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Use of broad spectrum antibiotics in six non-university Swiss hospitals

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Summary

Principles: Broad-spectrum antibiotics (BSAs) are costly and prone to misuse. Their use is associated with the emergence of resistant bacteria. This article describes the first step of an interhospital programme for the appropriate use of BSAs.

Methods: BSAs were defined as the iv antibiotics present in the formulary shared by the six participating institutions and considered to be antipseudomonal agents (i.e. cefepime, ceftazidime, ciprofloxacin, imipenem, meropenem, piperacillin/tazobactam) plus trovafloxacin. Annual utilisation rates and interhospital comparisons were provided to each institution using the "defined daily dosages" (DDDs) of the World Health Organization.

Results: From 1997 to 1999, the overall utilisation rate of BSAs increased from 20.6 treatment days (TD)/1000 patient days (PD) to 36.5 TD/1000 PD. Significant interhospital differences were detected (range: 12.1 TD/1000PD in 1997 – 66.5 TD/1000 PD in 1999). The highest relative risk for treatment with any BSA for each individual hospital in comparison to the others was determined for 1999 (RR = 2.92; 95% confidence interval: 2.81-3.04). In 1999, the most frequently used BSAs were cefepime, imipenem, and piperacillin/tazobactam respectively.

Conclusions: Although this programme does not provide information on the indications for using BSAs in various hospitals, it helps to identify those institutions where the selection pressure for resistant bacteria is highest, and that could particularly benefit from specific interventions aiming at decreasing this pressure and controlling drug expenditure. Moreover, the feedback of utilisation rates and interhospital comparisons to the prescribing physicians might have a positive impact on BSA use.

Key words: antibiotic use; broad-spectrum antibiotics; antibiotic resistance; benchmarking

Introduction

The continuing emergence of antibiotic resistant bacteria constitutes a threat to patients suffering from infection and a growing challenge for the health care system. [1, 2] Owing to selection pressure, antibiotic use has been identified as an important factor contributing to this public health problem [3–5]. In acute care hospitals, 20 to 30% of inpatients receive antibiotics every day, and antibiotics represent 20 to 25% of the total cost of drugs. [6, 7] A substantial proportion of the antimicrobial agents prescribed in this setting belongs to the costly category of broad-spectrum antibiotics (BSAs) which may be particularly prone to misuse or overuse and thus associated with the emergence of resistant bacteria [4, 8–10].

Since BSAs often constitute the last line of defence against nosocomial infections, their appropriate use should be promoted to avoid selection of potentially untreatable organisms. In addition, this could result in a better control of drug costs. Many strategies to improve antibiotic use in hospitals have been proposed [11, 12]. A global programme should allow the concomitant surveillance of utilisation rates and resistance, as well as the development and implementation of methods of control (e.g. guidelines). It would thus require an interdisciplinary approach including the prescribing physicians, the infectious diseases consultant, the pharmacist, the microbiologist, and the hospital epidemiologist.

This paper describes the first step of a global programme developed for six community hospitals in canton Valais, Switzerland. Currently, the programme provides every institution with annual utilisation rates for BSAs and allows interhospital comparisons (benchmarking).

Patients and methods

The six regional community hospitals of canton Valais provide a total of 857 acute care beds for a population of 275,000 (mean number of acute care beds per institution = 143; range: 92–241). All have intensive care units and surgical facilities. The largest hospital serves as a regional reference centre, particularly for cardiac surgery and neurosurgery. From 1997 to 1999, the overall acute care patient days for these six institutions varied between 284,667 and 247,300 (mean = 260,000). The Central Institute of the Valais Hospitals (CIVH) serves all six hospitals, providing laboratory, clinical (e.g. infectious diseases consultants), pharmaceutical, and epidemiological services.

