Short report

Use of parenteral antimicrobials in very small hospitals in inner Brazil: patterns, determinants, and opportunities for interventions in developing countries

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S U M M A R Y

Much of healthcare in developing countries takes place in small hospitals. Little is known about the use of antimicrobials in those settings. We studied the 60-day use of parenteral antimicrobials in 48 hospitals with up to 50 beds in inner Brazil. The overall use was 242.0 defined daily doses per 100 admissions, and broad-spectrum agents accounted for 26.8%. The existence of local guidelines, educational measures and restrictive policies for anti-microbial prescriptions, as well as infection control and microbiology resources, were significantly associated with lesser use. Those findings point to possible interventions aimed at preventing antimicrobial over-use in developing countries.

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Introduction

The World Health Organization's Global Action Plan on Antimicrobial Resistance includes among its main objectives the 'optimization of the use of antimicrobial medicines in human and animal health' [1]. It is estimated that BRIC countries (Brazil, Russia, India, and China) and South Africa account for three-quarters of the global increase in antimicrobial consumption from year 2000 to 2010 [2]. Still, little is known about patterns of antimicrobial use in those countries — and even less in settings outside large teaching hospitals.

In Brazil, hospitals with up to 50 beds comprise nearly two-thirds of the 6712 hospitals presently registered in the national database of healthcare settings (CNES, http://cnes.datasus.gov.br). Most of those hospitals are located in small cities, and deliver low-to-medium complexity medical, surgical, obstetric, and paediatric care [3]. They may be sites for the emergence and/or dissemination of antimicrobial resistance. Therefore, it is necessary to measure the magnitude of antimicrobial use and to identify opportunities for interventions aimed at optimizing anti-infective therapy in those settings.

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Methods

An ecological study was conducted, based on administrative data from 48 very small hospitals (VSH) from inner São Paulo State, Brazil. Since definitions for 'small' or 'very small' hospitals differ from country to country (and even within countries), VSH were defined arbitrarily as acute-care hospitals with up to 50 beds for inpatients. Psychiatric and other long-term-care hospitals, as well as emergency rooms that occasionally admitted patients, were not included in the definition. Hospitals were randomly selected from the CNES database. We were especially interested in studying VSH located far from the greatest cities, so we excluded those from the two metropolitan areas in the State (São Paulo City, 20 million inhabitants; Campinas, three million) and coastal cities (two million inhabitants). The remaining area comprises 570 municipalities, which collectively harbour 15 million inhabitants. In 2015, there were 286 VSH in São Paulo State. The 48 hospitals in our study were selected out of 195 VSH that were eligible on the basis of our geographic criteria. Hospital visits for data collection were conducted from March 2015 to December 2016.

Demographic data were collected from the cities where VSH were located. São Paulo State is divided into 17 administrative regions for healthcare, and hospital transfers of patients generally take place within a region. We used the number of teaching hospitals in each administrative region harbouring the study VSH as a proxy measure of interaction with high-complexity settings.

Characterization of VSH included financial nature and patterns of health care delivered. Of special interest, we collected evidence of the presence of infection control and antimicrobial stewardship: infection control committee (ICC), infectious diseases medical doctors, guidelines for anti-infective therapy, training on antimicrobial use for clinicians, restrictive control of antimicrobial prescription, and a reference microbiology laboratory. In order to adjust for possible seasonal variations in antimicrobial use, the season in which data were obtained was recorded.

The use of parenteral antimicrobials was collected from hospital pharmacies' records for the two months previous to our visit to each hospital. The magnitude of use was expressed in defined daily doses (DDD) per 100 admissions. Broad-spectrum agents were defined according to the classification proposed by Stenehjem *et al.* [4]. The following agents or classes met that definition: aminoglycosides, fluoroquinolones, aztreonam, ceftazidime, cefepime, ceftaroline, vancomycin, piperacillin–tazobactam, carbapenems, polymyxins, linezolid, and daptomycin.

As well as describing overall antimicrobial use, the aim was also to investigate the heterogeneity of patterns of antimicrobial use among different hospitals. Briefly, we attempted to find out whether there was a relatively homogeneous pattern for antimicrobial prescription, or if there were great differences in the use of specific agents or classes. In order to assess this topic, cluster analysis was performed, based on euclidean distances of values for individual agents or classes and unweighted pair group method with arithmetic mean (UPGMA). A threshold of one standard deviation was used for cluster definition.

Predictors of the magnitude of antimicrobial use were assessed using univariate and multivariate models of negative binomial regression with log link. Statistical analyses were carried out in SPSS 20 (IBM, Armonk, NY, USA), NCSS 9 (LLC, Kaysville, UT, USA) and STATA 14 (Stata, College Station, TX, USA).

Results

The study VSH had a median of 30 beds (range: 6–50) and collectively admitted 7325 patients in the study period. Even though 81.3% of hospitals were private, 95.8% delivered healthcare to patients covered by the Unified Health System — Brazilian programme of universal access to healthcare. The cities in which they were located had populations ranging from 6000 to 660,000 inhabitants. The proportion of VSH delivering medical, surgical, obstetric, and paediatric care were 97.9%, 62.5%, 64.6%, and 72.9%, respectively.

The overall use of parenteral antimicrobials was 242.0 DDD per 100 admissions. Broad-spectrum agents comprised 26.8% of total use. Results for specific agents or classes are presented in Table I. Cephalosporins and fluoroquinolones stood out as the most intensively used.

Cluster analysis identified 15 clearly distinct patterns of antimicrobial use. Briefly, there were three similarity clusters, comprising 31, three and two hospitals, respectively. The remaining 12 VSH presented unique patterns. This points to heterogeneity in prescribing patterns among hospitals.

Results from the analysis of factors associated with the magnitude of parenteral antimicrobial use were as follows. In univariate regression models, admission of medical patients and data collected in cold seasons (April to September) were significantly associated with greater antimicrobial use. On the other hand, the presence of an ICC active for at least five years, antimicrobial guidelines, training in anti-infective therapy, and restrictive policies were predictors of lesser use. When the outcome was switched to broad-spectrum agents, results were similar to the previous analysis for two predictors: admission of medical patients and training for clinicians.

Table II presents the effect of infection control and antimicrobial stewardship on the magnitude of use of parenteral antimicrobials in multivariate models adjusted for demographic variables and hospital characteristics. Besides factors previously identified, the presence of microbiology laboratory and ICC active for five years were associated with less use of overall and broad-spectrum agents, respectively.

Discussion

Presently, both the USA and Europe are facing the challenge of monitoring antimicrobial use in hospitals [5,6]. Metrics can provide useful information to direct interventions for optimizing prescriptions and, ultimately, prevent the emergence and spread of resistant organisms [7]. In order to achieve these goals, the available data must be comprehensive enough to include hospitals of different sizes and patterns of healthcare delivery. It has been previously noticed that, even in developed countries, there are scarce data on antimicrobial use in small hospitals [4].

Our results point to extensive use of antimicrobials in VSH in Brazil, including broad-spectrum agents. Roughly comparing, if we use the mean time of admission for patients in VSH in Brazil (which is 4.5 days, according to governmental data available at