Discussion

Newborn infants of diabetic mothers are at risk of developing severe hypoglycaemia. Good control of maternal diabetes during pregnancy increases the fetal survival rate. Recent reports support the hypothesis that neonatal hypoglycaemia is due to islet-cell hyperplasia, which in turn may be caused in utero by maternal hyperglycaemia. Since perfect control of maternal blood glucose is aimed at during pregnancy, it is logical to avoid excessive stimulation of fetal insulin secretion immediately before delivery.

The combined infusion of insulin and glucose is a simple way of controlling the maternal blood glucose concentration during labour. It also permits adequate hydration of the mother and prevents starvation ketosis. At the same time the stomach may be kept empty, so that a general anaesthetic can be given without delay.

Infused insulin is cleared extremely rapidly from the plasma, and by means of an insulin infusion the maternal plasma insulin concentration may be readily adjusted to achieve more-constant blood glucose concentrations. Immediately after delivery maternal insulin requirements fall, and the infusion rate of insulin may be lowered accordingly.

Measurement of blood glucose with Dextrostix and the reflectance meter is simple and may be performed by nurses on capillary blood samples obtained by finger-prick at the bedside. The result is available within two minutes and compares favourably with estimations performed by a standard laboratory method. Repeated estimations may be performed without undue discomfort to the patient. (During one premature labour over 100 capillary blood samples were taken in 48 hours.)

Provided that simple rules are observed and equipment is properly standardised, management of diabetes during labour with this method becomes a simple procedure suitable for all obstetric units.

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References


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CONDENSED REPORT

Prophylactic use of cephazolin against wound sepsis after cholecystectomy

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Summary

A trial of antibiotic prophylaxis with cephazolin against postoperative wound sepsis was carried out on 201 patients undergoing routine cholecystectomy. Wound sepsis occurred in 11 out of 65 controls (16.9%), who were not given the drug; two out of 63 patients (3.2%) given a single dose preoperatively; and four out of 73 patients (5.5%) given the single preoperative dose plus a five-day course postoperatively. The difference between the controls and patients given the single preoperative dose was significant.

Introduction

Antibiotic prophylaxis against wound sepsis should rarely be needed during "clean" operations. Elective procedures on the biliary system, however, are followed by wound infection in 11-20% of cases. In some 35-40% of such cases the organisms cultured from the biliary tract correlate closely with those recovered from the wound, suggesting an endogenous perioperative source.

Parenteral gentamicin and cephaloridine have potential for successful prophylaxis, but routine use may encourage the emergence of resistant strains, particularly if instilled into the wound. A recent semi-synthetic cephalosporin, cephazolin sodium, reaches concentrations in bile several times the serum concentration 90-120 minutes after injection. In a previous report on non-jaundiced patients with gall-bladder disease high concentrations of this antibiotic were found in the common bile duct one hour after injection. In addition, three doses of cephalazolin started preoperatively significantly reduced wound infection.

We report here the results of a single-blind trial comparing wound infection rates in controls, patients given a single dose of cephazolin, and patients receiving a five-day course.
Patients and methods
During February to October 1976, 214 patients at six hospitals entered the trial. All were admitted for non-urgent cholecystectomy and were under the care of 19 consultant surgeons. Patients were not included if they were jaundiced or had acute cholecystitis, if they had received antibiotics in the week before operation, or if they were known to be sensitive to cephalosporins. The patients were divided into three groups by means of a sealed-envelope system. One group was not given an antibiotic and served as controls, the second was given a single 1-g dose of cephalosporin sodium intramuscularly one hour before operation, and the third was given the same preoperative dose plus a five-day postoperative course of 500 mg intramuscularly every eight hours. Age, weight, and gall-bladder function (as assessed radiologically) were noted. Operations were performed by each surgeon in his usual way, resulting in variation in incision and drainage. Those who routinely removed the appendix continued to do so. Every patient underwent operative cholangiography. Duct exploration and operating time were recorded.

Bacteriology—Aspirates or swabs of bile were obtained from the gallbladder and common bile duct at operation, and a wound swab was taken after peritoneal closure. When organisms grown in a subculture was stored at −20°C for determination of the minimum inhibitory concentration (MIC) of cephalosporin for each isolate. MICs were determined in batches by a routine agar plate dilution method. Oxoid direct sensitivity test agar (pH 7–4) was used throughout. The organisms were grown overnight in nutrient broth at 37°C, and a multipoint inoculating device delivered about 100–1000 colony-forming units to the surface of the plate. The plates were then incubated at 37°C for 18 hours. The MIC was taken as the lowest concentration of cephalosporin to inhibit growth of the inoculated organism.

