The Therapeutic Effect of Contezolid in Complex Intra-Abdominal Infections

Yongsheng Zhao*, Xianlei Xin*, Bin Wang, Lei He, Qinghua Zhao, Weizheng Ren

Faculty of Hepato-Pancreato-Biliary Surgery, First Medical Center, Chinese PLA General Hospital, Beijing, People’s Republic of China

*These authors contributed equally to this work

Correspondence: Weizheng Ren; Qinghua Zhao, Faculty of Hepato-Pancreato-Biliary Surgery, First Medical Center, Chinese PLA General Hospital, 28 Fuxing Road, Haidian District, Beijing, 100853, People’s Republic of China, Email rwz301@163.com; zhaqinghuabj@163.com

Purpose: In this paper, we observed the use of contezolid in patients with complex intra-abdominal infections in the intensive care unit of the Hepatobiliary Surgery department at the Chinese PLA General Hospital.

Patients and Methods: The study collected data on complex intra-abdominal infections patients who received the antibiotic contezolid between January 2022 and April 2023.

Results: Contezolid was administered to 12 patients, including 8 with severe acute pancreatitis, 3 with intra-abdominal infections following abdominal surgery, and 1 with complicated intra-abdominal infection after trauma. Gram-positive bacteria, such as Enterococcus faecium, Enterococcus casseliflavus, Staphylococcus capitis, and Staphylococcus haemolytica, were detected in 11 patients. All patients who received contezolid had previously been treated with other anti-Gram-positive agents, including linezolid for 9 patients, teicoplanin for 6 patients, and vancomycin for 3 patients. The treatment with contezolid began 20.0 (15.0, 34.5) days after admission and lasted for 8.0 (6.0, 10.0) days. At the end of the treatment, the patients’ body temperature showed a significant decrease. After concomitant therapy, IL-6 levels decreased, and platelet count increased.

Conclusion: Contezolid has shown potential in treating complex intra-abdominal infections caused by Gram-positive bacteria by reducing fever and inflammatory response.

Keywords: intra-abdominal infection, contezolid, multiple drug-resistant bacteria, gram-positive bacteria

Introduction

Complicated intra-abdominal infections (cIAI) are infectious pathogens that penetrate the primary affected organs and enter the abdominal cavity, causing peritonitis or abdominal abscess.1 As they belong to the category of secondary intra-abdominal infections, they cannot be resolved by surgery alone. Therefore, anti-infective drug treatment is required to a greater extent.2,3 Intra-abdominal infection (IAI) is frequently seen in patients with diffuse or localized purulent peritonitis, appendiceal perforation, peri-appendiceal abscess, acute cholecystitis, cholangitis, trauma, perforation of hollow organs within 24 hours without surgery, intra-abdominal infection after abdominal surgery, and severe acute pancreatitis (SAP) with intra-abdominal or retro-peritoneal infections.4–6 It is important to note that this list is not exhaustive and other conditions may also lead to IAI. Patients with complex medical conditions and treatment histories often experience common multidrug-resistant bacterial infections, which limit the available antibiotics and require a relatively long course of treatment. Among Gram-positive bacteria, vancomycin-resistant enterococcal (VRE) infections are relatively more prevalent and difficult to treat.7 Contezolid is a new type of oxazolidinone antibiotic that was approved by the National Medical Products Administration of China (NMPAC) mainly for the treatment of complicated skin and soft tissue infections (cSSTI) with a broad antibacterial spectrum against staphylococci, streptococci as well as enterococci.8,9 It is also be used for the treatment of infections caused by methicillin-resistant Staphylococcus aureus (MRSA), methicillin-resistant Staphylococcus epidermidis (MRSE), penicillin-resistant Streptococcus pneumoniae
This study reviewed the disease progression of 12 patients with cIAI after treatment with contezolid, providing a reference for the treatment of cIAI patients in clinical settings.

