Montréal

19ICC MONTRÉAL 1995

19th International Congress of Chemotherapy
July 16-21, 1995
Montréal, Québec, Canada

Final Program and Abstracts

THE CANADIAN JOURNAL OF
INFECTIOUS DISEASES
JOURNAL CANADIEN DES MALADIES INFECTIEUSES
VOLUME 6 SUPPLEMENT C JULY 1995

2252 IN VITRO ACTIVITY OF FLEROXACIN VERSUS CIPROFLOXACIN, OFLOXACIN AND PEFLOXACIN AGAINST UROPATHOGENS.

Kurt G. Naber*, Karin Hollauer, Daniela Kirchbauer and Orlin Savov, Elisabeth Hospital, Straubing, Germany.

The minimal inhibitory concentration (MIC) of fleroxacin (FLE) versus ciprofloxacin (CIP), ofloxacin (OFL) and pefloxacin (PEF) were determined against 441 uropathogens cultured from the urine of hospitalized urological patients with complicated and/or hospital acquired UTI using an agar dilution method. The bacterial spectrum consisted of Enterobacteriacea (37.8%), enterococci (29.3%), staphylococci (20.6%) and non fermenting bacteria (12.2%). FLE inhibited 51.0% upto a MIC of 1mg/l, 57.6% upto 2mg/l, 68.9% upto 4mg/l and 82.8% upto 8mg/l of the isolates. If using breakpoints for sensitive (S) and resistant (R) of ≤ 2 and ≥ 16mg/l for FLE and PEF, ≤ 1 and ≥ 8mg/l for OFL and ≤ 0.5 and ≥ 4mg/l for CIP almost identical rates for S and R can be obtained.

Kurt G.Naber, Urologic Clinic, Elisabeth Hospital, Schulgasse 20, D-94315 Straubing, Germany, Tel.: +49-9421-710-0 (Ext. 1700) Fax:-710-270.

2253 COMPARATIVE ACTIVITIES OF OFLOXACIN AND CIPROFLOXACIN COMBINED WITH CEFTAZIDIME AND PIPERACILLIN AGAINST *PSEUDOMONAS AERUGINOSA*.

Michael E. Klepser, Kalpana B. Patel, David P. Nicolau, Richard Quintiliani and Charles H. Nightingale*, Hartford Hospital, Hartford, CT, USA.

As monotherapy, ciprofloxacin (CIP) is significantly more active against *P. aeruginosa* (PSA) than ofloxacin (OFX); however, in clinical practice, these agents are generally combined with other anti-pseudomonal agents such as ceftazidime (TAZ) or piperacillin (PIP). Under these circumstances, it is unknown whether or not CIP maintains its bactericidal advantage. We enrolled 12 healthy volunteers in this randomized, steady-state, six-way cross-over, open-label, comparative trial. Subjects received the following regimens : 1) OFX 400mg IV every 12 hours (Q12), 2) CIP 400mg IV Q12, 3) OFX 400mg IV Q12 plus TAZ 1g IV Q8, 4) CIP 400mg IV Q12 plus TAZ 1g IV Q8, 5) OFX 400mg IV Q12 plus PIP 4g IV Q8, and 6) CIP 400mg IV Q12 plus PIP 4g IV Q8. Blood samples were collected at specified times in conjunction with the third dose of the antimicrobials. Serum bactericidal titers (SBTs) with subsequent calculation of the area under the bactericidal curve (AUBC) were determined for three clinical isolates of PSA. CIP monotherapy demonstrated superior anti-pseudomonal activity compared to OFX. Combination of these agents with TAZ, however, yielded statistically comparable activity profiles. When combined with PIP, regimens including CIP retained a superior bactericidal advantage compared to OFX/PIP. TAZ-containing regimens displayed significantly greater anti-pseudomonal activity than PIP-quinolone regimens. Although CIP exhibits superior anti-pseudomonal activity when used as monotherapy, combinations of OFX or CIP with TAZ yield equivalent activity profiles against PSA.

Charles H. Nightingale, Hartford Hospital, 80 Seymour St, Hartford, Connecticut, USA. Phone: (203) 545-2865, FAX (203) 545-5112.

