The Experience of a Novel Glycylcycline Antibiotic for a Patient with Infection Caused by Multiple Drug-resistant Pathogens: What is the Benefit?

Po-Chin Chi, Chien-Liang Wu, Chung-Lieh Hung, Yu-Ling Weng, Ching-Chi Lin, Shih-Yi Lee

Department of Internal Medicine, Divisions of Pulmonary and Critical Care Medicine, and Cardiology, Mackay Memorial Hospital, and Mackay Medicine, Nursing and Management College, Taipei, Taiwan.

Introduction

In the intensive care unit (ICU), there is a high probability of infection due to resistant pathogens. When patients develop infections caused by more than one type of resistant bacteria, it is hard to find optimal antibiotics to cure the disease. In practice, physicians have been trying to prescribe antibiotics effectively according to reliable culture results. However, multiple antibiotic administration is usually accompanied by much fluid accumulation, which could be a problem for a critically ill elderly patient with compromised cardiorespiratory or renal function. Facing the requirement for infection management, tigecycline, a novel glycylcycline antibiotic, has a broad spectrum including vancomycin-resistant enterococci (VRE) and multiple-drug resistant (MDR) Acinetobacter species. It can be efficiently used to deal with ventilator-associated pneumonia (VAP) and can also minimize the amount of water administered for dissolving multiple antibiotics. In view of the superiority of tigecycline, fluid control can be achieved more easily while using a single antibiotic instead of multiple drugs, which is also important for care of a critically ill elderly man with compromised cardiorespiratory or renal function. Here, we present a patient infected with multiple drug-resistant pathogens, who improved clinically after being treated with tigecycline, to demonstrate the benefits of this antibiotic. [International Journal of Gerontology 2008; 2(3): 124–127]

Key Words: multiple antibacterial drug resistance, tigecycline, ventilator-associated pneumonia

Case Report

A 75-year-old man with bronchiectasis and chronic obstructive pulmonary disease complicated by cor pulmonale and type 2 diabetes mellitus accepted medical
Tigecycline for Multiple Drug Resistant Pathogens

care in the ICU because of septic shock induced by VAP. He was treated with empiric antibiotics, hemodynamic-guided therapy, inotropic agents, and mechanical ventilation. Later, sputum yielded MDR Acinetobacter baumannii that was only susceptible to colistin, and the central venous catheter tip culture yielded VRE, on hospital days 5 and 11, respectively. In accordance with the culture results and septic shock status, the patient was administered an antibiotic regimen comprising imipenem, sulbactam, colistin and linezolid for 18 days. During this period, the daily fluid input and output was around 4,000 mL and 1,500 mL, respectively. However, he developed episodes of cyanosis, hypoxemia with respiratory distress under 90% oxygen inspiration and mechanical ventilation support with pressure control of 24 cmH2O, bradycardia, and hypotension accompanied by increasing production of purulent sputum and size of pulmonary consolidation on a chest X-ray (Figure). At that time, his APACHE II score was 42 and C-reactive protein level was 26.03 mg/dL. Because initial antibiotics failed to improve his clinical condition, the antibiotic regimen was changed to tigecycline and ceftazidime under the preliminary diagnosis of acute respiratory distress syndrome complicated by VAP and pulmonary edema. Stress doses of hydrocortisone and diuretics were also administered. Two days later, his body temperature was around 36°C, heart rate was 92 beats per minute, respiratory rate was 24 inspirations per minute, white blood count was 6,800/µL, blood pressure was within the normal range without vasopres sor support, C-reactive protein level was 3.28 mg/dL, oxygenation was sufficient with 40% oxygen inspiration and mechanical ventilation support with pressure control of 24 cmH2O, the pulmonary consolidation size was decreased (Figure), and APACHE II score was 22. For four more days, the patient’s edema resolved because the daily water output became more than the input (3,000 mL vs. 2,000 mL per day, respectively). Unfortunately, on day 29, he suddenly developed sinus bradycardia, hypotension and a decreased level of consciousness. Cardiogenic shock was suspected, but the patient did not receive any further invasive intervention before passing away in hospice care at his family’s request.

