


**Oral prophylaxis in biliary tract surgery**

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Postoperative sepsis remains a major cause for concern for all surgeons undertaking gastrointestinal tract surgery. Any intra-abdominal procedure in which the integrity of the gastrointestinal tract is breached is likely to result in postoperative septic complications. Wound infection, though rarely fatal, causes considerable patient discomfort, significantly increases the risk of wound dehiscence or incisional hernia, and prolongs both the duration and cost of hospitalization. Wound infection may also be associated with more serious complications including deep intra-abdominal sepsis and septicemia which do produce significant morbidity and may sometimes prove fatal.

Postoperative wound infections affect at least 920,000 of the 23 million patients who undergo surgery each year in the USA (Wenzel, 1992). Eighteen percent of those with postoperative wound infections have disability lasting more than 6 months. The direct costs of the excess duration of hospitalization exceed $1.5 billion annually.

The principles of antibiotic prophylaxis are now well established. The choice of antibiotic depends on the pathogenic microorganisms likely to be present at the time of surgery, while the mode of administration should be chosen to achieve high tissue concentrations at this time, without provoking toxicity or precipitating the emergence of resistant organisms. In order to achieve high tissue concentrations antibiotics are usually administered parenterally.

Randomized prospective controlled trials undertaken in the late 1970s clearly demonstrated the value of prophylactic antibiotics in surgery. In most studies the wound infection rate fell from around 20% in the control group to less than 5% in the treated group. These findings have been widely accepted and absorbed into routine surgical practice (Haddock, Hansell & McArdle, 1988). Since then, a wide range of antibiotics have been evaluated but none has offered an obvious advantage. In a recent Dutch meta-analysis study, the results of 42 randomized, controlled trials with a total of 4129 patients were analysed (Meijer, Schmitz & Jeekel, 1990). In the control groups the overall wound infection rate was 15%; there was an overall advantage of 9% in favour of antibiotic prophylaxis. Comparison of wound infection rates in patients treated with 'first-' or 'second-' or 'third-' generation cephalosporins (1128 patients in 11 trials), as well as single-dose versus multi-dose regimens (1226 patients in fifteen trials) did not show any significant difference. The authors, therefore, concluded that the choice of antibiotics should be governed by cost. It is for this reason that the newer fluoroquinolones, for example ciprofloxacin, are of interest.

Ciprofloxacin is a 4-fluoroquinolone antibacterial agent which acts by inhibiting DNA gyrase, a bacterial topoisomerase which is responsible for negative supercoiling of DNA within the bacterial cell (Zeiler & Grohe, 1984). It has an extended antibacterial spectrum and is highly active against both Gram-negative and Gram-positive bacteria (Felmingham et al., 1985). Previous studies have shown that when given parenterally, it is an effective prophylactic agent for patients undergoing biliary tract surgery (Kögler et al., 1989; Kujath, 1989). Of particular interest, however, is the fact that it achieves high con-
Table. Incidence of postoperative wound infections and duration of hospitalization (cf. McArdle et al., 1991)

<table>
<thead>
<tr>
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<th>Cefuroxime iv (1.5 g)</th>
<th>Ciprofloxacin iv (200 mg)</th>
<th>Ciprofloxacin oral (750 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound infection</td>
<td>7 (10%)</td>
<td>6 (9.7%)</td>
<td>6 (9.0%)</td>
</tr>
<tr>
<td>Mean postoperative stay (days)</td>
<td>9</td>
<td>10</td>
<td>9</td>
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centration in tissues and bile following oral administration (Strachan & Thom, 1985; Dan et al., 1987). The mean bile/serum ratio observed following a single oral 750 mg dose of ciprofloxacin was 49. The mean values for bile and serum concentrations of ciprofloxacin were 99 and 6-03 g/mL, respectively (Dan et al., 1987). Both of these concentrations exceed the MIC90 of ciprofloxacin for the Enterobacteriaceae, faecal streptococci, and most other common biliary and gastric pathogens. Clearly the use of oral ciprofloxacin would offer significant advantages in terms of cost and ease of administration.

However, before advocating the use of oral quinolones for surgical prophylaxis, it is important to establish the effect of concomitant therapy on absorption in particular the agents used for pre-medication (Flowerdew & Karran, 1984). Temazepam given 1-2 h before induction of anaesthesia has no obvious adverse effect on the bioavailability of ciprofloxacin. However, the use of an opiate premedication reduces significantly the absorption of orally administered ciprofloxacin (Morran et al., 1989). Clearly, if oral ciprofloxacin is to be used for surgical prophylaxis, the use of an opiate premedicant should be avoided.

