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Comparison and Evaluation of Ticarcillin and Carbenicillin Using Disk Diffusion Methods

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Ticarcillin has proved to be two- to fourfold more active than carbenicillin against most strains of *Pseudomonas aeruginosa*. Although susceptibility of the *Enterobacteriaceae* to ticarcillin could be predicted from results obtained with carbenicillin disks, neither the 50-μg nor the 100-μg carbenicillin disk proved suitable for testing susceptibility of *P. aeruginosa* to ticarcillin. Forty-three percent of *Pseudomonas* strains judged to be resistant to carbenicillin by the 100-μg carbenicillin disk were susceptible to ticarcillin by agar dilution studies. Results obtained with a 75-μg ticarcillin disk showed excellent correlation between zone size and ticarcillin minimal inhibitory concentration values and produced good discrimination between resistant and susceptible strains of *Pseudomonas* as determined by agar dilution studies. Using a 75-μg ticarcillin disk, a zone size of 12 to 14 mm was appropriate for designating intermediate susceptibility, and a zone greater than or equal to 15 mm was appropriate for designating susceptible strains of both *P. aeruginosa* and the *Enterobacteriaceae*.

The susceptibility of *Pseudomonas* species and members of the *Enterobacteriaceae* to carbenicillin is routinely determined by the disk diffusion method, as is susceptibility to other antibiotics. Original work with disks of varying carbenicillin content (5, 9, 10) led to the approval of a 50-μg carbenicillin disk and the adoption of criteria for zone size interpretation (3). Recent work by Matsen et al. (6) and by Washington et al. (11) has suggested that the 100-μg carbenicillin disk is subject to less variation in content of antibiotic and produces zone sizes that correlate better with carbenicillin minimal inhibitory concentration (MIC) values determined by agar dilution methods.

The discovery of ticarcillin, a thienyl-carboxy-penicillanic acid derivative that is two- to fourfold more active than carbenicillin against *Pseudomonas aeruginosa*, has led to its clinical evaluation in infections caused by *Pseudomonas* and other gram-negative bacilli. During our evaluation of this antibiotic, we noted that disk diffusion data from carbenicillin disks were not adequate in many instances to determine the susceptibility of *P. aeruginosa* to ticarcillin. This was particularly true at ticarcillin MIC values between 50 and 200 μg/ml, concentrations that are achievable in serum (7). This prompted us to reevaluate the 50- and 100-μg carbenicillin disks and to compare these disks with the 75-μg ticarcillin disk in determining the susceptibility of gram-negative microorganisms to ticarcillin.

MATERIALS AND METHODS

Three hundred ten strains of gram-negative bacteria were studied. These included 124 strains of *P. aeruginosa*. All organisms were isolated from clinical specimens of blood, urine, sputum, or wounds of patients admitted to Columbia-Presbyterian Medical Center. Organisms were isolated and identified according to standard laboratory procedure (2, 4) in the clinical microbiology laboratories of Presbyterian and Babies Hospital. The isolated bacteria were inoculated onto brain heart infusion agar (Difco) slants, incubated at 35 C for 18 h, and then maintained at room temperature before testing.

Disk diffusion studies were performed according to the method of Bauer et al. (1) by inoculating a loop of stock culture into 2 ml of sterile Mueller-Hinton broth (BBL) and incubating the broth for 18 h at 35 C. The tubes were agitated, and a portion was adjusted to an 0.5 MacFarland opacity standard (99.5 ml of 0.36 N sulfuric acid plus 0.5 ml of 1.175% $BaCl_2 \cdot 2H_2O$) by diluting with sterile Mueller-Hinton broth. A sterile cotton swab was dipped into the standardized suspension, rotated against the side of the tube to remove excess fluid, and then streaked in three directions onto plates containing Mueller-Hinton agar (BBL) to a depth of 4 mm. Agar plates were made within 48 h of use, refrigerated, and allowed to reach room temperature before being inoculated. Antibiotic susceptibility disks used for the study were 50-μg carbenicillin disks (Pfizer, BBL), 100-μg carbenicillin disks (BBL), and 75-μg ticarcillin disks

(Beecham Laboratories). Three disks, one of each type, were placed randomly on the agar surface, allowing at least 40 mm between each disk. Zone sizes were read after 18-h overnight incubation at 35 C. Values were thus obtained simultaneously with each disk for each organism tested.

