Short Summary Of Swedres 2005, A Report On Swedish Antibiotic Utilisation And Resistance

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"Swedres 2005", the fifth report on Swedish antibiotic utilisation and resistance in human medicine, was presented in May 2006. Compared with the rest of Europe, antibiotic consumption and resistance levels in Sweden are relatively low. However, global travel and trade facilitate the spread of bacteria between countries and continents. As a consequence, also in Sweden, increasing resistance trends are seen for some pathogens, notably ESBL-producing enterobacteriaceae.

Introduction

"Swedres 2005", the fifth report on Swedish antibiotic utilisation and resistance in human medicine, was presented in May 2006. The report was published by Sweden's Strategic Programme for the Rational use of Antibiotics (Strategigruppen för Rationell Antibiotikaanvändning och Minskad Antibiotikaresistens - STRAMA) and the Swedish Institute for Infectious Disease Control (Smittskyddsinstitutet - SMI) [1].

STRAMA was formed as a network in 1995. In September 2006, it was appointed by the Swedish government to interact and coordinate between authorities and organisations in matters regarding antibiotic resistance.

Methods

Surveillance of antibiotic consumption

Since 1988, the WHO Anatomical Therapeutic Chemical (ATC) classification system has been used in Sweden for national drug statistics. All data on medicine sales, including hospital use, are collected by Apoteket AB (the National Corporation of Swedish Pharmacies). The drug consumption data can be obtained in various formats; in this report it is most often presented as the number of defined daily doses per 1,000 inhabitants per day (DDD/1,000/day) or as the number of prescriptions per 1,000 inhabitants per year (prescriptions/1,000/year).

Surveillance of antibiotic resistance

The national strategy for surveillance of antibiotic resistance consists of several components, all of which rely on the participation of Sweden's clinical microbiological laboratories.

The first component involves the mandatory reporting of certain bacterial resistances as regulated in the Swedish Communicable Disease Act. Notifications are sent to SMI and at present include infection with or carriage of four pathogens: strains of *Streptococcus pneumoniae* resistant to/with reduced susceptibility to penicillin G MIC >= 0.5 mg/L (PRP – penicillin-resistant pneumococci, notifiable since 1996), methicillin-resistant *Staphylococcus aureus* (MRSA, notifiable since 2000), and vancomycin-resistant *Enterococcus faecalis* and *Enterococcus faecium* (VRE – vancomycin-resistant enterococci, notifiable since 2000). The notifications are entered into a national computerised surveillance system. In addition, the MRSA and PRP strains are sent to SMI for epidemiological typing.

Drug-resistant isolates of *Mycobacterium tuberculosis* and *M. bovis* are also subject to epidemiological typing at SMI.

► The second component of antibiotic resistance surveillance consists in voluntary reporting from all clinical laboratories done on an annual basis within the Resistance Surveillance and Quality Control programme (RSQC). The laboratories are asked to collect quantitative data (zone diameters) for 100 consecutive clinical isolates of defined bacterial species and antibiotics. In each data set, four to six antibiotics are tested for each pathogen.

► The third component comprises the Swedish data on invasive bacteria presented to the European Antibiotic Resistance Surveillance System (EARSS, http://www.rivm.nl/earss), at present provided by 21 laboratories covering approximately 75% of the population.

Susceptibility testing of enteric pathogens is not performed on a regular basis. Existing data derive mainly from special investigations.

The National Reference Laboratory for Pathogenic Neisseria in Örebro provides the national quantitative data on *Neisseria gonorrhoeae* and *N. meningitidis*. Since 2002, national data on antibiotic resistance can be entered and accessed through a web-based software package, ResNet [3].

Results

Use of antibiotics

For the last 10 years, there has been a steady decrease in the consumption of antibiotics in Sweden. In 2005, the total use of antibiotics, methenamine excluded, was 14.8 DDD/1,000/day.

Out-patient care, representing approximately 90% of the total use of antibiotics, was 13.1 DDD/1,000/day, methenamine excluded. The most commonly used substances were beta-lactamase sensitive penicillins and tetracyclines (Figure 1).

Sweden has a long tradition of using beta-lactamase sensitive penicillin as the first-choice drug for many infections. In 2005, this substance corresponded to 26% of all antibiotic use in out-patient care (methenamine included).

