Differences in Susceptibility of Enterobacteriaceae and Penicillin-Resistant Staphylococcus aureus to Tetracycline and Minocycline

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Two hundred strains of penicillin-resistant Staphylococcus aureus and 311 isolates of Enterobacteriaceae were compared for their susceptibility to tetracycline and minocycline. Thirteen and one-half percent of the staphylococcal isolates were resistant to tetracycline but susceptible to minocycline. Similarly, 24% of the enterobacterial isolates were found to be tetracycline resistant but susceptible to minocycline. Of a total of 511 recent clinical isolates, 14.5% were susceptible to minocycline but were tetracycline resistant.

In the laboratory determination of antibiotic susceptibility of bacterial isolates, it is generally not necessary to test every member of a class of related drugs. This practice of avoiding redundancy in testing is based upon the concept that, although marked pharmacologic differences may exist among a class of drugs, their antimicrobial spectrum is essentially identical. In line with this practice, disks containing tetracycline are used to represent this class of antimicrobial agents (3). A number of reports however (1, 4-6) have indicated that significant differences in antimicrobial activity do exist among tetracycline analogues, and bacteria found to be resistant to tetracycline may, in fact, be susceptible to one or more analogues of the parent compound. A comparative evaluation (6) of the in vitro susceptibility of common bacterial patho gens to seven tetracycline antibiotics indicated that minocycline (7-dimethylamino-6-demethyl-6-deoxytetracycline) was the most active analogue. The present study presents comparative data on the in vitro susceptibility of penicillin-resistant Staphylococcus aureus and Enterobacteriaceae to tetracycline and its minocycline analogue.

MATERIALS AND METHODS

The antibiotic susceptibility of 200 fresh clinical isolates of S. aureus were routinely tested by the Kirby-Bauer technique (2). One hundred of these isolates were recovered from wounds or abscesses, 83 from respiratory sites, seven from female genital specimens, six from urine, and one each from blood, bone marrow, eye, and ear. Those strains showing resistance to penicillin (zone sizes less than 20 mm) were selected for further testing. Standardized suspensions of these organisms were inoculated onto 150-mm plates of Mueller-Hinton agar and 30-μg tetracycline and minocycline disks were placed on the plate. Three disks of each drug were placed on each plate. After incubation for 18 h at 35 C, the diameters of the zones of inhibition were measured and the mean zone diameter was determined for each of the drugs.

In a similar manner, 311 clinical isolates of Enterobacteriaceae showing tetracycline resistance on routine testing were selected for further evaluation against tetracycline and minocycline as described above. Two hundred and one of these isolates were recovered from urine, 53 from wounds or abscesses, 47 from respiratory sites, and 10 from genital specimens. The various species recovered are shown in Table 1. A single lot of Mueller-Hinton agar from one manufacturer was utilized for the entire study, and all testing of the selected strains was performed by the same technologist. Isolates giving mean zone diameters of 19 mm or greater were interpreted as susceptible; zones of 15 to 18 mm were considered as intermediate; and zone diameters of 14 mm or less were interpreted as resistant.

Both drugs were tested against standard reference strains of Escherichia coli (ATCC 25922) and S. aureus (ATCC 29213). Tetracycline disks produced mean zone diameters of 21 mm with E. coli and 26 mm with S. aureus; minocycline gave mean zone diameters of 20 mm with E. coli and 28 mm with S. aureus.

RESULTS

One hundred sixty-nine strains of penicillin-resistant S. aureus (84.5%) were found to be susceptible to both tetracycline and minocycline. Twenty-seven of the staphylococcal isolates (13.5%) were resistant to tetracycline but susceptible to minocycline. Thirteen of these strains were wound isolates, 11 strains came...
from respiratory sites, two from urine, and one from a cervical culture. Three strains were resistant to tetracycline but gave intermediate zones (16, 17, and 18 mm) to minocycline. A single isolate was resistant to both drugs.

Forty-eight of the enterobacterial isolates (24%) were resistant to tetracycline but susceptible to minocycline. Forty-two of these strains were urinary isolates, five were from respiratory sites, and one from a wound. These tetracycline-resistant, minocycline-susceptible species included 28 E. coli, eight Proteus mirabilis, eight Serratia, three Klebsiella, and one Enterobacter.

Of a total of 511 organisms tested, 74 (14.5%) were clearly resistant to tetracycline but susceptible to minocycline.

**DISCUSSION**

Minuth et al. (5) recently showed that significant numbers of S. aureus isolates were resistant to tetracycline but inhibited by minocycline. This confirmed the observations of Steigbigel et al. (6) who studied 56 strains of S. aureus and found that 35% of them were susceptible to minocycline but resistant to other tetracyclines. Minocycline was found to be more active against strains of E. coli, members of the Klebsiella-Enterobacter-Serratia group, and Acinetobacter than the other tetracycline analogues tested. Significant differences among tetracycline analogues were also observed by Klastersky and Daneau (4) who noted that minocycline was more active against strains of E. coli, Proteus mirabilis, Klebsiella-Enterobacter, and Pseudomonas aeruginosa than equal concentrations of doxycycline or tetracycline. Bach et al. (1) documented marked differences to exist in the susceptibility of Nocardia asteroides to minocycline and tetracycline; all of 49 strains were inhibited by 6.3 μg of minocycline per ml, whereas 12.5 μg of tetracycline per ml only inhibited eight of the strains.

It is clear from our results that the tetracycline disk does not detect susceptibility of staphylococci and members of the Enterobacteriaceae to all of the tetracycline analogues. It is also evident that significant numbers of bacterial pathogens considered resistant to tetracycline may be susceptible to minocycline. Minocycline may prove to be a useful drug in the treatment of infections caused by members of the Enterobacteriaceae, Nocardia, and under certain circumstances by penicillin-resistant staphylococci.

**LITERATURE CITED**