MIC values for carbenicillin and ticarcillin were determined by the agar dilution method. Agar plates were prepared using Mueller-Hinton agar (BBL) containing ticarcillin or carbenicillin in concentrations from 800 to 0.8 μg/ml in twofold dilutions. A control plate without antibiotic was included in each series. Plates were prepared 24 h in advance, refrigerated, and then allowed to reach room temperature before inoculation. Each organism was inoculated into 2 ml of sterile Mueller-Hinton broth and incubated for 18 h at 35 C. Approximately 10^4 organisms from the resulting culture suspension were inoculated onto the prepared plates by a replicating device, allowing 25 strains to be tested simultaneously. Plates were then incubated at 35 C. The MIC value was determined as the lowest antibiotic concentration that produced no visible growth after 18 h of incubation.

MIC values for both carbenicillin and ticarcillin, and disk diffusion data for the 50- and 100-μg carbenicillin disks and the 75-μg ticarcillin disks, were thus available for each of the 310 organisms and were determined simultaneously. Zone size was plotted against MIC value on semilogarithmic paper to produce a scattergram, and regression lines were determined by the method of least squares adapted for computer calculation.

Zone size criteria for the 50-μg carbenicillin disk were the accepted published criteria (3): less than or equal to 12 mm, resistant; 13 to 14 mm, intermediate; and greater than or equal to 15 mm, susceptible, for *P. aeruginosa*. Criteria for the 100-μg carbenicillin disk for *P. aeruginosa* were those in common use and as suggested by Matsen et al. (6): less than or equal to 13 mm, resistant; 14 to 16 mm, intermediate; and greater than or equal to 17 mm, susceptible.

Antibiotic content of the three disk types was determined by comparison with disk made in our own laboratory. Disk standards were prepared in 25-μg increments of 0, 25, 50, 75, 100, 125, and 150 μg. Disks were assayed by an agar plate technique with *P. aeruginosa* NCTC 10701 as the assay organism. Twenty disks of each type were assayed, and disk antibiotic content was determined by comparison with zone sizes produced by the disk standards.

RESULTS

The in vitro susceptibilities of 310 strains of gram-negative bacilli, as determined by the agar dilution method, are presented in Table 1. Ticarcillin inhibited 74% of *P. aeruginosa* strains at 25 μg/ml and 91% at 100 μg/ml. Carbenicillin was significantly less effective than ticarcillin, with 48% of strains susceptible to 25 μg/ml and 84% susceptible to 100 μg/ml ($P < 0.01$). Ticarcillin was consistently twice, and occasionally four times, as active as carbenicillin against *P. aeruginosa*. This was also true for other *Pseudomonas* species. The median ticarcillin MIC for *Pseudomonas* was 12.5 μg/ml, but the range of MIC values was from 0.8 to 400 μg/ml, with bimodal peaks at 0.8 and 25 μg/ml.

The *Enterobacteriaceae* exhibited similar susceptibility to both ticarcillin and carbenicillin. *Escherichia coli, Proteus mirabilis,* and indole-positive *Proteus* species *(Proteus vulgaris, P. rettgeri, P. morganii)* exhibited a biphasic distribution of MIC values, being either quite susceptible (≤50 μg/ml) or very resistant (>800 μg/ml). No strains of these organisms were found with MIC values between 50 and 800 μg/ml. The same was true for *Serratia,* although few susceptible strains (predominantly *Serratia liquefaciens*) are found in most hospital environments. *Enterobacter* and *Citrobacter* displayed a continuum of susceptibilities, with respective median ticarcillin MIC values of 3.1 and 100 μg/ml.

Zone size distribution using 100-μg carbenicillin disks is shown in Fig. 1. Carbenicillin MIC values, expressed in $\log_2$ scale, are plotted on the ordinate, versus zone diameter in millimeters on the abscissa. There is a continuum of zone sizes corresponding to MIC values with a greater splay of zone sizes for organisms susceptible to 0.8 μg/ml, since this represents a range of MIC values from 0.8 μg/ml to below this value.

