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ORIGINAL ARTICLE

Cost-minimization analysis of imipenem/cilastatin versus meropenem in moderate to severe infections at a tertiary care hospital in Saudi Arabia

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Abstract *Aim:* The aim of this study was to compare the costs of management of moderate to severe infections in patients treated with imipenem/cilastatin (IC) and meropenem (MEM). Pharmacoeconomic studies in Saudi Arabia are scarce. The current hospital formulary contains 2 carbapenems: IC and MEM. These antibiotics share a similar spectrum of activity. There are conflicting reviews with regard to the relative cost-effectiveness of these two agents. *Methods:* A retrospective, single-centre cohort study of 88 patients of IC versus MEM in moderate to severe infections was performed, applying cost-minimization analysis (CMA) methods. In accordance with CMA methods, the assumption of equivalent efficacy was first demonstrated by literature retrieved and appraised. Adult patients (⩾18 years old) diagnosed with moderate to severe infections, including skin and skin structure infections (SSIs), sepsis, intra-abdominal infections (IAIs), respiratory tract infections, urinary tract infections (UTIs) and hospital-acquired infections (HAIs), who were prescribed IC 500 mg every six hours intravenously (2 g per day) or MEM 1 g every eight hours (3 g per day), were included in the study. Only direct costs related to the management of the infections were included, in accordance with a payer perspective. *Results:* Overall there was no difference in

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the mean total daily costs between IC (SAR 4784.46, 95% CI 4140.68, 5428.24) and MEM (4390.14, 95% CI 3785.82, 4994.45; $p = 0.37$). A significantly lower medicine acquisition cost per vial of IC was observed when compared to MEM, however there was a significantly higher cost attached to administration sets used in the IC group than the MEM group. Consultation, nursing and physician costs were not significantly different between the groups. No differences were observed in costs associated with adverse drug events (ADEs). *Conclusion:* This study has shown that while acquisition costs of IC at a dose of 500 mg q6 h may be lower than for MEM 1 g q8 h, mean total costs per day were not significantly different between IC and MEM, indicating that medicine costs are only a small element of the overall costs of managing moderate to severe infections.

1. Introduction

As in almost every health system, medication costs at the King Abdulaziz Hospital (KAH) have increased noticeably over time (Saggabi, 2012). High prices of essential medicines are a heavy burden on the government budget (Saggabi, 2012). Policymakers are thus in search of the most cost-effective options for the government and society as a whole.

Data from KAH show that the carbapenem antibiotics were the third most expensive pharmacological class procured during 2009. The current hospital formulary lists two carbapenems: the fixed-dose combination of imipenem/cilastatin (IC) and meropenem (MEM). MEM is restricted to infection control physicians, while IC is restricted to infection control, intensivists and haematology/oncology practitioners. These antibiotics share a similar spectrum of activity, but the unit cost of IC (500 mg/500 mg) is less than that for the equipotent dose of MEM (1 g). There are conflicting reviews with regard to the relative cost-effectiveness of these two medicines (Attanasio et al., 2000; Edwards et al., 2006).

An unpublished pharmacoeconomic review, at the Ministry of National Guard Health Affairs, showed that an interchange programme, substituting MEM with IC, would lead to a cost saving of 2,306,257 Saudi Riyals (SARs) per year (614,309 US dollars per year). Hospital antimicrobial usage data since 2004 showed that usage of IC had been markedly lower than the usage of MEM. There have been limited applications of pharmacoeconomic evaluations in Saudi Arabia (Al Aqeel and Al-Sultan, 2012). It would be appropriate, therefore, to test the economic impact of the proposed substitution as well as the main factors influencing hospital costs, in this setting, based on pharmacoeconomic principles. In this regard, cost-minimization analysis (CMA) could provide an estimate of the economic impact of these therapeutically equivalent medicines, using local Saudi Arabian data.

The aim of this study was to contribute to the rational selection of medicines, in order to achieve efficiencies and better patient outcomes, by focusing on high-cost medicines used in the Saudi Arabian health system.

2. Background

In 2012, total annual expenditure on MEM at KAH placed it in the top 10 medicines at the institution in value terms. The Department of Infection Control, Department of Microbiology and Pharmacy attempted to minimize usage of MEM by suppressing mention of this agent in sensitivity reports appearing in the hospital's electronic health information system. This was implemented in an attempt to encourage usage of alternative antibiotics, including IC. The Pharmacy and Therapeutics Committee (PTC) also restricted the use of MEM to infection control practitioners only. IC was restricted to infection control, intensivists and haematology/oncology practitioners. The Infection Control Department developed usage guidelines for IC and MEM. An unpublished pharmacoeconomic review examined the acquisition costs of the study drugs, but did not include the resource costs associated with the primary infection. A CMA was therefore proposed in an attempt to investigate the overall costs associated with the use of these two clinically equivalent medicines.

2.1. Pharmacoeconomic principles

The field of pharmacoeconomics identifies the costs and consequences of alternative medicines therapy in order to make the best possible decision, while ensuring the maximum benefit and efficiency of budgets or resources (Drummond, 2006). In this study, a CMA approach was selected, which assumes that the consequences are clinically equivalent and then determines the least costly alternative (Newby and Hill, 2003). Studies on the local population may be more applicable to the context of Saudi Arabia and hence a study of this nature was considered.

2.2. Pharmacology

IC and MEM are both carbapenem antibiotics. These beta-lactam antibiotics are similar to penicillins and cephalosporins, but differ in their structure. Carbapenems inhibit bacterial cell wall synthesis. Both IC and MEM exhibit activity against a wide range of Gram-positive and Gram-negative aerobic and anaerobic bacteria.

The first carbapenem (imipenem) became commercially available in 1985 for the treatment of complex microbial infections (Papp-Wallace et al., 2011). The fixed-dose combination IC (including the dehydropeptidase inhibitor cilastatin) has been marketed by Merck Sharp and Dome with the trade name Tienam® in Saudi Arabia (Anonymous, 2013). The United States Food and Drug Administration (FDA) has approved the dose of IC from between 250 mg q6 h to a maximum of 1 g q8 h, depending on the severity of the infection. The dose should be adjusted in patients with impaired renal function. MEM is a broad spectrum carbapenem, subsequently approved by the US FDA (Mohr, 2008; Baldwin et al., 2008). It has been marketed by AstraZeneca in Saudi Arabia as Meronem®