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Comparative healthcare-associated costs of methicillin-resistant *Staphylococcus aureus* bacteraemia-infective endocarditis treated with either daptomycin or vancomycin

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ABSTRACT

Complex infection with methicillin-resistant *Staphylococcus aureus* (MRSA) is associated with high healthcare and societal costs; thus, evaluation of the costs and health benefits of interventions is an important consideration in a modern healthcare system. This study estimated the cost consequences of the use of daptomycin compared with vancomycin for the first-line treatment of patients with proven MRSA-induced bacteraemia-infective endocarditis (SAB-IE) with a vancomycin minimum inhibitory concentration (MIC) >1 mg/L in the UK. A decision model was developed to assess total healthcare costs of treatment, including inpatient, outpatient and drug costs. Data were sourced from the literature (treatment efficacy and safety), a physician survey (resource use) and publicly available databases (unit costs). Assuming the same length of stay for daptomycin and vancomycin, the total healthcare costs per patient were £17 917 for daptomycin and £17 165 for vancomycin. However, extrapolating from published studies and supported by a physician survey, daptomycin was found to require fewer therapeutic switches and a shorter length of stay. When the length of stay was reduced from 42 days to 28 days, daptomycin saved £4037 per person compared with vancomycin. In conclusion, daptomycin is an effective and efficient alternative antibiotic for the treatment of SAB-IE. However, the level of cost saving depends on the extent to which local clinical practice allows early discharge of patients before the end of their antibiotic course when responding to treatment.

1. Introduction

Daptomycin is indicated for the treatment of *Staphylococcus aureus* bacteraemia-infective endocarditis (SAB-IE). It has been suggested that daptomycin could be used in outpatient parenteral antibiotic therapy (OPAT) to reduce the time that patients with SAB-IE spend in hospital [1]. Reduction in length of hospital stay is a key financial and quality indicator in the National Health Service (NHS) in the UK. As a result, the higher drug acquisition costs of daptomycin compared with established therapies such as vancomycin must be balanced against the potential shorter duration of hospitalisation. This study examined the cost consequences of daptomycin as an alternative to vancomycin in the treatment of SAB-IE in the UK.

Despite a recent reduction in methicillin-resistant *S. aureus* (MRSA) rates in the UK [2], MRSA still makes up 13.6% of invasive blood isolates [3] and 6% of isolates in surgical site infections [4]. MRSA is associated with increased morbidity, mortality and duration of stay compared with methicillin-sensitive *S. aureus* (MSSA) [5].

The glycopeptides, such as vancomycin, are established standard treatment for SAB-IE [6]. However, increasing awareness of vancomycin intermediate resistance [7], particular in MRSA with high vancomycin minimum inhibitory concentrations (MICs) [8], has caused concern among infection specialists. *Staphylococcus aureus* isolates with a vancomycin MIC $\geq$ 2 mg/L have increased from 4.0% in 2004 to 7.7% in 2009 [9].

Daptomycin provides an alternative to vancomycin when there are concerns regarding efficacy or toxicity. Daptomycin has a

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Table 1
Length of treatment and second-line drug use.

Resource	Unit	Base-case input	Input for scenario analysis	Source
First-line drugs				
Treatment duration				
Daptomycin, complete course	Days	42.0	28.0	Physician survey [16]
Vancomycin, complete course	Days	42.0	–	
Average length of inpatient stay				
Daptomycin	Days	42.0	28.0	Assumed same as treatment duration
Vancomycin	Days	42.0	–	
Second-line drugs				
After daptomycin failure				
Linezolid	%	24.7	–	Physician survey [16]
Teicoplanin	%	1.7	–	
Vancomycin	%	73.7	–	
After vancomycin failure				
Linezolid	%	18	–	Physician survey [16]
Teicoplanin	%	1.7	–	
Daptomycin	%	80.3	–	
Treatment duration				
Second-line treatment	Days	42.0	–	Physician survey [16]

unique mode of action and is rapidly bactericidal against Gram-positive bacteria, including methicillin-sensitive and -resistant staphylococcal species [10]. A matched retrospective cohort study demonstrated a significantly lower rate of clinical failure at 30 days for MRSA bacteraemia with vancomycin MIC > 1 mg/L in patients using daptomycin compared with vancomycin (20.0% vs. 48.2%, respectively; $P < 0.001$) [11].