FIGURE 1

Antibiotics used in out-patient care in 2005, percentage of total DDD/1,000/day (defined daily doses per 1,000 inhabitants per day)

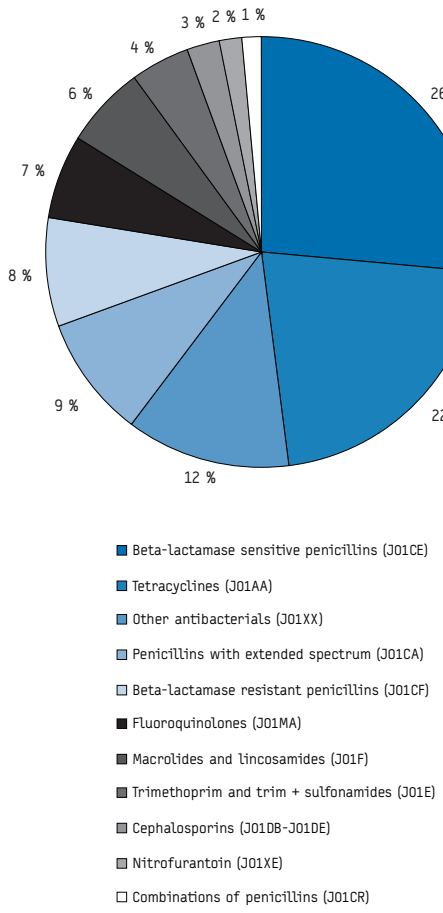


FIGURE 2

Antibiotics mostly used against urinary tract infections, out-patient care 2000-2005. Women, prescriptions/1,000/year

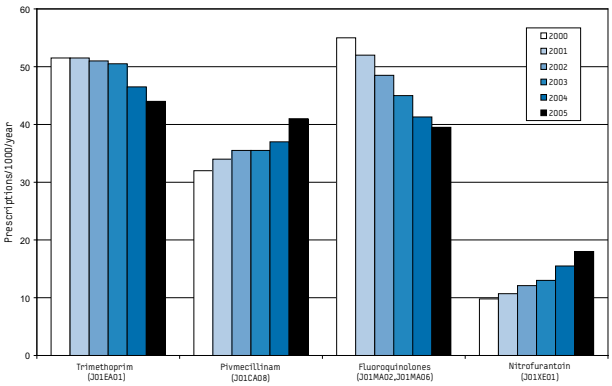
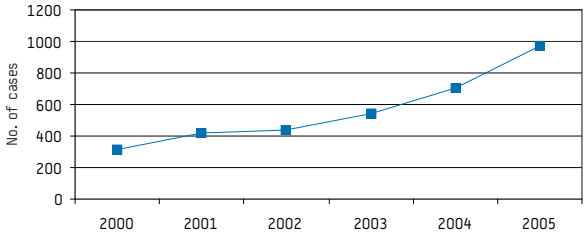


FIGURE 3

Number of reported cases of MRSA per year, Sweden 2000-2005



The most commonly used tetracycline, taking into account the number of prescriptions, is doxycycline. This substance is mainly used in the treatment of respiratory tract infections, which may be one reason why it is mostly used during the winter.

The fluoroquinolones used most frequently in out-patient care during the last few years were norfloxacin and ciprofloxacin. During 2005, the use of ciprofloxacin increased and the use of norfloxacin decreased at approximately the same rate. The introduction of generic ciprofloxacin available at a lower price might explain this trend.

Fluoroquinolones are still commonly used in the treatment of urinary tract infections. However, during the last six years their use has steadily decreased, whereas the use of pivmecillinam and nitrofurantoin has increased (Figure 2). This trend reflects the national and local recommendations to restrict the use of fluoroquinolones in the treatment of lower urinary tract infections in women.

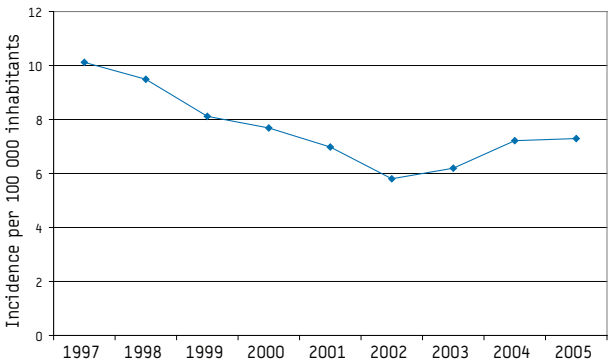
The use of antibiotics in hospitals has increased since 1996, especially in terms of DDD/100 patient-days (42% increase), but also in terms of DDD/100 admissions (19%). The most commonly prescribed classes were cephalosporins, penicillins, tetracyclines and fluoroquinolones.

Antibiotic resistance

The incidence of multi-resistant *Staphylococcus aureus* (MRSA) in Sweden is relatively low compared to many other

FIGURE 4

Annual incidence of penicillin-resistant pneumococci (PRP) 1997-2005



European countries [4]. However, during 2005, a total of 975 cases were reported, representing an increase of 37%, compared to 2004 (Figure 3). Fifty-five percent of the patients acquired MRSA in Sweden, 23% were infected abroad, and for 22% the place of infection was unknown or not reported. In 2005, invasive isolates of MRSA constituted 1% of all invasive *S. aureus*, according to the data presented through EARSS [4].

