

CLINICAL TRIAL OF NORFLOXACIN IN URINARY TRACT INFECTION

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Abstract

Forty six patients, with acute pyelonephritis or cystitis and a significant colony count were treated with Norfloxacin 400mg, 12 hourly for 7 days. The prevalent organisms were E.Coli (83%) and Ps pyocyanea (11%). Cure rate after one week's treatment was 98%. Nine patients (20%) had recurrence of infection one to six weeks after stopping the drug. Tolerance to the drug was excellent. Norfloxacin is safe and effective in uncomplicated as well as complicated urinary tract infections (JPMA 37: 152, 1987).

INTRODUCTION

Norfloxacin is a quinoline carboxylic acid antibacterial agent for oral administration. It is highly effective against typical urinary pathogens.¹⁻³ Norfloxacin is structurally related to nalidixic acid, pipemidic acid, cinoxacin and oxolinic acid. It is rapidly distributed to peripheral tissues and tissue fluid, resulting in higher urine concentrations than concomitant serum levels⁴. Norfloxacin is mainly eliminated via the kidneys, attaining high and prolonged urinary concentrations which makes it suitable for dosage every 12 hours.

This study was done to evaluate the efficacy of Norfloxacin in the complicated and uncomplicated urinary tract infections in our population.

MATERIAL AND METHODS

Patients attending the outpatient department were, after clinical evaluation and diagnosis of urinary tract infection, included in the study.

A mid-stream urine specimen, after due precaution, was collected and cultured. Urinary tract infection was diagnosed on a colony count of 100,000 bacteria per millilitre of urine. A sensitivity zone of more than 15 mm diameter was taken significant. Pre-trial haematological, renal and liver function tests were done. Urine culture and colony counts were repeated on 3rd or 4th day, 7th day and after every two weeks for 6 weeks. Haematological, renal and liver function tests were repeated after 6 weeks.

RESULTS

There were 35 females and 11 males, with a mean age of 38.4 years. Common presenting features were dysuria(34), lumbar pain(31), increased frequency(26), fever (11) and haematuria (10). Thirty one (67.4%) patients had pyelonephritis and 32.6% had cystitis.

The causative micro-organisms isolated were E. Coli (82.7%), Pseudomonas pyocyanea (10.8%), Klebsiella (4.3%) and staphylococcus aureus 2.2%.

Twenty four patients had uncomplicated and 22 complicated UTI associated with calculus disease, diabetes mellitus, urethral stricture and other urological problems.

Pre- and post- trial haematological, and liver and kidney function tests remained unchanged in almost all cases.

The drug was well-tolerated except by one patient who developed gastrointestinal symptoms: flatulence, loss of appetite, epigastric pain and vomiting which improved after withdrawal of the drug. All patients except one (98%) were cured of UTI after one week's treatment. Nine patients had a relapse one to six weeks after stopping the drug. The organisms were still sensitive to Norfloxacin except in one patient. All patients with relapse had complicated UTI. One female patient was given Norfloxacin in 5th month of pregnancy with no after effects on mother or foetus. Four patients with moderately impaired kidney functions were given Norfloxacin 400mg 12 hourly for 7 days. There was no worsening of renal functions and in one case, renal function improved and the patient underwent surgery for ureteric stone.

DISCUSSION

Infections of the urinary tract (UTI) are probably second only to infections of the respiratory tract in frequency. Females are affected about twice as often as males. If not treated properly it can result in progressive and irreversible impairment of kidney function.

The most common causative organism is *Escherichia Coli* (*E. Coli*)⁵ followed by *proteus*, *Klebsiella* and *staphylococcus aureus*. *Pseudomonas pyocyanea* infections occur in patients with major complications following surgery, instrumentation, antibiotic therapy or catheterisation⁶. *E. Coli* were also the commonest infecting organism in the present series, followed by *pseudomonas pyocyanea*. The appearance of the *Ps. pyocyanea* as the second commonest infecting organism was due to associated urological problems in most cases. In the 5 year period (1976-1980), *staphylococcus aureus* was the second commonest organism in our department (unpublished data).

Urinary tract infections caused by *pseudomonas pyocyanea* were previously treated with parenteral antibiotics (aminoglycosides, carbenicillin), which are inconvenient, toxic and expensive. Studies of Norfloxacin after an oral dose of 400mg show high concentration in the genito urinary system⁸. It is non-toxic and shows a high effectivity against *Ps. pyocyanea* as well as other common pathogens. Our results agree with those of other workers^{6,9,10}. The overall cure rate varied from 75-95 percent, this study showed a cure rate of 98 percent at 1 week and 80 percent at six weeks.

In patients with moderate renal failure (GRF 30ml/rnin) no untoward side effects were observed.

Hughes et al (1984)¹¹ used the drug in patients with renal failure, but have not mentioned any side effects.

The drug was well tolerated by all except one patient. Overall compliance of the patients was good, due to a 12 hourly dosage. Norfloxacin appears to be a drug of choice in both, uncomplicated and complicated urinary tract infections.

REFERENCES

1. Ito, A., Hirai, K., Inoue, M., Koga, H., Suzue, S., Irlkuia, T. and Mitsuhashi, S. In vitro antibacterial activity of AM-i 15, a new nalidixic acid analog. *Antimicrob. Agents Chemother.*, 1980; 17: 103.
2. Gadebusch, H.H., Shungu, D.L., Weinberg, E. and Chung, S.K. Comparison of the antibacterial activity of norfloxacin (MK 0366, AM715), a new organic acid, with that of other orally absorbed chemotherapeutic agents. *Infection*, 1982; 10: 41.
3. King, A., Warren, C., Shannon, K. and Phillips, I. In vitro antibacterial activity of norfloxacin (MK-0366). *Antimicrob. Agents Chemother.*, 1982; 21 :604.
4. Norrby, S.R. Pharmacokinetics of norfloxacin; dinical implications. *Ear. J. Chemother. Antibiot.*, 1983; 3: 19.

5. Cattell, W. R. Urinary infection in adults - 1985. *Postgrad. Medical J.*, 1985; 61: 907.
6. Leigh, D.A. and Emmanuel, F.X.S. Norfloxacin therapy for complicated urinary tract infections, in *Proceedings of IV Mediterranean Congress of Chemotherapy*. Edited by Daikos, G.K. and Giamareliou, H. Italia, II Sedicesimo, 1985, p. 475.
7. Unpublished report.
8. Swanson, B.N., Boppana, V.K., Viasses, P.H., Rotmensch, H.H. and Ferguson, R.K. Norfloxacin disposition after sequentially increasing oral doses. *Antimicrob. Agents Chemother.*, 1983; 23:284.
9. Palumbo, M. and De Rosa, F. Comparison between Norfloxacin and Pipemidic acid in secondary urinary tract infections, in *Proceedings of IV Mediterranean Congress of Chemotherapy*, Edited by Daikos, G.K. and Giamarellou, H. Italia, II Sedicesimo, 1985, p.483.
10. Schmidbauer, C.P., Graninger, W., Ganzinger, U. and Jesch, E. Treatment of complicated and uncomplicated urinary tract infections with a new Oxalinic acid derivative (MKO 366), in *Proceedings of IV Mediterranean Congress of Chemotherapy*. Edited by Daikos, G.K. and Giamarellou, H. Italia, II Sedicesimo, 1985, p. 473.
11. Hughes, P. J., Webb, D.B. and Asscher, A.W. Pharmacokinetics of norfloxacin (MK366) in patients with impaired kidney function some preliminary results. *J. Antimicrob. Chemother.*, 1984;13 (Suppl.B) :55.