NORFLOXACIN IN THE TREATMENT OF CHRONIC BACTERIAL PROSTATITIS

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SUMMARY

The efficacy of norfloxacin in chronic bacterial prostatitis (CBP) was investigated in this prospective study. Twenty-two patients with CBP documented by sequential localization cultures were treated with norfloxacin 2x400 mg orally. The duration of the treatment ranged between 10 and 20 weeks (mean 13.2 weeks). The results of sequential cultures were evaluated after six months and one year from the completion of therapy. Sixteen of the 19 evaluable patients (84 %) had sterile cultures in six months. In one year follow-up, this figure was 79 % (11 patients out of 14). These findings suggest that long-term norfloxacin can cure CBP.

Key Words: Chronic Bacterial Prostatitis, Treatment, Norfloxacin

INTRODUCTION

It is estimated that about 50 % of adult men will experience some type of chronic prostatitis syndrome (CPS) during their lifespan (1). Such a high prevalence of CPS in men attracted much interest from physicians for the management of the syndrome. The use of numerous drugs including various antibiotics and different treatment durations resulted in large scale changes in the mangement over the last 30 years (2,3). One of the infrequent but may be the most challenging cause of CPS is chronic bacterial prostatitis (CBP). This clinical entity has two important features: One is recurrent urinary tract infection and the other is persistence of mainly Gram-negative bacteria in the prostatic secretions(2). The period of treatment in CBP ranged between 10 days to six months with various antimicrobial agents. These studies with many succesful as well as unsatisfactory results were reviewed by Pfau (4) and Nickel(5). This study was undertaken to evaluate the efficacy of long-term norfloxacin treatment in men with CBP.

MATERIALS AND METHODS

The data of this prospective study were collected in three and a half years period (September 1991-February 1995). The men with CPS symptoms such as frequency, urgency, dysuria, genital or pelvic pain and discomfort during ejaculation as well as recurrent urinary tract infection symptoms were evaluated in the outpatient clinic. Possible diseases apart from prostatitis were ruled-out by necessary tests. Patients with CPS other than CBP and the patients with CBP previously treated by norfloxacin were excluded from the trial. Known allergic diathesis to quinolones was another exclusion criterion.

The investigated group with CPS symptoms consisted of the patients with urinary tract infection detected by a midstream urine culture and treated for one week by appropriate antibiotic according to the sensitivity test. Among these patients, twenty-two with CBP, proven by sequential localization cultures described by Meares and Stamey (6), were enrolled in the study. The age range of the patients was between 20 and 56 (median 37). The duration of symptoms before therapy was minimum of eight months (8 months to 7 years) with a mean of 20 months.

Either of the two reguirements fulfilled the CBP diagnosis: 1- The colony count of the pathogen microorganism should be at least ten times more in specimens of expressed prostatic secretion (EPS) or first voided urine after prostatic massage (VB_3) than in urethral (VB_1) or bladder specimen (VB_2); 2- There should be bacterial growth in EPS or VB_3 specimen while VB_1 and VB_2 specimens were sterile (4). Quantitative cultures were done by a surface plate method. After 24 hours of incubation, the colonies were counted and identified by standard methods. Sensitivity to antibacteriel agents was determined by Bauer-Kirby disc diffusion technique (7).

The patients were prescribed 2x400 mg of norfloxacin p.o. when the diagnosis was concluded to be CBP. The drug was scheduled for a minimum of 10 weeks.

If the prostatitis symptoms persised after 10 weeks, the medication was continued two more weeks. Then, if necessary, the duration was increased by four weeks each time. Sequential quantitative cultures with sensitivity tests were performed before and one month, six months, one year and two years after the withdrawal of the drug.

Nitrofurantoin (4x100 mg) was administered 24 hours before the specimen collection in order to sterilize the bladder urine and clear the urethra of prostatic microorganisms without altering the prostatic microbial flora (4,8). Ejaculation was refrained at least five days prior to specimen collection for sufficient prostatic secretion. Although all of the patients were circumcised, glans penis was washed with soap and rinsed by sterile saline prior to collecting the localization cultures. While taking the VB_3 specimen, it was tried to get no more than 10 ml of urine after prostatic massage to prevent the excessive dilution of prostatic secretion with urine. Transrectal ultrasonograhy (TRUS) was applied to patients to see any evidence of prostatic calculi. Chi-square test was used for statistical analysis.

RESULTS

All of the pathogen microorganisms were Gram negative bacteria. All of the microorganisms were detected to be susceptible to norfloxacin according to the sensitivity test. Seven patients ingested norfloxacin for 10 weeks, eight patients for 12 weeks, four patients for 16 weeks and three patients for 20 weeks. Sypmtoms subsided in the patients at most after 20 weeks. The details of the infective microorganisms and the duration of norflaxacin administration is shown on table I.

