ABSTRACT

Background: The Canadian Bacterial Surveillance Network (CBSN) is a network of Canadian clinical laboratories across Canada with a central repository in Toronto. Since amoxicillin remains essential in the treatment of SPN infections, we looked at the impact of amoxicillin usage and pneumococcal conjugate vaccine (PCV7) introduction on the rapid emergence of resistance to penicillin.

Methods: SPN isolates submitted to CBSN from 1988-2007 were reviewed (n=25,584). IMS Health Canada provided the total number of antimicrobial prescriptions dispensed in Canadian retail pharmacies and data on use of the pneumococcal conjugate in clinics. SPN MICs were obtained using standard broth microdilution methods per CLSI. Serotypes were determined using pneumococcal antisera (Statens Serum Institut, Copenhagen, DK). Pre-PCV7 era (1995-2001), PCV7 era (2002-5), and post-PCV7 era (2006-2007) AMOXIR SPN isolates were compared by multi-locus sequence typing (MLST) (http://www.mlst.net/).

Results: Between 1988 and 2007 we noted a significant increase in AMOXIR SPN isolates (0 to 3.9%, p < 0.0001, n=174). β-lactam usage pre-PCV7 remained above 300 prescriptions per 1000 persons. Serotyping demonstrated that while the majority of post-PCV7 AMOXIR SPN continue to be 19F (pre-PCV7 55.6%, post-PCV7 48%), serotype 19A (pre-PCV7 0%, post-PCV7 42%) is an emerging contributor to rising AMOXIR. MLST of a subset AMOXIR 19A post-PCV7 identified clonal complex (CC) 320 as dominant serotype (100%, n=17). Pre-PCV7 AMOXIR 19A were not present. Instead pre-PCV7 AMOXIR SPN CC320 was found amongst serotype 19F (100%, n=12). We are characterizing the genetic event that led to putative capsular switch from CC320 19F to 19A.

Conclusions: We hypothesize that drug selection pressure exerted on AMOXIR CC320 19F pre-PCV7 sustained its presence in Canada. During the PCV7 era immune selection pressure likely drove a capsular switch resulting in AMOXIR CC320 19A emergence post-PCV7. The propensity for vaccine escape of genetically labile organisms like SPN should be taken into account when designing vaccine strategies.

RESULTS

A total of 25,584 Streptococcus pneumoniae isolates from the Canadian Bacterial Surveillance Network database (1988-2007) were available for study, from which multi-drug resistant serotype 19A and amoxicillin-resistant 19F isolates from pre-PCV7 era (1995-2001), PCV7 era (2002-2005), and post-PCV7 era (2006-2007) were taken. MICs were obtained by standard CLSI broth microdilution methods and serotypes were determined using pneumococcal antisera. Genotyping was performed by multi-locus sequence typing (MLST) as previously described. IMS Health Canada provided total number of antimicrobial prescriptions from retail pharmacies and data on PCV7 use in clinics.

METHODS

BACKGROUND

S. pneumoniae is the leading cause of acute otitis media, sinusitis, and bacterial pneumonia in children. Invasive pneumococcal disease (IPD) leads to sepsis, bacteremia and meningitis and is most common in infants (28 cases per 100,000 population per year), elderly and immunocompromised (13.3 cases/year)1.

The haemophilus influenzae conjugate vaccine Prevenar (PCV, Wyeth-Ayerst) was introduced to provincial universal vaccination programs between 2002-2005. PCV7 protects against 7 of the 9 pneumococcal serotypes [4, 6b, 9V, 14, 18C, 19F, and 23F].

Following PCV7 introduction in Canada the incidence of pneumococcal disease cause by PCV7 serotypes decreased significantly. However, disease caused by non-vaccine serotypes such as 19A significantly increased in the post-PCV7 era2.

Taiwan 19F-14 is a penicillin-resistant pandemic strain that spread globally in the pre-PCV7 era, and belongs to a family of closely related S. pneumoniae genotypes called clonal complex (CC)320.

OBJECTIVE: To characterize the epidemiological and genetic events that contributed to the increase in amoxicillin-resistant S. pneumoniae serotype 19A following introduction of the haemophilus influenzae conjugate vaccine, PCV7.

REFERENCES & ACKNOWLEDGEMENTS

