Short Communication

Impact of meningococcal vaccination with combined serogroups A and C polysaccharide vaccine on carriage of *Neisseria meningitidis* C

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Received 26 March 2002
Accepted 27 August 2002

Two studies of meningococcal carriage state were carried out in Galicia (Spain) before and after a mass vaccination campaign between December 1996 and January 1997 against *Neisseria meningitidis* serogroup C with meningococcal serogroups A and C polysaccharide vaccine. The studies covered two areas with different incidence rates of meningococcal disease in 1996 (high and low incidence). Carriage rates of serogroup C showed a decrease in both areas, 47 and 65 % respectively, before and after the vaccination. Results showed a decrease in carrier state in the age groups 10–14- and 15–19-year-olds, but not in the 5–9-year-olds. These results demonstrate the effect of immunization on the reduction of the carriage state.

INTRODUCTION

In Galicia, a region situated in north-west Spain (population, 2·7 million), meningococcal disease is an endemic disease. During the early part of the 1990s, the approximate incidence rate of meningococcal disease was three cases per 100 000 population, but by 1995/1996, the incidence had risen sharply to 11 cases per 100 000 population. Unlike previous years, when *Neisseria meningitidis* serogroup B was the most frequently isolated serogroup, the increased incidence registered in 1995/1996 was caused by *N. meningitidis* serogroup C (Dirección Xeral de Saúde, 1995). Faced with this situation, the Galician Regional Public Health Authorities looked into different disease prevention and control measures, and eventually decided to conduct a *N. meningitidis* C vaccination campaign, using meningococcal group A and C polysaccharide vaccine and targeting all residents in Galicia aged 18 months to 19 years. The campaign was carried out in the period December 1996–January 1997, with a total of 472 465 vaccinated persons.

In the wake of the vaccination campaign, a marked decline in the incidence of meningococcal disease was observed. By 1998, 1 year after vaccination, the incidence rate had declined from a pre-vaccination figure of 10·42 to 4·3 cases per 100 000 population (Dirección Xeral de Saúde, 1998). At this time, it was decided that, in view of the importance of healthy carriers in the epidemiology of meningococcal disease

(Broome, 1986), a study should be undertaken immediately prior to vaccination, aimed at ascertaining the incidence of carriers of *N. meningitidis* C:2b:P1.2.5 – the strain most frequently isolated during the epidemic period – and studying the relationship between carriage and incidence of meningococcal disease (Fernández *et al.*, 1999). For study purposes, two areas that registered different meningococcal disease incidence were therefore demarcated.

In 1998, 1 year after the vaccination campaign, a new *N. meningitidis* C carriage study was carried out, with the aim of determining any possible differences in carriage prevalence before and after vaccination with meningococcal group A and C polysaccharide vaccine. This paper reports the differences between the above two studies, which covered the segment of the population aged 5–19 years.

METHODS

Population and selection of sample. On the basis of meningococcal disease incidence for the 1995/1996 epidemiological year (week 41, 1995 to week 40, 1996), the pre-vaccination study conducted from December 1996 to January 1997 identified two geographical areas in Galicia, Spain, which were duly denominated high- and low-incidence areas. The study population was selected from one administrative zone in each of these geographical areas, and a stratified two-stage design was then used to obtain the respective pre-vaccination samples in the population aged 2–19 years (Fernández *et al.*, 1999).

In the study conducted 1 year after vaccination (1998), with the same geographical areas and individuals, the age range was 5–19 years. The 2–4 year age group was not included in this second study, owing to the

Abbreviation: CI, confidence interval.

fact that the prevalence of serogroup C carriers reported by the pre-vaccination study was very low and that the possibility of finding differences between the two studies was therefore judged negligible.

Prevalences were calculated with the aid of a ratio estimator, and 95 % confidence intervals obtained. To compare the prevalences reported by the two studies, the variance of the estimators was estimated using the delta method, and a normal-distribution test applied. The samples were weighted to compensate for the different selection probabilities, and the complexity of the design thereby incorporated into the data analysis.

Specimen collection and analysis. Nasopharyngeal specimens were collected by trained staff, plated on Thayer–Martin agar (Oxoid) and, after incubation in 5 % CO₂ at 37 °C for 24 h at regional laboratories, sent to the National Reference Laboratory in Majadahonda, Madrid, Spain, for isolation and identification of strains. Serosubtyping *N. meningitidis* serogroup C was done under the above-described conditions (Fernández *et al.*, 1999).

RESULTS

The approximate total population of 5–19-year-old Galicians is 505 483. The pre-vaccination study analysed 8727 specimens. Prevalence of *N. meningitidis* serogroup C carriers was 1.51 % (95 % CI, 0.92–2.11) in the meningococcal disease high-incidence area and 0.94 % (95 % CI, 0.14–1.74) in the low-incidence area. The meningococcal group A and C polysaccharide vaccination campaign achieved an overall vaccination coverage of 85.02 %, ranging from over 90 % in the 5–9 and 10–14 age groups to around 60 % in the 15–19 age group.

