A 3 year survey on the use of antibacterial agents in five Italian hospitals

Alberto Vaccheri*, Maria Chiara Silvani, Laura Bersaglia, Domenico Motola, Petar Strahinja, Antonio Vargiu, Elisabetta Poluzzi and Nicola Montanaro

Department of Pharmacology and Interuniversity Research Centre for Pharmacoepidemiology, University of Bologna, Bologna, Italy

Received 2 July 2007; returned 20 August 2007; revised 21 December 2007; accepted 31 December 2007

Background: Misuse of antimicrobial agents in hospitals may cause the emergence of resistant microorganisms, as well as increased costs and unnecessary exposure of patients to drugs. We investigated the pattern of antibiotic consumption in 2002–04 in a sample of Italian hospitals, and compared this with antibiotic consumption data in primary healthcare in the Emilia-Romagna region.

Methods: The study was carried out in five hospitals of the Emilia-Romagna region and 2002–04 drug use data were obtained from the pharmacy services. Data were analysed by clinical areas and single wards and were expressed by ATC classification and defined daily doses (DDD)/100 bed days. Prescription data of antibacterials in primary care in the same period were also analysed.

Results: Antibiotic consumption increased by 18% in the 3 year period. Combinations of penicillins and \(\beta\)-lactamase inhibitors were the most used drugs, followed by fluoroquinolones and third-generation cephalosporins. Penicillins plus \(\beta\)-lactamase inhibitors increased in all the clinical areas by over 40%, and fluoroquinolones sharply increased in medical units (+29%). Third-generation cephalosporins remained fairly stable in paediatrics and surgery, but increased in medicine (+18%). Glycopeptides accounted for 4.3% of total antibiotic consumption with a peak of 10% in intensive care units. Antibacterial prescription in primary care showed a pattern similar to that of hospitals.

Conclusions: We found a considerable increase in antibiotic use over time and a marked preference for wide-spectrum antibiotics such as penicillins plus \(\beta\)-lactamase inhibitors, fluoroquinolones and third-generation cephalosporins; thus raising concern about appropriate use. These results could represent the basis for educational initiatives aimed at rationalizing the use of antibiotics in hospitals.

Keywords: drug utilization, penicillins plus \(\beta\)-lactamase inhibitors, fluoroquinolones, glycopeptides, third-generation cephalosporins

Introduction

Misuse of antimicrobial agents in hospitals may cause the emergence of resistant microorganisms, as well as increased costs and unnecessary exposure of patients to drugs.\(^1,2\)

A well accepted relationship exists between antibiotic use and increasing resistance, probably due to an increased use of new as well as older broad-spectrum antibacterials.

In several European countries, despite efforts to limit excessive use of antibiotics, consumption as well as resistance are increasing. In published reports of the European Surveillance of Antimicrobial Consumption (ESAC) project, Italy had a high consumption of antibacterials in ambulatory care in 2003, as was found for most of the other Mediterranean European countries.\(^3\)

At present only a few and limited studies on antibiotic consumption in Italian hospitals have been performed; the findings of these studies suggest that hospital antibiotic use is very high and the adoption of measures aimed at rationalizing the use of these drugs is necessary.\(^4-6\)

The aim of this study was to investigate the pattern and trends of antibiotic consumption over the period 2002–04 in a sample of Italian hospitals, to compare this with antibiotic consumption data in primary healthcare in the Emilia-Romagna region and to evaluate the variability between clinical areas inside hospitals.

*Corresponding author. Tel: +39-51-2091856; Fax: +39-51-248862; E-mail: alberto.vaccheri@unibo.it

© The Author 2008. Published by Oxford University Press on behalf of the British Society for Antimicrobial Chemotherapy. All rights reserved. For Permissions, please e-mail: journals.permissions@oxfordjournals.org
Methods

The study was carried out in five hospitals of Emilia-Romagna region, three university hospitals and two general hospitals, with a catchment area of ~1.5 million inhabitants. We considered consumption of antibacterials for systemic use (ATC group J01) in the period 2002–04. Data for antimicrobial drug consumption were obtained from the pharmacy records of each hospital which provided, for each ward, the code of the medicinal product, the number of unit doses and the reference year. The number of bed days of the single wards was also available. The data for day hospital facilities, both in terms of drug consumption and of bed days, were added to those of the corresponding wards.

Prescription data of antibacterial agents by the general practitioners of the Emilia-Romagna region (~4 million inhabitants) in the period 2002–04 were retrieved from the Emilia-Romagna Health Authority Database (Italy). The study was carried out in five hospitals of Emilia-Romagna region (one million inhabitants) in the period 2002–04 and changes between 2002 and 2004 were observed among the hospitals.

