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ORIGINAL ARTICLE

Invasive meningococcal disease in Navarra in the era of a meningococcal C vaccine☆

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Meningococcal disease;
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Abstract
Introduction: Systematic childhood vaccination against meningococcus C has had a considerable impact on meningococcal invasive disease (MID). The aim of this study is to perform an analysis on the epidemiology, the clinical features, and the factors associated with a worse prognosis of MID, in the era of a meningococcal C vaccine.
Material and methods: The study included confirmed cases of MID in children less than 15 years of age in Navarra, Spain, between 2008 and 2014. The risk of death or permanent sequelae was evaluated according to the presence of clinical features and analytical parameters at diagnosis.
Results: The average annual incidence was 7.9 cases per 100 000 children, with the highest attack rate in children <1 year. Of 53 cases analysed, 87% were due to meningococcus B. Fever (100%), rash (91%), and elevation of procalcitonin (94%) were the most frequent findings at diagnosis. Some sign of shock was observed in 70% upon arrival at the hospital. The case-fatality rate was 3.8% and 10% survived with permanent sequelae. Glasgow coma scale <15 (odds ratio [OR] = 9.2), seizure (OR = 8.3), sepsis without meningitis (OR = 9.1), thrombocytopenia (OR = 30.5), and disseminated intravascular coagulation (OR = 10.9) showed a greater association with a worse prognosis.
Conclusion: The MID continues to be a significant cause of morbidity and mortality in children. Therefore, new advances are needed in the prevention, early diagnosis, and detection of the factors associated with poor prognosis.

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PALABRAS CLAVE
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Enfermedad meningocócica invasiva en Navarra en la era de la vacuna conjugada antimeningocócica C

Resumen
Introducción: La vacunación sistemática infantil frente al meningococo C ha tenido un impacto considerable en la enfermedad meningocócica invasiva (EMI). El objetivo de este estudio es analizar la epidemiología, las manifestaciones clínicas y los factores asociados a un peor pronóstico de la EMI en la era de la vacuna antimeningocócica C.
Material y métodos: Se analizaron los casos de EMI confirmados en menores de 15 años diagnosticados en Navarra entre 2008 y 2014, y se evaluó el riesgo de muerte o secuelas permanentes, según la presencia de determinados hallazgos clínicos o analíticos al diagnóstico.
Resultados: La incidencia media anual fue 7,9 casos por 100.000 niños, con mayor tasa de ataque en niños < 1 año. De 53 casos analizados, el 87% fueron por meningococo B. Fiebre (100%), exantema (91%) y elevación de la procalcitonina (94%) fueron los hallazgos más frecuentes al diagnóstico. El 70% de los casos presentaba algún signo de shock a su llegada al hospital. La letalidad fue del 3,8% y un 10% sobrevivió con secuelas permanentes. Una puntuación en la escala de coma de Glasgow < 15 (odds ratio [OR] = 9,2), convulsión (OR = 8,3), sepsis sin meningitis (OR = 9,1), trombocitopenia (OR = 30,5) y coagulación intravascular diseminada (OR = 10,9) se asociaron con un peor pronóstico.
Conclusión: La EMI continúa causando una morbimortalidad importante en la población infantil, por lo que sigue siendo necesario avanzar en su prevención, en su diagnóstico temprano y en reconocer los factores asociados a mal pronóstico.

Introduction

Invasive meningococcal disease (IMD), caused by the bacterium *Neisseria meningitidis* (*N. meningitidis*, known as meningococcus), is a severe infection that primarily affects young children.[1–4]

In Spain, the inclusion of the conjugate vaccine against group C meningococcus (MenC) in the routine immunisation schedule in 2001 was followed by a decline in the incidence of IMD, which was down to approximately 0.8 cases per 100 000 inhabitants per year by 2012–2013.[5] However, compared to other transmissible infectious diseases, it still is a considerable social, health care and economic burden and remains a top health priority.[6,7]

Invasive meningococcal disease typically manifests with acute sepsis and/or meningitis that may result in death within a few hours.[2] In Spain, despite adequate treatment, its associated mortality is 10%, and 10%–20% of survivors experience sequelae.[8,9]

Invasive meningococcal disease poses a challenge to clinicians due to the difficulty of early diagnosis in some patients and to the complexity of the care required by the most severe cases. The initial signs and symptoms are often nonspecific, especially in infants,[10] which complicates differential diagnosis.[11,12] Early administration of antibiotics and initiation of life support are the cornerstones of treatment.[7,13,14] In IMD, early identification of patients at risk of having a poor outcome from the first contact with primary care is of vital importance,[12] as early treatment and transfer to intensive care is associated with increased survival and a decreased incidence of sequelae.[15] To this end, several predictors of severity have been proposed.[16]

The aim of our study was to explore the epidemiology and clinical characteristics of IMD in the paediatric population of Navarra in the age of universal vaccination against meningococcus C, and to identify the clinical and laboratory findings at diagnosis that are associated with a poor prognosis.

Materials and methods

We conducted a retrospective study between 2008 and 2014, a period in which the routine immunisation against meningococcus C was well established that we considered to be long enough to reflect the current situation of IMD. The population under study included every child aged less than 15 years residing in Navarra, which amounted to approximately 95 500 inhabitants. We defined a case as any patient aged less than 15 years with clinical manifestations compatible with IMD and with microbiological confirmation of *N. meningitidis* in blood or cerebrospinal fluid (CSF) samples (isolation in culture, DNA detection by polymerase chain reaction, or antigen detection by immunoassay).

We obtained the epidemiological and microbiological data of all cases from the active IMD surveillance system records included in the Register of Notifiable Diseases of Navarra. We completed this information with data from medical records in 46 cases.

We calculated the incidence of IMD using the population size recorded in the census on January 1 for each