In the post-vaccination study, a total of 5742 specimens was obtained. Prevalence of *N. meningitidis* serogroup C carriers was now 0.79 % (95 % CI, 0.45–1.13) in the meningococcal disease high-incidence area and 0.32 % (95 % CI, 0.04–0.60) in the low-incidence area. The percentage decline observed in prevalence of *N. meningitidis* C was thus 47 % in the high and 65 % in the low-incidence areas. Table 1 shows these results for both studies, with the respective carriage prevalences of *N. meningitidis* serogroup B and C: 2b:P1.2.5 strains for the two incidence areas. The prevalence of other serogroups and non-groupable strains is likewise shown. While the *N. meningitidis* B carriage rate also declined, it was only the decrease in *N. meningitidis* C carriers in the high-incidence

area that proved statistically significant ($P = 0.03$). A statistically significant rise in the carriage rate for other serogroups and non-groupable strains was in evidence in the meningococcal disease high-incidence area. Shown also in Table 1 are the P -values for the differences observed between the studies in the two areas.

A breakdown of serogroup C carriers by age group is depicted in Fig. 1. There was a post-vaccination decline in prevalence of carriers aged 10–14 and 15–19 years in both areas. With the single exception of those in the 15–19 age group in the high-incidence area, the relative decline in all these age groups exceeded 70 %. A slight rise of around 20 % in the 5–9 age group was also noted.

DISCUSSION

In view of the importance of the carrier state in meningococcal disease (Broome, 1986), the effect of meningococcal group A and C polysaccharide vaccine on carrier state has long been regarded as an aspect which merits proper prospective study in the context of meningococcal disease epidemiology (Gotschlich *et al.*, 1969). Although other *N. meningitidis* C carrier studies have also reported a decline in carriage rates, over different periods of time, following vaccination with polysaccharide vaccine (Gotschlich *et al.*, 1969; Stroffolini *et al.*, 1990; Di Martino *et al.*, 1990; Neal *et al.*, 1998), we nevertheless feel that the high number of specimens analysed renders the data yielded by our study of considerable interest.

The decrease in carriers observed among the 10–14 and 15–19 age groups is similar to that observed by Neal *et al.* (1998), yet in this latter study subjects received chemoprophylaxis in addition to vaccine, a factor which could be expected to exert an effect on the reduction in carriers. The slight rise in prevalence observed in the 5–9-year-olds could, in part, be explained by the attenuated effect that polysaccharide vaccine has among the youngest age groups.

Furthermore, the results display no increase in the *N. meningitidis* B carriage rate 1 year after vaccination, which might mean that in this period of time serogroup B had failed

Table 1. *N. meningitidis* carriage rates and p -values for differences in each area

	High-incidence area					Low-incidence area				
	Pre-vacc' ($n = 4004$)		Post-vacc' ($n = 3083$)		P -value	Pre-vacc' ($n = 4723$)		Post-vacc' ($n = 2659$)		P -value
	%	95 % CI	%	95 % CI		%	95 % CI	%	95 % CI	
All <i>N. meningitidis</i>	9.62	7.63–11.60	10.01	8.62–11.39	0.751	8.38	7.08–9.67	6.54	5.20–7.88	0.053
Serogroup C	1.51	0.92–2.11	0.79	0.45–1.13	0.037	0.94	0.14–1.74	0.32	0.04–0.60	0.149
Serogroup B	6.48	4.87–8.08	5.69	4.75–6.62	0.404	5.47	4.68–6.26	4.46	3.37–5.56	0.145
C: 2b:P1.2.5	0.67	0.30–1.04	0.25	0.02–0.48	0.059	0.42	0.00–1.04	0.00	—	0.177
Non-groupable	1.34	0.85–1.83	2.71	2.11–3.31	0.000	1.49	0.98–1.99	1.04	0.25–1.82	0.669
Other serogroups	0.28	0.07–0.49	0.90	0.45–1.36	0.015	0.47	0.09–0.93	0.42	0.17–0.66	0.841

Fig. 1. Pre- (solid bars) and post- (open bars) vaccination *N. meningitidis* serogroup C carriage rates by age group and area.

to replace serogroup C in the asymptomatic nasopharyngeal carriers. The increase in the percentage of non-groupable strains was not the result of down-regulation of capsular expression; genogrouping of these strains by PCR (data not shown) showed a similar proportion of B and C serogroups to the percentage found by conventional methods. Therefore, serogroup C was not over-represented in these non-groupable isolates.

Finally, we feel that, while the effect of the natural evolution of meningococcal infection on carrier state cannot be ruled out, the results of our study must be taken to support the effect of polysaccharide vaccination on *N. meningitidis* C

carrier state, since 1 year after vaccination the decline in prevalence was not only statistically significant but indeed coincided with the decline in disease incidence in the oldest groups among which the effect of vaccination is most marked. In 1996, 1997 and 1998, serogroup C meningococcal disease registered a downward trend, with rates of 14.04, 3.63 and 0.79 cases per 100 000 population, respectively. Broken down by age group, disease incidence declined by 79 % in the 5-9 age group, 91 % in the 10-14 age group and 67 % in the 15-19 age group.

ACKNOWLEDGEMENTS

The authors wish to thank the Galician regional team of epidemiologists and all *Neisseria* Reference Laboratory staff for their assistance in specimen collection and analysis.

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