Each medicinal product was assigned the ATC code and the defined daily dose (DDD), according to the international classification published by the WHO Collaborating Centre for Drug Statistics Methodology, 2005 edition.8

Antimicrobial drug consumption was expressed as DDD/100 bed days and data were analysed by active substance (ATC fifth level) or by therapeutic subgroups (ATC fourth level).

Results

The overall consumption of antibacterial agents increased in the 3 year period by 18%, from 64.9 in 2002 to 76.7 DDD/100 bed days in 2004 (Table 1).

Figure 1 shows the trend of antibiotic use in the period 2002–04 in the individual hospitals participating in the survey. No relevant variations in the trend of antibiotic consumption were observed among the hospitals.

In 2004, the intensive care units (ICUs) showed the highest consumption of antibacterials, followed by surgical units, medical units and paediatric units. Consumption increased in all four clinical areas, from 7% in paediatric units to 22% in medical units.

Table 2 shows the overall ranking of the antibacterial agents used in the hospitals participating in this survey. Combinations of penicillins and β-lactamase inhibitors ranked first with 23.2 DDD/100 bed days in 2004, followed by fluoroquinolones and third-generation cephalosporins. Penicillins plus β-lactamase inhibitors were the antibacterials with the highest increase between 2002 and 2004. A considerable increase was also observed for fluoroquinolones, third-generation cephalosporins, macrolides and glycopeptides.

Co-amoxiclav was largely the most used penicillin plus a β-lactamase inhibitor in 2004 (18.1 DDD/100 bed days; 78% of the group) and its consumption increased by 50% (+6.0 DDD) in comparison with 2002. Among fluoroquinolones, levofloxacin and ciprofloxacin together represented ~95% of the group in 2004, with 7.4 and 6.7 DDD, respectively; levofloxacin showing the sharpest increase (+2.0 DDD; +38%). Ceftriaxone was the highest among the third-generation cephalosporins (6.4 DDD), with an increase of 1.05 DDD (+20%) from 2002, followed by ceftazidime (1.7 DDD; −0.2 DDD; −9%) and cefotaxime (1.5 DDD; +0.1 DDD; +4%).

Clarithromycin ranked first among macrolides, representing 78% of the group (4.4 DDD; +0.5 DDD; +12%), followed by
Azithromycin (0.9 DDD; +0.5 DDD; +131%). Teicoplanin represented ~75% of the glycopeptides (2.5 DDD; +0.3 DDD; +15%).

Table 3 shows the ranking of the antibacterial agents used by the general practitioners of the Emilia-Romagna region in the period 2002–04. The pattern was similar to that observed in the hospitals participating in this survey, with penicillins plus β-lactamase inhibitors ranking first and macrolides, fluoroquinolones and third-generation cephalosporins included in the first five positions of the list. Penicillins plus β-lactamase inhibitors also showed a sharp increase in consumption in the 3 year period (+23%).

Table 4 shows the breakdown of the antibacterial groups in the four clinical areas. The medical units showed a pattern of antibiotic utilization similar to the overall figures of the hospitals, with penicillins plus β-lactamase inhibitors ranking first, followed by fluoroquinolones, third-generation cephalosporins and macrolides. A similar pattern of utilization was also observed in surgical units, with penicillins plus β-lactamase inhibitors first, followed by fluoroquinolones and third-generation cephalosporins; in those units, a considerable consumption was also observed for extended-spectrum penicillins, first-generation cephalosporins and glycopeptides. Also in the paediatric units, penicillins plus β-lactamase inhibitors were the first group, followed by third-generation cephalosporins, but consumption of fluoroquinolones was considerably lower than in the other areas. As reported above, intensive care was the area with the highest consumption of antibiotics. In this area, several antibiotic groups showed high utilization, namely penicillins plus β-lactamase inhibitors, fluoroquinolones, aminoglycosides, glycopeptides and others.

Table 5 shows the consumption of penicillins plus β-lactamase inhibitors, fluoroquinolones, third-generation cephalosporins and glycopeptides in the individual wards within each clinical area. Penicillins plus β-lactamase inhibitors showed the highest consumption in the maxillofacial/plastic surgery ward among all surgical wards and in the emergency medicine ward within medical units.

Haematology wards had the highest consumption of fluoroquinolones while third-generation cephalosporins were most used in emergency medicine wards and pneumology wards within medical units, in thoracic/vascular surgery within surgical units and in ICUs. Consumption of glycopeptides was particularly high in ICUs, haematology, cardiac surgery and orthopaedics, with values >10 DDD/100 bed days. In the medical units, consumption was >2 DDD in infectious disease control units, internal medicine and pneumology wards, while it was higher than 2 DDD in most wards of the surgical units.
Antibiotic use increased in our hospital sample in the 3 year period by 18%. Literature on antibiotic use in Italian hospitals for comparison is scarce, but our findings appear consistent with data published in other European countries.