The 100-μg carbenicillin disk produced good correlation between MIC values and zone size (Table 2) with only moderate scatter around the regression line. Mean standard deviation of zone sizes around the regression line was 3.01 mm. The regression line intersects the ordinate (the 6-mm or "no-zone" point) at a carbenicillin MIC value of 631 μg/ml, well above the critical MIC value for resistance. Using the 100-μg disk, we found good discrimination between susceptible and resistant strains of *P. aeruginosa* (Fig. 2). All strains of *P. aeruginosa* with a carbenicillin MIC value of 50 μg/ml or less, and 13 of 17 (76%) with a carbenicillin MIC value of 100 μg/ml were considered susceptible or intermediate by disk criteria (zone size greater than or equal to 14 mm), whereas 17 or 18 strains with MIC values greater than or equal to 200 μg/ml were counted as resistant. Using the 100-μg carbenicillin disk for testing susceptibility of the *Enterobacteriaceae* (Fig. 2), all organisms with MIC values less than or equal to 25 μg/ml were susceptible (zone size greater than or equal to 18 mm), but only 9 of 12 (75%) with MIC values of 50 μg/ml and 0 of 7 with MIC values of 100 μg/ml were called sus-

TABLE 1. *Comparison of in vitro activity of ticarcillin and carbenicillin*

Organism and agent	No. of strains tested	MIC (μg/ml)										
		≤0.8	1.6	3.1	6.2	12.5	25	50	100	200	400	≥800
Pseudomonas aeruginosa	124											
Ticarcillin		23	9	6	11	15	28	15	6	10	1	
Carbenicillin		17	9	8	5	4	16	30	17	9	9	
Pseudomonas (other)	10											
Ticarcillin		1		2				3	2	1	1	
Carbenicillin			1		2			1	1	2	2	1
Proteus mirabilis	26											
Ticarcillin		15	7	2		1		1				
Carbenicillin		7	16		1		1	1				
Proteus (Indole +)	25											
Ticarcillin		4	5		3	5	4					4
Carbenicillin		4	6		3	5	2	1				4
Escherichia coli	31											
Tircarcillin		4	10	7	4	1	1					4
Carbenicillin		2	3	11	6	4	1					4
Enterobacter	34											
Ticarcillin		3	1	16	6	1	2	2	2			1
Carbenicillin			4	7	11	5	1	3	2			1
Citrobacter	29											
Ticarcillin			3	5	1	1	2	1	7	7	1	1
Carbenicillin				3	5	2	1	3	4	6	4	1
Klebsiella	8											
Ticarcillin							2	2	1	2		1
Carbenicillin								3	1	2	1	1
Serratia	12											
Ticarcillin				1	5	1		1				4
Carbenicillin					5	2		1				4
Acinetobacter	10											
Ticarcillin						4	3	1				2
Carbenicillin						1	5	2				2

ceptible to carbenicillin. These latter MIC values correspond to easily achievable serum levels of carbenicillin. The 19 strains of *Enterobacteriaceae* with carbenicillin MIC values of 50 or 100 μg/ml included only one *P. mirabilis* and no *E. coli*, but were predominantly *Citrobacter* (seven strains) and *Enterobacter* (five strains).

Results obtained with the 50-μg carbenicillin disk were less satisfactory. Although scatter was small (Table 2), the regression line intersected the 6-mm coordinate at an MIC value of 364 μg/ml, much closer to the critical MIC values for resistance, and resulted in poorer discrimination between susceptible and resistant strains. Three of 30 strains (10%) of *P. aeruginosa* with carbenicillin MIC values of 50 μg/ml and 9 of 17 strains (53%) with carbenicillin MIC values of 100 μg/ml were called resistant to carbenicillin (zone size less than 13 mm). However, all strains of *P. aeruginosa* with MIC values greater than or equal to 200 μg/ml of carbenicillin were called appropriately resistant (Fig. 2). Similar to results obtained with the 100-μg carbenicillin disk, *Enterobacteriaceae* with carbenicillin MIC values of 50 and 100 μg/ml were usually called resistant to carbenicillin if the 50-μg disk was used.