In the first month control, 20 of the 21 patients (95 %) had post- therapy negative prostatic fluid cultures (Table II). The eradication of the pathogen microorganism could not be achieved in one patient. Of the 22 patients at he beginning of the study, 19 were evaluable at six months. Sixteen (84 %) of these had sterile sequential cultures while urinary pathogens were detected in three. The follow-up of 14 patients was completed after one year. The cultures in 11 patiends (79 %) showed no growth. At the end of the second year, it was possible to contact only 10 patients. Five refused the control, three indicating no symptoms after therapy. The cultures of the all remaining five patients remained sterile.

Relapse was encountered after one month in one patient and after six months in the other. These two patients underwent suppressive therapy with a daily dose of 80 mg trimethoprime and 400 mg sulphametoxazole. One patient experienced reinfection in the sixth month.

TRUS investigations revealed that prostatic calculi were present in seven patients (32 %). The mean duration of the symptoms before norfloxacin therapy in these patients was 49 months (23 to 74 months). Of these, only one (14 %) could be cured at the end of one year. This figure was 67 % for the patients with no calculi. The difference was statistically significant between the two groups ($p<0.05$.).

No significant adverse effects were encountered. The treatment was not discontinued by any patient. Two patients complained from mild nausea and one from skin rashes. All side-ffects lasted approximately five days and subsided spontaneosly.

Table I: Norfloxacin Administration Period and the Infecting Microorganisms

		Treatment Duration (weeks).			
Pathogen	No. (%)	10w	12w	16w	20w
E. coli	16 (72)	6	6	3	1
P. aureginosa	2 (9)	-	1	-	1
P. mirabilis	2 (9)	1	-	1	-
P. vulgaris	1 (5)	-	-	-	1
K. pneumoniae	1 (5)	-	1	-	-
Total patients	22 (100)	7	8	4	3

Table II: Sterile EPS Cultures in Evaluable Patients

	Sterile	Evaluable	(%)
Pre - treatment	22	22	0
1 month	20	21	95
6 months	16	19	84
1 year	11	14	79

DISCUSSION

The incidence of CBP in CPS ranges between 5 and 17 % in different studies (4, 5, 16). The incidence was 8.3 % (22/183) in this study. CBP mostly affects men who are sexually active (10, 11, 13, 14). The median age of the patients was 37 years in our study. The pathogens were mainly Gram-negative microorganismis in CBP(9), however, Gram-positive bacteria were reported to play a role in some cases (10-12). In the present study, infecting microorganisms consisted of Gram-negative bacteria. E.coli was the predominant pathogen (73 %) as reported previously (2,8,12).

WBC count of more than 10 per high-power field in PMS is accepted as the indicafor of prostatic inflammation (8, 16, 17). As WBC count has no place in distinguishing between CBP and other CPS (5), only microbiological assessment was used for the diagnosis of CBP. While Pfau suggests to omit VB_3 culture because of the dilution of prostatic expressate which yields low bacteria counts(2), other investigators and we perform VB_3 culture (6, 15). Nevertheless we tried not to get more than 10 ml of urine after prostatic massage. However Rosette et al claimed even only VB_1 culture would be enough in interpreting CBP(13), which is expected to be misleading(15).

To evaluate the results of treatment a minimum of one-year follow-up is needed(9). Of the numerous norfloxacin studies in CBP, many lack localization cultures and/or long-term follow-up(19). Proper studies reported cure rates of 64 and 92 % (14,20). This figure was 79 % at the end of the first year in the present study. Although absence of previous antibiotic administration implies better response to therapy(21-23), patients have been prescribed antibacterial drugs in inappropriate dosage to a great extent preceeding the long-term treatmeni. Somewhat low cure rate reported by Schaeffer and Darras (14) may bu due to this condition.

Another -and more important- factor influencing the efficacy of the therapy is the calculi within the prostate. When calculi harboring microorganisms are present it is nearly impossible to eradicate the infection(9). It was evident that when TRUS revealed prostatic calculi, the cure rate would be dramatically low. In these patients another treatment such as transurethral resection of the prostate should be instituted(9).

Despite in vitro tests indicated susceptibility, disppointing results with various antibiotics, probably due to poor diffusion into or non-accumulation in the prostatic fluid, have been reported(14). Fluoroquinolones with unique and favorable pharmacokinetic properties for concentrating in the prostatic fluid(19) and with a broad spectrum against pathogen microorganisms(14) may be a good alternative in CBP.

As the long-term use of a drug may produce pronounced side-effects and/or development of resistance would be a problem, selection of the antimicrobial agent has utmost importance in CBP. Norfloxacin, one of the members of newer quinolones, with no serious side-effects and with acceptible efficacy (5,14,20) is one of the antimicrobials of choice. Also, the over-all frequency of clinical resistance to norfloxacin has been reported to be low(24).

In conslusion, long-term norfloxacin -used at least three months- may be a viable and safe treatment option in men with CBP. Although, the data of this study suggest promising results, especially controlled studies are needed to determine the efficacy of various drugs including norfloxacin.

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