A similar increase was described in Denmark over the period 1997–2001. Two studies in Dutch hospitals also showed increased antibiotic use by 14% between 1991 and 1996, and by 24% between 1997 and 2002, respectively. However, absolute consumption of antibiotics in our hospital sample was considerably higher than that reported in Denmark, with a marked preference for broad-spectrum antibiotics in Italian hospitals as compared with the Danish ones.

Our finding of high consumption of combinations of penicillins with β-lactamase inhibitors and other wide-spectrum antibiotics is consistent with some recent publications performed in several European Countries, particularly in the Mediterranean area, to the detriment of narrow-spectrum penicillins, β-lactamase-resistant penicillins and first-generation cephalosporins, preferred by Nordic countries. To our knowledge, no change in guidelines or recommendations has been introduced in the hospitals of our study regarding penicillins plus β-lactamase inhibitors, so that market pressure is more likely to have caused the observed increase in consumption of these drugs.

Hospital glycopeptide consumption was highest in surgical units and ICUs and increased in the 3 year period. A study of glycopeptide use in German hospitals showed high consumption in the ICUs with a sharp increase in the period 1998–2000. The authors suggested that prophylactic and empirical indications may therefore account for more than 50% of all prescriptions, so that a substantial amount of glycopeptide prescriptions may be inappropriate. Irrespective of the reasons for such high consumption of glycopeptides, this is a matter of great concern because their excessive use enhances the risk of resistance among enterococci and staphylococci.
The high antibiotic consumption observed in ICUs is not surprising because almost all the patients admitted to these units usually receive daily antimicrobial therapy. Moreover, the use of DDD to analyse antibiotic consumption could have caused an overestimate in those wards or clinical areas in which patients usually require high doses. The opposite problem occurs in evaluating antibiotic use in children who usually take antibiotic dosages lower than adults: the DDD definition does not account for dose adaptation in childhood, and this is a limitation of the DDD methodology.16

In our study, surgical units used more antibiotics than medical units. Antibiotic prophylaxis in surgery is one of the matters of discussion about hospital use of antimicrobial agents, since surgical procedures are often associated with unnecessary prescription of antibiotics.17

International guidelines suggest that the more suitable antibiotics for prophylaxis are first-generation (cefazolin) or second-generation (cefuroxime) cephalosporins. The third- and fourth-generation cephalosporins, carbapenems, aztreonam and fluoroquinolones are more expensive and promote the emergence of resistant strains, and they should not be used for routine prophylaxis in surgery. Our survey showed instead a very high, and probably inappropriate, consumption of these groups of antibiotics.

A limitation of our study is the lack of patient/infection information. Microbiological data could probably give additional information about isolated bacterial strains and development of resistance. Preliminary data obtained from one of the university hospitals participating in this study indicate that only 1 out of 4–5 patients admitted to hospital underwent a microbiological test. In the same hospital, total consumption of antibiotics was ∼75 DDD/100 bed days, roughly indicating that ∼75% of the patients received antibiotics during hospital stay. This suggests that a considerable amount of antibiotics is prescribed without evidence of a documented infection.

An intrinsic limit of antibiotic utilization studies based on DDD methodology is that DDD is intended for evaluating drug consumption data in primary care, and the DDDs of a number of antibiotics are much lower than the dosages usually prescribed to some hospital patients. An example has been reported by de With et al. concerning co-amoxiclav. The DDD listed in the ATC/WHO index is 1 g for oral formulations and 3 g for parenteral formulations. In our data, oral formulations accounted for 70% of co-amoxiclav consumption and this could be associated with a substantial overestimation of this drug, owing to the low value of oral DDD. We chose to follow the standard DDD methodology anyway, in order to allow data comparison.

This study offers information on the pattern and trend of antibiotic use in a sample of Italian hospitals, only based on hospital pharmacy records. A more detailed understanding of the problems related to hospital use of antibiotics should involve prescription data linked to patients’ data, particularly in terms of diagnosis and microbiological findings. Further studies are therefore needed using linkage techniques between pharmacy and medical records, also taking into account information about possible adoption of local guidelines or recommendations.

Results like those showed in this paper could also represent the basis for educational initiatives aimed at rationalizing the use of antibiotics in hospitals.

Acknowledgements

We wish to thank the pharmacists of the participating hospitals for supplying pharmacy record data: Stefano Bianchi, Francesca Carnaccini, Paola Fiacchi, Fabio Pieraccini, Giovanna Rametta, Stella Sfera, Vera Viti and Anna Zuccheri. We also thank the Drug Policy Service of Regione Emilia-Romagna for kindly supplying drug primary care prescription data.

Funding

The study was supported by grants from the Regione Emilia-Romagna and the University of Bologna, and by an institutional unrestricted grant from Roche S.p.A.

Transparency declarations

None to declare.

References