Since 1997 the use of the BSAs listed in the formulary shared by the six hospitals and defined as iv antipseudomonal agents plus trovafloxacin has been surveyed and regularly communicated to hospital chief-physicians by the CIVH pharmacy and hospital epidemiology unit. To date, cefepime, ceftazidime, ciprofloxacin, imipenem, meropenem, piperacillin/tazobactam, and trovafloxacin have been monitored. Utilisation rates were determined from annual deliveries for each acute care department, assuming constant stocks within each of them. Defined daily dosages (DDDs), as defined by the World Health Organization (WHO) [13], served to establish treatment days with BSAs. DDDs for the various antibiotics were as follows: cefepime 2 g; ceftazidime 4 g; ciprofloxacin 0.5 g; imipenem 2 g; meropenem 2 g; piperacillin/tazobactam 14 g; and trovafloxacin 0.2 g. Rates were treatment days / 1000 patient days / year. Annual costs for BSAs and antibiotics in general were derived from the annual total drug expenditures for each hospital.

Results were determined annually for each hospital including secular trends and interhospital comparisons, each individual institution being blinded to the others. Statistics were performed with the Epi Info software, version 6.04 (Centers for Disease Control and Prevention, Atlanta, and WHO, Geneva). The relative risks (RR) were calculated for each hospital as follows: number of days on BSA in hospital H / total days in hospital H divided by number of days on BSA in all other hospitals / total hospital days in all other hospitals. P values were calculated by using the Chi square test.

Results

As shown in Figure 1, the global utilisation rate of BSAs for patients hospitalised in acute care beds increased over the three years observed from 20.6 treatment days / 1000 patient days in 1997 to 29.5 in 1998, and 36.5 in 1999. With the exceptions of cefepime, which was used increasingly, and trovafloxacin, which was only briefly available, use of the different substances appears to be quite constant.

In 1997, 1998, and 1999, the costs for BSA represented 30.1%, 32.3%, and 34.9% respectively of the total costs for antibiotics in the six hospitals, a statistically significant increase for both the 1997–1998 and 1998–1999 period ($p < 0.0001$).

Although this survey does not allow adjustment for case mix, figure 2 demonstrates that utilisation rates varied significantly between and within hospitals from one year to the other. Extremes were 12.1 treatment days / 1000 patient days in 1997 in one hospital and 66.5 treatment days / 1000 patient days in 1999 in another hospital. In three hospitals, BSA use increased continuously during the observation period, whereas random fluctuations were observed in the remaining three.

All but one annual interhospital difference, and all within hospital temporal differences were statistically significant. The highest and lowest RR for treatment with any BSA when comparing an individual institution to the remainder were determined in 1999 (RR = 2.92 and 0.32 respectively; 95% CI = 2.81–3.04 and 0.30–0.35 respectively).

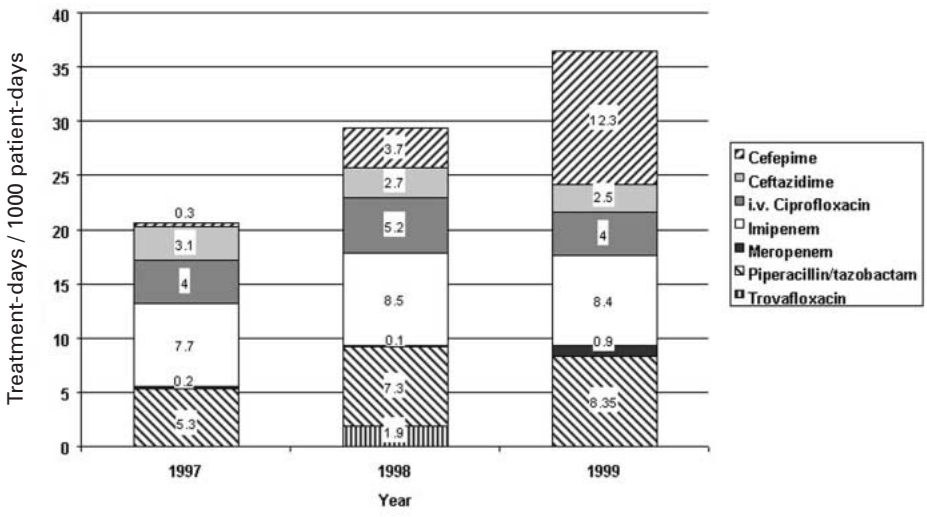

Figure 1

Overall utilisation rates of broad-spectrum antibiotics in the acute care departments of six Swiss non-university hospitals from 1997 to 1999.