Assessment of wound sepsis—Wounds were regularly inspected by a microbiologist, or occasionally another surgeon, unaware of which treatment the patient was receiving. Infection was defined as the discharge of pus, irrespective of culture results, or of non-purulent material if it contained pathogenic bacteria. The length of stay in hospital after operation was recorded.

Withdrawal from trial—Any patient given antibiotics postoperatively (other than cephalosporin in the five-day group) was withdrawn.

Results
Of the 214 patients who entered the trial, 13 were given antibiotics other than cephalosporin postoperatively and were therefore withdrawn: all were in the control and single-dose groups. Overt duct sepsis was found in three of these patients at operation, and the rest developed infections of the respiratory and urinary tracts. Only one of the 13 (a control) developed a wound infection. The 201 patients who completed the trial comprised 65 in the control group, 63 given the single-dose regimen, and 73 given the five-day course. The mean ages and sex distribution in the three groups were similar (table A*). The accepted and possible risk factors associated with cholecystectomy—namely, organisms in bile, exploration of common bile duct, age over 70, radiologically non-functioning gall bladder, and concomitant appendectomy—were distributed evenly between the three groups (table B), and we examined their presence in relation to the incidence of wound sepsis in the control group alone (table C). Out of 13 patients (46.2%) with organisms in the bile developed wound infection compared with five out of 52 patients (9.6%) with sterile bile (P < 0.01), and five out of 12 patients (41.7%) subjected to duct exploration had wound sepsis compared with six out of 53 patients (11.3%) who did not undergo this procedure (P < 0.05). No other risk factor was associated significantly with wound sepsis. Concomitant appendicectomy resulted in an infection rate of 21.4%, whereas after cholecystectomy alone the rate was 15.7%.

Out of 108 organisms found on bile culture, 81 (75%) were tested for MIC (table I). Only three isolates were not susceptible to a cephalosporin, one a Staphylococcus aureus, one Streptococcus faecalis, and one Klebsiella sp. One Staphylococcus coagulase positive, one Staphylococcus aureus, one Klebsiella sp., two Staphylococcus aureus, two Streptococcus faecalis, one Streptococcus faecalis, five other streptococci, four Klebsiella sp., two Staphylococcus aureus, two Streptococcus faecalis, one Acinetobacter. On 14 occasions the same organism was also cultured from bile.

Though there was no significant difference between the two treatment groups in the incidence of wound sepsis, the single-dose group differed significantly from the controls in this respect (P < 0.025) when Yates's correction was applied (table II).

<table>
<thead>
<tr>
<th>TABLE I—MIC of cephalosporin for biliary isolates</th>
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<tbody>
<tr>
<td>Organism</td>
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<tr>
<td>----------</td>
</tr>
<tr>
<td>E coli</td>
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<tr>
<td>Klebsiella sp</td>
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<tr>
<td>Sr faecalis</td>
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<tr>
<td>Other streptococci</td>
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<tr>
<td>Others</td>
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*Tables A-D may be obtained on request from the authors.

Discussion
Many surgeons strongly oppose the use of prophylactic antibiotics during any form of surgery. Most would agree that clean operations need no antibiotic cover. Cholecystectomy, however, is associated with a high incidence of wound sepsis related to certain well-recognised risk factors, one of the most important of which is the presence of bacteria in the bile at operation.18 Because such organisms are present in 20–40% of cases, the operation has been termed "clean-contaminated."11,13 Even with duodenal intubation "contaminated" patients cannot be detected preoperatively,14 and few hospitals have the time and resources at their disposal. In addition the decision to explore the common bile duct (table C) is usually made after intravenous cholangiography. Thus more than one in four of our controls proceeded to surgery at risk. If this many are at risk then they merit prophylaxis with an appropriate antibiotic.

The choice of antibiotic is important. Organisms recovered from the biliary tree are predominantly E coli, Klebsiella, and Sr faecalis. In view of the broad spectrum required, previous
antibiotic cover has been with ampicillin and tetracycline, rifamide, gentamicin, and cephaparin, all with varying degrees of success. Fewer than half these organisms, however, are now sensitive to ampicillin or tetracycline. Rifamide, excreted wholly in bile, has yet to be studied in sufficient depth in a prophylactic trial excluding jaundiced patients. Gentamicin fails to reach bactericidal concentrations in bile, and many bacteriologists believe that it should be reserved for life-threatening sepsis and not used prophylactically.

