Cefoperazone Versus Clindamycin Plus Gentamicin for Obstetric and Gynecologic Infections

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Cefoperazone was compared with clindamycin plus gentamicin for the treatment of pelvic infections. Of 102 women, 95 (93%) demonstrated a good clinical response (47 with cefoperazone and 48 with clindamycin plus gentamicin). Of the seven failures, four were secondary to side effects and three were clinical failures.

Cefoperazone provides broad-spectrum coverage against many of the organisms encountered in obstetric and gynecologic infections (2, 8, 11, 13). The present study was undertaken to compare cefoperazone with clindamycin plus gentamicin for the treatment of women with pelvic infections (postpartum endometritis, posthysterectomy vaginal cuff infections, or acute pelvic inflammatory disease). Reasons for exclusion included breast-feeding, pregnancy, and hypersensitivity to penicillin. The clinical diagnosis of pelvic infection was based primarily on the presence of fever, pain, and leukocytosis. Specifically, patients with salpingitis had cervical motion and adnexal tenderness or an adnexal mass or both. Patients with endometritis had uterine and parametrical tenderness and foul lochia. Patients with posthysterectomy cellulitis had exceptional tenderness and induration of the vaginal cuff.

 Cultures had been obtained from all patients before therapy. For women with endometritis, specimens were obtained from endometrial washings (7). For women with posthysterectomy cuff cellulitis, specimens were obtained by direct sampling of the vaginal cuff. Women with acute salpingitis had specimens taken via culdocentesis for aerobic and anaerobic organisms, as well as Neisseria gonorrhoeae, and directly from the endocervix for isolation of N. gonorrhoeae. Specimens for isolation of the gonococcus were plated directly onto Thayer-Martin medium, whereas all others were transported to the laboratory in a Port-A-Cul (BBL Microbiology Systems) vial or tube. Techniques for isolation and identification of aerobic and anaerobic organisms have been previously described (9, 10, 12, 15).

 MICs for cefoperazone and clindamycin were determined for anaerobes, as well as for enterococci and group B streptococci, by the agar dilution method of Sutter et al. (16). For the remaining aerobes, disk susceptibility tests were performed by the method of Bauer et al. (1). The patients were randomized to either cefoperazone or a combination of clindamycin and gentamicin according to a computer-generated list of numbers. Cefoperazone was administered in a dose of 2 g intravenously every 12 h. Clindamycin was administered in a dose of 600 mg intravenously every 6 h, and gentamicin was administered in a dose of 1 to 1.5 mg/kg of body weight intravenously every 8 h. Patients received the antibiotics for a mean of 5.6 days. There was no significant difference between the study groups with regard to duration of therapy (5.5 ± 1 versus 5.7 ± 1 days). Antibiotics were discontinued after the patient had been afebrile for at least 24 h. Patients with acute salpingitis were discharged with oral tetracycline to complete a 10-day course of therapy. Clinical failures were defined as patients who showed no significant improvement after 48 h or whose conditions worsened during therapy. Patients were monitored before, during, and after therapy with complete blood counts, serum creatinine and blood urea nitrogen tests, urinalysis, and liver function test.

 Most of the patients were parous (58%) and between the ages of 20 and 39 (62%). There were no significant differences in these factors with regard to antibiotic regimens. Of the 51 patients treated with cefoperazone and the 51 patients treated with clindamycin-gentamicin, 28 (27%) had postcesarean section endometritis (12 versus 16, respectively), 27 (26%) had posthysterectomy cuff, pelvic cellulitis, or both (14 versus 13), 25 (25%) had acute salpingitis (18 versus 7), and 22 (22%) had endometritis (7 versus 15) after vaginal delivery or incomplete abortion. The mean highest temperature was similar in both groups (38.8°C for the cefoperazone group and 38.9°C for the clindamycin-gentamicin group). Two patients in the cefoperazone group and three in the clindamycin-gentamicin group had a positive blood culture. Isolates from these cultures were Klebsiella pneumoniae, Proteus mirabilis, Enterobacter cloacae, Bacteroides fragilis, and a Bacteroides species (nonviable). The bacterial isolates were similar in both antibiotic groups, with the exception of the isolation of a few more gram-negative bacilli and Bacteroides bivius in the clindamycin-gentamicin group. The results of susceptibility testing are summarized in Table 1.

