International Journal of Clinical Medicine, 2021, 12, 1-6
https://www.scirp.org/journal/ijcm
ISSN Online: 2158-2882
ISSN Print: 2158-284X

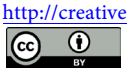
Tigecycline Use in Surgical Intensive Care Unit for the Treatment of Complicated Intra-Abdominal Infections: A Real-World Study

Yao Nie, Fei Pei, Luhao Wang, Xiang Si, Xiangdong Guan

Department of Surgical Intensive Care Unit, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China
Email: nieyao@mail.sysu.edu.cn

How to cite this paper: Nie, Y., Pei, F., Wang, L.H., Si, X. and Guan, X.D. (2021) Tigecycline Use in Surgical Intensive Care Unit for the Treatment of Complicated Intra-Abdominal Infections: A Real-World Study. *International Journal of Clinical Medicine*, **12**, 1-6.
https://doi.org/10.4236/ijcm.2021.121001

Received: December 10, 2020
Accepted: January 8, 2021
Published: January 11, 2021



Abstract

OBJECTIVES: To describe real-world use of tigecycline in cIAIs patients. METHODS: A retrospective, observational study enrolled cIAIs patients hospitalized in The First Affiliated Hospital, Sun Yat-sen University from January 1, 2013 to June 30, 2017 was conducted. Patients' data were collected and matched based on age, gender, and Acute Physiologic Assessment and Chronic Health Evaluation II (APACHE II) score according to receiving first-line, later-line, or no tigecycline during hospitalization. RESULTS: Data were collected for 52 patients. 82.6% were male. Mean age was 57.8 years and APACHE II score was 14.8. The incidence of both extended-spectrum beta-lactamase producing and carbapenem-resistant pathogens was high on initial culture; however, few patients received first-line tigecycline. No significant difference in mortality rate was identified among first-line, later-line and no tigecycline users. Of surviving patients, shorter hospital length of stay was observed for patients receiving first- vs later-line or no tigecycline, respectively. ICU length-of-stay was shorter in patients receiving first- vs later-line or no tigecycline. CONCLUSIONS: First-line tigecycline use was rare in our surgical intensive care unit. Resistant organisms were commonly cultured from initial specimens. Although these results are limited by small patient numbers and single center, our results suggest that early tigecycline use may have significant benefits with similar mortality. Further research is warranted to demonstrate the values of early tigecycline use in cIAIs patients.

Keywords

Tigecycline, Complicated Intra-Abdominal Infection, Multidrug-Resistant

1. Introduction

Intra-abdominal infections have a high incidence and are often associated with poor prognosis [1]. Complex intra-abdominal infections (cIAIs) refer to bacteria passing through defects in the digestive tract and invading the peritoneal cavity, leading to abscess formation or peritonitis. The clinical treatment of complex intra-abdominal infections is complicated, and patients admitted to the ICU are generally difficult to solve by a single treatment. The treatment includes drainage of effusion or control of infection under surgical and interventional guidance, supplemented by broad-spectrum antibiotics. Appropriate empirical antimicrobial therapy can increase the success rate of clinical treatment, reduce the length of hospital stay and hospitalization costs, and minimize antimicrobial resistance caused by selective pressure. Inappropriate treatment can lead to treatment failure, prolong hospital stay, and increase mortality.

The conditions of critically ill patients are complex, and most of them have used a variety of anti-infective drugs in the early stage. As a result, it is very difficult to choose antibiotics after being transferred to ICU [2] [3]. Tigecycline, as a new type of glycyl-type broad-spectrum antibacterial drug, is the first antibiotic approved by the U.S. FDA for the treatment of complex intra-abdominal infections [4]. It is particularly effective to multiple pathogens isolated from patients with complex intra-abdominal infections and has good antibacterial activity *in vitro*. This article retrospectively analyzes the real-world data of tigecycline use in a surgical ICU for the treatment of complex intra-abdominal infections, and provides a basis for the selection of antibiotics for clinical complex intra-abdominal infections.

2. Methods

2.1. Data Source

We performed a retrospective analysis of hospitalization data obtained from the surgical intensive care unit of The First Affiliated Hospital, Sun Yat-sen University.

Patients

All patients hospitalized in our surgical ICU from January 1, 2013 to June 30, 2017 were screened. The inclusion criteria are: 1) diagnosed with cIAIs; 2) ≥18 years old. The exclusion criteria include: 1) tigecycline administration is not for abdominal infections; 2) severe infection in other parts of the body; 3) existence of immunodeficiency (e.g. HIV); 4) history of alcohol abuse; 5) no drug susceptibility results, or no culture specimens obtained within one week after using antibiotics. Patients were categorized into the case group if they received tigecycline within 24 hours of confirmed pathogen test results. Those who did not receive tigecycline during this time period were categorized into the control group. Matched controls were selected based on age, gender, the Acute Physiologic Assessment and Chronic Health Evaluation II (APACHE II) score, lab results, and previously used antibiotics. First-line TGC users were those who received TGC

as the first antibiotic during hospitalization. Later-line TGC users were those who received TGC after prior antibiotic administration. All patients were followed up to discharge or death, which came first.