Although cephaparin may reduce wound sepsis, cephaparin reaches higher concentrations in both serum and bile. High concentrations in bile have been found in patients with biliary disease, and the peak concentrations in common duct bile occur 60–90 minutes after injection. It seemed rational to provide the patient with a peak concentration in the biliary tree when surgical manipulation was at its height. Hence a 1-g injection was given to both treatment groups one hour before operation.

Recently the trend has been to reduce the duration of prophylaxis. Stone et al. in a trial including patients undergoing biliary surgery, showed that preoperative administration of cephaparin reduced wound infection to 2%. When prophylaxis began after operation the infection rate was similar to that in controls. Stokes et al. found that two doses of a combination of an aminoglycoside with lincomycin effectively reduced sepsis after bowel surgery and encountered no bacterial resistance, nor did they feel that this would be likely to occur after short-term treatment. Few studies have been made of the efficacy of single-dose antibiotic prophylaxis, a concept that bacteriologists favour in principle but for which there is little practical evidence. In one such study 500 mg ampicillin intravenously failed to reduce wound sepsis. Leigh et al. however, reduced wound sepsis after appendicectomy by giving a 600-mg intramuscular dose of lincomycin after wound closure.

We have confirmed that wound infection is associated with duct exploration and the presence of bacteria in the bile (table C). These risk factors were evenly distributed among the three groups. Possibly because jaundiced patients were excluded and few patients were aged over 70, age and non-functioning gall bladder were not demonstrable risk factors in our series. In the control group concomitant appendicectomy resulted in a 21.4% infection rate compared with a rate of 15.7% after cholecystectomy alone. This differs from the figures of 41% and 16% respectively in a study by Pollock and Evans.

Cephaparin prophylaxis did not affect the rate of recovery of bacteria from bile at operation (table B). There was, however, a highly significant reduction in wound sepsis after cholecystomy (P < 0.02) in the two treatment groups, which suggests that cephaparin had not exerted its full bactericidal potential when the specimens were taken.

Only three strains of the most common biliary organisms were not inhibited by the reported average common bile duct concentration of cephaparin in patients with biliary disease (table I). Two of these were Klebsiella. There was, however, little correlation between biliary isolations (108) and the few organisms subsequently found in infected wounds (6). Since cephaparin reaches adequate concentrations in bile, blood, and tissues, it is unlikely that any one of these was solely responsible for the prophylactic effect shown in this trial.

The most significant finding was the reduction in wound sepsis from 16.9% in the controls to 3.2%, in the single-dose group. The full five-day course was less effective, with 5.5% of wounds infected, although not significantly different from the single-dose group.

Surgeons opened the abdomen in their usual manner. Three-quarters of the incisions were subcostal, the remainder being paramedian rectus-shifting (table D). Neither incision nor type of drainage significantly influenced the incidence of wound infection, which agrees with the finding of Gordon et al. All patients underwent on-table cholangiography. There were no deaths, which may reflect the increasing use of low-dose heparin prophylaxis against thromboembolism.

Cephalosporins are powerful broad-spectrum antibiotics with few specific indications. Cephaparin is clinically effective and appears to be a rational choice in the prophylaxis of wound infection after biliary surgery. This study shows that it is effective when given as a single dose, which reduces cost, saves nursing time, and is less likely to produce bacterial resistance.

The following centres, listed in order of the number of patients contributed, took part in the trial; we thank our consultant surgical colleagues at these hospitals: Queen Elizabeth Hospital, Birmingham (F Ashton, A P Barnes, V S Brookes, A Gourvestich, J D Hamer, D M Morrissey, and G Slaney); General Hospital, Northampton (K Cronin); North Staffs Royal Infirmary, Stoke (L J Lawson and H S Trafford); General Hospital, Birmingham (R M Baddeley, N J Doorlock, G D Oates, and J A Williams); Dudley Road Hospital, Birmingham (P G Bevan and M A Feldman); Walsgrave Hospital, Coventry. We thank the house surgeons, registrars, nursing staff, and technicians of the participating hospitals for their co-operation; Dr C Wicks, Mr D Varnham, Mr M A Jones, and Mr R Cones, of Ell Lilly & Co (Basingstoke), for help in co-ordinating the trial; Miss Pat Cole for preparing the manuscript; and Mr A R McLeish (Milton) for help in formulating the trial.

Tables A–D may be obtained from: Mr Colin J L Strachan, Department of Surgery, Queen Elizabeth Hospital, Birmingham B15 2TH.

References

8 Pollock, A V, and Evans, M, Lancet, 1975, 2, 1251.
17 Forsman-Smith, W R, British Journal of Hospital Medicine, 1975, 14, 529.

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