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ScienceDirect
Vaccine 25 (2007) 7233–7237
Vaccine
www.elsevier.com/locate/vaccine

Age-specific seroprevalence of serogroup C meningococcal serum bactericidal antibody activity and serogroup A, C, W135 and Y-specific IgG concentrations in the Turkish population during 2005

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Received 8 August 2006; received in revised form 7 March 2007; accepted 13 July 2007
Available online 1 August 2007

Abstract

Like many other developing countries; there is no accurate information about the antibody levels against *Neisseria meningitidis* in Turkey. We collected serum samples from four health centers located in different geographic regions and stratified according to age in order to obtain a baseline seroprevalence of protective antibodies to meningococcal serogroup C and provide data on seroprevalence of IgG antibodies to serogroups A, C, W135 and Y. Sera were tested for serum bactericidal antibodies (SBA) to serogroup C meningococci using rabbit serum as the complement source and by a bead based assay for serogroup A, C, W135 and Y-specific IgG. It was observed that 30% and 12% of individuals within the study population had SBA titers of $\geq$8 and $\geq$128, respectively. Overall; at least 70% of the population are susceptible (SBA titer <8) to meningococcal serogroup C disease. The rate of susceptibility was highest in infants aged 7–12 months and young children (1–4 years). Regardless of age, for serogroup A, C, W135 and Y, 60.5%, 27.2%, 12.3% and 19.2% of subjects, respectively, had serogroup-specific IgG concentrations $\geq$2 μg/mL. These data highlight that a large proportion of the Turkish population are susceptible to serogroups C, W135 and Y and should be considered, along with serogroup-specific disease incidence data, in future decisions on possible meningococcal vaccination programmes.

Keywords: Meningococcal; Serum bactericidal antibody; Seroprevalence

1. Introduction

Disease due to *Neisseria menigitidis* infection remains a global problem. Meningococci are classified into 13 different serogroups based on capsular polysaccharide structure, but serogroups A, B, C, W135 and Y account for the majority of disease [1]. Epidemics of meningococcal disease occur in sub-Saharn Africa, in a region known as the meningitis belt. These epidemics are mainly due to serogroup A whereas serogroups B and C cause endemic disease in Europe and North America. An increase in incidence of serogroup Y in the USA has recently been observed [2]. Outbreaks have also been associated with the Hajj pilgrimage, traditionally due to serogroup A, but more recently in 2000 and 2001 outbreaks due to serogroup W135 occurred [3,4].

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doi:10.1016/j.vaccine.2007.07.019

There are limited epidemiologic data on the incidence of meningococcal disease and serogroup distribution in Turkey. In 1990, a study reported a total meningococcal carriage rate of 28%, with serogroup C the most frequent serogroup identified [5]. The *N. meningitidis* carriage rate among primary school children in Turkey has been reported as 6.2% with serogroups A, B and C identified as the dominant serogroups [6]. In 2004, 624 cases of meningococcal disease were reported to the Ministry of Health in Turkey, but no data are available on the serogroup distribution except for 6 cases that were reported to be serogroup W135 [7,8].

The World Health Organisation (WHO) recommended serosurveillance studies representing the country population before the decision to use meningococcal vaccines [9].

The determination of serum bactericidal antibody (SBA) is regarded as the surrogate of protection for serogroup C [10,11]. A SBA titer ≥4 or ≥8, using either human or baby rabbit, respectively as a source of exogenous complement, have been established as the protective SBA level for serogroup C and have been previously used to analyze serosurveillance data [10,12–14]. These earlier studies demonstrated an age-dependent acquisition of protective SBA which inversely correlated with meningococcal serogroup C disease incidence.

The objective of this study was to measure serogroup C SBA titers in a representative cross-section of the Turkish population to determine the susceptibility of individuals in different age groups to serogroup C meningococcal disease and provide a baseline seroprevalence of serogroup C SBA and serogroup A, C, W135 and Y-specific IgG.

2. Materials and methods

2.1. Study design

Three geographical regions, where the majority of the country's population (55%) are located and where the inhabitants are representative of the socioeconomical and ethnicity of Turkey, were selected for the study. Twenty-eight of the largest health centers of these regions were evaluated and a unique number was given to each center. Four hospitals were then selected from a table of random numbers.

During a 3-month period beginning from April 1 2005, a total of 1629 serum specimens were collected for the national vaccine preventable diseases surveillance programme in Turkey. Sera were stored at −20 °C until sending to the central laboratory at Hacettepe University, Medical School, Department of Pediatric Infectious Diseases, Ankara, Turkey where they were anonymized and stored at −80 °C. Fifty sera from each of seven different age groups were selected by simple random sampling. A total of 350 serum samples were sent to Vaccine Evaluation Unit, Health Protection Agency North West, Manchester, United Kingdom for SBA determination and detection of serogroup-specific IgG. Three hundred twenty nine were available for SBA determination and 349 available for detection of serogroup-specific IgG. Seven different age groups, 0–6 months, 7–12 months, 1–4 years, 5–14 years, 15–24 years, 25–39 years and ≥40 years were analyzed with 46, 47, 46, 50, 47, 46, and 47 results available in each age group, respectively for SBA and 50 results available for serogroup A, C, W135 and Y in each age group, except for 15 to 24 years olds where 49 were available.

2.2. Serologic assays

Sera were tested using standardized complement-mediated SBA against *O*-acetylated serogroup C strain C11 (phenotype C:16:P1.7) as described by Maslanka et al. [15] at the Meningococcal Reference Unit, Health Protection Agency North West Laboratory, Manchester Royal Infirmary, Manchester, UK. The complement source was pooled 3–4-week-old baby rabbit serum (Pelfreeze Biologicals, WI, USA). SBA titers were expressed as the reciprocal of the final serum dilution giving ≥50% killing at 60 min. SBA titers of <4 were assigned a value of 2 for computational purposes. A positive control serum with an assigned serogroup C titer was included to quality control the assay.

Meningococcal serogroup-specific immunoglobulin G (IgG) levels were quantified using a tetraplex immunoglobulin bead assay [16]. *N. meningitidis* capsular polysaccharides; serogroup A (NIBSC code 98/730), serogroup C (NIBSC code 98/730), serogroup Y (NIBSC code 01/426), and serogroup W-135 (NIBSC code 01/428) obtained from National Institute for Biological Standards and Control (NIBSC; Potters Bar, United Kingdom) were conjugated to carboxylated microspheres (Luminex Corp.; Austin, Texas). Seven fourfold dilutions (1:20 to 1:81,920) of standard reference serum sample CDC 1992 (NIBSC code 99/706; obtained from 14 adults who had received one dose of meningococcal A, C, Y, and W-135 polysaccharide vaccine) were utilized in the assay. All results were read on a Bio-plex reader (Bio-Rad, Hemel Hempstead, United Kingdom) and a computer software package (Bio-plex Manager; Bio-Rad) was used for analysis. The calibration factors of the standard CDC1992 serum were 91.8, 24.1, 25.23 and 28.92 μg/mL for serogroups A, C, W135 and Y, respectively [17,18]. Two positive control samples were included to quality control the tetraplex assay.

2.3. Statistical analysis

Geometric mean SBA titers and 95% confidence intervals were calculated for each age group. SBA data were categorised as follows: <8, 8–64 and ≥128 and the percentage of individuals within each age group calculated. A chi-squared test was used to assess the change in proportions with age. The proportion with serogroup-specific IgG antibody ≥2 μg/mL and the geometric mean concentration was calculated overall and within each age group along with 95% confidence intervals (CI). For proportions exact 95% confidence intervals were used. The SBA titers for individuals were compared to