Comparative In Vitro Evaluation of the Effects of Ticarcillin and Carbenicillin upon Pseudomonas aeruginosa

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An in vitro comparison of the effects of ticarcillin and carbenicillin was performed upon 164 strains of Pseudomonas aeruginosa. The two drugs displayed nearly identical inhibitory activities: for each, about 82.5% of the strains were inhibited by doses of 256 µg/ml or less. A low bactericidal activity was also observed. Strains of P. aeruginosa that were highly resistant to carbenicillin were also resistant to ticarcillin.

Pseudomonas aeruginosa has an important role as a causative organism of intrahospital epidemics, which have increased in frequency in recent years. Carbenicillin has been used successfully in the treatment of these infections (2, 4). The appearance of resistant strains of P. aeruginosa has created an imperative need for the detection of new active drugs. In this paper we present data on the comparative susceptibility of recent clinical isolates of P. aeruginosa to carbenicillin and to ticarcillin, a new semisynthetic penicillin.

MATERIALS AND METHODS

Ticarcillin (6-[-D-α-carboxy-3-thienylacetamido] penicillanic acid) and carbenicillin (6-[-D-α-carboxyphenylacetamido] penicillanic acid) were supplied by Beecham Pharmaceuticals as a dry powder. A total of 164 strains of P. aeruginosa was isolated from different pathogenic materials from patients hospitalized at the National Hospital of Athens "King Paul." These strains were identified by growth on MacConkey agar, oxidase and pigment production, growth at 4 and 42 C, gluconate oxidation, failure to ferment lactose and sucrose, gelatin liquefaction, and citrate utilization. Pyocine typing was performed by the method of Gillies and Govan (3).

Minimal inhibitory concentrations (MICs) were determined by serial twofold dilutions in tubes containing Mueller-Hinton broth (Oxoid). The inoculum used in these tests was 3 ml of a 10⁻³ dilution of an overnight broth culture added to 3 ml of fresh broth, yielding an inoculum density of 5 × 10⁶ colony-forming units/ml. The MIC was defined as the lowest concentration of drug that prevented macroscopically visible growth after incubation at 37 C for 18 h. Minimal bactericidal concentrations were determined by subculturing 0.01 ml of broth from clear tubes onto blood agar plates and noting the lowest antibiotic concentration resulting in the growth of less than 10 colonies.

RESULTS

The activities of carbenicillin and ticarcillin against the 164 strains of P. aeruginosa are shown in Fig. 1. In general, the two drugs displayed virtually identical activities, with about 82.5% of the strains having an MIC of 256 µg/ml or less and with 50% of the strains being inhibited by doses between 64 and 128 µg/ml. Apparently the susceptibility of different

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*Fig. 1. Comparison of minimal inhibitory concentrations (MIC) and minimal bactericidal concentrations (MBC) for the two semisynthetic penicillins carbenicillin and ticarcillin, applied to 146 strains of P. aeruginosa.
strains of *P. aeruginosa* to the drugs is variable and not predictable for all strains.

A comparison of minimal bactericidal concentrations for the two drugs (Fig. 1) shows a low bactericidal activity for the semisynthetic penicillins. The bactericidal concentrations for the two drugs exceeded the respective MICs by approximately two to four serial dilutions for 43.6% of the strains. Of eleven strains that were highly resistant to ticarcillin, seven were also very resistant to carbenicillin. Five strains with various MICs for the two drugs were exposed to 0.1, 1, 10, 100, and 1,000 × MIC concentrations of the drugs separately; under a phase-contrast microscope they displayed similar morphological variations after 1, 1.5, and 4 h.

**DISCUSSION**

In this study the in vitro actions of ticarcillin and carbenicillin on *P. aeruginosa* were essentially identical. These results contrast with several reports (1, 5, 6) that claim a greater activity for ticarcillin than for carbenicillin against *P. aeruginosa*. Further experiments using different broths and agars will be necessary to determine the consistency of the responses of these drugs, and animal experiments will have to be performed to determine whether the observed in vitro response is similar in vivo. A nearly uniform lack of in vitro bactericidal activity against strains of *P. aeruginosa* was noted in our study. Eleven strains were highly resistant to ticarcillin; and of these, four had relatively low MICs for carbenicillin. This is of some interest since ticarcillin is a new drug that has not yet been used in Greece. According to Neu and Winshell (5), strains of *Pseudomonas* or members of the *Enterobacteriaceae* resistant to carbenicillin will also be resistant to ticarcillin.

Results for the activity of ticarcillin on different members of the *Enterobacteriaceae* as well as the in vitro synergy with gentamicin will be presented later.

**LITERATURE CITED**