Discussion

Infection caused by MDR pathogens is a common problem in the ICU1,2. However, it is still a requirement to deal with infection caused by MDR Acinetobacter baumannii and VRE. Agents frequently reported as being effective for treating MDR Acinetobacter baumannii include imipenem/cilastatin, colistin, ampicillin/sulbactam, amikacin, rifampin, and tetracyclines3. Those currently approved for treating VRE are quinupristin/dalfopristin, linezolid, and tigecycline4. The success rate of these antibiotics in treating pneumonia caused by MDR Acinetobacter baumannii has been reported to vary from 25% to 93%5, while for pandrug-resistant Acinetobacter baumannii, success is only around 40%6. The clinical response rate of quinupristin/dalfopristin for VRE was reported to be 70.5%6,7 and that for linezolid was 92.6%4. Although a recent study indicated

Figure. Size of pneumonia consolidation decreased after antibiotics were changed from imipenem, sulbactam, colistin and linezolid to tigecycline.
that combination carbapenem-sulbactam therapy significantly decreased the minimal inhibitory concentration of carbapenem for treating pandrug-resistant *Acinetobacter baumannii*, it has been shown that there is no significant difference in clinical outcome from patients treated with traditional combination regimens. These clinical results are still disappointing to physicians. In addition, none of the regimens can deal with infection caused by MDR *Acinetobacter baumannii* and VRE at the same time.

Selection of antibiotics should be based on the principle of de-escalation, which implies starting with a broad spectrum antibiotic regimen and then tailoring the individual therapy based on culture results and local hospital antibiograms. Tigecycline, a novel glycyliclcline antibiotic, which has bacteriostatic effects for multiple resistant pathogens including VRE, methicillin-resistant *Staphylococcus aureus*, extended-spectrum β-lactamase-producing *Enterobacteriaceae* and MDR *Acinetobacter* species, may be an additional choice in this situation. It is normally used to treat skin and soft tissue infections, and intra-abdominal infections, with success rates of 90% and 86.6%, respectively. However, there is still minimal evidence for the use of tigecycline in nosocomial pneumonia caused by MDR *Acinetobacter baumannii* and VRE, the benefits of tigecycline, with a broader anti-resistant microbial spectrum, lower cost and easier fluid balance control than traditional regimens, make it a better choice in this field, especially as classical regimens are ineffective in improving the clinical condition.

In conclusion, as patients in the ICU usually have compromised cardiopulmonary status and may have infection caused by MDR *Acinetobacter baumannii* and VRE, the benefits of tigecycline, with a broader anti-resistant microbial spectrum, lower cost and easier fluid balance control than traditional regimens, make it a better choice in this field, especially as classical regimens are ineffective in improving the clinical condition. Here, we report a case of a critically ill elderly man with underlying cardiopulmonary disease, MDR *Acinetobacter baumannii* VAP, and VRE catheter-related infection, with improved clinical condition after being treated with tigecycline.

**Table.** The dose, cost and fluid requirement of antibiotics against highly resistant Acinetobacter or enterococci

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose for normal renal function</th>
<th>Cost per bottle (US$)</th>
<th>Daily cost (US$)</th>
<th>Fluid required for drug dilution (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tigecycline</td>
<td>50 mg q12h</td>
<td>54.28 (50 mg)</td>
<td>108</td>
<td>100</td>
</tr>
<tr>
<td>Imipenem/Cilastatin</td>
<td>0.5 g q6h</td>
<td>33 (0.5 g)†</td>
<td>132</td>
<td>400</td>
</tr>
<tr>
<td>Sulbactam</td>
<td>1 g q6h</td>
<td>7.8 (0.5 g)</td>
<td>62.4</td>
<td>400</td>
</tr>
<tr>
<td>Piperacillin/Tazobactam</td>
<td>3.375 g q6h</td>
<td>18 (3.375 g)†</td>
<td>72</td>
<td>400</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>2 g q8h</td>
<td>21–28.93 (2 g)†</td>
<td>63–84</td>
<td>300</td>
</tr>
<tr>
<td>Amikacin</td>
<td>7.5 mg/kg q12h</td>
<td>34.26 (0.5 g)†</td>
<td>68.52</td>
<td>200–400</td>
</tr>
<tr>
<td>Colistin</td>
<td>80–160 mg q8h</td>
<td>17 (150 mg)</td>
<td>51</td>
<td>300–600</td>
</tr>
<tr>
<td>Quinupristin/Dalfopristin</td>
<td>5–7.5 mg/kg q8h</td>
<td>138 (350 mg)</td>
<td>300–350</td>
<td>300 (central line); 750 (peripheral line)</td>
</tr>
<tr>
<td>Linezolid</td>
<td>600 mg q12h</td>
<td>82 (600 mg)</td>
<td>115</td>
<td>600</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>50 mg q12h</td>
<td>54.28 (50 mg)</td>
<td>108</td>
<td>100</td>
</tr>
</tbody>
</table>

*Adapted from reference 17; †new brand. q12h = every 12 hours; q6h = every 6 hours; q8h = every 8 hours.
References

7. Swoboda S, Hoppe-Tichy T, Geiss HK, Hainer C, Nguyen TH, Knaebel HP, et al. [Septic shock due to vancomycin-resistant enterococci infection. Tigecycline monotherapy.] Anaesthesist 2007; 56: 169–74. [In German]