Cost of bacteraemia caused by methicillin-resistant vs. methicillin-susceptible *Staphylococcus aureus* in Spain: a retrospective cohort study

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Abstract

The aim of this study was to determine the impact on healthcare resource utilization and associated costs of bacteraemia due to methicillin-resistant *Staphylococcus aureus* (MRSA) vs. methicillin-susceptible *S. aureus* (MSSA) strains in Spain. An observational, retrospective, cohort multicentre study was conducted during 2005. The target population comprised Spanish patients with *S. aureus* bacteraemia (five and ten cases per hospital for resistant and susceptible strains, respectively). The resources used were obtained from the hospital patient records. The unit costs were obtained from the participating hospitals and from Spanish databases; the costs of a bacteraemic episode were estimated from resource utilization results and expressed in euros (€). Univariate sensitivity analyses were performed. The clinical records of 366 valid patients with *S. aureus* bacteraemia (121 MRSA and 245 MSSA) from 27 Spanish hospitals were reviewed. Resource use per bacteraemic episode was higher for MRSA cases than for MSSA cases, with longer antibiotic treatment (3.1 additional days) and greater length of hospital stay (LOS) (2.2 additional days), more diagnostic tests, and higher rates of admission to the intensive-care unit (ICU) (7.6%). As a consequence, a higher cost per episode was incurred, with an additional €1205 in episodes of MRSA infections (1.12-fold increase). The main drivers of the cost difference were the higher rates of ICU admission and hospital re-admission and increased LOS. The analysis confirmed that there were additional costs due to resistant strains, ranging from €293 to €5188. Overall, MRSA was associated with higher costs in bacteraemic patients, and this was attributable mainly to the greater rate of ICU admissions and increased LOS.

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Introduction

Bacterial resistance is increasing both in outpatient clinics and in hospitals, and has become the subject of much research. The impact of infections caused by resistant bacteria is reflected by higher mortality, increased length of hospital stay (LOS), and increased healthcare costs [1]. In addition, this increased resistance reduces the therapeutic options available for the treatment of infections involving these microorganisms.

One of the microorganisms whose incidence has recently increased dramatically in Spanish hospitals is methicillin-resistant *Staphylococcus aureus* (MRSA). At present, both in Spain and in many countries around the world, more than 25% of *S. aureus* isolates are resistant to methicillin (although low prevalences of these strains are also found in some European regions, including The Netherlands and Scandinavian countries) [2–5].

MRSA strains are resistant to currently available β-lactam agents and frequently also to other families of antibiotics, with the notable exception of most of the so-called community-acquired MRSA strains; but these strains, as compared with sensitive strains, also cause infections, increasing the LOS and healthcare costs [6–8].

Bacteraemia is a complex clinical syndrome that is constantly changing and causes high and increasing morbidity and mortality [9]; bacteraemias caused by MRSA are rapidly becoming a serious problem in Spanish hospitals [10].

This study was aimed at the calculation of the impact of MRSA vs. methicillin-susceptible *S. aureus* (MSSA) bacteraemia on healthcare resources and associated costs in Spain.

Materials and Methods

The present study was a Spanish multicentre, retrospective, observational cohort study of the use of healthcare resources and the associated costs in the treatment of bacteraemia caused by MRSA and MSSA.

The inclusion criteria were as follows: (i) either sex; (ii) age 18 years or over; (iii) bacteraemia caused by *S. aureus* (resistant or sensitive to methicillin); and (iv) strains isolated between 1 January and 31 December 2005. Pregnant patients and cases of bacteraemia resulting from a previous stay in hospital were excluded.

Hospitals with an interest in the investigation from throughout Spain were able to participate in the study. All participating centres were required to have the study protocol approved by their respective ethics committees.

The microbiology department of each participating hospital selected five MRSA and ten MSSA cases by systematic sampling [11] in the following way. A skipping factor, $k = n/5$, was calculated, with n being the number of MRSA bacteraemias in the hospital during the study time period. The first case was selected through a random number provided in a centralized way, and the following cases were selected by applying k repeatedly until all MRSA bacteraemia cases were selected. MSSA cases were selected similarly. *S. aureus* was identified in every participating centre with conventional methods, usually automated identification–susceptibility systems [12].

To find notable economic differences ($\geq$ €300) in the overall cost per patient between patients with MRSA and those with MSSA, for a standard deviation of €600, a bilateral α-risk of 0.05, and a β-risk of 0.10, 94 patients with MRSA and 188 patients with MSSA were needed.

The study was performed from the perspective of the National Health Service; therefore, only the use of healthcare resources was recorded. The costs of bacteraemia were expressed as direct healthcare costs.

Use of resources was documented by reviewing the clinical records of all the patients who met the inclusion criteria. The following data were retrieved from the clinical history for each episode of bacteraemia: (i) patient demographic and clinical characteristics; (ii) antibiotic therapy; (iii) complementary tests; (iv) rates of hospitalization, admission to the intensive-care unit (ICU), re-admission to the ward, and LOS; (v) rates of outpatient clinics; and (vi) resources consumed during the reconstitution of the vials of antibiotics and their intravenous infusion.

The mean costs of an episode of bacteraemia caused by resistant or sensitive strains of the microorganisms studied were calculated. The cost of the antimicrobial treatments was estimated by using the recommended retail price and the rates of use per episode of bacteraemia, and taking two possible treatments into account: (i) empirical antibiotics (those administered before the results of the microbiological study were known); and (ii) targeted antibiotics (those started or continued on the day when the results of the antibiogram of the cultured microorganisms became available). The costs of the other resources per episode of bacteraemia were calculated by using their rates of use and the unit costs obtained from the hospitals that participated in the study, and from a database of Spanish healthcare costs in the sensitivity analysis. All costs are presented in euros (€) as of October 2006.

The cost per episode of bacteraemia was calculated on the basis of the following tests: (i) general analysis; (ii) monitoring of vancomycin and/or aminoglycoside levels; (iii) diagnostic imaging studies; (iv) microbiological tests; and (v) other tests, such as electrocardiogram, bronchoscopy, laparoscopy, and lumbar puncture.

In the analysis of base-case costs, the average values of the resources used and of the unit costs obtained from the study were applied. The sensitivity analysis involves modifying the values of the variables with respect to which there is uncertainty in verifying to what extent the results of the base case are affected.

In order to verify the robustness of this analysis, several unifactorial simple sensitivity analyses were performed in the following scenarios: (i) use of unit costs from a database of healthcare costs in Spain; (ii) lower and upper limits of the 95% CI of the use of healthcare resources; (iii) minimum and maximum values of the unit costs of the resources obtained in the study; and (iv) minimum and maximum values of the resources and unit costs taken together.

Qualitative and quantitative descriptive analyses were performed for all variables. The qualitative variables were analysed using absolute frequencies and percentages, whereas the quantitative variables were analysed using the mean, 95% CI for the mean, median, standard deviation, minimum, and maximum. All demographic data and histories were analysed to examine any difference between the groups, using the Student *t*-test for independent measures in the case of continuous data distributed normally, or the Mann–Whitney *U*-test if the parametric requirements were not met. A chi-squared test (or Fisher exact test, where necessary) was used to compare the categorical variables between the treatment groups. The Kolmogorov–Smirnov test was used to compare the normality of the distribution of the continuous variables, whereas the Levene test was used to analyse the homogeneity of the variances. All analyses were performed using the statistical program SPSS 13.0.