**Materials and Methods**

**Patient Population**

In this study, we observed the treatment of patients with cIAI who were treated with contezolid in the intensive care unit of our hospital’s Hepatobiliary and Pancreatic Surgery Department from January 2022 to April 2023. The diagnostic criteria for cIAI were based on the guidelines provided by the Surgical Infection Society and the Infectious Diseases Society of America.

**Treatment Plan**

The patients’ treatment plan adheres to the guidelines, with critical care physicians formulating and implementing antibiotic treatment plans and senior doctors in the Department of Hepatobiliary Surgery formulating and implementing surgical treatments. The treatment group comprises at least two hepatobiliary surgeons and two hepatobiliary Intensive Care Unit (ICU) surgeons, with expert support in clinical pharmacy, interventional radiology, nutrition, and other related disciplines. The general treatment principles involve fasting and decompression of the gastrointestinal tract, analgesia, proton pump inhibitors, maintenance of water-electrolyte balance, nutritional therapy, and non-prophylactic use of antibiotics. Senior ICU physicians develop invasive treatments, such as vasoactive drugs, mechanical ventilation, and continuous kidney replacement therapy. Surgical treatment is an option if the site of infection is clear or if there are symptoms of compression, as determined by a senior surgical attending in accordance with guidelines.

**Data Collection**

Patient information was collected and observed, including age, gender, Body Mass Index (BMI), length of ICU stay, respiratory support (mechanical ventilation), renal function support (continuous renal replacement therapy), circulatory support (vasoactive drugs), length of stay, treatment outcomes, results of bacterial detection and drug sensitivity, use of various antibiotics, initial treatment time with contezolid, and vital signs and laboratory results on the day of treatment, 3 days after treatment, and the day after treatment ended. Statistical analysis was performed. Using R3.5.2 statistical software, M (Q1, Q3) represents econometric data with non-normal distribution while counting data is represented by percentages.

**Results**

**Patient Characteristics**

From January 2022 to April 2023, our center admitted 12 patients who received treatment with the new domestic drug contezolid for cIAI. Of these patients, 8 had SAP, 3 had intra-abdominal infections after abdominal surgery, and 1 had intra-abdominal infection after trauma. The median age of the patients was 58 years (46.0, 63.5), with an equal distribution of 6 males and 6 females. The study found that the median BMI was 22.66 (21.31, 23.89). The patients received various types of organ function support, including respiratory support in 11 cases (92%), continuous renal replacement therapy in 10 cases (83%), and circulatory support in 11 cases (92%). Before using contezolid, all patients had used other anti-Gram-positive bacterial drugs, such as linezolid (9 cases), teicoplanin (6 cases), and vancomycin (3 cases). 5 of the 12 patients in the study had previously received treatment with at least 2 anti-Gram-positive bacterial drugs. The patients were treated with contezolid at a dosage of 800mg/d, on average, 20 days after hospitalization. The treatment course lasted for an average of 8 days. The patients spent an average of 41.5 days in the ICU and a total of 50.5 days in the hospital. Two patients died during their hospital stay, resulting in an in-hospital mortality of 16.7% (2/12). The mortality rate within 90 days was 41.7%.
Gram-Positive Bacteria Culture and Drug Sensitivity results
Out of the 12 patients, bacterial culture revealed mixed infection in 11 cases, with only 1 case showing no detection of Gram-positive bacteria. The Gram-positive bacteria detected were Enterococcus faecium (found in bile, tracheal aspirates, urinary catheters, abdominal drains, and central venous catheters) and Enterococcus casseliflavus (found in venous blood). Staphylococcus capitis was found in venous blood, Staphylococcus hemolyticus in central venous catheters, Staphylococcus epidermidis in abdominal drainage, Staphylococcus aureus in bile, and Staphylococcus mimicus in bile. Enterococcus faecium was the most commonly detected bacteria, with a total of 7 patients and 9 sites. Gram-positive bacteria were most frequently detected in bile, with a total of 7 patients. Out of the 12 patients, only 1 patient exhibited vancomycin resistance in Staphylococcus aureus (venous blood), while 2 patients showed resistance to linezolid in Staphylococcus cephalococcus (urinary tract) and Enterococcus faecium (peritoneal drainage fluid). The cultivation results are presented in Table 1.