 Of the 102 women, 95 (93%) demonstrated a good clinical response to antibiotic therapy (47 [92%] of 51 in the cefoperazone group and 48 [94%] of 51 in the clindamycin-gentamicin group). Side effects in four patients required discontinuation of the study antibiotics: severe diarrhea in two patients in the clindamycin-gentamicin group and an allergic skin reaction in two patients in the cefoperazone group. Of the three treatment failures, two patients were receiving cefoperazone for vaginal cuff and pelvic cellulitis. One of these patients had an enterococcus for which the MIC was 64 μg/ml. The remainder of isolates in this patient (as well as in the other patient) were susceptible to cefoperazone. Both of these patients were changed to clindamycin-
gentamicin therapy with a good clinical response. The remaining clinical failure was in the clindamycin-gentamicin group (postcesarean section endometritis), and no resistant organisms were isolated. This patient responded favorably to the addition of ampicillin. Six patients in the cefoperazone group and two patients in the clindamycin-gentamicin group had transient minimal elevations of glutamic-oxaloacetic transaminase in serum. In addition, one patient in the cefoperazone group had an unexplained transient elevation in the eosinophil count while on therapy, and two patients in the clindamycin-gentamicin group had an elevated serum creatinine or blood urea nitrogen level.

Because of the inherent risks with regimens consisting of combinations of antibiotics, single-agent therapy would be preferred provided that the individual antibiotics were successful (i.e., had a high cure rate) in most pelvic infections treated. Fortunately, most newer cephalosporins and penicillins do provide a wide spectrum of coverage and have been reported to be quite efficacious as well as relatively safe for the patient (3–6, 9, 14, 17). The major drawback with these newer antibiotics is cost. In the present study, cefoperazone was both safe and efficacious for treating women with polymicrobial pelvic infections. Although this study included only 102 patients, cefoperazone appeared to be as effective as clindamycin-gentamicin, although a type II error cannot be ruled out. Moreover, side effects were infrequent and generally minor in nature. In addition, most organisms tested with the antibiotic were susceptible to clinically achievable levels.

**TABLE 1. Results of susceptibility testing**

<table>
<thead>
<tr>
<th>Isolates (n)</th>
<th>Cefoperazone</th>
<th>Clindamycin</th>
<th>Gentamicin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aerobes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group B streptococci (17)</td>
<td>17 (100)</td>
<td>17 (100)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Enterococci (44)</td>
<td>14 (32)</td>
<td>1 (2)</td>
<td>44 (100)</td>
</tr>
<tr>
<td>Staphylococcus aureus (2)</td>
<td>2 (100)</td>
<td>2 (100)</td>
<td>2 (100)</td>
</tr>
<tr>
<td>Escherichia coli (48)</td>
<td>46 (96)</td>
<td>NT*</td>
<td>48 (100)</td>
</tr>
<tr>
<td>Other gram-negative (26)</td>
<td>26 (100)</td>
<td>NT</td>
<td>26 (100)</td>
</tr>
<tr>
<td>Neisseria gonorrhoeae (2)</td>
<td>2 (100)</td>
<td>2 (100)</td>
<td>2 (100)</td>
</tr>
</tbody>
</table>

| Anaerobes                    |              |             |            |
| Gram-positive cocci (11)     | 10 (91)      | 11 (100)    | NT         |
| Bacteroides bivius (42)      | 41 (98)      | 42 (100)    | NT         |
| Bacteroides fragilis (17)    | 7 (44)       | 17 (100)    | NT         |
| Other Bacteroides species (3)| 3 (100)      | 3 (100)     | NT         |
| Clostridium species (6)      | 6 (100)      | 6 (100)     | NT         |
| Fusobacterium species (8)    | 8 (100)      | 8 (100)     | NT         |
| Eubacterium species (3)      | 3 (100)      | 3 (100)     | NT         |

* Breakpoints were ≤16 μg/ml (MIC) or zone diameter of ≥21 mm for cefoperazone, ≥8 μg/ml (MIC) or zone diameter of ≥16 mm for clindamycin, and zone diameter of ≥14 mm for gentamicin.

* NT, Not tested.

**REFERENCES**