

中文題目: Doripenem 使用在醫療照護相關感染的臨床經驗

英文題目: Clinical experience in patients with doripenem-containing regimens for treatment of healthcare-associated infections

作者: 趙建銘<sup>1</sup>、賴志政<sup>2</sup>、陳志忠<sup>3</sup>、湯宏仁<sup>4</sup>

服務單位: 柳營奇美醫院加護醫學部<sup>1,2</sup>、奇美醫院醫學研究部<sup>3</sup>、奇美醫院內科部感染科<sup>4</sup>

## **Introduction:**

In this era of increasing antimicrobial-resistant bacteria, broad-spectrum antibiotic, such as carbapenems have become recommended as one of the most effective in the treatment of serious infections caused by these pathogens, especially multidrug-resistant gram-negative bacilli (MDR-GNB) (Baldwin, Lyseng-Williamson, & Keam, 2008; Rodloff, Goldstein, & Torres, 2006). Among the category of carbapenem, imipenem and meropenem are the most common used agents for healthcare-associated infections (HCAI), and ertapenem is indicated for community-acquired infections. However, as well as the increasing use of imipenem or meropenem, more and more bacteria showed the decreased antimicrobial susceptibility to carbapenems (Kanj & Kanafani, 2011; Pogue, Mann, Barber, & Kaye, 2013). In this context, doripenem - the newly introduced agent of the carbapenem class into clinical use may be another drug of choice due to its comparable in vitro antimicrobial activity with other carbapenems (Castanheira, Jones, & Livermore, 2009; Fritsche, Stilwell, & Jones, 2005; Jones, Huynh, Biedenbach, Fritsche, & Sader, 2004; Livermore, 2009; Mushtaq, Ge, & Livermore, 2004).

Because most automated susceptibility testing panels (Hagihara, Kuti, & Nicolau, 2012) did not test doripenem, and the knowledge about in vitro activity of doripenem against clinically isolates in the context of increasing carbapenem resistance was limited (Dong, Wang, & Chang, 2012; Lee, Ko, Song, & Peck, 2011), clinicians are usually prescribe much more imipenem or meropenem than doripenem in clinical practice. Thus, the clinical experience of doripenem use is limited. However, we should need other carbapenems than imipenem and meropenem for treating HCAI, which is commons caused by MDR-GNB. Nowadays, doripenem only obtained its FDA-approved indications - treatment of adults with complicated intra-abdominal infections and complicated

urinary tract infections. Doripenem as one member of carbapenem, we would expect its usefulness can be expanded. Therefore, we retrospectively reviewed the clinical experience in patients with doripenem-containing regimens for treatment of HCAs in a tertiary care center and assessed its clinical usefulness in this clinical setting.

## **Method:**

### **Patients and hospital setting**

This study was conducted in Chi Mei Medical Center, a tertiary referral hospital which has 1288 beds. In this retrospective study, all of the adult patients ever received doripenem-containing for treating HCAI were enrolled between September 1, 2012 and August 31, 2014. After we obtained the approval of the Institutional Review Board of Chi Mei Medical Center, we reviewed the medical records of all the recruited patients and collected the following information: age, gender, type of infection, severity scores as Acute Physiology and Chronic Health Evaluation II (APACHE II) score, underlying comorbidities or conditions including cancer, stroke, liver cirrhosis, diabetes mellitus, congestive heart failure, chronic obstructive pulmonary disease, chronic respiratory failure on mechanical ventilator, chronic kidney disease, autoimmune disease, use of steroid or immunosuppressant, HIV infection, and recent operation within three months, and laboratory data. Additionally, we also collected the data regarding mortality, clinical and microbiologic response.

### **Definitions**

HCAI was defined as patients who had any one of the following risk factors including receiving parenteral antibiotic treatment, chemotherapy or wound management within 30 days, living in nursing home or long-term care facility, having hospital admission for more than two days within 90 days, receiving hemodialysis therapy in dialysis facilities, and clinical manifestations of infections requiring antibiotic treatment (Horan, Andrus, & Dudeck, 2008). The diagnosis of infection focus of HCAI was made based on clinical, bacteriological, and radiological investigations as previous study (Tan et al., 2010). Mortality was defined as death from all causes during the study episode of hospitalization. Like previous report (Kuo et al., 2011), clinical response success defined as the

resolution or improvement of signs and symptoms of infection and no further antibiotic treatment after discontinues of doripenem. In contrast, clinical failure was defined as persistent presence of sign and symptoms of the infection during doripenem treatment. Microbiological eradication was defined as absence of the original baseline pathogens in a follow-up specimen.

### **Statistical Analysis**

Continuous variables were reported as means and standard deviation, and categorical variables were presented as counts and portion. The differences among groups, and survival and mortality groups at hospital discharge were examined by univariate analysis with a Student T test or a chi-square test. A p value <0.05 was considered statistically significant. Those significantly associated with in-hospital mortality in univariate analysis ( $p < 0.05$ ), were further tested for logistic regression analysis. Statistical analysis of the data was done using SPSS 19.0 for Windows (SPSS, Inc., Chicago, IL, USA).

### **Results:**

During the study period, a total of 184 adult patients with HCAI received doripenem-containing therapy were enrolled in this survey (table 1). The mean age of the patients was 72.4 years, and 145 (78.8%) patients were classified as elderly patients  $\geq 65$  years old. Men comprised 61.4% of patients. Respiratory tract infection ( $n = 91$ , 49.5%) was the most common type of infections, followed by urinary tract infection, intra-abdominal infection and skin and soft tissue infection. About 45% of patients had various devices, such as foley tube, central venous catheter, and endotracheal tube. The mean APACHE II score was 14.5. Diabetes mellitus was the common underlying disease, followed by cancer and stroke. The uses of immunosuppressant and steroid were found in 7.6% and 29.3% of cases, respectively. The average duration of doripenem use was 9.6 days. About clinical response, 144 (78.2%) patients had clinical success after doripenem-containing management. Among 50 patients had the data of microbiologic response, microbiologic eradication was only found for 19 (38%) patients.

### **Conclusions:**

The most common indication of doripenem prescription was respiratory tract infection – non-FDA approval indication, not urinary tract infections or intra-abdominal infections in our institution. However, we found that the overall in-hospital mortality rate was low and the clinical success rate was high in HCAIs patients. It should suggest that doripenem with adequate treatment duration can be judiciously used for patients with HCAIs, including respiratory tract infections, and other FDA-approved indications.