Healthcare costs are closely related to length of hospitalisation, which in turn can be influenced by utilisation of OPAT [1]. Current endocarditis treatment guidelines recommend that patients are treated as inpatients until treatment has been demonstrated to be successful [6]. The use of OPAT is, however, becoming increasingly popular as a way of treating patients with complex MRSA infections, including endocarditis [12–15].

In this paper, the cost consequences of the use of daptomycin compared with vancomycin for the first-line treatment of patients with proven MRSA-induced SAB-IE with a vancomycin MIC > 1 mg/L in the UK were estimated.

2. Methods

2.1. Model description

A decision analytical model was developed (Fig. 1). In the model, patients have SAB-IE caused by MRSA with a vancomycin MIC > 1 mg/L. First-line treatment was assumed to be either daptomycin or vancomycin. In the base case, patients remained in hospital until treatment was completed. Initial treatment success was evaluated at 7 days after commencement of treatment [16]. If treatment was assessed as successful, first-line treatment was completed before discharge. If treatment failed [due to lack of efficacy or to adverse events (AEs)], second-line treatment was assumed and thus hospital stay was prolonged. The choice of second-line antibiotic (daptomycin, linezolid, teicoplanin or vancomycin) is influenced by prior treatments (Table 1). Patients were assumed to be successfully cured after completing second-line treatment.

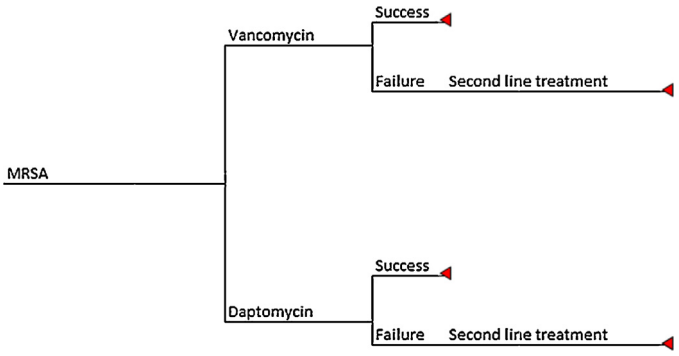

Fig. 1. Treatment pathway for patients with MRSA-induced bacteraemia-infective endocarditis (SAB-IE) with a vancomycin MIC >1 mg/L. MRSA, methicillin-resistant *Staphylococcus aureus*; MIC, minimum inhibitory concentration.

The model estimated the total healthcare costs of treatment (in 2012 GBP), including drugs, inpatient stay, laboratory tests and outpatient care. A UK NHS perspective was adopted; hence, only direct medical costs were included. Indirect costs due to potential work loss of patients or carers were not taken into account. The time horizon was from hospital admission until resolution (less than a year), therefore no discounting was required.

2.2. Model inputs

Clinical success rates used in the model were calculated using one minus the rate of bacteraemia persisting for ≥7 days taken from Murray et al. (18.8% for daptomycin vs. 42.4% for vancomycin; $P = 0.001$) [11]. Interviews with three clinical experts[1] in microbiology and infectious diseases provided information on first- and second-line treatment options, concomitant medications, treatment duration, frequency of patient monitoring and length of hospital stay (Table 1). If all three values from the three experts differed, a mean value was used. If two of the three experts agreed, the agreed upon estimate was used in the model.

Unit costs were obtained from publicly available databases (Table 2) [20–23]. If 2012 costs were unavailable, earlier costs were inflated using the Hospital and Community Health Services (HCHS) pay and price inflation [24]. Daily drug costs were £88.57 for daptomycin 500 mg vial and £14.50 for vancomycin 1 g vial twice daily [21]. Second-line treatments after daptomycin and vancomycin are shown in Table 1. The daily cost of linezolid 600 mg oral/vial and teicoplanin 400 mg vial were £89.00 and £6.10, respectively. Monitoring tests consisted of serum creatine phosphokinase, serum drug levels, blood counts, urinalysis, and liver and kidney function tests. Weekly monitoring requirements were based on those recommended by the British National Formulary 2012 [21] for various

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