Changes in Vital Signs and Laboratory Examination Indicators Before and After Treatment
Compared to pre-treatment, the patient’s body temperature at the end of treatment. The IL-6 levels decrease both at 3 days after treatment and at the end of treatment. The patient’s platelet count tended to increase at the end of treatment. There were no significant changes in the patient’s white blood cell count (WBC), C-reactive protein (CRP), BNP, troponin T, aspartate aminotransferase, alanine aminotransferase, total bilirubin, urea nitrogen, or creatinine after contezolid administration, as shown in Table 2.

Simultaneous Mixed Infections and Coadministration of Antimicrobials
Upon admission, 11 out of 12 patients were treated with linezolid, vancomycin, and teicoplanin as their preferred anti-Gram-positive bacterial therapeutic agents. The median time for patients to adjust to contezolid treatment was 20.0 (15.0, 34.5) days, with an average of 24.9 days after admission.

Of all the patients, only 1 patient preferred contezolid tablets on the second day of admission. The patient was initially diagnosed with intra-abdominal infection, septic shock, and renal insufficiency after abdominal surgery. Her temperature fluctuated around 39°C for three days before admission, and she had a persistent fever. On the day of treatment, the patient’s body temperature was 38.6°C, her WBC was 41.86 × 10^9/L, neutrophil percentage was 97%, and platelet count was 12 × 10^9/L. The bacteriologic examination revealed that only Acinetobacter baumannii was pan-resistant. Based on the patient’s history of abdominal surgery and culture results, we administered a combination of antibiotics, including polymyxin, caspofungin acetate, and imipenem with cilastatin. The patient was discharged from the ICU after 7 days of treatment but unfortunately passed away within 90 days.

The 12 patients in this study were infected with multidrug-resistant Gram-negative bacteria (Acinetobacter baumannii in 11 patients; Klebsiella pneumoniae in 7 patients). The antibiotics used to treat the infections included Ceftazidime/Avibactam (3 patients), polymyxin (2 patients), Imipenem/Cilastatin (3 patients) and tigecycline (7 patients). Table 3 shows the drug usage of each patient during their stay in the ICU.

Discussion
Complex intra-abdominal infection refers to a range of clinical scenarios that vary in severity, duration, and complexity. Immediate intervention is often necessary due to the severity of the condition. The guidelines recommend multidisciplinary participation, including surgery, intensive care, infectious disease experts, and nutritionists, to effectively treat complex intra-abdominal infections. Experts recommend a tiered approach to achieve the best treatment outcomes for cIAI. This approach includes early identification, adequate infection source control, appropriate antimicrobial therapy, and nutritional support. As per the guidelines, several patients possess risk factors linked to treatment failure and mortality. These include advanced age, organ failure (SOFA ≥1), high temperature, elevated leukocytes, inadequate debridement or drainage, emergence of drug-resistant organisms, positive enterococcal cultures, and worsening of thrombocytopenia after the initial infection control procedure.
Table 1 The Results of Gram-Positive Bacteria Culture and Drug Sensitivity Test of 12 Patients

