Comparison of the MicroScan System and the Agar Dilution Assay for Quinupristin/Dalfopristin Susceptibility of Enterococcus faecium

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Abstract. We compared the results of Quinupristin/Dalfopristin (Q/D) susceptibility tests by the Positive Combo Panel (Type 11) of the MicroScan Walk Away 96 analyzer (Dade Behring, Inc.) with those obtained by the reference agar dilution method. From September 2003 to August 2004, a total of 410 E. faecium isolates were obtained from clinical samples. Of these, 65 (15.9%) strains were non-susceptible, and 345 (84.1%) strains were susceptible to Q/D. We collected consecutively 65 Q/D non-susceptible E. faecium isolates (42 resistant, 23 intermediate), and randomly selected 32 Q/D susceptible E. faecium isolates using the MicroScan system. The minimal inhibitory concentrations (MICs) of Q/D, vancomycin, and teicoplanin were determined by the agar dilution method according to CLSI guidelines. The agreement rates between the two methods were 100% for Q/D-susceptible strains, 85.7% for Q/D-resistant strains, and 26.1% for Q/D-intermediate strains of E. faecium. The major error rate (S→R) was 11.9%, and the minor error rate (S→I) was 13.0%. No very major errors were found. We conclude that for MicroScan ‘non-susceptible’ test results for Q/D, it is necessary to confirm the result using a reference method. The Q/D-resistance rate was higher in glycopeptide-susceptible (78.0% for vancomycin, 82.0% for teicoplanin) than glycopeptide-resistant E. faecium (22.0% for vancomycin, 16.0% for teicoplanin). Further studies are needed to determine whether Q/D use in hospitals or virginiamycin use in animals, or other factors, are responsible for the high rates of glycopeptide-susceptible and Q/D-resistant E. faecium strains in Korea.

Keywords: quinupristin/dalfopristin, Enterococcus faecium, antimicrobial susceptibility testing

Introduction

Enterococcus faecium (E. faecium) is an important nosocomial pathogen and vancomycin resistance in this species is increasing worldwide. Quinupristin/Dalfopristin (Q/D) is a mixture of the semisynthetic streptogramin A (dalfopristin) and B (quinupristin) compounds, and is an effective antimicrobial for treating vancomycin-resistant E. faecium (VRE). In Korea and Taiwan, the Q/D resistance rate is high (9-15%) [1-3], and an accurate susceptibility test is needed for appropriate therapeutic drug selection for VRE. The MicroScan system is frequently used for identification and antimicrobial susceptibility testing in clinical laboratories, but the results do not always agree with the reference method [4]. In this study, we compared the results of a Q/D susceptibility test by the Positive Combo Panel (Type 11) of the MicroScan Walk Away 96 analyzer (Dade Behring, Inc., Newark, DE, USA) with those obtained by the reference agar dilution...
method. We also determined the glycopeptide resistance rate among Q/D-susceptible and Q/D-resistant isolates of *E. faecium*.

**Materials and Methods**

From September 2003 to August 2004, a total of 410 *E. faecium* isolates were obtained from clinical samples. We found that 65 (15.9%) strains were non-susceptible to Q/D, and 345 (84.1%) strains were susceptible. We collected consecutively 65 *E. faecium* isolates that were non-susceptible to Q/D (42 resistant, 23 intermediate). We also randomly collected 32 *E. faecium* isolates that were susceptible to Q/D according to the MicroScan system. All isolates were identified in the Kangnam St. Mary’s Hospital using the MicroScan system. The MIC of Q/D, vancomycin, and teicoplanin were determined using the standard agar dilution method according to the CLSI guidelines [5]. The agar dilution tests were performed in duplicate, and *E. faecalis* ATCC 29212 was included for quality control.

**Results and Discussion**

Of the 42 Q/D-resistant *E. faecium* strains, 5 were susceptible to Q/D by the reference method, giving a major error (false resistance) rate of 11.9%. This is above the maximum limit (3%) of major errors recommended by NCCLS [6].