2254 THE ANTIBACTERIAL ACTIVITY OF SPARFLOXACIN.

Athanasios G. Paradelis*, Kyriaki Delidou, Dimitrios Kouvelas, Slobodan M. Jankovic and Andreas Pangalis, Aristotle University of Thessaloniki, Macedonia, Greece.

The in vitro antibacterial activity of sparfloxacin, a new quinolone, was compared with that of ciprofloxacin against 2000 clinical isolates of Gram-negative bacteria including: E. coli (800), K. pneumoniae (150), K. oxytoca (100), E. cloacae (100), P. mirabilis (450), Ps. aeruginosa (250), P. rettgeri (50), P. stuartii (50), Acinetobacter (50) and with that of ciprofloxacin, methicillin, erythromycin and vancomycin against 500 clinical isolates of S. aureus, (150) methicillin resistant and (150) methicillin susceptible, S. epidermitus, (50) methicillin resistant and (50) methicillin susceptible, S. saprophyticus (40), Str. group A beta hemolytic (20) and Str. group B beta hemolytic (20). The minimal inhibitory concentrations (MICs/ $\mu g \cdot ml^{-1}$) determined by the broth dilution method using an inoculum size of 10^6 colony forming units per ml showed that sparfloxacin has a spectrum similar to that of ciprofloxacin, with excellent activity against Gram-negative bacteria. The MIC_{90} (μg/ml) were: for E. coli 0.02, for K. Pneumoniae 0.1, for K. oxytoca 0.1, for E. cloacae 0.1, for P. mirabilis 0.1, for Ps. aeruginosa 0.25, P. rettgeri 0.25, P. stuartii 0.25 and for Acinetobacter 0.25, including ß-lactamase-producing strains. Concerning the Gram-positive microorganisms the antibacterial activity of sparfloxacin was superior to that of ciprofloxacin; the $MICs_{90}$ (μg/ml) were: for S. aureus 0.3 and 0.1 for methicillin resistant and susceptible strains, respetively, for S. epidermitis 0.1 for methicillin resistant and susceptible strains, for S. saprophyticus 0.20, for Str. group A beta hemolytic 0.20 and finally for Str. group B beta hemolytic 0.4. These results suggest that sparfloxacin could be an effective alternative drug in the empiric treatment of respiratory and urinary tract infections.

Correspondence: Prof. A.G. Paradelis, 5, Themistokli Sofouli Str, 546 46 Thessaloniki, Greece, Tel. & Fax: (3031) 999 324
email: PARADELIS @ OLYMP.CCF.AUTH.GR

2255 COMPARATIVE CLINICAL STUDY OF AZITHROMYCIN WITH TOSUFLOXACIN TOSILATE IN THE TREATMENT OF ACUTE ODONTOGENIC INFECTIONS.

Jiro Sasaki*, Akihiro Kaneko, Kazunari Karakida and Haruo Sakamoto, Department of Oral Surgery, School of Medicine, Tokai University, Japan.

For the purpose of objectively assessing azithromycin (AZM) for its clinical efficacy and safety in the treatment of acute odontogenic infections (periodontitis, pericoronitis and osteitis of jaw), a double-blind, randomized, multi-centre trial was conducted where tosufloxacin tosilate(TFLX) was used as the control drug. AZM was administered to 90 patients at once-daily 500mg dose for 3 days, while TFLX was given to 90 patients at a 150mg t.i.d. dose for 7 days. Taking into account the findings of body temperature, redness, swellings, induration, pain and the results of bacteriological findings and clinical lab tests, the drugs were evaluated until Day 8.
1) The clinical efficacy rate was 87.1% (74/85) in the AZM group, 73.3% (66/90) in the TFLX group with statistical significant difference between the two groups($p=0.006$).
2) The bacteriological elimination rate in the AZM group was 97.5% (39/40) and that in the TFLX group, 85.7% (30/35), without significant difference.
3) Adverse reactions rate was 12.5%(11/88) in the AZM group and 5.6%(5/90) in the TFLX group. Six of 85 cases (7.1%) in the AZM group and 5 of 85 cases (5.9%) in the TFLX group found laboratory abnormalities. However, either for adverse reactions or for laboratory abnormalities, difference of statistical significance between the treatment groups was not detected.
4) Adverse reactions found in AZM group include diarrhea, anthema and nausea as well as elevation in eosinophile and GOT, etc. None of them were severe, and they all disappeared in a short period of time.

