Thesis Title Effectiveness of Single Oral Dose of Pefloxacin in the Treatment of Cystitis in Thai Women

Name Yupaporn Natesungnoen

Degree Master of Science (Pharmacy)

Thesis Supervisory Committee

Busba Chindavijak, Doct. Sc. Pharm.

Amorn Leelarasamee, M.D., M.Med. Sc.

Jinda Wangboonskul, Ph.D.

Date of Graduation 20 May B.E. 2536 (1993)

ABSTRACT

Effectiveness of pefloxacin in the treatment of Thai women with cystitis was studied in order to find out its usefulness and to see whether the drug has low adverse effects and cause no noncompliance problems. The study was randomized and comparable design. Single oral dose of 800 mg pefloxacin was compared with short course pefloxacin taken as 400 mg twice daily for three days The former treatment was given to 13 female patients with cystitis and the latter was given to 19 patients. Effectiveness outcome was determined from the level of drug in urine, the result of urine culture at the first and the second follow-up and the clinical effect. The level of pefloxacin in urine was found to be 53.23 $\pm$ 8.09 and 22.45 $\pm$ 3.13 mg/L in the first group of patients and to be 39.91 $\pm$ 4.67 and 67.64 $\pm$ 6.91 mg/L in the second group at 24 and 48 hours after drug administration. The drug levels in both groups of patients at different time are significantly different ($p \leq 0.05$), yet several hundred times the minimum inhibitory

concentration (MIC_{90}). Norfloxacin, an active metabolite of pefloxacin was also determined in urine at the same time and found to have much higher concentration than its MIC_{90}. The urine culture of patients of both treatments were negative at the first follow-up, 1-7 days after drug administration, in addition to the disappearance of symptoms. At the second follow-up, 7-30 days after drug administration, the sterile urine was found in 87.5% of single dose therapy group and 90.9% of short course therapy group. A single dose of 800 mg pefloxacin was thus demonstrated to be as effective as a short course therapy in the treatment of acute cystitis in Thai women ($p \geq 0.05$).

Pefloxacin pharmacokinetic was also studied in the healthy subjects in order to have a background data for the consideration of pefloxacin usage. Five healthy female volunteers participated in pharmacokinetic studies. The mean age was 22.4 $\pm$ 2.1 years and the mean weight was 49.8 $\pm$ 4.4 kg. After the single oral dose of two 400 mg pefloxacin tablets, the level of drugs in urine was determined by HPLC method with UV-detector. The analytical method showed high precision (%CV = 3.7 and 2.4 at concentration of 6 and 14 mg/L, respectively) and high sensitivity with detection limit of 0.03 mg/L. The pharmacokinetic parameter values were calculated, using urine data. The mean maximum urine concentration, time to maximum concentration, elimination rate constant, urinary excretion rate constant, renal clearance and elimination half-life were 74.14 $\pm$ 14.65 mg/L, 8.4 $\pm$ 2.7 hr, 0.0689 $\pm$ 0.0054 hr^{-1}, 4.83 x 10^{-3} $\pm$ 0.47 x 10^{-3} hr^{-1}, 0.44 $\pm$ 0.06 L/hr and 10.32 $\pm$ 0.84 hr, respectively. The results also showed that 5.6% of unchanged drug was excreted in urine within 24 hours and almost disappeared within 60 hours.

The present study suggest pefloxacin to be chosen in the treatment of cystitis with the advantages of vast quantity excreted in urine, long half-life in urine, high effectiveness of bacterial eradication, having active metabolite and causing no noncompliance problems.