Serotype incidence and antibiotic susceptibility of Streptococcus pneumoniae causing invasive disease in Scotland, 1999–2002

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Pneumococcal disease remains an important cause of invasive and non-invasive disease in Scotland and elsewhere. The Scottish Meningococcus and Pneumococcus Reference Laboratory receives isolates of Streptococcus pneumoniae from diagnostic laboratories around Scotland. Here, the serogroups/types and antibiotic-susceptibility patterns of invasive isolates received between 1999 and 2002 are described. There were a total of 1741 invasive isolates received, the most common serogroups/types being 14 (19.8 %), 9 (10.2 %), 6 (8.3 %), 19 (7.9 %), 23 (7.9 %), 4 (6.5 %), 8 (6.4 %), 3 (5.7 %), 1 (3.8 %), 7 (3.8 %) and 18 (3.4 %). Importantly, serotypes 7 and 8 are not represented in the 7-, 9- and 11-valent pneumococcal conjugate polysaccharide vaccines. There were 67 (3.8 %) isolates considered penicillin non-susceptible, although no penicillin resistance (MIC > 0.002 mg ml−1) was recorded. One hundred and ninety-four (11.1 %) isolates, predominantly of serotype 14, were resistant to erythromycin, and 12 (0.7 %) were resistant to ciprofloxacin. This information provides an important dataset that will prove essential prior to and during the implementation of pneumococcal conjugate vaccines in the UK.

Introduction

Streptococcus pneumoniae is responsible for invasive and non-invasive pneumococcal diseases worldwide, such as pneumonia, bacteraemia and meningitis. It remains a leading cause of morbidity and mortality worldwide, especially in the young and old (Mohan & Heath, 2001; Obaro & Adegbola, 2002). There are more than 90 known pneumococcal serotypes, although the majority of invasive and non-invasive disease is associated with a much smaller number of serotypes. Pneumococcal disease surveillance has improved in many countries in recent years in an effort to improve public health management and inform vaccine policy (Bos et al., 2003; Clarke et al., 2001; Gertz et al., 2003; Kyaw et al., 2003; Muhlemann et al., 2003; Skoczynska & Hryniewicz, 2003; Whitney et al., 2003). A number of multivalent pneumococcal conjugate polysaccharide (Pnc) vaccines have now been developed and a 7-valent Pnc vaccine has been licensed in a number of countries and is in use in the USA. The need for improved epidemiological information, as well as serotype and genotype data, is unmistakable.

The Scottish Meningococcus and Pneumococcus Reference Laboratory (SMPRL) was established in 1992 and led to the improved availability of data relating to pneumococcal infection in Scotland, particularly in relation to serogroup/type and antibiotic susceptibility. All diagnostic laboratories in Scotland are encouraged to submit pneumococcal isolates, but, historically, not all invasive isolates were sent, whilst some non-invasive isolates were sent for confirmation of identity or because they were resistant to one or more antibiotics. Therefore, in November 1999, the SMPRL and the Scottish Centre for Infection and Environmental Health (SCIEH) started an enhanced invasive pneumococcal disease surveillance programme in order to gain an improved understanding of the actual incidence of different serogroups/types and the occurrence of antibiotic resistance.

Information from the SMPRL has previously been used to describe the serogroups/types and antibiotic susceptibility of invasive pneumococci between 1988 and 1999 (Kyaw et al., 2000, 2002b). The proportion of penicillin non-susceptible isolates was 4.2–12.6 %, whilst the proportion of erythromycin non-susceptible isolates was 5.6–16.3 % (Kyaw et al., 2002b). Although 5659 and 6007 invasive pneumococcal isolates were used in these studies, respectively, and this data...
proved useful in providing a baseline level for serotype and antibiotic resistance information, the number of invasive pneumococcal isolates actually sent to the SMPRL was low compared with the number of diagnostic laboratory reports of invasive pneumococcal disease. Here, we report the successful introduction of enhanced invasive pneumococcal disease surveillance in Scotland and the reference laboratory data that was gained during the first 3 years of its implementation.

**Methods**

In Scotland, an enhanced invasive pneumococcal disease surveillance programme began in November 1999 as an active collaboration between the diagnostic laboratories, SMPRL and SCIEH. For the purposes of this study, information was included from January 1999, to indicate the success of the enhanced surveillance, through to December 2002. Pneumococci from patients with invasive pneumococcal disease were isolated at diagnostic laboratories throughout Scotland between 1999 and 2002 and sent to the SMPRL. Isolates were serogrouped/typed by coagglutination and MICs determined using E-tests as previously described (Kyaw et al., 2003; Smart, 1986). MIC breakpoints were used according to the British Society for Antimicrobial Chemotherapy (http://www.bsac.org.uk/). Isolates showing MICs of ≤0.06 mg ml⁻¹, 0.1–1.0 mg ml⁻¹ and >2 mg ml⁻¹ to penicillin were considered susceptible, intermediate and non-susceptible, respectively. Isolates susceptible and non-susceptible to erythromycin were defined by MICs of <1 and >1 mg ml⁻¹, respectively. Ciprofloxacin susceptibility and non-susceptibility were defined by MICs of <2 and >4 mg ml⁻¹, respectively.