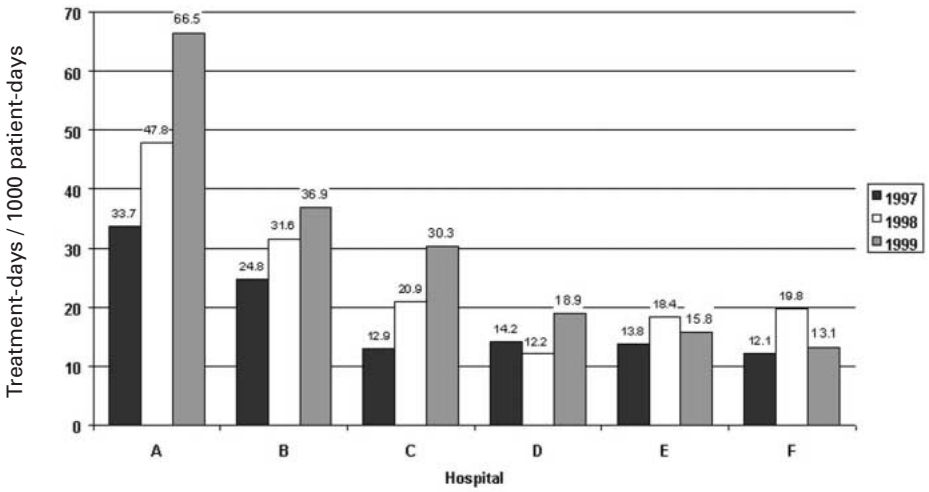

Figure 2

Utilisation rates of broad-spectrum antibiotics in the acute care departments of six Swiss non-university hospitals from 1997 to 1999, by institution.

Discussion

In 1996, Lew et al published a similar study comparing antibiotic use in five Swiss university hospitals and six non-university hospitals from 1990 to 1994 [6]. The authors observed trends towards an increase in utilisation rates over the years and differences between university and non-university hospitals in the use of iv antibiotics, particularly third generation cephalosporins, broad spectrum penicillins, and carbapenems.

In the present study, utilisation rates of BSAs were compared over three years in six non-university hospitals. As in the 1996 study, a significant increase in use was observed over the years. Irrespective of the reasons for this increase (inpatients in 1999 might have needed more BSAs than previously), this obviously corresponds to an increase in the selection pressure for BSAs. Consequently, physicians in these hospitals could be increasingly confronted with patients suffering from nosocomial infections due to resistant microorganisms, either directly selected by the treatment they received or transmitted from another patient exposed to BSAs. Providing every attending physician with this kind of data should sensitise them and might elicit some change in their prescription habits, without having to use less well accepted methods such as critical reviews of prescriptions, requiring infectious diseases consultations, or the completion of order forms. Furthermore, these data might help to increase the awareness of drug costs among clinicians.

However, a more detailed analysis showed that baseline utilisation rates of BSAs, as determined in 1997, and their subsequent evolution until 1999 varied greatly between hospitals. Since no data were collected at the patient level to adjust for case mix, the surveillance programme does not allow any assumption as to whether these differences were medically justified or not. Nevertheless it aids the identification of those institutions, which were more at risk of eventually having to deal with difficult to treat infections as well as those institutions, which should anticipate such problems and initiate specific programmes to prevent the emergence of resistant microorganisms and their secondary spread. Such programmes can be developed according to the 1997 guidelines of the Society for Healthcare Epidemiology of America and the Infectious Diseases Society of America [11]. These identify the elements of an optimal antimicrobial control programme and propose several methods to implement antibiotic control or restriction policies (i.e. written hospital guidelines, educational efforts aimed at changing prescribing practices of physicians, restriction of hospital formulary through pharmacy and therapeutics committee, utilisation review, requirement of consultation with infectious diseases specialists for certain antimicrobial choices, antimicrobial susceptibility reporting, and restriction of pharmaceutical promotion).