Zone size distribution using the 75-μg ticarcillin disk is shown in Fig. 3; ticarcillin MIC value is plotted on the ordinate in $\log_2$ scale, and zone diameter is plotted in millimeters on the abscissa. A distribution of zone sizes similar to those obtained with the carbenicillin disks was observed. The regression line intersects the

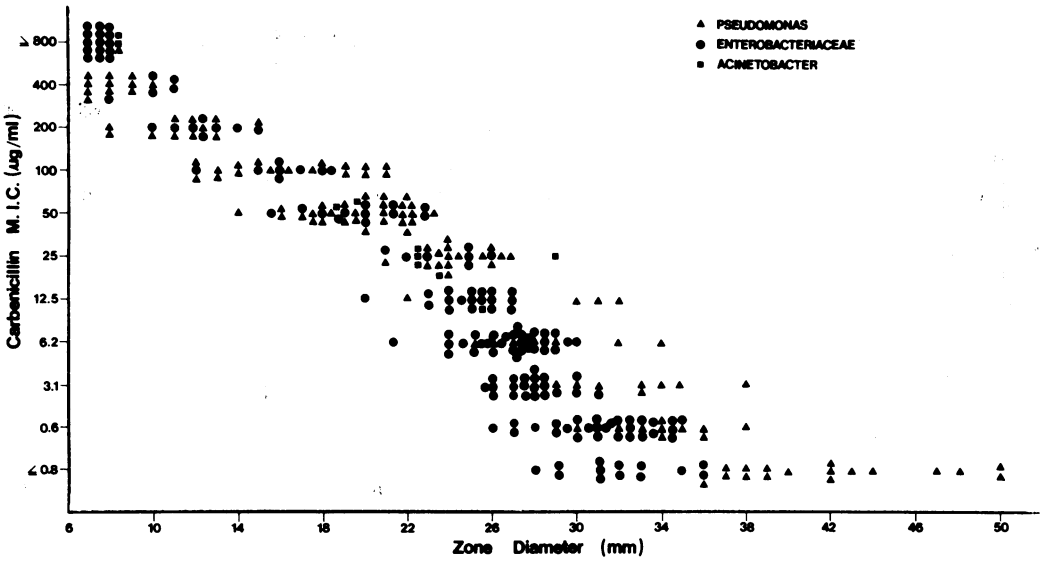

FIG. 1. *Zone diameter distribution obtained using 100-μg carbenicillin disks and MIC determined by the Bauer-Kirby method.*

TABLE 2. *Mathematical analysis of susceptibility data*

Antibiotic disk content	No. of strains tested	Correlation coefficient	Slope[a]	Y intercept[a]	No-zone point[b]	Standard deviation
Carbenicillin, 100 μg	310	−0.9398	−0.3104	+11.1105	631.0	3.01
Carbenicillin, 50 μg	310	−0.9432	−0.2969	+10.290	364.1	2.90
Ticarcillin, 75 μg	310	−0.9404	−0.2932	+10.377	392.6	2.73

[a] Expressed in $\log_2$ scale.
[b] No-zone point, expressed as the MIC value in micrograms per milliliter corresponding to a zone of 6 mm.

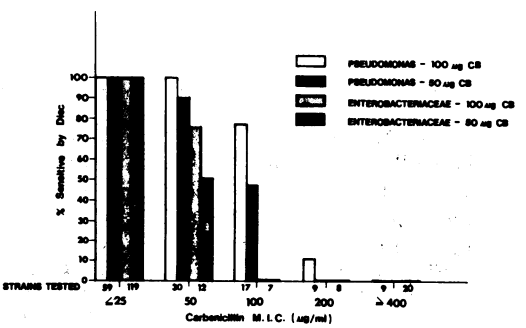

FIG. 2. *Carbenicillin susceptibility of P. aeruginosa and Enterobacteriaceae determined with 50- and 100-μg carbenicillin disks.*

6-mm coordinate (Table 2) at a ticarcillin MIC value of 393 μg/ml, and correlation between zone size and MIC values is high. The mean standard deviation of points around the regression line was only 2.73 mm, less than that observed with either the 50- or 100-μg carbenicillin disks. The regression line for the 75-μg ticarcillin disks intersects the 125 μg/ml coordinate at a zone diameter of 11.6 mm, and it is apparent that a zone of 12 mm or greater is most discriminating between susceptible and resistant strains. Using these criteria, 11 of 11 strains of *P. aeruginosa* with ticarcillin MIC values greater than or equal to 200 μg/ml appropriately were called resistant, and five of six strains with MIC values of 100 μg/ml appropriately were read as being susceptible to ticarcillin (Fig. 4). The regression line intersects the 60-μg coordinate at a zone of 15 mm and was judged appropriate for dividing intermediate and susceptible organisms. A zone size greater than or equal to 15 mm included all strains of *P. aeruginosa* with MIC values less than 50 μg/ml and 13 of 15 strains with MIC values equal to 50 μg/ml. It excluded all but one of those with ticarcillin MIC values of 100 μg/ml.