2.2. Analyses

Descriptive analyses were conducted on patient baseline characteristics. Clinical and economic outcomes were compared between the treatment groups. Antibiotic use prior to TGC administration was assessed among patients treated with later-line TGC therapy and confirmed carbapenem-resistant or extended spectrum beta-lactamase (ESBL)-producing organisms.

3. Results

3.1. Patient Characteristics

Data from 52 patients were collected. 82.6% of the patients were male, with the mean age of 57.8 years and the mean APACHE II 14.8. Despite matching patients receiving TGC to those not receiving TGC therapy on APACHE II score, the score was lower in patients not receiving TGC vs those receiving TGC. Patients not receiving TGC may not be comparable to patients receiving TGC due to their underlying conditions. Therefore, comparisons between the TGC and no TGC treatment groups were not performed. APACHE II scores were similar in patients receiving first- vs later-line TGC. The incidence of both carbapenem-resistant pathogens and ESBL-producing organisms was high on the initial abdominal culture; however, few patients received first-line TGC (Table 1).

3.2. First-Line vs Later-Line TGC

Among TGC users, no statistically significant differences were found in mortality. Of surviving patients, shorter hospital length of stay was observed for patients who received first- vs later-line TGC therapy. Of survivors admitted to the ICU, length of ICU stay was shorter in patients receiving first- vs later-line TGC, but with no statistical significance. No statistically significant difference was found in antibiotic costs between patients receiving first- and later-line TGC therapy.

Table 1. Baseline Characteristics by TGC Use.

		No TGC	First-line TGC	Second-line TGC	P value
Age		61.7 ± 9.68	55.4 ± 16.4	51.2 ± 17.0	0.066
Gender	Male	25	10	8	0.222
	Female	3	2	4	
APACHE-II		13.7 ± 5.7	15.8 ± 8.6	17.4 ± 4.9	0.348
Bacteria	Gram-Negative	19	10	6	0.219
	Gram-Positive	9	2	6	
ESBL (N)		15	6	1	0.069
Carbapenem-resistant (N)		4	2	2	0.821

3.3. Antibiotics Used Prior to TGC Therapy

Among patients with carbapenem-resistant infections, imipenem, teicoplanin, and meropenem were the most frequently used antibiotics before initiation of TGC therapy. Among patients with ESBL infections, imipenem was the most frequently used antibiotics before initiation of TGC therapy.

4. Discussion

Since the pathogenic bacteria of early complicated intra-abdominal cavity infections are mostly Enterobacteriaceae, such as Escherichia coli, *Klebsiella pneumoniae*, *Enterobacter cloacae*, etc., the sensitivity rate of carbapenems to *Enterobacteriaceae* was almost 100% in early years; therefore, carbapenem antibiotics have always been the most effective antibiotics for the treatment of severe cIAIs. However, in recent years, bacteria resistant to carbapenem antibiotics in local areas have gradually shown an increasing trend, and the related mortality rate has also been climbing [5] [6]. This shows that for these patients, the sensitivity of carbapenem antibiotics has a downward trend.

There are many reasons for the increase in drug resistance, and some studies suggest that overexposure may be one of the important factors. A prospective study in Greece showed that frequent use of carbapenems and polymyxins and a longer treatment course were factors influencing carbapenem antibiotic resistance, and polymyxins was an independent risk factor for multiple drug resistance (Multidrug-resistant, MDR) [7]. Recently, the resistance of non-fermenting bacteria such as *Acinetobacter baumannii* and *Pseudomonas aeruginosa* has increased by years. Particularly, the sensitivity of carbapenems has decreased significantly. The emergence of some pan-resistant strains is of more concern.

Tigecycline belongs to a new type of glycylcycline antibacterial drug. Its mechanism is similar to that of tetracycline antibiotics. After administration, it can bind to bacterial 30S ribosomes to prevent transfer RNA from entering, thereby effectively inhibits peptides chain formation, interrupts bacterial structure and makes it difficult for bacteria to perform certain functions, which ultimately exerts antibacterial effect and inhibits bacterial reproduction. Tigecycline has a strong binding ability to ribosomes. After injection, about 22% of the drug will be excreted in the urine, with an average elimination half-life of 27 h. The antibacterial spectrum is very broad, mainly including *Acinetobacter baumannii*, *Escherichia coli*, *Enterobacter cloacae*, *Klebsiella oxytoca*, *Aeromonas hydrophila*, *Citrobacter klebsiella*, and *Klebsiella pneumoniae*. These pathogens are highly sensitive to Tigecycline and have obvious therapeutic effects.