We have recently completed a study of oral ciprofloxacin in patients undergoing biliary tract surgery (McArdle et al., 1991). Two hundred and eight consecutive patients were randomized to receive either cefuroxime (1.5 g) or ciprofloxacin (200 mg) iv on induction of anaesthesia or ciprofloxacin (750 mg) orally 1 h before anaesthesia. The groups were comparable in terms of physical characteristics, demographic data, biochemical parameters, degree of urgency, ease, and duration of surgery. There were no significant differences in the incidence of septic complications or postoperative hospital stay among the three treatment groups (Table). Similar results have been obtained from a group in Southampton, UK (Karran et al., 1991; Ranabaldo et al., 1993). Preliminary analysis of studies of oral ciprofloxacin in patients undergoing upper gastrointestinal surgery and endoscopic mani-

References


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Brief Prescribing Information
Indications: Pneumonia, septicemia, meningitis, bone, skin and soft tissue infections, infections in neutropenic patients, gonorrhoea, per-operative prophylaxis of infections associated with surgery. Treatment may be started before the results of susceptibility tests are known. Dosage and Administration: Rocephin should be administered by deep intramuscular injection, slow intravenous injection, or as a slow intravenous infusion after reconstitution of the solution. Adults and children: 12 years and over: Standard dosage: 1g once daily. Severe infections: 2-4g normally once daily. Duration of therapy varies according to course of disease. Gonorrhoea: single dose of 250mg i.m. Per-operative prophylaxis: usually single dose of 1g, colorectal surgery 2g in conjunction with a suitable agent against anaerobic bacteria. Children under 12 years: Standard dosage: 20-50mg/kg once daily. Severe infections: maximum 80mg/kg once daily. Doses of 50mg/kg or over should be given by slow intravenous infusion over at least 30 minutes. Renal and hepatic impairment: In the absence of hepatic impairment, dose reduction is required only in severe renal failure (creatinine clearance <10ml/min). When the daily dose should be 2g or less, no dose reduction is required in liver damage provided renal function is intact. In severe renal impairment accompanied by hepatic insufficiency, the plasma concentration should be determined at regular intervals and dosage adjusted. Serum concentrations should be monitored in dialysis patients. Contra-indications, Warnings etc: Cephalosporin hypersensitivity. Premature infants: Full-term infants during first six weeks of life. Safety in pregnancy has not been established. Precautions: Stated dose should not be exceeded. Cautions in patients with a history of hypersensitivity (especially anaphylactic reaction) to penicillins or other non-cephalosporin beta-lactam antibiotics. Anaphylactic shock requires immediate countermeasures. Severe renal impairment accompanied by hepatic insufficiency (see Dosage). Side-effects and Adverse Reactions: Gastro-intestinal side-effects including loose stools, diarrhoea, nausea, vomiting, stomatitis and glossitis. Gastrointestinal reactions including maculopapular rash, pruritus, urticaria, oedema and erythema multiforme. Haematological reactions including anaemia (all grades), leucopenia, neutropenia, thrombocytopenia, eosinophilia, agranulocytosis, positive Coombs' test and prolongation of prothrombin time. Regular blood counts should be carried out during treatment. Other reactions include headache, dizziness, drug fever and transient elevations in liver function tests. Rarely, glosoula, oliguria, haematuria, anaphylaxis and bronchospasm. Very rarely, precipitation of ceftriaxone calcium salt in urine in patients on higher than recommended dose. Reversible precipitates of calcium ceftriaxone have been detected by gallbladder sonograms. In symptomatic cases (which are rare), conservative non-surgical management is recommended. Superinfections with yeasts, fungi or other resistant organisms. Rare instances of pseudomembranous colitis. Injection site pain and local phlebitis. Legal Category: POM. Presentations and Basic NHS Cost: 250mg vials i.m. and i.v. (containing 250mg ceftriaxone) - £11.46, 1g vials i.m. and i.v. (containing 1g ceftriaxone) - £11.46, 2g vials for infusion (containing 2g ceftriaxone) - £22.92. Product Licence Numbers: PL 0031/0165 (250mg vials), PL 0031/0171 (1g vials), PL 0031/0172 (2g vials) Product Licence Holder: Roche Products Limited. PO Box 8, Welwyn Garden City, Hertfordshire. AL7 3AY. Full prescribing information is available on request. Roche®