The agreement rate between the agar dilution and MicroScan methods is shown in Table 1. The MICs of Q/D resistant isolates by the agar dilution method was 4 µg/ml in all but one isolate. That is considered a low-level resistance. Of the 23 isolates that showed intermediate resistance to Q/D by MicroScan, 3 (13.0%) were susceptible to Q/D when tested by the agar dilution method. In summary, 8 (12.3%) of 65 isolates were falsely non-susceptible to Q/D by MicroScan.

Sader et al [7] stated that automated systems, including the MicroScan WalkAway system, showed unacceptable levels of very major errors for selected β-lactams in strains of *Pseudomonas aeruginosa*. D’Azvedo et al [4] reported that for enterococci tested with the MicroScan WalkAway and agar MIC tests, the percentages of agreement for the detection of resistance was 90.2% for ampicillin, 90.6% for high-level resistance to streptomycin, 96.4% for high-level resistance to gentamicin, and 100% for vancomycin.

Of 50 Q/D-resistant isolates of *E. faecium* that we tested, most were susceptible to vancomycin and teicoplanin (78.0% and 82.0%, respectively). The glycopeptide susceptibility rate was much higher in Q/D-resistant *E. faecium* than in Q/D-susceptible *E. faecium* (Table 2). This observation is consistent with previous reports [1,3,8], and it supports the suggestion that Q/D-resistant *E. faecium* emerged before Q/D use in medicine because virginiamycin (another streptogramin) had been widely used in agriculture [9]. But there may

| No. of isolates according to susceptibility category by agar dilution method | Susceptibility category by MicroScan (No. of isolates) |
|---|---|---|
| | Resistant (42) | Intermediate (23) | Susceptible (31) |
| Resistant | 36/42 (85.7%) | 14/23 (60.9%) | 0/31 (0.0%) |
| Intermediate | 1/42 (2.4%) | 6/23 (26.1%) | 0/31 (0.0%) |
| Susceptible | 5/42 (11.9%) | 3/23 (13.0%) | 31/31 (100.0%) |

Table 2. Glycopeptide susceptibility of *E. faecium* isolates by agar dilution method.

<table>
<thead>
<tr>
<th>Susceptibility category</th>
<th>Q/D-resistant</th>
<th>Q/D-susceptible</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>E. faecium</em> (50)</td>
<td>39/50 (78.0%)</td>
<td>16/39 (41.0%)</td>
</tr>
<tr>
<td></td>
<td>11/50 (22.0%)</td>
<td>23/39 (59.0%)</td>
</tr>
<tr>
<td></td>
<td>0/50 (0.0%)</td>
<td>(0.0%)</td>
</tr>
<tr>
<td></td>
<td>8/50 (16.0%)</td>
<td>9/39 (23.1%)</td>
</tr>
<tr>
<td></td>
<td>0/31 (0.0%)</td>
<td>9/39 (23.1%)</td>
</tr>
<tr>
<td></td>
<td>1/50 (2.0%)</td>
<td>21/39 (53.8%)</td>
</tr>
<tr>
<td></td>
<td>41/50 (82.0%)</td>
<td></td>
</tr>
</tbody>
</table>

* Significantly different susceptible rate between Q/D-resistant and susceptible *E. faecium* by Chi-square test (p < 0.01)
be other factors leading to Q/D resistance of *E.
faecium*, considering that the Q/D resistance rates
are high in Korea (10.0%) and Taiwan (9 to 15%)
[1-3], in contrast to low rates (0 to 3.8%) in America
and Europe where virginiamycin has also been
used [10-14].

In conclusion, to our knowledge, this is the first
publication on the accuracy of the MicroScan
Q/D susceptibility test. We found that it has a
major error rate of 11.9%, which exceeds the
acceptable range (≤3%). The minor error rate (S→
I) is also high (13.0%). Until the MicroScan
achieves better correlation of antibiotic susceptibility
results with those obtained by agar dilution, it may
be advisable to confirm Q/D-resistant results by
use of a reference method.

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