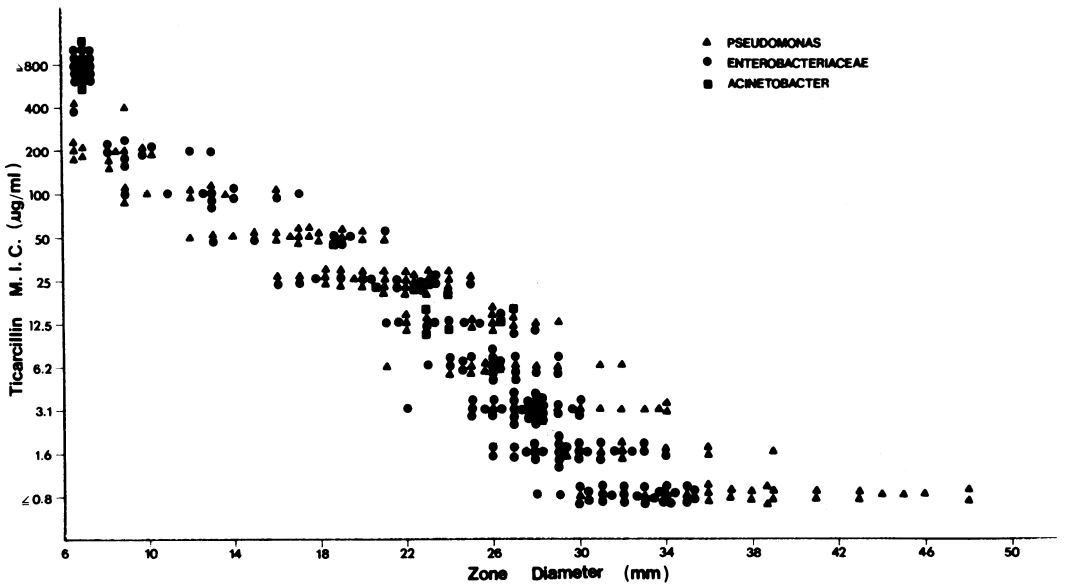

FIG. 3. *Zone diameter distribution obtained using 75-µg ticarcillin disks and MIC by the Bauer-Kirby method.*

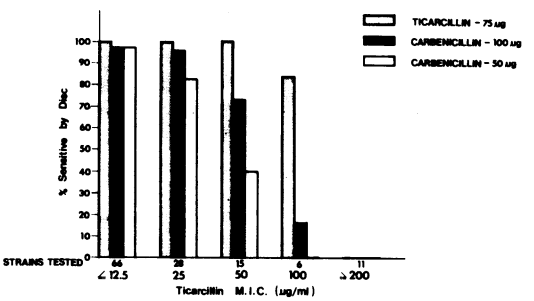

FIG. 4. *Susceptibility of P. aeruginosa to carbenicillin and ticarcillin, using disk criteria, according to ticarcillin MIC values.*

Although the *Enterobacteriaceae* and *P. aeruginosa* exhibited a relation of zone size to ticarcillin MIC value with the ticarcillin disks, the regression line was steeper for the *Enterobacteriaceae* than for *Pseudomonas* if each group was evaluated separately. This was because no zone size greater than 35 mm was found for *Enterobacteriaceae*, implying that there were few strains with MIC values below 0.8 µg/ml. In contrast, 17 strains of *P. aeruginosa* were highly susceptible to ticarcillin and demonstrated zone sizes greater than 36 mm. A similar relationship was observed when carbenicillin disks were used. However, a zone size of 12 mm or more obtained with the ticarcillin disk also correlated well with susceptibility of the *Enterobacteriaceae* to ticarcillin, excluding only two of ten organisms (one *Klebsiella* and one *Citrobacter*) with MIC values of 100 µg/ml. A zone size of 15 mm, dividing intermediate and susceptible strains, excluded all but 2 of 10 organisms (both *Citrobacter*) with MIC values of 100 µg/ml and included all but 1 *(Klebsiella)* of 7 with MIC values of 50 µg/ml. All strains with MIC values less than 50 µg/ml were read as susceptible to ticarcillin (zone size greater than or equal to 15 mm).