Prof. Jiro Sasaki, Department of Oral Surgery School of Medicine, Tokai University, Isehara, Kanagawa 259-11, Japan. Tel 0463-93-1121 Fax 0463-93-1153

2256 POST-MARKETING SURVEILLANCE OF LEVOFLOXACIN IN JAPAN.

M. Sawada*, Y. Saishu, S. Hayashi, Y. Onaka, K. Yoshioka, Y. Sano and A. Yamada, Daiichi Pharmaceutical Co., Ltd., Tokyo, Japan.

Levofloxacin, the S-(-)-isomer of ofloxacin, was first introduced in Japan in December 1993. We conducted a Drug Use Investigation (Phase IV trial) to confirm the safety of oral levofloxacin under conditions of actual use. Reports on 2,552 patients were compiled during the 6-month period from January to June 1994. We also had received 415 spontaneous reports on adverse drug reactions (ADRs) to levofloxacin by the end of 1994. On the basis of these data, we assessed oral levofloxacin for safety in clinical usage. Drug Use Investigation: A total of 58 ADRs were reported in 40 of 2,552 patients, representing an occurrence rate of 1.6% - lower than that recorded in the similar Phase IV trial of ofloxacin (2.6%) carried out from 1985 to 1990. The most frequent ADRs were gastrointestinal system disorders, liver system disorders, skin disorders, and nervous system disorders, in that order. Spontaneous Reporting on ADRs: We received 415 spontaneous reports on ADRs in about 1 year after the launch of levofloxacin. Skin disorders such as rash were reported most frequently, accounting for 28% of the total number. Several very rare but serious ADRs such as anaphylactic shock and convulsions were reported for the first time as spontaneous reports. All ADRs reported with levofloxacin were known to be attributable to ofloxacin as well. Here, we will present updated data on ADRs of levofloxacin.

Masahiro Sawada, Ph.D. 16-13, Kita-Kasai 1-Chome, Edogawa-ku, Tokyo 134 Japan Tel: 3-5696-8094 Fax: 3-5696-8351

2257 CLINICAL EVALUATION OF GREPAFLOXACIN (GPFX), A QUINOLONE ANTIMICROBIAL DRUG, FOR ORAL USE IN SURGICAL INFECTIONS.

Nagao Shinagawa* (Group Chairman), Nagoya City University Medical School, Nagoya, Japan; and GPFX Surgery Study Group, Japan.

The clinical efficacy and safety of grepafloxacin (GPFX) was evaluated in patients with surgical infections. GPFX was administered to 183 patients at a dose of 150-400 mg once or twice a day for 3-14 days. Eight patients either were excluded or dropped out. The overall clinical efficacy rate was 85.3% in 177 patients in whom clinical effects could be evaluated. The clinical efficacy rates were especially high in patients with periproctitis (93.8%) and in patients with cholecystitis or cholangitis (94.7%), reflecting a profile of GPFX that indicates a high rate of biliary excretion. Of 116 patients in which bacteria were isolated before dosing, clinical and bacterial efficacy was observed in 99 patients (85.3%) and 83 patients (83.8%), respectively. With regard to safety, slight and transient adverse reactions, mainly consisting of a bitter taste in the mouth, were observed in 7 of the 177 subjects. In clinical laboratory tests, an abnormal change in s-GPT was observed in one patient. The above results suggest that GPFX is highly useful for the treatment of surgical infections.

Nagao Shinagawa, M.D., 1st Department of Surgery, Nagoya City University Medical School, 1 Kawasumi, Mizuho-ku, Nagoya 467, Japan, Tel: 81-52-853-8225, Fax: 81-52-842-3906