pharmacother 2007, 41(11): 1859-66.
28. Shkarupeta, M.M., Lazarev, V.N, Akopian, T.A. Afrikanova TS, Govorun, V.M. *Analysis of antibiotic resistance markers in Chlamydia trachomatis clinical isolates obtained after ineffective antibiotic therapy.* Bull Exp Biol Med 2007, 143(6): 713-7.
29. Jang, T.L., Schaeffer, A.J. *The role of cytokines in prostatitis*. World J Urol 2003, 21(2): 95-9.
30. Al-Mously, N., Eley, A. *Interaction of Chlamydia trachomatis serovar E with male genital tract epithelium results in secretion of proinflammatory cytokines*. J Med Microbiol 2007, 56(Pt. 8): 1025-32.
31. Hawkins, R.A., Rank, R.G., Kelly, K.A. *A Chlamydia trachomatis specific Th2 clone does not provide protection against a genital infection and displays reduced trafficking to the infected genital mucosa.* Infect Immun 2002, 70(9): 5132-9.
32. Shahed, A.R., Shoskes, D.A. *Correlation of beta-endorphin and prostaglandin E2 levels in prostatic fluid of patients with chronic prostatitis with diagnosis and treatment response.* J Urol 2001, 166(5): 1738-41.
33. Fukuda, E.Y., Lad, S.P., Mikolon, D.P., Iacobelli-Martinez, M., Li, E. *Activation of lipid metabolism contributes to interleukin-8 production during Chlamydia trachomatis infection of cervical epithelial cells.* Infect Immun 2005, 73(7): 4017-24.
34. Mascellino, M.T., Ciardi, M.R., Oliva, A., Cecinato, F., Hassemer, M.P., Borgese, L. *Chlamydia trachomatis detection in a population of asymptomatic and symptomatic women: Correlation with the presence of serological markers for this infection*. New Microbiol 2008, 31(2): 249-56.