

EFFECT OF OFLOXACIN IN THE TREATMENT OF GENITOURINARY TRACT INFECTION WITH UREAPLASMA UREALYTICUM

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Ofloxacin was administered to 26 males infected with *Ureaplasma urealyticum*. The infection was confirmed by urine or semen culture. Ofloxacin, administered at daily dose of 300~600 mg for 7 to 28 days, eradicated *U.urealyticum* in 25 of 26 patients (92.2%).

Key words: *Ureaplasma urealyticum*, NGU, STD, OFLX.

INTRODUCTION

Urinary tract infection by *Ureaplasma urealyticum* (Uu) is widespread among pet animals and the organism is frequently found in the urine of man¹⁾. It is suspected as a causative agent of non-gonococcal urethritis, but greater importance is attached to its etiologic role in male infertility and in salpingitis²⁻⁷⁾.

Transmission of Uu is generally thought to be via sexual intercourse in most instances and, accordingly, its infections are widely recognized as a sort of sexually transmitted disease (STD). If and when such an infection is discovered, therefore, the patient should immediately be begun on appropriate theapeutic agents and his (or her) sex partner, if known, should also be treated simultaneously for the same length of period.

Several chemotherapeutic agents, ie. streptomycin, erythromycin and such tetracyclines as doxycycline and minocycline are known to be effective in the treatment of Uu infection^{3,8,9)}. Besides, certain quinolones have been demonstrated to possess anti-Uu activity. It is known that ciprofloxacin and ofloxacin have anti-Uu activity.

This report describes the results of a study we have recently conducted to assess

the clinical effect of ofloxacin (OFLX) in the treatment of Uu infection.

SUBJECTS AND METHODS

Treated in the study were patients whose urine or semen proved positive for Uu among those examined at the Outpatient Service during the past two years. Detection of Uu was performed by the Taylor-Robinson method.

Patients received 300 to 600 mg of OFLX daily for 2 to 4 weeks, followed by re-examination of urine or semen for Uu by the Taylor-Robinson method. Their therapeutic responses were evaluated according to whether or not Uu was still demonstrable the re-examination.

RESULTS

Of the twenty-six patients treated with OFLX, the treatment proved effective in twenty-five patients (96.2%).

The cases treated in this study are summarized in the tables. The treatment eradicated Uu in all but one case. Twelve patients had concomitant *Chlamydia trachomatis* infection, of whom eleven patients were cured of *Chlamydia* infection following the OFLX therapy. It remains uncertain whether or not the treatment was effective against *Chlamydia* infection in the other case since no post-treatment examination

Table 1. Summary of patients in the study

Case No.	Age	Urine findings		at initial examination post treatment			OFLX dose		Efficacy to U. urealyticum
		U. urealyticum	C. trachomatis	Gonococcus	Other pathogens	Leukocyte	mg/day	day	
1	25	+	+	+	S. epidermidis 10 ²	+	600	10	Eradicated
2	38	+	+	+	—	0~0	600	14	Eradicated
3	22	+	ND	—	—	15~20 10~15	300	19	Eradicated
4	22	+	+	—	—	20~30	600	14	Eradicated
5	39	+	+	—	—	8~10 0~1	300	21	Eradicated
6	25	+	+	—	GPC	30† 5~9	600	7	Eradicated
7	32	+	+	—	—	1~3	300	26	Eradicated
8	40	+	+	—	—	1~4 1~4	300	9	Eradicated
9	37	+	+	—	Lactobacillus (++) micrococcus (+)	1~2 0~1	300	14	Eradicated
10	40	+	+	—	—	0~1 0~1	300	14	Eradicated
11	46	+	+	—	—	0~2 0~1	600	7	Eradicated
12	36	+	+	—	—	0~1	600	7	Eradicated
13	42	+	+	—	X. maltophilia GPC (2 colonies)	30† 5~9	600	15	Eradicated
14	28	+	—	—	T. vaginalis	— ND	600	14	Eradicated
15	19	+	—	—	M. hominis Coryneb. sp. 10 ³	+++ 20~30	300	4	Eradicated
19	48	+	—	—	Enterococci 10 ³ S. epidermidis 10 ³	2~3	300	10	Eradicated
20	49	+	—	—	—	ND	300	14	Eradicated
21	21	+	—	—	—	—	300	5	Eradicated
22	21	+	—	—	—	—	600	14	Eradicated
23	?	+	—	—	S. epidermidis 10 ³ ND	— ND	600	21	Eradicated
24	?	+	—	—	—	—	600	5	Eradicated
25	19	+	—	—	S. aureus 10 ³ S. epidermidis 10 ³	— —	600	28	Eradicated
26	36	+	+	—	—	10~15	300	21	Persisted

for the organism was performed.

