Antimicrobial resistance of invasive
Streptococcus pneumoniae in Slovenia from
1997 to 2000

Milan Čizmana,*, Marko Pokornaa, Metka Paragib and
the Slovenian Meningitis Study Group

aDepartment of Infectious Diseases, University
Medical Centre Ljubljana, Japljeva 2, SI-1525
Ljubljana; bInstitute of Public Health of Slovenia,
Trubarjeva 2, Ljubljana, Slovenia

*Corresponding author. Tel: +386-1-522-2110;
Fax: +386-1-2302-781;
E-mail: milan.cizman@mf.uni-lj.si

Sir,
Antimicrobial resistance of Streptococcus pneumoniae demonstrates geographical variability and is increasing worldwide.1,2 The evolution of resistance and different resistance patterns are probably most influenced by local antibiotic consumption,3,4 and this relationship, with regard to Slovenia, is reported here.

The data on the use of antibiotics were obtained from the Institute of Health Insurance, which covers all medical costs in Slovenia. All isolates of S. pneumoniae from blood, CSF and other normally sterile body fluids in all but one Slovenian hospital in the period from 1997 to 2000 were included in the study. Duplicate isolates from the same patient were excluded. Susceptibility tests were carried out at the Institute of Public Health according to the methods described previously.5

The data on antibiotic consumption and antimicrobial resistance of invasive S. pneumoniae isolates are shown in the Figure. During the study period, the total outpatient consumption of antibiotics in Slovenia increased from 17.47 defined daily doses per 1000 persons per day (DDD/1000/day) in 1997 to 18.49 DDD/1000/day in 2000. The use of most classes of antibiotics remained stable, on average 10.89 DDD/1000/day for penicillins, 0.89 DDD/1000/day for cephalosporins, 0.93 DDD/1000/day for tetracyclines and 1.16 DDD/1000/day for trimethoprim/sulfamethoxasole (TMP/SMX). In contrast, the use of macrolides increased from 2.85 to 3.57 DDD/1000/day.

The resistance of invasive S. pneumoniae to penicillin remained stable during the study period. Resistance to TMP/SMX increased from 15.7% in 1997 to 27.6% in 2000. Resistance to tetracyclines demonstrated year-to-year variation with no trend. Resistance to erythromycin and clindamycin increased from 3.6% (4/109) to 9.0% (10/111) and from 0% (0/108) to 6.3% (7/111), respectively. Resistance to ciprofloxacin, assessed in the years 1999 and 2000 only, was not detected in invasive S. pneumoniae isolates. All strains had MICs of ≤1 mg/L. No resistance to vancomycin was detected in invasive S. pneumoniae isolates during the study period.

Resistance of invasive S. pneumoniae to penicillin in Slovenia is moderate and stable. Compared with The Netherlands, consumption of penicillins in Slovenia is 3.2-fold higher on average and the resistance is 10-fold higher.1 When comparing other European countries (e.g. Finland, Denmark and The Netherlands) with low resistance rates of S. pneumoniae to penicillin in 1997 and Slovenia with its moderate resistance rate, a difference in consumption of broad-spectrum penicillins between these other countries (average 3.0, range 2.39–3.78 DDD/1000/day) and Slovenia (4 year average 8.02 DDD/1000/day) is seen.1,3,4 In Spain in 1997 the consumption of broad-spectrum penicillins was 18.01 DDD/1000/day and the resistance of S. pneumoniae was 59.6%.5,6 In the 4 year study period in Slovenia the consumption of broad-spectrum penicillins increased from 7.15 to 7.75 DDD/1000/day (8.99 in 1999), due exclusively to an increase in amoxicillin/clavulanic acid consumption with no influence on the penicillin resistance rate of S. pneumoniae. A higher consumption of cephalosporins in Finland than in Slovenia (2.11 versus 0.92 DDD/1000/day) indicates that the aminopenicillins could have a greater influence on the development of resistance than the cephalosporins. The resistance of S. pneumoniae to TMP/SMX increased during the study period in Slovenia, despite a decrease in TMP/SMX consumption. Twenty percent of TMP/SMX-resistant isolates were also resistant to macrolides. Without any increase in TMP/SMX consumption in the study period, the increase in TMP/SMX resistance was at least partly caused by an increase in macrolide resistance. A difference in resistance to TMP/SMX between children and adults was observed (30.4%, 46/151 versus 18.9%, 53/279), which could be explained by differences in TMP/SMX consumption in children and adults. For TMP/SMX during the study period, there were, on average, 91 prescriptions/1000 inhabitants/year in children less than 15 years old and 57 prescriptions/1000 in adults. In contrast, the consumption of tetracyclines was 25-fold higher in adults than in children (25/1000 versus 1/1000 prescriptions per year), but the resistance was higher in children than adults (11.9%, 18/151 versus 3.9%, 11/279), which also...
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contrasts with the data from The Netherlands. All isolates resistant to tetracyclines isolated in children were also resistant either to TMP/SMX (16/18) and/or penicillin (13/18) or, less commonly, to other antibiotics. The consumption of macrolides has been continuously increasing in Slovenia, except in the year 2000, when the consumption decreased for the first time in the last decade. The resistance of invasive \( S. \) pneumoniae to macrolides has increased each year from 3.6% in 1997 to 9% in 2000. The increased use was first associated with an increase in resistance of \( S. \) pneumoniae followed by non-invasive \( S. \) pneumoniae strains. The increased resistance to macrolides was associated with increased resistance to clindamycin, indicating the presence of the MLS/\beta\)-lactam phenotype. Seven out of 10 strains resistant to erythromycin were also resistant to clindamycin. Increased use of quinolones was not associated with the emergence of resistance to quinolones during the last 2 years of the study period.

Our data indicate that the consumption of antibiotics in outpatients in Slovenia is comparable to other European countries. Increased use of macrolides was associated with an increase in resistance of \( S. \) pneumoniae to macrolides and lincosamides. The relationship between the use of antibiotics and the development and evolution of resistance is complex and needs further study.

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References