If the disk susceptibility to carbenicillin was used as an indication of susceptibility to ticarcillin, although it was acceptable for the *Enterobacteriaceae*, it proved unreliable for *P. aeruginosa* at any corresponding ticarcillin MIC value greater than 25 µg/ml (Fig. 4). Of 21 *P. aeruginosa* strains with ticarcillin MIC values of 50 or 100 µg/ml, only 57%, with the 100-µg carbenicillin disk, and 29% with the 50-µg carbenicillin disk, would have been called susceptible to carbenicillin. Furthermore, using accepted zone size criteria for the 100-µg carbenicillin disk, 9 of 21 strains (43%) of *P. aeruginosa* called resistant to carbenicillin were either intermediate or susceptible to the 75-µg ticarcillin disk (Fig. 5). An additional nine strains considered only intermediately susceptible to carbenicillin were completely susceptible to ticarcillin. Therefore, a total of 18 strains or 15% of all strains of *P. aeruginosa* tested using the 100-µg carbenicillin disk would not have been called susceptible to ticarcillin.

Analysis of the utility of carbenicillin disks for determining the susceptibility of *P. aerugi-*

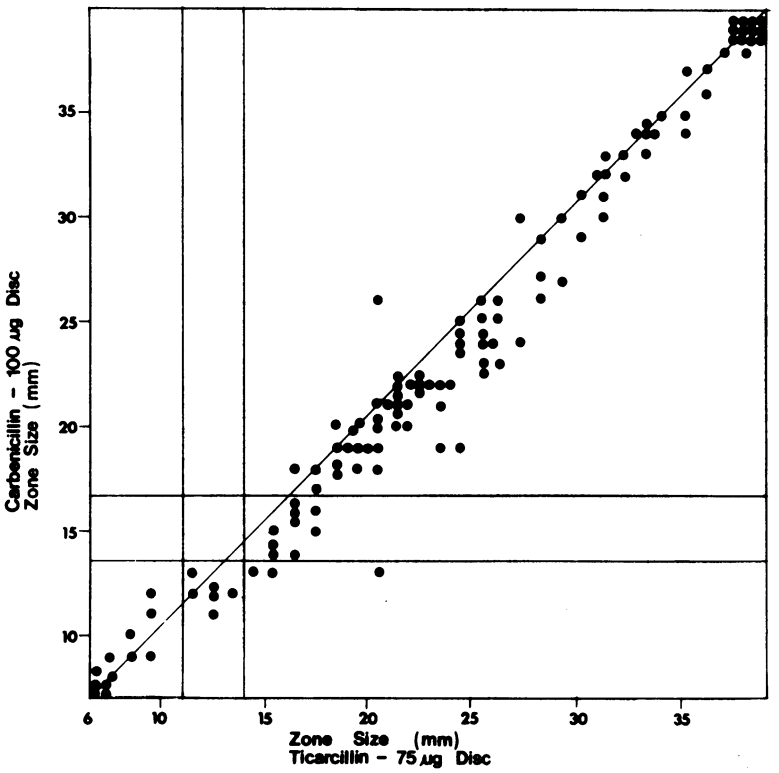

FIG. 5. *Correlation between zone sizes obtained with the 100-µg carbenicillin disk and 75-µg ticarcillin disk for P. aeruginosa.*

nosa to ticarcillin by using different zone size criteria is shown in Fig. 6; ticarcillin MIC values in the $\log_2$ scale are plotted on the ordinate, and zone sizes obtained using the 50-µg carbenicillin, 100-µg carbenicillin, or 75-µg ticarcillin disk are plotted on the abscissa. The regression line of *Pseudomonas* for the 50-µg carbenicillin disk intersects the ordinate, or no-zone point, at approximately 95 µg/ml (Table 3), making it virtually impossible to evaluate susceptibility to ticarcillin at any MIC value greater than 50 µg/ml. The regression line for the 100-µg carbenicillin disk parallels that of the 75-µg ticarcillin disk, but even here it intersects the ordinate at less than 200 µg/ml. The dividing line between susceptible and resistant strains of *Pseudomonas* would therefore correspond to a zone size of less than 9 mm, clearly difficult to read. The regression line of *P. aeruginosa* for the 75-µg ticarcillin disk intersects the ordinate at 260 µg/ml, well above the critical MIC value for resistance. The zone size of 12 mm, corresponding to an MIC value of 116 µg/ml, is easy to read and discriminates well between susceptible and resistant strains of *Pseudomonas*.

