RESEARCH NOTE

Meningococcal group C disease in Greece during 1993–2006: the impact of an unofficial single-dose vaccination scheme adopted by most paediatricians

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ABSTRACT

The aim of this study was to evaluate the impact of the meningococcal C conjugate vaccine on the epidemiology of meningococcal C disease in Greece. Data from the National Reference Laboratory for Meningococcal Disease and a questionnaire distributed to Greek paediatricians were assessed. Since the introduction of the vaccine in 2001, 72% of Greek paediatricians have administered it as one single dose to patients aged ≥12 months. This vaccination scheme has probably contributed to a dramatic decrease in the number of meningococcal C infections, which reached zero in 2004.

Keywords Conjugate vaccine, epidemiology, Greece, meningococcal C disease, *Neisseria meningitidis*, vaccination strategy

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International concern regarding meningococcal disease has always been significant because of the accompanying high mortality and possible long-term sequelae. In Greece, sporadic use of the polysaccharide vaccine against meningococci belonging to groups A and C did not halt the four-fold rise in cases of meningococcal disease, caused predominantly by serogroup C meningococcus (clone C:2a:P1.5), during 1996–1998 [1] (National Reference Laboratory for Meningococcal Disease, unpublished data). Although it is not yet included in the official vaccination schedule, Greek paediatricians have subsequently been administering the meningococcal C (Men-C) conjugate vaccine since its introduction in January 2001. The present study concerned the entire paediatric population aged ≤15 years in Greece between January 1993 and June 2006. The 0.5-mL Men-C vaccine contains 10 μg of *Neisseria meningitidis* C (serotype C11) oligosaccharide, conjugated with either CRM197 *Corynebacterium diphtheriae* protein (Wyeth, Madison, NJ, USA) or with tetanus toxoid (Baxter Vaccines, Wein, Austria). The study was approved by the ethics committee of the P & A Kyriakou Children's Hospital, Athens, Greece.

A questionnaire focusing on Men-C vaccination practice was distributed to 493 paediatricians. In total, 348 responses were received; 65.1% of responders answered the questionnaire during three successive nationwide conferences, while the remaining responders were distributed randomly throughout the country. In total, 70.8% of responders were practising in the two largest cities (Athens and Thessalonica). Interpretation of data was based on the following assumptions: (i) that all children have visited a paediatrician at least once; (ii) that the number of children each paediatrician followed-up was the same; and (iii) that all paediatricians completed the questionnaire accurately. However, although interpretation of questionnaire data would be impossible without the assumption that the number of children each paediatrician followed-up was the same, this may not be realistic.

The number of vaccine doses sold, which was obtained from a national statistical surveillance programme and the suppliers' logistics departments, together with the number of live births, were used to determine a rough estimate of vaccination coverage. Problems concerning the use of vaccine sales data as a surrogate marker were taken into consideration, including a failure to use the vaccine (which was the most frequent reason), an ineffective vaccine, or an erroneous route of administration.

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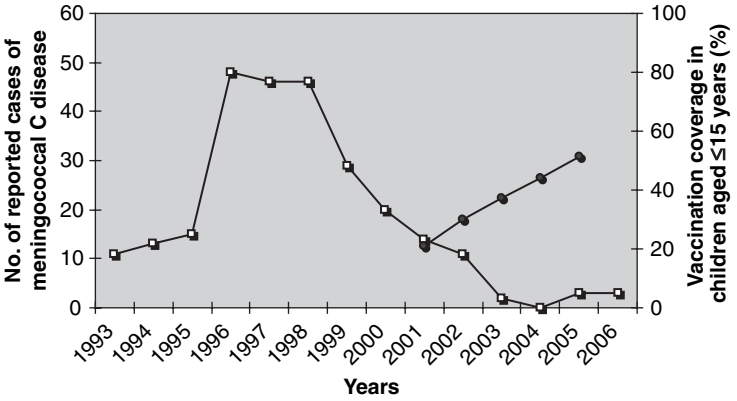

Fig.1. Cases of meningococcal C disease in Greece (squares) between January 1993 and May 2006, and vaccination coverage (circles) of children aged 0–15 years since the introduction of the Men-C vaccine in 2001.

All statistical tests for normality were conducted with the Shapiro–Wilk test, while median comparisons of independent samples were performed with the Mann–Whitney test. All statistical values were considered significant at $p \leq 0.05$.