For critically ill patients with sepsis and septic shock in surgical ICU, tigecycline treatment can significantly reduce the mortality rate [8]. Especially in sepsis patients with multi-drug-resistant bacteria infection, tigecycline is an important antibiotic. A meta-analysis from 15 studies showed that tigecycline could increase clinical treatment inefficiency and mortality [9]. However, some studies suggested that the increased mortality caused by failure of tigecycline treatment

may be related to the low dose of tigecycline [10]. A recent study comparatively analyzed the effects of tigecycline and other antibacterial drugs in the treatment of complex intra-abdominal infections, and found that the short-term prognosis of the two groups of patients was similar, suggesting that tigecycline is one of the options for patients with complex intra-abdominal infections [11].

5. Limitations

Our study results are limited by small patient numbers and data from single hospital, but our results suggest that early TGC use may have significant economic benefits with similar mortality. Additional research is warranted to further demonstrate the value of early TGC therapy in patients hospitalized with cIAIs in China.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Kanj, S.S. and Kanafani, ZA. (2011) Current Concepts in Antimicrobial Therapy against Resistant Gram-Negative Organisms: Extended-Spectrum β-Lactamase-Producing Enterobacteriaceae, Carbapenem-Resistant Enterobacteriaceae, and Multidrug-Resistant *Pseudomonas aeruginosa*. *Mayo Clinic Proceedings*, **86**, 250-259. https://doi.org/10.4065/mcp.2010.0674

[2] Fu, Y.Q., Zhou, J.Y., Zhou, H., Yang, Q., Wei, Z.Q., Yu, Y.S., *et al.* (2010) Wide Dissemination of OXA-23-Producing Carbapenem-Resistant *Acinetobacter Baumannii* Clonal Complex 22 in Multiple Cities of China. *Journal of Antimicrobial Chemotherapy*, **65**, 644-650. https://doi.org/10.1093/jac/dkq027

[3] Wang, H., Guo, P., Sun, H., *et al.* (2007) Molecular Epidemiology of Clinical Isolates of Carbapenem-Resistant *Acinetobacter* spp. from Chinese Hospitals. *Antimicrobial Agents and Chemotherapy*, **51**, 4022-4028. https://doi.org/10.1128/AAC.01259-06

[4] Rose, W.E. and Rybak, M.J. (2006) Tigecycline: First of a NEW Class of Antimicrobial Agents. *Pharmacotherapy*, **26**, 1099-1110. https://doi.org/10.1592/phco.26.8.1099

[5] Boucher, H.W., Talbot, G.H., Bradley, J.S., Edwards, J.E., Gilbert, D., Rice, L.B., *et al.* (2009) Bad Drugs, No Drugs: No ESKAPE! An Update from the Infectious Disease Society of America. *Clinical Infectious Diseases*, **48**, 1-12. https://doi.org/10.1086/595011

[6] Morrissey, I., Hackel, M., Badal, R., Bouchillon, S., Hawser, S. and Biedenbach, D. (2013) A Review of Ten Years of the Study for Monitoring Antimicrobial Resistance Trends (SMART) from 2002 to 2011. *Pharmaceutical*, **6**, 1335-1346. https://doi.org/10.3390/ph6111335

[7] Mantzarlis, K., Makris, D., Manoulakas, E., *et al.* (2013) Risk Factors for the First Episode of *Klebsiella pneumoniae* Resistant to Carbapenems Infection in Critically Ill Patients: A Prospective Study. *BioMed Research International*, **2013**, Article ID: 850547. https://doi.org/10.1155/2013/850547

[8] Schafer, J.J., Goff, D.A., Stevenson, K.B. and Mangino, J.E. (2007) Early Experience

with TGC for Ventilator-Associated Pneumonia and Bacteremia Caused by Multi-drug-Resistant *Acinetobacter baumannii*. *Pharmacotherapy*, **27**, 980-987. https://doi.org/10.1592/phco.27.7.980

[9] Shen, F., Han, Q.P., Xie, D., Fang, M., Zeng, H.K. and Deng, Y.Y. (2015) Efficacy and Safety of Tigecycline for the Treatment of Severe Infectious Diseases: An Updated Meta-Analysis of RCTs. *International Journal of Infectious Diseases*, **39**, 25-33. https://doi.org/10.1016/j.ijid.2015.08.009

[10] Xie, J., Roberts, J.A., Alobaid, A.S., Roger, C., Wang, Y., Yang, Q.T., *et al.* (2017) Population Pharmacokinetics of Tigecycline in Critically Ill Patients with Severe Infections. *Antimicrobial Agents and Chemotherapy*, **61**, e00345-17. https://doi.org/10.1128/AAC.00345-17

[11] Solomkin, J., Mullins, C.D., Quintana, A., Eckmann, C., Shelbaya, A., Ernst, F.R., *et al.* (2016) Evaluation of Tigecycline Efficacy and Post-Discharge Outcomes in a Clinical Practice Population with Complicated Intra-Abdominal Infection: A Propensity Score-Matched Analysis. *Surgical Infections*, **17**, 402-411. https://doi.org/10.1089/sur.2015.075