<table>
<thead>
<tr>
<th>Case</th>
<th>Pathogen</th>
<th>Detection Location</th>
<th>Drug Sensitivity Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>PEN</td>
</tr>
<tr>
<td>1</td>
<td>EF</td>
<td>Bile, Sputum</td>
<td>/</td>
</tr>
<tr>
<td>2</td>
<td>EF</td>
<td>Bile, UT</td>
<td>R</td>
</tr>
<tr>
<td>3</td>
<td>E. casseliflavus</td>
<td>VB</td>
<td>S</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>5</td>
<td>EF</td>
<td>Bile</td>
<td>R</td>
</tr>
<tr>
<td>6</td>
<td>EF</td>
<td>PDF</td>
<td>R</td>
</tr>
<tr>
<td></td>
<td>S. capitis</td>
<td>UT</td>
<td>R</td>
</tr>
<tr>
<td>7</td>
<td>EF</td>
<td>PDF</td>
<td>R</td>
</tr>
<tr>
<td></td>
<td>SH</td>
<td>CVC</td>
<td>R</td>
</tr>
<tr>
<td></td>
<td>SE</td>
<td>PDF</td>
<td>R</td>
</tr>
<tr>
<td></td>
<td>S. hominis</td>
<td>Bile</td>
<td>R</td>
</tr>
<tr>
<td>8</td>
<td>EF</td>
<td>Bile</td>
<td>R</td>
</tr>
<tr>
<td>9</td>
<td>EF</td>
<td>VB</td>
<td>R</td>
</tr>
<tr>
<td>10</td>
<td>SE</td>
<td>Bile</td>
<td>R</td>
</tr>
<tr>
<td>11</td>
<td>EF</td>
<td>PDF</td>
<td>R</td>
</tr>
<tr>
<td></td>
<td>EF</td>
<td>CVC</td>
<td>R</td>
</tr>
<tr>
<td>12</td>
<td>S. simulans</td>
<td>Bile</td>
<td>S</td>
</tr>
</tbody>
</table>

Abbreviations: AMP, Ampicillin; CPFX, Ciprofloxacin; CVC, Central venous catheter; E. casseliflavus, Enterococcus casseliflavus; EF, Enterococcus faecium; EM, Erythromycin; GM, Gentamicin; LVFX, Levofloxacin; LZD, Linezolid; PDF, Peritoneal drainage fluid; PEN, Penicillin; Q/D, Quinupristin/Dalfopristin; R, Drug resistance; S. capitis, Staphylococcus capitis; SE, Staphylococcus epidermidis; SH, Staphylococcus haemolyticus; S. hominis, Staphylococcus hominis; SM, Streptomycin; S, Sensitive; S. simulans, Staphylococcus simulans; TC, Tetracycline; TGC, Tigecycline; UT, Urinary tract; VAN, Vancomycin; VB, Venous blood; /, not done.
Out of the cIAI cases in this group, 8 were SAP with intra-abdominal infection, which is defined as critical acute pancreatitis. According to international reports, this type of infection has a mortality rate as high as 55%. The remaining 4 cases were trauma and postoperative intra-abdominal infections. Two patients, both with pancreatitis, died during the mediation process, with a mortality rate lower than the internationally reported rate. The main cause of death is the worsening of infection due to the prolonged course of the disease and the inability to effectively drain and debride. Additionally, while 10 patients improved and were discharged, 3 patients died within 90 days after discharge, including 2 deaths from lung infections and 1 death due to tumor progression. This suggests that persistent ICU-acquired weakness after improvement in critically ill cases urgently needs to be aided by better individualized rehabilitation strategies after ICU treatment. Survivors of critical illness face an increased risk of late death, which is even higher when patients had experienced ICU-acquired weakness.

To treat cIAI, the initial step is to control the source of infection. This can be accomplished through surgical debridement, abscess or fluid drainage, and removal of infected tissue. Early intervention is crucial in preventing the spread of infection and reducing mortality rates. Intraperitoneal infections can be caused by various microorganisms, including Gram-negative, Gram-positive, anaerobic bacteria, and fungi. If bacterial culture results are not obtained, it is recommended to use broad-spectrum antibiotics immediately to cover potential pathogenic bacteria and begin empirical antibacterial treatment. However, adjustments or downgrades should be considered once the cultivation results are obtained. The total duration of antibacterial therapy should be 4–7 days. Bacterial culture was highly suspicious for abdominal Gram-positive bacterial infection in patient No.4, but the patient was unable to have another sample taken and no NGS was done. Typically, the application of antibiotics in the early stages of sepsis is empirical, and ultimately there may be no definitive evidence for this either. Then in septic shock with very low platelets, linezolid was not appropriate, and the broad antimicrobial spectrum of contezolid, with little adverse effects such as myelosuppression, suggests that it could be an empirical agent for abdominal infections with anti-positive bacteria.