During 1997-2002, the annual incidence rate per 100,000 population of Streptococcus pneumoniae resistant to/with reduced susceptibility to penicillin (PRP) decreased from 10.1 to 5.9 but increased to 7.3 in 2005. Most cases were identified through nasopharyngeal swabs. Fifty-nine percent of the PRP cases reported were below 5 years of age. In 30 cases (5%) the PRP isolates came from invasive sites, that is blood and/or spinal fluid. Multi-resistance (resistance to penicillin and at least two more antibiotics) was common among PRP accounting for 30-50% of the isolates. Of these, the most common serotypes/groups found were types 9, 14, 19, 23, 6 and 35.

Although vancomycin resistant enterococci (VRE) have become an important cause of nosocomial outbreaks in many parts of the world, only 47 VRE cases were reported in Sweden in 2005. They were mainly infections caused by *Enterococcus faecium* carrying the *vanB* gene.

Escherichia coli, mainly derived from urinary tract infections, has been included in the Swedish national surveillance programme since 1996. Ampicillin resistance has increased from 17 to 26% during this period. More alarmingly, the level of resistance to third-generation cephalosporins among blood isolates has increased to 1.3%, and in the majority of these the resistance was caused by plasmid-mediated Extended Spectrum Beta-Lactamases (ESBLs). Resistance to fluoroquinolones has increased every year and was almost 10% in 2005. The rates were the same in blood (EARSS data [4]) and in urine isolates (ResNet data [3]).

Klebsiella pneumoniae was included in the EARSS programme in 2005, and ESBL-producing strains have been identified. As part of the voluntary reporting system, a high number of ESBL-containing and multi-resistant isolates were reported from one Swedish county, both hospital- and community-related.

Concerning *Pseudomonas aeruginosa*, the most alarming feature is the high prevalence of carbapenem resistance (17.5% resistance to imipenem in 2005). Resistance to fluoroquinolones (ciprofloxacin) remained at 9%.

The average level of beta-lactam resistance in respiratory isolates of *Haemophilus influenzae* has not increased during the last four years, but the range between individual laboratories and counties was 5 to 27%. An average increase in strains resistant to trimethoprim-sulfamethoxazole was seen in 2005, but again with a wide range between individual laboratories (4-18%).

Resistance to clarithromycin in *Helicobacter pylori* has been increasing, with over 10% registered at one laboratory.

Gonorrhoea is a notifiable disease, and 691 clinical cases of the disease were reported in 2005. Isolates from 486 cases (70%) were completely characterised. During the last three years approximately 25% of the isolates were beta-lactamase producing and ampicillin resistant, and almost 50% were resistant to ciprofloxacin.

During 2005, there was a 24% increase in the total number of newly diagnosed tuberculosis (TB) cases (575 as compared to 465 in 2004). Resistant TB was reported in 8.7% of the Swedish born patients and in 10.7% of those foreign-born. Resistance to isoniazid was most common, reported in 10.3% of the patients, followed by pyrazinamide 1.3%, rifampicin 1.1% and ethambutol 0.7%.

Discussion

The Swedish government recently approved of a national strategy for coordinated efforts to prevent antibiotic resistance [5]. The strategy emphasises that coordinated work is required in several areas. The measures proposed regard the use of antibiotics in humans and animals as well as in food and environmental sectors. A number of legislative amendments have been proposed to prevent the spread of healthcare-associated infections.

For the last 10 years, there has been an integrated surveillance of antibiotic use and resistance in Sweden. Sweden participates in the European networks for surveillance of antibiotic resistance and consumption (European Antibiotic Resistance Surveillance System – EARSS [4] and European Surveillance of Antibiotic Consumption – ESAC [6]). Compared with the rest of Europe, antibiotic consumption and resistance levels in Sweden are relatively low. However, global travel and trade facilitate the spread of bacteria between countries and continents. As a consequence, also in Sweden, increasing resistance trends are seen for some pathogens, notably ESBL-producing enterobacteriaceae.

Annual reports on antibiotic use and resistance are important tools to increase awareness on rapid dynamics of antibiotic resistance development and the need to further optimise antibiotic use and infection control.

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Citation: Cars O, Olsson-Liljequist B, Lundh K, . Short summary of Swedres 2005, a report on Swedish antibiotic utilisation and resistance. Euro Surveill 2007;12(3)[Epub ahead of print]. Available online: http://www.eurosurveillance.org/em/v12n03/1203-225.asp