All paediatricians questioned confirmed administration of the conjugate vaccine. There was no statistically significant difference in vaccination practice among paediatricians in Athens and the rest of the country. The preferred regimen of 72.0% of paediatricians was to give a single dose at an age of ≥12 months. The age at which the vaccine was administered varied from 2 months to a maximum of 24 months, and vaccination coverage for this specific age group was almost 100%. Each year, vaccinated children were added to the pool aged ≤15 years, while unvaccinated children were excluded. Therefore, vaccination coverage rose from an estimated 20.7% in 2001 to 51.4% of the total Greek paediatric population (n = 1.5 million) in 2005 (Fig. 1).

In 1996–1998, i.e., before the introduction of the conjugate vaccines, there was an increase in meningococcal C cases [1]. Between 1999 and 2001, a decline in cases to pre-1996–1998 levels was observed, with a further decrease being observed in 2002 after the introduction of the Men-C vaccine. No cases of meningococcal C infection were reported during 2004, although there were three cases in 2005, and four cases in the first 6 months of 2006. The proportion of meningitis cases caused by serotypes B, A, W135 and Y changed, and while serogroup B predominated, the A serotype became the second most frequent [2] (National Reference Laboratory for Meningococcal disease, unpublished data) (Table 1). After 1998, serogroup C disease decreased, probably as a result of herd immunity that developed after the circulation of the epidemic clone in the community in previous years. The introduction of the conjugate vaccine during 2001 was followed by almost complete elimination of serogroup C disease from the

Table 1. Distribution of meningococcal serogroups between 1993 and 2004 (data collected from the National Meningococcal Reference Laboratory, Athens, Greece)

		Serogroup									
		B		C		A		W-135 and Y		NG	
Year	No. of specimens	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
1993	29	14	48.3	11	37.3	0		0		5	17.2
1994	30	16	53.3	13	43.4	0		0		1	3.4
1995	32	16	50.0	15	46.9	1	3.1	0		0	
1996	88	25	28.4	48	54.5	0		6	6.8	7	7.9
1997	72	25	34.7	46	63.9	1	1.4	0		0	
1998	109	49	44.9	46	42.2	5	4.6	3	2.8	6	5.5
1999	127	70	55.1	29	22.8	6	4.7	3	2.3	19	15.0
2000	161	80	49.6	20	12.4	9	5.6	15	9.3	37	23.0
2001	158	69	43.7	14	8.9	31	19.6	11	7.0	33	20.9
2002	174	75	43.1	11	6.3	19	10.9	20	11.5	49	28.1
2003	101	53	52.5	2	2.0	17	16.8	6	5.9	23	22.8
2004	63	43	68.2	0		3	4.8	0		17	27.0

NG, not grouped.

population studied. Although this reduction may be the result of a natural variation in meningococcal disease epidemiology, it is likely that the introduction of vaccine contributed considerably to the reduction.

In France, a vaccination campaign triggered by a rapid increase in cases of serogroup C disease resulted in no new cases [3], while surveillance following the introduction of the vaccine in Spain revealed a reduction in the incidence of serogroup C disease [4]. In locations where recent outbreaks have been reported, e.g., Quebec, Canada, an expanded vaccination strategy might be needed [5]. In the UK, although there has been a reduction of up to 86.7% in the number of cases of meningococcal C disease, a decline in the number of related deaths (67 in 1999; five in 2001) and a 66.0% reduction in the carriage of serogroup C meningococci in the 1-year period following the introduction of the Men-C vaccine [6,7], predictive models suggested the need for catch-up campaigns to induce herd immunity [8]. Although the long-term effectiveness of the vaccine is being studied, accumulated data suggest that a booster dose may be needed [9,10]. The UK Department of Health will change the timing of the three doses of the Men-C vaccine from ages 2, 3 and 4 months to ages 3 and 4 months, with a booster at 12 months, as the protection offered by the original dosage scheme wanes 1 year after the last dose (http://www.dh.gov.uk/PublicationsAndStatistics/PressReleases/PressReleasesNotices/fs/en?CONTENT_ID = 4128036&chk = PI8e57). Immunisation of infants aged ≥1 year is less costly than administration of two or three doses during the first year of life, and was shown in the present study to contribute effectively to disease control. Further enhanced surveillance of meningococcal disease is required to evaluate the effectiveness of the vaccine when administered at this age.

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