To ensure appropriate and standardized selection of antimicrobial agents, this study adhered to objective evaluations and precise selection. To treat infections caused by multidrug-resistant or pan-drug-resistant Gram-negative bacteria, particularly to control CRE infections, a combined treatment plan was followed after obtaining precise etiological diagnostic results. Recommended protocols outlined in consensus guidelines were followed in this plan. All patients in this group had one or more concurrent Gram-negative bacterial infections and carbapenem-resistant bacterial

### Table 2 Changes in Patients’ Vital Signs and Laboratory Examination Indicators Before and After Treatment

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Before Treatment</th>
<th>3 Days Post-Treatment</th>
<th>End of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M (Q1, Q3)</td>
<td>M (Q1, Q3)</td>
<td>M (Q1, Q3)</td>
</tr>
<tr>
<td>T (°C)</td>
<td>37.8 (36.9, 38.8)</td>
<td>37.6 (37.0, 38.2)</td>
<td>36.8 (36.5, 36.9)</td>
</tr>
<tr>
<td>WBC (×10⁹/L)</td>
<td>10.7 (4.3, 21.9)</td>
<td>14.6 (9.5, 26.5)</td>
<td>14.6 (8.6, 23.3)</td>
</tr>
<tr>
<td>N (%)</td>
<td>87.8 (65.8, 94.4)</td>
<td>84 (70.6, 87.1)</td>
<td>88 (82.1, 93.5)</td>
</tr>
<tr>
<td>CRP (mg/dL)</td>
<td>5.8 (4.0, 7.0)</td>
<td>5.6 (3.3, 8.4)</td>
<td>9.2 (5.0, 13.6)</td>
</tr>
<tr>
<td>Platelet (×10³/L)</td>
<td>63.7 (45.0)</td>
<td>69.6 (48.2)</td>
<td>96.6 (88.6)</td>
</tr>
<tr>
<td>IL-6 (pg/mL)</td>
<td>150 (98.3, 516)</td>
<td>132.6 (55.5, 381)</td>
<td>58.3 (20.5, 176.8)</td>
</tr>
<tr>
<td>BNP (pg/mL)</td>
<td>849.2 (538.2, 2708.5)</td>
<td>1065.6 (376.6, 6252.3)</td>
<td>1784.5 (330.1, 15,803.3)</td>
</tr>
<tr>
<td>TNF (ng/mL)</td>
<td>0.06 (0.03, 0.10)</td>
<td>0.05 (0.04, 0.07)</td>
<td>0.06 (0.02, 0.1)</td>
</tr>
<tr>
<td>AST (μL)</td>
<td>43.6 (24.0, 100.6)</td>
<td>47.9 (23.9, 80.9)</td>
<td>31.8 (19.0, 55.7)</td>
</tr>
<tr>
<td>ALT (μL)</td>
<td>51.8 (9.3, 108.5)</td>
<td>47.3 (18.8, 71.3)</td>
<td>30.3 (16.0, 47.1)</td>
</tr>
<tr>
<td>TB (μmol/L)</td>
<td>42.0 (25.0, 124.8)</td>
<td>58.3 (26.9, 179.3)</td>
<td>63.9 (37.1, 185.0)</td>
</tr>
<tr>
<td>BUN (mmol/L)</td>
<td>11.8 (7.68, 21.8)</td>
<td>10.0 (7.1, 25.8)</td>
<td>10.3 (6.1, 17.6)</td>
</tr>
<tr>
<td>Cr (μmol/L)</td>
<td>75.1 (41.6, 103.7)</td>
<td>88.2 (52.3, 118.4)</td>
<td>74.7 (53.4, 158.3)</td>
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<tr>
<td>UA (μmol/L)</td>
<td>206.6 (126.0, 273.1)</td>
<td>190.8 (122.5, 243.2)</td>
<td>159.6 (71.1, 285.1)</td>
</tr>
</tbody>
</table>