There was one patient in whom the course of OFLX therapy failed to bring about eradication of Uu. The dosage in this case was 300 mg g.d. for a period of twenty-one days, with a total dose of 6.3 g (case No. 26). The patient had concurrent Chlamydia trachomatis infection, which was eradicated by the treatment. As seen in Table 2, the treatment was effective even in both patients receiving dosages of 2.1 g

Table 2. Summary of therapeutic responses in patients classified according to total dosage

Total dose	No. of cases	Poor responder
≤2.1 g	2	0
2.2~4.2 g	10	0
4.3~8.4 g	11	1
≥8.5 g	4	0
Total	27	1

or less and it appeared unlikely that a greater dosage was necessary in this par-

ticular case. Analysis of the therapeutic response data by classification according to daily dose level (Table 3) also did not reveal any significant difference between the two dose levels since only one poor responder was available. Furthermore, it cannot be inferred from the data that the longer the duration of medication, the more gratifying was the therapeutic response (Table 4).

Table 3. Summary of therapeutic responses in patients classified according to daily dose level

Daily dose level	No. of cases	Poor responder
300 mg q.d. (100 mg t.i.d)	13	1
600 mg q.d. (200 mg t.i.d)	14	0
Total	27	1

Table 4. Summary of therapeutic responses in patients classified according to treatment duration.

Treatment duration	No. of cases	Poor responder
5~7 days	7	0
8~14 days	10	0
15~21 days	7	1
≥22 days	3	0
Total	27	1

COMMENT

OFLX shows an MIC value of about 0.8 mg against *Uu*. The antibiotic has been reported to be effective against *Chlamydia trachomatis* and *Mycoplasma hominis* and also against *Neisseria gonorrhoeae*¹⁰⁾. It would be highly desirable if, in a patient undergoing chemotherapy for an STD, an effective control of other concomitant pathogens of STD is also attained.

When compared with pyridoncarboxylic acid antibiotics, tetracyclines are as active against *Uu* at significantly lower concentrations and are more active against gonococci than the former. Against *Chlamydia trachomatis*, nevertheless, both groups of drugs are virtually equipotent; and our impression is that pyridoncarboxylic acid antibiotics may usually be of value in the treatment of STD in general.

As for gonococci, at present, it is said that infections by penicillin-and/or tetracycline-resistant organisms have been encountered with increasing frequency. Under

such circumstances, some physicians use such antibiotics as spectinomycin as the drugs of first choice in the treatment of gonococcal infection. Pyridoncarboxylic acid antibiotics, likewise, may become the drugs of first choice since they possess anti-gonococcal activity. It is desirable in such circumstances to attain a cure of concomitant other STD as well. To this effect, OFLX which is active against gonococci as well as against such other pathogens as *Chlamydia trachomatis*, *Uu* and *Mycoplasma hominis* is considered to be of considerable usefulness. For appraisal of efficacy of the drug in *Neisseria gonorrhoeae* and *Chlamydia trachomatis* infections, in fact, clinical trials led by Kumamoto are under way nation-wide in which we are also participating. Concomitant eradication of *Uu* has been observed among patients undergoing treatment in these trials¹¹⁾.

With minocycline (MINO), it usually takes a considerable length of period in order to achieve eradication of *Uu*, e.g. consecutive course of 4-week medication with one-week withdrawals between courses. With OFLX, it appears from the data presented here that three to four weeks of medication suffices. Sex partners, needless to mention, were also treated similarly, of whom only several cases have been followed by post-treatment examination^{12,13)}.

There were equal numbers of patients distributed in the two groups according to daily dose levels, and the poor responder was among the patients receiving 300 mg q.d. It would be reasonable to assume, therefore, that there was no significant intergroup difference between the two dose-level groups in terms of therapeutic response to OFLX in that the relative incidence was 1/13 vs. 0/13. As viewed with reference to total dosage of OFLX, one patient failed to respond at a total dosage of 6.3 g while the sixteen others were cured of the infection at smaller total dosages. The OFLX therapy for *Uu* infection, accordingly, appears not requiring any particularly large dose.

The only patient whose therapeutic response was rated as poor (persisted) was

completely relieved of symptoms of urethritis and Chlamydia trachomatis infection following treatment with OFLX. It was possibly because the patient was content with the therapeutic outcome, thus did not return to the clinic for further follow-up examination. It is presumed in this case that the patient became asymptomatic probably due to a substantial elimination of the organism by the treatment.

In this paper the evaluation of therapeutic response was based solely upon a criterion of whether or not eradication of *Uu* was attained, and the paper does not deal with the clinical progress of accompanying symptoms of urethritis. The observation eventually did not include enumeration of *Uu* in clinical specimens, nor in occasional cases any examination for Chlamydia trachomatis infection.

As in cases 16 and 17 where symptoms of urethritis were present with no laboratory evidence of any pathogenic organisms beside *Uu*, the *Uu* had no sooner disappeared than the symptoms of urethritis subsided. Together with a consideration of such findings, the clinical data heretofore obtained seem to imply that *Uu* is capable of causing urethritis even without involvement of other pathogenic microorganisms.