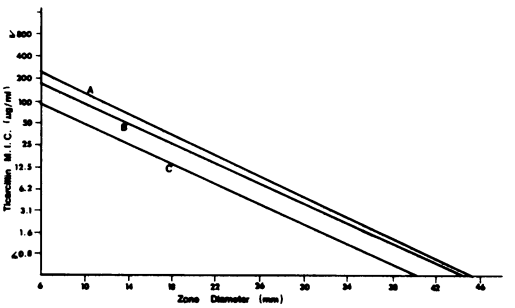

FIG. 6. *Comparison of regression lines for P. aeruginosa isolates using the 75-µg ticarcillin disk (A), 100-µg carbenicillin disk (B), and 50-µg carbenicillin disk (C) using ticarcillin MIC values.*

Freshly prepared 75-µg ticarcillin disks supplied by Beecham Laboratories contained 75 ± 10 µg of ticarcillin. After 6 to 12 months of intermittent use and storage at 4 C, the remaining disks contained 53 ± 4.9 µg of ticarcillin. This is within Food and Drug Administration specifications for allowable error in disk content (3).

TABLE 3. *Mathematical analysis of pseudomonas susceptibility data by ticarcillin agar dilution studies*

Antibiotic disk content	No. of strains tested	Correlation coefficient	Slope[a]	Y intercept[a]	No-zone point[b]
Ticarcillin, 75 μg	110	−0.9539	−0.2415	+9.457	259
Carbenicillin, 100 μg	110	−0.9412	−0.2300	+8.973	193
Carbenicillin, 50 μg	110	−0.8935	−0.2107	+7.841	95

[a] Expressed in $\log_2$ scale.

[b] No-zone point, expressed as the MIC value in micrograms per milliliter, corresponding to a zone of 6 mm.

DISCUSSION

In assessing the utility of any disk for use in diffusion susceptibility testing, the disk must meet several criteria. Disk content variation should be minimal. The line of regression, determined by the method of least squares from a plot of zone size versus $\log_2$ of the MIC value, should intersect the ordinate, representing MIC values, well above the critical MIC for resistance so that zone sizes can easily be read at higher MIC values. Scatter of zone sizes around the regression line should be small, so that a given zone size does not overlap a number of different MIC values. If these principles are met, discrimination between different MIC values should be such that very few organisms could be called either inappropriately susceptible or resistant by zone size criteria. On the basis of the zone size distribution and the regression line, criteria for designating susceptible, intermediate, and resistant organisms can be constructed.

Matsen (6) and Washington (11) found that 50-μg carbenicillin disks were not suitable. Both disk content variation and ability to detect susceptibility at higher MIC values was a problem. We have also found that a high percentage of organisms with MIC values of 50 and 100 μg/ml inappropriately were called resistant to carbenicillin. Furthermore, the Y intercept of the regression line obtained with the 50-μg carbenicillin disk was unacceptably close to the critical MIC value for resistance, although scatter around the regression line was not as great as with the 100-μg carbenicillin disk.

Results obtained using the 100-μg carbenicillin disk were satisfactory. The regression line intersected the ordinate well above the critical MIC value for resistance, making it easy to read zone sizes corresponding to carbenicillin MIC values of 100 and 200 μg/ml. Furthermore, although both the 50- and 100-μg disks excluded organisms with MIC values of 200 μg/ml from being called susceptible, the 100-μg disk did not result in inappropriately designated resistance and correlated well with MIC values. We found that the recommended zone size criteria for *P. aeruginosa* (<14 mm, resistant; 14 to 16 mm, intermediate, and ≥17 mm, susceptible) were appropriate from our study.