**Abbreviations:** ALT, Alanine transaminase; AST, Aspartate Transaminase; BNP, Brain natriuretic peptide precursor; BUN, Urea nitrogen; Cr, Creatinine; CRP, C-reactive protein; IL-6, Interleukin-6; N, Neutrophil percentage; T, Body temperature; TB, Total bilirubin; TNF, Tumor necrosis factor; T, Urine accl; WBC, White blood cells.
<table>
<thead>
<tr>
<th>Case</th>
<th>Diagnosed Disease</th>
<th>Surgery</th>
<th>SOFA</th>
<th>Type of Infection</th>
<th>Pre-order Therapy</th>
<th>Reason for Replacement</th>
<th>Other Aetiological Findings</th>
<th>Combined Antimicrobial Regimen</th>
<th>Antibiotic Treatment Outcomes</th>
<th>Hospitalization Outcomes</th>
<th>90-Day Treatment Outcomes</th>
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<tr>
<td>1</td>
<td>SAP</td>
<td>PN</td>
<td>3.00</td>
<td>IAI</td>
<td>VAN / LZD</td>
<td>Efficacy</td>
<td>KPN, PM (PDF), AB (bile, urine)</td>
<td>FLC, LVFX, TGC, I/C, VCZ, CAZ/ AVI</td>
<td>Effective</td>
<td>Discharge</td>
<td>Survive</td>
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<tr>
<td>2</td>
<td>Trauma</td>
<td>/</td>
<td>4.00</td>
<td>IAI, UT</td>
<td>TEC</td>
<td>Efficacy</td>
<td>AB (bile), KPN (urine), BC (urine)</td>
<td>TGC, BPM, CAZ/AVI, PB, I/C, CAS CAZ/AVI</td>
<td>Effective</td>
<td>Discharge</td>
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<tr>
<td>3</td>
<td>CCA</td>
<td>/</td>
<td>2.00</td>
<td>IAI, Li</td>
<td>LZD</td>
<td>LP</td>
<td>AB (PDF)</td>
<td>TGC, CAS</td>
<td>Death</td>
<td>Death</td>
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<tr>
<td>4</td>
<td>PC</td>
<td>/</td>
<td>4.00</td>
<td>IAI, Li</td>
<td>Conteozolid /</td>
<td>AB (PDF)</td>
<td>KPN, PAE, Ecl, CF (PDF), AB (bile), CT, SM, CA (airways)</td>
<td>I/C, TGC, FLC</td>
<td>Effective</td>
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<td>Death</td>
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<td>SAP</td>
<td>PN</td>
<td>4.00</td>
<td>IAI, Li</td>
<td>LZD</td>
<td>LP</td>
<td>AB (PDF)</td>
<td>TGC, FLC, CS</td>
<td>Death</td>
<td>Death</td>
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<td>6</td>
<td>CCA, CC</td>
<td>Robotic-assisted radical resection for pCCA and radical resection of colon cancer</td>
<td>4.00</td>
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<td>TEC / LED</td>
<td>LP</td>
<td>E. coli, CA, CG (urine)</td>
<td>TGC, CAS</td>
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<td>TEC / LZD</td>
<td>LP</td>
<td>KPN (PDF), AB, SM, EM (airways)</td>
<td>I/C, TGC, FLC</td>
<td>Effective</td>
<td>Discharge</td>
<td>Death</td>
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<tr>
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<td>SAP</td>
<td>PN</td>
<td>4.00</td>
<td>IAI, Li</td>
<td>LZD</td>
<td>LP</td>
<td>KPN, SMA (PDF, bile), AB, CA (urine)</td>
<td>TGC</td>
<td>Effective</td>
<td>Discharge</td>
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<td>IAI, Li</td>
<td>VAN / LZD</td>
<td>LP</td>
<td>AB (PDF), KPN (bile)</td>
<td>TGC, FLC, CS</td>
<td>Death</td>
<td>Death</td>
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<tr>
<td>10</td>
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<td>PN</td>
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<td>LZD</td>
<td>LP</td>
<td>E. coli (PDF), AB (urine), KPN (airways)</td>
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<td>Effective</td>
<td>Discharge</td>
<td>Survive</td>
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<tr>
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<td>IAI, Li</td>
<td>VAN/ TEC/ LZD</td>
<td>LP</td>
<td>AB (bile)</td>
<td>LVFX, AMPH, PB</td>
<td>Effective</td>
<td>Discharge</td>
<td>Survive</td>
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<td>/</td>
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<td>IAI</td>
<td>TEC</td>
<td>Efficacy</td>
<td>A. caviae (bile), AB (urine)</td>
<td>Effective</td>
<td>Discharge</td>
<td>Survive</td>
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</tr>
</tbody>
</table>