Our initial programme also permitted the identification of which BSAs were preferentially used, namely cefepime, imipenem, and piperacillin/tazobactam. This knowledge is of interest since not every BSA is similarly associated with the emergence of resistance among specific species of bacteria [8, 14, 15].

Moreover, the yearly analysis stratified by agent as well as the growing proportion of costs due to BSAs relative to other antibiotics suggest that the introduction of new BSAs to the formulary (e.g. cefepime) might encourage their use instead of agents with narrower, more specific spectra or older BSAs with similar antimicrobial and pharmacokinetic profiles. This observation, which was already made by Lew et al. [6] argues in favour of keeping the number of BSAs available through the formulary constant. However, a too drastic restriction in the choice of BSAs available could be counterproductive unless it is part of a policy of periodic shifts from one class of agents to another

(the so-called "antibiotic cycling" strategy). Indeed, the long-term use of same class agents may induce the emergence and spread of bacterial species with particular resistance profiles such as imipenem resistant *Pseudomonas* spp, cephalosporin resistant *Enterobacter* spp, *Stenotrophomonas maltophilia* or bacteria producing extended spectrum beta-lactamases [7, 12, 13]. In contrast, allowing some diversity in the BSAs used inside a hospital might better control for the selection of specific resistant strains.

As already pointed out by others [7], comparing antibiotic use between hospitals should be done with caution since many factors could confound their utilisation rates. The lack of adjustment for these factors certainly constitutes the main limitation of this study. Indeed, no information was available on the patients, the severity of their illnesses, and the wards on which they were staying. A larger number of acute beds or a shorter average length of stay could be associated with a higher use of BSAs, because these variables may reflect the case mix or have an impact on utilisation rates of BSAs. However, no such links could be detected in this study (data not shown).

Moreover, although all six hospitals have intensive care units, they may still not be comparable. In particular, one of them serves as a reference centre for certain specialties and might thus care for more severe cases, requiring more BSAs. In addition, some "low consumers" could use more combinations of antibiotics (such as amoxillin / clavulanate with an aminoglycoside) instead of the studied BSAs. Furthermore, some WHO DDDs are lower than the dosages commonly used in Switzerland and their use may have lead to an overestimation of treatment days with some BSAs (e.g. cefepime or ciprofloxacin). These limitations allow no grading of the participating hospitals. They nevertheless still provide data on each of them enabling better control of their use of BSAs.

In conclusion, though efforts are still needed to correlate the use of broad-spectrum antibiotics with data on resistance to allow analyses at the ward or patient level and to design interventions aimed at improving the use of BSAs, we believe that a simple surveillance system constitutes the mainstay of a global programme to control the use of BSAs in hospitals. Such a simple system may generate interesting and useful information. In addition, it could have a positive impact on the use of BSAs by providing feedback to physicians and allowing cautious interhospital comparisons.

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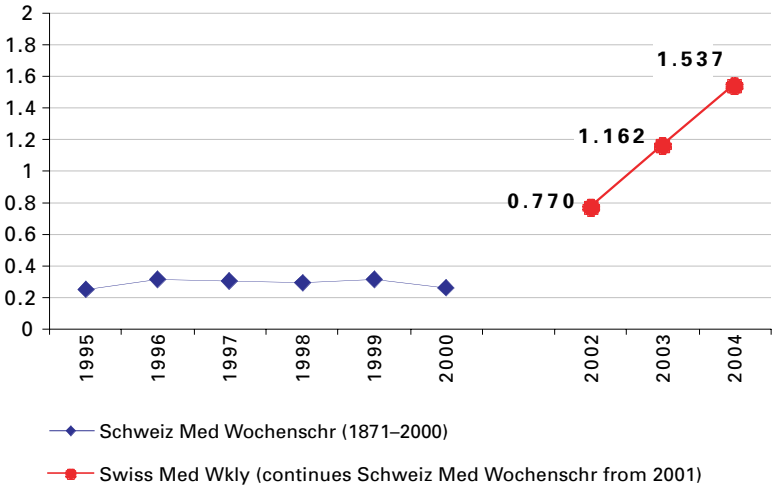

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