NOTES

Double-Blind Comparison of Phlebitis Produced by Cefazolin Versus Cephalothin

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In a double-blind study with each patient as his own control, 1 g of cefazolin and 2 g of cephalothin were administered intravenously every 6 h to 20 patients in opposite arms for a period of 48 h each. The degree of phlebitis was significantly more severe with cephalothin than with cefazolin ($P < 0.05$); however, neither the incidence of phlebitis nor the time of onset of phlebitis was significantly different between the two drugs.

Cefazolin sodium, a new cephalosporin C antibiotic for parenteral use, has a spectrum of activity similar to that of cephalothin but gives higher and more sustained concentrations in serum (3). It has been the impression that cefazolin administered intravenously causes less phlebitis than cephalothin (2, 4).

The purpose of the present study was to determine in a double-blind manner, with each patient as his own control, whether the phlebitis-producing potential of intravenously administered cefazolin was the same as cephalothin.

The patients studied were 20 adults hospitalized at the Hospital of the Medical College of Pennsylvania, all of whom had suspected or confirmed bacterial infections. Informed consent was obtained from all patients.

An intravenous infusion was started in an arm or hand vein with a 21-gauge scalp vein needle. The area was first swabbed with 70% alcohol or an iodophor iodine compound. According to the double-blind schedule, either cefazolin or cephalothin was administered intravenously every 6 h for the first 48 h. After the initial 48 h, the intravenous infusion was changed to the identical vein in the opposite arm and the alternate antibiotic was begun. The antibiotic powder in each vial was reconstituted with 100 ml of saline solution just prior to administration and was infused over a period of 15 to 20 min.

Both cefazolin and cephalothin powder were supplied by Smith Kline & French Laboratories in vials marked "A" and "B." Vial A contained cefazolin (1 g), and vial B contained cephalothin (2 g). The choice of dose reflects the fact

that 1 g of cefazolin intravenously gives at least equivalent blood levels to 2 g of cephalothin administered intravenously (1), and that these are the usual doses of each drug used in the treatment of serious infections. The contents of the vials were not known to the investigators. The order in which the vials (i.e., A or B) were administered was randomly assigned in advance. During the study, the infusion site was kept open with 5% dextrose in water and was not used for administration of any other drug.

The infusion sites were examined after 24 and 48 h. Phlebitis was graded from 1 to 3+ as follows: 1+, erythema and mild tenderness extending along the vein more than 2.5 cm above the infusion site; 2+, erythema and moderate tenderness extending along the vein more than 2.5 cm above the infusion site; 3+, erythema and severe tenderness extending along the vein more than 2.5 cm above the infusion site.

At the conclusion of the study it was determined that 11 patients had received cefazolin first, and 9 patients had received cephalothin first. Among the 20 patients, 7 developed phlebitis when cefazolin was infused and 12 developed phlebitis when cephalothin was infused.

Six of these patients developed phlebitis with both drugs. On a scale of 1 to 3+, five patients receiving cefazolin had 1+ phlebitis, two had 2+ phlebitis, and zero had 3+ phlebitis; three patients receiving cephalothin had 1+ phlebitis, five had 2+ phlebitis, and four had 3+ phlebitis.

In this study, no significant difference was observed in the frequency of development of

phlebitis or in the time of onset of phlebitis produced by intravenously administered cefazolin or cephalothin ($P > 0.05$ by the chi-square test). However, when patients with more severe phlebitis (arbitrarily defined as $\geq 2+$) were compared, the difference was significant (9 of 20 with cephalothin versus 2 of 20 with cefazolin; $P < 0.05$ by chi-square test). This difference may have been due to the larger dose of cephalothin used as compared with cefazolin, but these are the dosages commonly used clinically.

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LITERATURE CITED

1. Kirby, W. M., and C. Regamey. 1973. Pharmacokinetics of cefazolin compared with four other cephalosporins. *J. Infect. Dis.* **128**:S341-S346.
2. Reinarz, J. A., C. M. Kier, and J. C. Guckian. 1973. Evaluation of cefazolin in the treatment of bacterial endocarditis and bacteremia. *J. Infect. Dis.* **128**:S392-S396.
3. Ries, K., M. E. Levison, and D. Kaye. 1973. Clinical and in vitro evaluation of cefazolin, a new cephalosporin antibiotic. *Antimicrob. Agents Chemother.* **3**:168-174.
4. Turck, M., R. A. Clark, H. N. Beaty, K. K. Holmes, W. W. Karney, and L. B. Reller. 1973. Cefazolin in the treatment of bacterial pneumonia. *J. Infect. Dis.* **128**:S382-S385.