Healthcare-associated, community-acquired and hospital-acquired bacteraemic urinary tract infections in hospitalized patients: a prospective multicentre cohort study in the era of antimicrobial resistance

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Abstract

The clinical and microbiological characteristics of community-onset healthcare-associated (HCA) bacteraemia of urinary source are not well defined. We conducted a prospective cohort study at eight tertiary-care hospitals in Spain, from October 2010 to June 2011. All consecutive adult patients hospitalized with bacteraemic urinary tract infection (BUTI) were included. HCA-BUTI episodes were compared with community-acquired (CA) and hospital-acquired (HA) BUTI. A logistic regression analysis was performed to identify 30-day mortality risk factors. We included 667 episodes of BUTI (246 HCA, 279 CA and 142 HA). Differences between HCA-BUTI and CA-BUTI were female gender (40% vs 69%, p <0.001), McCabe score II–III (48% vs 14%, p <0.001), Pitt score $\geq$2 (40% vs 31%, p 0.03), isolation of extended spectrum β-lactamase-producing Enterobacteriaciae (13% vs 5%, p <0.001), median hospital stay (9 vs 7 days, p 0.03), inappropriate empirical antimicrobial therapy (21% vs 13%, p 0.02) and mortality (11.4% vs 3.9%, p 0.001). *Pseudomonas aeruginosa* was more frequently isolated in HA-BUTI (16%) than in HCA-BUTI (4%, p <0.001). Independent factors for mortality were age (OR 1.04; 95% CI 1.01–1.07), McCabe score II–III (OR 3.2; 95% CI 1.8–5.5), Pitt score $\geq$2 (OR 3.2 (1.8–5.5) and HA-BUTI OR 3.4 (1.2–9.0)). Patients with HCA-BUTI are a specific group with significant clinical and microbiological differences from patients with CA-BUTI, and some similarities with patients with HA-BUTI. Mortality was associated with patient condition, the severity of infection and hospital acquisition.

Keywords: Bacteraemia, community acquired, healthcare-associated, hospital-acquired, urinary tract infection
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Introduction

Urinary tract infections (UTI) are one of the most frequent bacterial infections in the community and in hospitals. It has an estimated overall incidence rate of 17.5 per 1000 person-years [1]. Around 1 million cases of nosocomial UTI occur in the USA annually [2]. In the Spanish national prevalence study (EPINE) performed annually since 1990 UTI represented between 26% of nosocomial infections in the 1990s and 20% in 2011 [3]. Between 15% and 25% of episodes of UTI have positive blood cultures at the time of presentation [4–6]. In bacteraemic episodes mortality can vary between 4% and 30% depending on baseline conditions and age. Inadequate or delayed antimicrobial treatment might influence the outcome under some circumstances [6–9].

In the last years, there have been important changes in healthcare delivery. Some traditionally inpatient procedures are now routinely performed on an outpatient basis. Infections acquired by these patients cannot be classified as hospital-acquired (HA) or community-acquired (CA), so they have been named healthcare-associated (HCA) infections [10]. Recent studies of bloodstream infections, pneumonia and endocarditis have shown that community-onset HCA infections are more similar to HA than to CA infections [10–13]. Taking into account this classification, there is little information regarding bacteraemia of urinary source and its possible impact on healthcare delivery. It is a matter of concern that rates of bacterial resistance of uropathogens have significantly increased worldwide [14]. This has important implications not only in acute uncomplicated UTI [15], but also in bacteraemic forms (BUTI) [16]. Delay in appropriate antimicrobial therapy can lead to adverse outcomes and potentially increased mortality, a longer hospital stay, and higher costs in patients with severe forms of UTI [9,17,18].

The aim of this study is to describe the epidemiological, clinical and microbiological features and appropriateness of empirical antimicrobial therapy in patients with HCA-BUTI by means of a prospective multicentre study. We also compared HCA with HA-BUTI and CA-BUTI, and assessed mortality-related factors.

Materials and Methods

Setting and patients

A prospective cohort observational study was conducted at eight tertiary-care hospitals in Spain (total beds 6500 and inhabitant coverage of 3 701 600). We included all consecutive patients over 18 years of age with BUTI requiring hospitalization or those who were already hospitalized and developed BUTI from October 2010 up to June 2011. Exclusion criteria included bacteraemia from another source or primary bacteraemia. Cases were identified from a prospective clinical chart review of all patients with a potential uropathogen isolated in blood cultures reported daily by microbiology laboratories in each hospital. Enterobacteriaceae, *Pseudomonas aeruginosa*, other non-fermenteing gram-negative bacilli, *Enterococcus* spp. and *Staphylococcus saprophyticus* were considered potential uropathogens. Assessment was performed by the local investigator in each centre following the same criteria. Patients were followed up until 30 days after the bacteraemic episode.

Sample size was calculated to detect differences in the appropriateness of empirical antimicrobial therapy between CA-BUTI and HCA-BUTI. Taking into account a significance level of 95%, a power of 80% and 10% losses, and based on our previous experience [19], to detect a difference of 8% in the appropriateness of empirical antimicrobial therapy between CA-BUTI (15%) and HCA-BUTI (23%), sample size should be 210 patients per branch. This sample size is large enough to detect a difference in mortality between the two groups of 6% (4% vs 10%).

Study variables

Main outcome variable: 30-day all-cause mortality.

Explanatory variables: Demographic characteristics, the McCabe Score [20], urological history, previous antibiotic therapy, clinical symptoms, the Pitt Score [21] assessed at the time of positive blood culture, causative microorganisms, antibiotic susceptibilities, empirical treatment and the length of stay.

Definitions

BUTI was defined following the CDC/National Healthcare Safety Network (NHSN) bacteraemia definition criteria plus accompanying symptomatic UTI (urinary tract symptoms that included dysuria, frequency, gross haematuria, flank or abdominal pain) with or without positive urine culture ($>10^5$ CFU/mL) or asymptomatic UTI with the isolation of the same uropathogen in a urine culture (NHSN Specific infection type—asymptomatic bacteraemic urinary tract infection) [22].

HCA-BUTI was defined as an episode detected at hospital admission or within the first 48 h after admission, which fulfilled any of the following Friedman criteria with modifications [23]:

(i) Receiving intravenous therapy, wound care or specialized nursing care at home by qualified healthcare workers within 30 days of the episode. (ii) Attending a hospital, haemodialysis ward or receiving intravenous chemotherapy within 30 days of the episode. (iii) Being hospitalized in an acute-care hospital for 2 or more days within 90 days of current hospitalization. (iv) Residing in a nursing home or long-term care facility. (v) Being subjected to an invasive urinary procedure within 30 days of the episode or having a long-term indwelling urethral catheter.

CA-BUTI was defined as episodes detected at hospital admission or within the first 48 h without fulfilling any of the above criteria for HCA-BUTI.

Episodes detected beyond 48 h of hospital admission were considered *HA-BUTI*.

Prior antibiotic therapy was defined as antibiotics given for at least 2 days within the previous 90 days before the episode. These data were collected by direct interview with the patient or the family if that information was not in the clinical chart.

Severe sepsis or septic shock was defined according to the 2001 International Sepsis Definitions Conference [24].

Appropriate empirical treatment was considered if the initial treatment regimen included one or more antibiotics with *in*