The present clinical response data indicate potential usefulness of OFLX in the treatment of *Uu* infection.

REFERENCES

- 1) Viareng J, Herbrant E and Piot P: Ureaplasma urealyticum in the urethra of healthy men. *Br J Vener Dis* 56: 169-172, 1980
- 2) Klousia JM, Madden DL, Fucillo DA, Traub RG, Mattson JM, Krezlewicz AG: The etiology of non-specific urethritis in active duty marines. *J Urol* 120: 67-70, 1978
- 3) Mattheus CD, Clapp KH, Tansing JA and Cox LW: T-Mycoplasma genital infection; the effect of doxycycline therapy on human unexplained infertility. *Fertil Steril* 30: 98-99, 1978
- 4) Idriss WM, Patton WC and Taymor ML: On the etiologic role of Ureaplasma urealyticum (T-Mycoplasma) infection in infertility. *Fertil Steril* 30: 293-296, 1978
- 5) McDonald MI, Lam MH, Birch DF, D'Arcy AF, Fairley KF and Pavillard ERJ: Ureaplasma urealyticum in patients with acute symptoms of urinary tract infection. *J Urol* 128: 517-519, 1982
- 6) Toth A and Lesser ML: Ureaplasma urealyticum and infertility; the effect of different antibiotic regimens on the semen quality. *J Urol* 128: 705-707, 1982
- 7) Brunner H, Weidner W and Schiefer H-G: Studies on the role of Ureaplasma urealyticum and Mycoplasma hominis in prostatitis. *J Infect Dis* 147: 807-813, 1983
- 8) Prentice MJ, Taylor-Robinson D and Csonka GW: Non-specific urethritis; a placebo-controlled trial of minocycline in conjunction with laboratory investigations. *Br J Vener Dis* 52: 269-275, 1976
- 9) McNeil PJ, Fiumara NJ, Calibando JJ, Benes S, and McCormack WM: Evaluation of doxycycline cyclate in the treatment of nongonococcal urethritis. *STD* 8: 127-131, 1981
- 10) Aznar J, Caballero MC, Lozano MC, deMiguel CP, Palomares JC and Perea EJ: Activities of new quinolone derivatives against genital pathogens. *Antibicrob Agents Chemother* 27: 76-78, 1985
- 11) Kumamoto Y, Sakai S, Hirose T, Tsunekawa T, Machida T, Kiyota H, Okazaki T, Kishi H, Higashihara E, Aso Y, Nijima T, Taitoh I, Yoshida M, Kataniwa Y, Taguchi S, Yamazaki M, Kojima H, Noguchi Y, Hashimoto S, Osada T, Yamagoe M, Hirano A, Murakami S, Kawamura N, Kawashima T, Ohkoshi M, Koinuma A, Ohara A, Ban Y, Kanematsu M, Deguchi T, Hisazumi H, Ohkawa M, Kameda K, Kawada YY, Isomatsu Y, Kamidono S, rakawa S, Fujii A, Kataoka N, Tsugami H, Ohmori H, Kumon H, Kishi M, Tanaka H, Amano M, Tatsumoto A, Usui H, Nagano H, Sanda N, Usui T, Tanaka H, Tanaka M, Matsumoto T, Ogata N, Kumazawa J, Nagayama A, Saito Y, Jodai A, Kawahara M, Shimada T, Ohi Y, Matsuda T, Suzuki M, Mizuno M, Kawana T, Sugae M, Noguchi M, Okamoto T, Ishihara M, Okada H, Yasuda J, Yamamoto T, Fuchi I, Noda K, Hirakawa O, Hirota M, Tsuneoka H and Motomura R: Efficacy of ofloxacin in sexually transmitted male urethritis and cervicitis. *Jpn J Antibiot* 41: 1445-1479, 1988
- 12) Kiriya T and Yoshida O: Ureaplasma urealyticum infection of semen and male infertility. *Acta Urol Jpn* 27: 623-636, 1981
- 13) Kawamura N, Hoshino H and Nakajima N: Clinical trials no Minocycline in urinary tract infection on Ureaplasma urealyticum. *Prog Med* 4: 1123-1126, 1984

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和文抄録

Ureaplasma urealyticum の尿路感染に対する ofloxacin の効果について

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26例の患者に OFLX を投与し，25例に有効（有効率96.2％）の結果を得た．患者の一覧表を呈示する．1例を除いて Uu が消失している．26例中12例は *Chlamydia trachomatis* の感染を伴っており，うち11例では OFLX 投与後 *Chlamydia* の感染も消失している．残りの1例については，投与後の

Chlamydia 検査が行われなかったため，効果は不明である．無効例は1例であったが，300 mg を21日間投与した症例であり，*Chlamydia trachomatis* を併存していたが，そちらの方は消失している．総投与量は 6.3 g であった．

（泌尿紀要 35：2149-2153，1989）