OFLOXACIN CONCENTRATION IN HUMAN BENIGN PROSTATIC TISSUE AFTER ORAL ADMINISTRATION

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The penetration of ofloxacin (OFLX) into prostatic tissue was examined on 11 patients with benign prostatic hypertrophy. OFLX was administered orally in a dose of 200 mg, three times one day before and twice on the day of operation. The blood sample was taken 30 minutes before operation and prostatic tissue specimens were collected during operation. The mean concentration of OFLX in prostatic tissue was 5.51±1.79 μg/g (mean±SD) and 5.36±1.28 μg/ml in serum. The mean ratio of these concentrations was 1.06±0.31 (range 0.55~1.54). These findings indicate that OFLX will be valuable against bacterial prostatitis.

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Key words: Ofloxacin, Prostatic concentration

INTRODUCTION

Ofloxacin (OFLX) is a new broad spectrum antibacterial agent of the quinolone-azaquinolone class for oral administration. It is intended to be used against both systemic and local infections caused by a variety of gram-positive and gram-negative bacteria such as *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Because of the poor diffusion of most antibiotics into the prostatic gland, the number of antimicrobial alternatives for treatment of bacterial prostatitis is lmited. Recently published results suggest that in the quinolone group, there are derivatives which penetrate well into the prostatic tissue and reach levels exceeding corresponding serum concentrations and the minimal inhibitory concentration (MIC) of many prostatic pathogens. The present study was undertaken to evaluate the penetration of orally administered OFLX into human prostatic tissue.

PATIENTS AND METHODS

Eleven elderly patients with benign prostatic hypertrophy were studied. The mean age was 74.2 years (ranging from 70~82 years). All patients had normal kidney and liver function tests. OFLX was administered orally in a dose of 200 mg, three times one day before and twice on the day of operation. Blood samples were taken 30 minutes before operation, i.e. 2.1 hours on average (ranging from 2.0~2.5 hours) after the final administration. Prostatic tissue samples were taken during transurethral resection. The mean weight of the resected chips was 9.5 g (ranging from 4.0~22.0 g). The serum obtained by centrifugation was frozen together with the prostatic tissue and stored at −20°C until the concentration of OFLX was assayed.

The samples of prostate were homogenized and centrifuged. The supernatants were used for assay of OFLX. The concentrations of OFLX in serum and prostate were determined by the microbiological agar well diffusion method. The test strain was *Escherichia coli* KP. The concentrations were calculated from standard solutions with known concentrations of OFLX. Standard solutions were prepared in pooled human serum for serum assays and in phosphate buffer for assays of prostate.

RESULTS

Table 1 shows the mean concentrations of OFLX in serum and prostatic tissue

Table 1. Individual and mean (±SD) ofloxacin concentrations in the serum and the prostatic tissue, 2.1 hrs after the final administration.

Patient No.	Prostatic Tissue (μg/g wet tissue)	Serum (μg/ml)	Prostate/ Serum Concentration
1	4.52	8.24	0.55
2	3.70	4.99	0.74
3	9.70	6.72	1.44
4	3.67	5.61	0.65
5	5.14	5.58	0.92
6	7.19	4.68	1.54
7	7.16	5.42	1.32
8	4.80	3.87	1.24
9	5.92	5.26	1.13
10	5.16	5.44	0.94
11	3.62	3.12	1.16
mean	5.51	5.36	1.06
SD	1.79	1.28	0.31

Ofloxacin detection limits: 3.0μg/g in prostatic tissue; 0.5μg/ml in serum

are presented.

The serum levels about two hours after the final oral administration were 3.12~8.24 μg/ml (mean 5.36±1.28 μg/ml). The prostatic tissue levels were 3.62~9.70 μg/g (mean 5.51±1.79 μg/g). The mean ratio between the prostatic tissue and serum concentration was 1.06±0.31 (range 0.55~1.54). There was no correlation between the size or histology of prostate and the OFLX level in the prostatic tissues.

DISCUSSION

Antibiotics used for the treatment of urogenital infections in uro-andrologic patients have to fulfill certain criteria; (1) bacteriocidal effects against the relevant pathogens, (2) good penetration into reproductive organs, (3) no effects on spermatogenesis or sperm mortality, and (4) pH-independency. Recent results indicate that related quinolones such as enoxacin (ENX), norfloxacin and ciprofloxacin penetrate into human prostatic tissue at effective concentrations[1-3] and prove to be useful as potent antibiotics in clinical care.

In our study, the OFLX concentrations in the prostatic tissue exceeded over one-fold the corresponding serum level; the mean tissue-serum ratio was 1.06. There was no significant difference between OFLX and ENX in the serum or prostatic levels or the ratio[1].

Class[4] recently reported that the OFLX concentration was 5.10 μg/g in prostatic tissue, 1.81 μg/ml in serum and 3.17 in prostate/serum concentration. As compared with our results, the ratio of Claes seems to be very high because the serum level of OFLX was lower by his trial. It is difficult to explain the reason for this.

OFLX concentration by oral administration seems to achieve tissue levels high enough to be effective in the treatment of bacterial prostatitis due to susceptible organisms because the prostatic concentration exceeded the MIC-values of the common urinary tract and prostatic pathogens.

It is well known that the pH is raised to 7.4 in prostatitis patients. According to the study of influence of pH and human urine on the antibacterial activity of a new quinolone derivative, Zeiler[5] showed that cultivation in urine at pH 5.7 increased the MIC values for all three quinolones 8-, 16- and 32-fold compared with those at pH 7.1, which was a very important finding for oral treatment of bacterial prostatitis.

In conclusion, our study has shown that OFLX given orally penetrated well into the prostatic tissue suggesting the drug can be effective in the treatment of prostatitis due to susceptible organisms.

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和文抄録

オフロキサシンの前立腺組織への移行について

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オフロキサシンを術前日 600 mg，手術日当日 400 mg を経口投与した後の前立腺組織への移行について検討した．その結果，前立腺組織内濃度は平均 5.51±1.79 μg/g（range 3.62-9.70）で，同時に採血した血清濃度との比率（前立腺/血清比）は 1.06±0.31（range 0.55-1.54）であった．オフロキサシンが前立腺組織に良く移行し，前立腺炎の起炎菌の最小発育阻止濃度に比べ高い値を示したことは，この薬剤が前立腺疾患の治療に役立つ薬剤と考えられた．

（泌尿紀要 **34**：1097～1099，1988）