Epidemiology of bacterial meningitis in the USA from 1997 to 2010: a population-based observational study

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Summary

Background **Bacterial meningitis continues to be a substantial cause of morbidity and mortality, but the epidemiological trends after adjunctive dexamethasone recommendations are unknown in the USA. We aimed to describe the changing patterns among the most common bacterial causes in the USA after conjugate vaccination and to assess the association between adjunctive dexamethasone and mortality.**

Methods **For this population-based observational study, we searched information available from hospital discharges about incidence and inpatient mortality for the most important causes of community and nosocomial bacterial meningitis based on International Classification of Diseases coding across all hospitals in the USA between 1997 and 2010 with the HealthCare Cost Utilization Project (HCUP) network database. We calculated incidences according to US Census Bureau data and used a negative binomial regression model to evaluate the significance of changes over time. We assessed mortality from pneumococcus for three periods 1997–2001 (baseline), 2002–04 (transition years), and 2005–08 (after corticosteroid recommendations were available).**

Findings ***Streptococcus pneumoniae*** **incidence fell from 0·8 per 100 000 people in 1997, to 0·3 per 100 000 people by the end of 2010 (RR 0·3737, 95% CI 0·1825–0·7656). Mortality from pneumococcal meningitis decreased between 2005 (0·049 per 100 000 people) and 2008 (0·024 per 100 000 people) compared with between 2002 (0·073 per 100 000 people) and 2004 (0·063 per 100 000 people; RR 0·5720, 95% CI 0·4303–0·7582). The incidence of** ***Neisseria meningitidis*** **infection decreased from 0·721 per 100 000 people in 1997, to 0·123 per 100 000 people in 2010 (RR 0·1386, 95% CI 0·048–0·4284), which has placed this pathogen close to common bacterial causes of nosocomial meningitis such as staphylococcus and Gram-negative bacteria and to** ***Haemophilus influenzae*****.**

Interpretation ***S pneumoniae*** **continues to be the leading identifiable cause of bacterial meningitis in the USA, but with a significant decrease in incidence and mortality associated with the introduction of conjugated vaccines and a mortality decrease that is associated with the introduction of recommendations for use of adjunctive dexamethasone for pneumococcal meningitis.**

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Introduction

Bacterial meningitis continues to cause substantial neurological morbidity and mortality worldwide. The epidemiology of bacterial meningitis continues to shift with the ongoing introduction of conjugate vaccines for the most common meningeal pathogens.[1,2] *Streptococcus pneumoniae* remains the leading cause of bacterial meningitis and is associated with a 30% mortality rate.[2,3] Besides timely antibiotic treatment, only adjunctive dexamethasone decreases pneumococcal meningitis mortality in adults.[4] The addition of adjunctive dexamethasone to antibiotic treatment in bacterial meningitis was endorsed by the Infectious Diseases Society of America (IDSA) guidelines in 2004 and has now become routine practice.[5] Nationwide implementation of adjunctive dexamethasone in the Netherlands was associated with a 20–30% decrease in mortality of cases of pneumococcal meningitis.[6] The effect of adjunctive dexamethasone in the mortality of patients with bacterial meningitis in the USA is unknown. The objective of our study was to assess the temporal association between conjugate vaccine introduction of pneumococcal seven-valent conjugate vaccine (PCV7) in 2000 and the meningococcal conjugate vaccine (MCV4) introduced in 2005, the trends of the most important community-acquired and nosocomial meningeal pathogens in the USA from 1997 to 2010, and to explore whether the introduction of adjunctive dexamethasone was associated with a decrease of mortality from pneumococcal meningitis.

Methods

Data source

We searched information available for all principal diagnoses including bacterial meningitis based on International Classification of Diseases (ICD) 9 coding across the USA during 14 years between 1997 and 2010 with the Agency for Healthcare Research and Quality National Inpatient Sample database (NIS), which is part of the Healthcare Cost and Utilization Project (HCUP) network. The HCUP-network national inpatient sample is the largest publicly available inpatient care database in the USA and is a free online query system that provides access to health statistics and information about hospital

inpatient and emergency department use across the USA since 1988. The database contains data from roughly 8 million hospital stays each year from about 1000 hospitals and is designed to be a representative cross-section of institutions comprising about 20% of the US community hospitals including public hospitals, academic medical centres, and specialty hospitals such as obstetrics and gynaecology, ear, nose, and throat, orthopaedic, and paediatric institutions (appendix). The database is based on statewide data collected by individual state and private data organisations, hospital associations, and the federal government.