Separate zone size criteria have been established for *Proteus* and *E. coli* when tested with the 50- or 100-μg carbenicillin disk. We believe that this creates a great deal of confusion and accomplishes little. Although the regression line of the *Enterobacteriaceae* was steeper than for *Pseudomonas* in our study, the main reason for this was the large number of highly sensitive strains of *P. aeruginosa*. At carbenicillin MIC values greater than or equal to 25 μg/ml, mean zone diameters of the *Enterobacteriaceae* for their corresponding MIC values were not different from those obtained with *P. aeruginosa*. This is in agreement with the data of other investigators. Furthermore, with the exception of *Enterobacter* and *Citrobacter*, most *Enterobacteriaceae*, by virtue of their mechanisms of resistance, are either quite susceptible (MIC ≤25 μg/ml) or highly resistant (MIC >800 μg/ml) to carbenicillin or ticarcillin (8). Since blood levels achieved by administration of these antibiotics are not dependent on the species of bacterial infection, and since the *Enterobacteriaceae* do not produce different zone sizes for a given MIC value, we feel that using different zone size criteria is inappropriate and misrepresents the susceptibility of a large number of microorganisms. Indeed, we found that, using recommended criteria for the 100-μg carbenicillin disk, all *Enterobacteriaceae* with MIC values of 100 μg/ml were called resistant and none of these were strains of *E. coli* or *Proteus*. Using the same zone size criteria as those for *P. aeruginosa*, we could differentiate between *Enterobacteriaceae* susceptible or resistant to 100 μg of carbenicillin per ml. This concentration is achievable in the serum with recommended dosage programs (7).

Neither the 50-μg nor the 100-μg carbenicillin disk is appropriate for evaluating the susceptibility of *P. aeruginosa* to ticarcillin. We found that 43% of all strains of *P. aeruginosa* called resistant to carbenicillin were inhibited

by ticarcillin in the disk and agar dilution studies. The results with the 50-μg carbenicillin disk were worse.

We were interested to see if different zone size criteria could be established with carbenicillin disks to determine the susceptibility of *Pseudomonas* to ticarcillin. Although correlation between the 50-μg carbenicillin disk or the 100-μg carbenicillin disk and ticarcillin MIC values was quite good, the Y intercept for the regression line made interpretation of susceptibility or resistance to ticarcillin at higher MIC values impossible. The regression line for the 50-μg carbenicillin disk intersected the ordinate at a ticarcillin MIC value of less than 100 μg/ml, making it impossible to read zone sizes corresponding to ticarcillin MIC values greater than 25 μg/ml. The 100-μg carbenicillin disk intersected the ordinate at a ticarcillin MIC value of approximately 190 μg/ml. To read zone sizes produced by the 100-μg carbenicillin disk corresponding to ticarcillin MIC values of 100 to 200 μg/ml, one would have to perform the difficult task of discriminating between zone sizes in the range of 6 to 9 mm.

The use of a 75-μg ticarcillin disk obviated these problems, since it produced zone sizes that correlated well with the ticarcillin MIC values for both *P. aeruginosa* and the *Enterobacteriaceae* and produced a regression line that intersected the ordinate at approximately 400 μg/ml, well above the critical MIC value for resistance. A zone of 12 mm or more was found to have good discriminatory value between those organisms judged to be susceptible on the basis of agar dilution and those judged to be resistant. This zone size was discriminatory for both *P. aeruginosa* and the *Enterobacteriaceae*.

We believe that a separate ticarcillin disk is needed to determine the susceptibility of *P. aeruginosa* to ticarcillin. A ticarcillin disk could be used to determine susceptibility to ticarcillin and carbenicillin, but it would require that a larger zone size be used to indicate susceptibility to carbenicillin, and this might lead to confusion. Furthermore, we cannot justify the use of different zone size criteria for *P. aeruginosa* and the *Enterobacteriaceae*, but we recommend the same criteria for both groups, whether carbenicillin or ticarcillin susceptibility is being tested. Zone sizes of 11 mm or less, 12 to 14 mm, and 15 mm or more were appropriate for designating resistant, intermediate, and susceptible organisms, respectively, when tested with the 75-μg ticarcillin disk. The argument in favor of a double set of standards to interpret carbenicillin susceptibility has been based on the assumption that lower doses of carbenicillin are used to treat *E. coli* or *Proteus* infections. Since the majority of isolates of *E. coli* and *P. mirabilis* are inhibited by a carbenicillin or ticarcillin concentration of 6.2 μg or less per ml, even if the *Pseudomonas* zone size criteria were used and the dosage programs recommended in package inserts for carbenicillin were employed, blood levels would be more than adequate. However, if we consider the data with regard to *Enterobacter, Citrobacter, Acinetobacter,* and *Serratia,* use of the *Pseudomonas* zone size criteria is more in keeping with the in vitro susceptibilities.

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