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Letter to the Editor

High rate of confirmatory penicillin MIC test after oxacillin disk screening for invasive pneumococcal disease

Dear Editor,

Pneumococcal infection is associated with high rates of morbidity and mortality, especially in children and the elderly, necessitating prompt reporting of penicillin susceptibility for effective management of patients [1,2]. According to the Clinical and Laboratory Standard Institute (CLSI) guidelines, an oxacillin zone size ≥20 mm demonstrates susceptibility to penicillin, whereas the minimum inhibitory concentrations (MIC) of penicillin and cefotaxime, ceftriaxone, or meropenem should be determined for isolates with an oxacillin zone size ≤19 mm [3]. We found that the rate of confirmatory MIC testing was high during the Korea Global Antimicrobial Resistance Surveillance System (Kor-GLASS) project [4]. Therefore, we evaluated the efficiency of the oxacillin disk-diffusion test as a screening method.

A total of 217 non-duplicated *S. pneumoniae* isolates obtained between 2016 and 2022 in Korea were included in this study. All pneumococcal isolates were isolated from blood cultures. The collection and analysis of all strains were conducted using Kor-GLASS. For susceptibility testing, 1-μg oxacillin disks (BD 2321319; Becton Dickinson, Franklin Lakes, NJ, USA) and the MicroScan MICroSTREP panel (Siemens Healthcare Diagnostics, Sacramento, CA, USA) were used. The oxacillin disk test was performed on Mueller–Hinton agar supplemented with 5 % defibrinated sheep blood (Micromedia, Korea), and the test samples were incubated for 20 h at 35 °C in a 5 % CO_2 atmosphere. The results were interpreted according to the CLSI guidelines for non-meningitis (S ≤ 2 μg/mL). If the oxacillin zone size of inhibition was ≥20 mm, the *S. pneumoniae* isolate was considered susceptible to penicillin. *S. pneumoniae* ATCC 49619 was used for quality control in this study. We analyzed the efficiency of the oxacillin disk test by calculating the number of confirmatory MIC tests and by comparing the results of the oxacillin disk zone size with the MICs of penicillin.

Of the 217 isolates, 44 showed an oxacillin zone size ≥ 20 mm, and all were susceptible to penicillin in the MIC tests, as expected. The MIC values for all isolates were ≤ 0.03 μg/mL, except for one isolate that showed an MIC value of 0.12 μg/mL (Table 1). On the basis of these results, we concluded that the oxacillin disk test is a good predictive tool. However, only 20.3 % (44/217) of the isolates that demonstrated an oxacillin zone size of ≥ 20 mm were determined to be penicillin-susceptible by the oxacillin disk test, whereas the remaining 173 isolates (79.7 %) with a zone size of ≤ 19 mm showed indeterminate findings requiring confirmatory MICs. Thus, 390 tests (217 oxacillin-screening tests and 173 confirmatory MIC tests) were eventually conducted to confirm penicillin susceptibility in 217 *S. pneumoniae* isolates. Surprisingly, among the 36 recently collected isolates from 2021 to 2022, only one showed an oxacillin zone size ≥20 mm. Thus, almost all recent strains required confirmatory MICs tests, which increased costs, required more labor, and delayed the final report.

Among the 173 isolates showing a zone size of ≤ 19 mm, 55.0 % (n = 95), 35.3 % (n = 61), and 9.8 % (n = 17) were confirmed to be susceptible, intermediate, and resistant to penicillin, respectively. Interestingly, most strains showed no inhibition zone around the oxacillin disk, with the exception of 13 strains (disk diameter = 6 mm). Horna et al. [5] reported that 253 of 302 strains with a zone size of ≤ 19 mm were confirmed as susceptible, similar to our findings. While Jette et al. [6] suggested that the absence of an inhibition zone around the oxacillin disk could be regarded as an indicator of resistance to penicillin, we confirmed that 83 of the 160 strains that showed no inhibition zones were susceptible to penicillin. We assume that this difference is due to the change in the breakpoint for penicillin in 2008.

Table 1
Comparison of zone of inhibition of the oxacillin disk diffusion test to minimum inhibitory concentrations (MICs) of penicillin.

Zone diameter	Penicillin MIC (μg/mL)									
Oxacillin (mm)	< =0.03	0.06	0.12	0.25	0.5	1	2	4	>4	Total
40	1									1
38	1									1
34	1									1
33	2									2
30	5									5
29	3									3
28	9									9
25	7									7
24	3									3
23	4									4
22	2		1							3
20	4									4
17		1								1
16		1								1
15		1								1
13				1						1
11			2							2
10			1	1				1		3
8							1			1
6				4	1	20	43	48	12	128
Total	42	3	4	6	1	20	44	49	12	181

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In conclusion, oxacillin disk screening increases costs, delays reporting, and requires many additional MIC tests. In addition, since the oxacillin disk result may be the sole screening tool in developing countries, this approach may yield false predictions of resistance if the laboratory cannot perform confirmatory MICs tests. Therefore, we recommend that proceeding with the MIC test initially may be a more efficient approach than oxacillin disk screening for evaluating penicillin susceptibility of *S. pneumoniae*.

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Ethical approval

Not required.

Competing interests

None declared.

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