See Online for appendix

Procedures

We obtained information from the NIS database starting from 1997 until 2010 because this was when the greatest number of states was represented (22 in 1997 and 46 states included in 2010; appendix) and statistics on the specific diagnosis of bacterial meningitis per organism were available since 1997. After an initial analysis, we excluded all causes that did not have a specific ICD code 9 or if data were incomplete for the years included in the study. We calculated mortality, incidence, routine discharge, home health care, length of stay, and charges for admission to hospital for bacterial meningitis caused by specified pathogens if this information was available.

Statistical analyses

We calculated all rates by dividing the annual rate of hospitalisation and mortality by the annual population of the USA according to the US Census Bureau with rates expressed as hospitalisation and mortality per 100 000 people. To assess the changes in the meningitis incidence rate, we analysed the differences between the first and the last years of the study with NIS data. We also assessed annual meningitis hospitalisation rates from 1997–2010 by age group (age <1 year, 1–17 years, 18–44 years, 45–64 years, 65–85 years, and >85 years) for pneumococcal and meningococcal meningitis that were adjusted for specific denominators per age group based on US Census Bureau information. To assess the changes in mortality rate from pneumococcus, we divided the available information into three periods: 1997–2001 (baseline), 2002–04 (transition years; because this was the period of time when the first evidence of corticosteroids affecting pneumococcal meningitis mortality appeared in 2002 and when guidelines made this recommendation widely available in 2004), and 2005–08 (after corticosteroid recommendations). To estimate the effect of corticosteroids, we calculated the average weighted pneumococcal mortality rates for the baseline years and for the years after the recommendation of corticosteroids. All analyses were done with SAS 9.3 (SAS Institute) assuming statistical significance at $p<0·05$. We did a negative binomial regression model to assess the significance of rate changes across time.[7,8] Hospitalisation charges were adjusted for the USA inflation index from 1997 until 2010 and also accounted for the number of discharges in the NIS, weighted for national estimates changes from 1997 until 2010 (appendix).

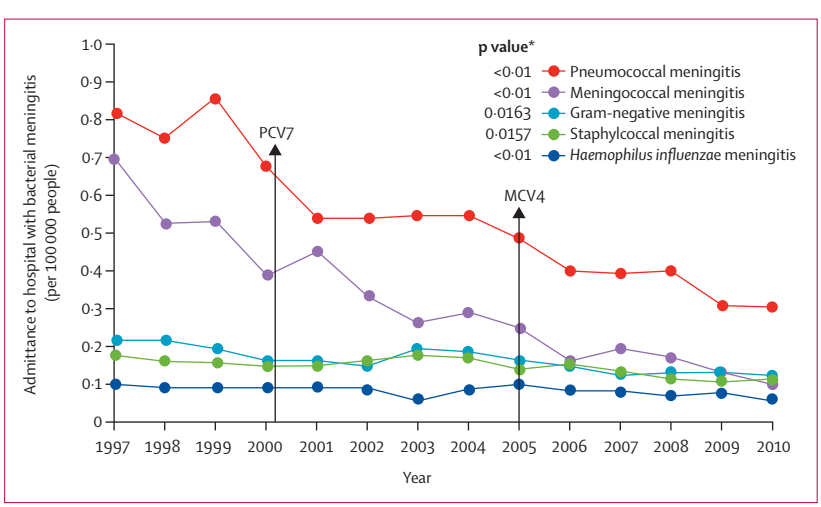

Figure 1: **Meningitis trends for different bacteria, 1997–2010**
Case estimation based on total number of cases per 100 000 people by International Classification of Diseases code (320·0, 320·1, 320·3, 320·82, and 036) from hospital discharges across the USA with the nationwide inpatient sample Healthcare Cost and Utilization Project net database. *p values calculated on the basis of the comparison between 1997 and 2010.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Incidence of admittance to hospital due to bacterial meningitis was available in the NIS for 50 822 cases reported from 1997 to 2010 for five of the most commonly identified bacterial pathogens: *S pneumoniae, Neisseria meningitidis, Haemophilus influenzae,* staphylococcus species, and Gram-negative bacteria (figure 1). The most common identifiable bacterial pathogen was *S pneumoniae,* with 21 858 cases and an incidence rate of 0·306 per 100 000 people (95% CI 0·250–0·374) by the end of 2010. *N meningitidis* accounted for 12 833 cases and an incidence rate of 0·123 per 100 000 people (0·082–0·185) in 2010. During these 14 years, 3404 cases of *H influenzae* meningitis were reported with a rate of 0·058 per 100 000 people (0·036–0·071) by the end of 2010. *H influenzae* has now been displaced as one of the most common causes of meningitis by other bacterial causes such as staphylococcal species (6031 cases) and Gram-negative bacteria (6696 cases) between 1997 and 2010 with an incidence rate of 0·114 per 100 000 people (95% CI 0·086–0·142) for staphylococcal species and 0·127 per 100 000 (95% CI 0·094–0·168) for Gram-negative bacteria, in 2010 (figure 1).