**Results**

Pneumococci (1741 isolates) were isolated from blood (1646), cerebrospinal fluid (75), and blood and cerebrospinal fluid (20) during the 4-year period 1999–2002. Overall, the 11 most common serogroups/types in order of prevalence were 14 (19.8 %), 9 (10.2 %), 6 (8.3 %), 19 (7.9 %), 23 (7.9 %), 4 (6.5 %), 8 (6.4 %), 3 (5.7 %), 1 (3.8 %), 7 (3.8 %) and 18 (3.4 %) (Fig. 1). Serotype 14 was by far the most common serotype in each year, accounting for 55 (21 %), 66 (18.3 %), 104 (20 %) and 119 (19.7 %) isolates, respectively.

MICs against penicillin, erythromycin and ciprofloxacin were determined (Fig. 2). Overall, there were 67 (3.8 %) isolates considered penicillin non-susceptible, although none of these was fully resistant. Penicillin MICs were mostly less than 0.016 mg l⁻¹ in 1999 and 2000, although 15 (5.7 %) and 20 (5.5 %), respectively, were intermediately resistant; no penicillin-resistant strains were isolated. In 2001 and 2002, penicillin MICs were mostly less than 0.019 mg l⁻¹ although 19 (3.6 %) and 13 (2.2 %), respectively, were intermediately resistant. Over the 4 years, erythromycin MICs ranged from 0.006 to >256 mg l⁻¹. Resistance was recorded in 49 (18.7 %), 40 (11.1 %), 74 (14.3 %) and 31 (5.1 %) isolates, respectively. Ciprofloxacin MICs ranged from 0.38 to 2.0 mg l⁻¹ between 1999 and 2002. Overall, 12 isolates were considered resistant to ciprofloxacin.

**Discussion**

Awareness of pneumococcal disease has increased due to the need for improved public health interventions and the development of Pnc vaccines. A substantial dataset relating to invasive pneumococcal disease in Scotland is available and data has previously been published in relation to serotype prevalence and antibiotic susceptibility (Kyaw et al., 2000, 2002a, b). Some of this has been linked to patient record data in order to provide information relating to pneumococcal disease and medical conditions (Kyaw et al., 2003). This study therefore, updates the dataset available for serogroup and antibiotic susceptibility up to and including 2002. This information can be used to help inform vaccine policy now that a Pnc vaccine has been licensed in the UK and will also provide ongoing data for the surveillance of serogroups/types during and after any implementation of such vaccines.

In Scotland, between 1988 and 1999, a twofold increase in the incidence of invasive pneumococcal disease was observed (Kyaw et al., 2002b). Although an increase was also noted between 1999 and 2002, from 261 to 603 cases, this increase was most likely due to the introduction of the enhanced surveillance scheme rather than a true increase in disease. The prevalent serogroups/types changed slightly from year to year, but the most common in the 4-year period were serogroups/types 14, 9, 6, 19, 23, 4, 8, 3, 1, 7 and 18. This is only slightly different from the serogroup/type incidence reported between 1988 and 1999, when the most prevalent serogroups/types were 14, 9, 19, 6, 23, 1, 3, 4, 7, 8 and 18 (Kyaw et al., 2000). Our data does not provide full serotype-specific information so it is difficult to draw conclusions on the coverage that would be provided by new Pnc vaccines. However, if the assumption is made that a proportion of pneumococcal serogroups in Scotland contain serotypes represented in the new Pnc vaccines, then most serogroups/types in Scotland would be represented in the 7-valent Pnc vaccine. However, serotype 3 (the eighth most common serotype) is only represented in the 11-valent Pnc vaccine and serotype 1 (the ninth most common serotype) is only represented in the 9- and 11-valent Pnc vaccines. Importantly, serotypes 7 and 8 are not represented in the 7-, 9- or 11-valent Pnc vaccines.

There is relatively little antibiotic resistance amongst Scottish pneumococci causing invasive disease. There was no recorded penicillin resistance in this study, although a small percentage was intermediately resistant. The incidence reported in this study is lower than that previously reported in Scotland and again may be due to the improved data now available through the enhanced surveillance scheme. Erythromycin resistance is not uncommon amongst invasive pneumococci in the UK and was observed at levels of 18.7, 11.1, 14.3 and 5.1 % for 1999, 2000, 2001 and 2002, respectively. It is not known why there was less erythromycin resistance during 2002, as preliminary data from 2003 suggests a resistance level of around 12 %. This is particularly interesting as the incidence of invasive serotype 14 pneumococci remained at around 20 % between 1999 and 2002.
**Fig. 1.** Serogroups/types of invasive *S. pneumoniae* in Scotland during 1999 (a), 2000 (b), 2001 (c) and 2002 (d).
Fig. 2. Penicillin, erythromycin and ciprofloxacin MICs against invasive S. pneumoniiae in Scotland during 1999 (a), 2000 (b), 2001 (c) and 2002 (d). Black bars, penicillin; grey bars, erythromycin; white bars, ciprofloxacin.

Antibiotic MIC (mg l−1)
Our laboratory data confirm the on-going public health burden of invasive pneumococcal disease in Scotland and provide an initial insight into the current incidence of serogroups/types and antibiotic susceptibility. Full serotyping and multi-locus sequence typing is now performed as part of the enhanced surveillance scheme and will help improve our understanding of the incidence of certain pneumococcal clones circulating in Scotland, as well as help clarify the relationship between serotype and sequence type. The availability of such data is essential prior to and after the introduction of Pnc vaccines and requires continued enhanced surveillance.

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References