**Abbreviations:** AB, Acinetobacter baumannii; A. caviae, Aeromonas cavae; AMPH, Amphotericin B; AP, Acinetobacter pittii; BC, Burkholderia cepacia; BPM, Biapenem; CA, Candida albicans; CAS, Caspofungin; CAZ/AVI, Cefazidine/Avibactam; CC, Colon cancer; CCA, Cholangiocarcinoma; CF, Citrobacter freundii; CG, Candida glabrata; CS, cefoperazone/sulbactam; CT, Candida tropicalis; Ecl, Enterobacter cloacae; E. coli, Escherichia coli; EM, Elizabethkingia meningoseptica; FLC, Fluconazole; IAI, Intra-abdominal infection; I/C, Imipenem/Cilastatin; KPN, Klebsiella pneumoniae; LI, Lung Infection; LP, Low platelets; LVFX, Levofloxacin; LZD, Linezolid; PAE, Pseudomonas aeruginosa; PB, Polymixin B; PC, Pancreatic cancer; pCCA, perihilar cholangiocarcinoma; PM, Proteus mirabilis; PN, pancreatic necrosectomy; SM, Serratia marcescens; SMA, Stenotrophomonas maltophilia; TEC, Teicoplanin; TGC, Tigecycline; UT, Urinary infection; VAN, Vancomycin; VCZ, Voriconazole.
infections, indicating a critical condition. The 2 hospital deaths in this group were related to sepsis caused by pan-
resistant Klebsiella pneumoniae infection. The achievement of a favorable outcome for patients is closely related to
effective antimicrobial therapy against both Gram-negative and Gram-positive bacteria, as well as practical surgical
drainage.

The treatment of infections caused by Gram-positive bacteria usually requires specialized antibacterial treatments that
target these microorganisms, such as vancomycin or linezolid.\textsuperscript{21,22} In recent years, Enterococcus resistance has increased,
making treatment more challenging, particularly for Enterococcus faecalis and Enterococcus faecium. All patients were
treated with a standard anti-Gram-positive bacterial infection prior to using contezolid due to its availability (off-label use
and lacking of evidence-based medicine). Of the patients, 9 had a poor response. Most of these patients experienced
significant and persistent thrombocytopenia, leukopenia, and other myelosuppression, which was related to the use of
linezolid or due to the infection (agranulocytosis due to infection and Panton-Valentine leukocidin production by
Staphylococcus aureus).\textsuperscript{23} Others showed a significant increase in leukocytes and neutrophils. In these complex cases,
where antibiotic options are limited, we attempted to use contezolid, a new generation of oxazolidinones. Following the
change in medication, some patients with agranulocytosis experienced a recovery in their white blood cell count, while
others showed a decrease in white blood cells and neutrophils due to the improvement of the infection. There are 2
patients died before reaching the point of drug discontinuation, which may have contributed to the lack of significant
changes in the leukocyte index at the end of therapy. Not all patients changed medication due to severe platelet
decompensation. Although significant platelet increases were observed in some patients, platelets did not change
significantly in the group as a whole.

Among these patients, linezolid resistance was detected in 2 cases and vancomycin resistance in 1 case. Although
there is a risk of cross-resistance between contezolid and linezolid, continuous passage studies of Staphylococcus aureus
have shown that the rate of resistance of contezolid in Staphylococcus aureus is significantly slower than that of linezolid,
indicating a lower risk of resistance and more durable antibacterial activity.\textsuperscript{24} Based on the above characteristics, we
carefully chose to use contezolid in these patients. After treatment with contezolid, their body temperature was quickly
controlled and its anti-infective effect was effective. Therefore, we suggest that contezolid could be used as an alternative
regimen with excellent efficacy and a favorable safety profile in the treatment of Gram-positive bacterial infections that
have shown poor response to conventional drugs and are associated with platelet drop and resistance.

The study patients had poor baseline conditions, including varying degrees of hepatic, renal, and cardiac
insufficiency. Additionally, the use of linezolid, vancomycin, or teicoplanin was either ineffective or had intolerable
side effects. Additionally, all patients had contraindications to oral antibiotics. Specifically, three patients had
enterocutaneous fistulae. Contezolid is currently available only as tablets, not in intravenous form. With the patients’
full knowledge, we chose to administer contezolid through nasogastric tube for sympathetic treatment and achieved
clinical results similar to those of the tablets. High doses of contezolid against Gram-positive bacteria were also found
to be safe and effective in these challenging situations. The future development and marketing of intravenous
formulations of contezolid will resolve the issue of oral contraindications, better meeting complex clinical anti-
infective needs.

Patients with complex intra-abdominal infections face limited antibiotic options due to the long treatment course and
the presence of multidrug-resistant bacteria in hospitals.\textsuperscript{7} The challenge of antibiotic treatment increases in the later
stages of the disease, which can be compounded by the pressure of longterm illness. Unfortunately, the research and
development cycle for new antibiotics is lengthy, resulting in a limited number of new antibiotics available. Furthermore,
the prolonged use of linezolid has been linked to myelosuppression, lactic acidosis, and optic neuropathy.\textsuperscript{25} On the other
hand, contezolid exhibits non-inferior antibacterial activity to linezolid, with fewer adverse effects and fewer drug
interactions.\textsuperscript{26} Considering the benefits of contezolid and the patient characteristics in this study, it is suggested to use
contezolid as a combination antibacterial treatment regimen for empiric coverage of Gram-positive bacteria. This may
provide significant clinical benefits. A case report describes the successful treatment of VRE pneumonia in a centenarian
using sequential therapy of linezolid and contezolid.\textsuperscript{27} The study showed that switching to contezolid when experiencing
a platelet decrease while using linezolid for anti-infective purposes resulted in excellent, safe, and effective antibacterial
outcomes. No serious adverse reactions were observed in this study, consistent with the literature.
Conclusion
More than a dozen case reports have been published since the launch of contezolid describing its anti-infective effects in various clinical disease areas. Our report is the first to report the successful use of contezolid in the treatment of cIAI with satisfactory clinical results. Taken together, contezolid can be considered an effective and safe therapeutic agent for the treatment of cIAI. However, further randomized controlled trials in relevant treatment areas are necessary to confirm its efficacy and safety.

Data Sharing Statement
The data presented in this study are available on request from the corresponding author.

Ethics Approval and Informed Consent
The protocol and informed consent form were reviewed and approved by the Ethics Committee of Chinese PLA General Hospital (no. 2023-352). Informed consents were obtained from the study participants prior to study commencement.

Consent for Publication
All authors read and approved the final manuscript.

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