ORIGINAL ARTICLE

Preventable infectious diseases using vaccination in developmental age in the Province of Frosinone, Italy

E. LANGIANO, L. LANNI, M. FERRARA, P. ATREI, G. MARTELLUCCI*, E. DE VITO
Department of Motor Sciences and Health, University of Cassino, Italy; * Local Health Agency Frosinone, Lazio Region, Italy

Key words

Statutory notifications • Vaccine preventable diseases • Epidemiology

Summary

Introduction. *A study has been made of the behaviour of preventable infectious diseases by means of vaccination in the developmental age, reported between 1995 and 2003, in the area of Frosinone and Province, Italy.*
Results. *Analysis of the distribution of the 185 cases of hepatitis B notified, demonstrates that the mean age has increased from 26.5 to 41.1 years. Notifications of invasive diseases due to haemophilus influenzae type b (Hib) refer exclusively to 13 cases of meningitis. As far as concerns pertussis, 119 cases have been reported (median age 4.0 years, mode 1.0). Overall 850 cases of measles were reported (median age 7.0 years, mode 5.0), the highest number being recorded in 1997 (349 cases: median age 7.0 years, mode 5.0) and 2002 (199 cases: median age 8.0 years, mode 8.0). Rubella occurred in 411 cases (median age 12.0 years, mode 11.0), with 53.3% involving females. As far as concerns mumps, the last peak of the epidemic occurred in 2001 (median age 7.0 years, mode 6.0) with 137 cases.*
Discussion and conclusion. *Results emerging from the study demonstrate a reduction in time in the number of notifications for almost all the diseases under consideration.*
The distribution of the cases of rubella in fertile females, in 2002, stresses the need to promote campaigns in order to recuperate still-susceptible women of childbearing age. The cases of hepatitis B, pertussis and meningitis due to Hib confirm the high rate of protection resulting from vaccination.
The incidence rates of measles, mumps, rubella and pertussis when compared with those of the paediatric sentinel surveillance system (SPES) clearly demonstrate not only that these are underestimated but also reveal controversial findings with respect to data provided by Infectious Diseases Italian Surveillance System (SIMI).

Introduction

In Italy, the epidemiology of infectious diseases, typical of infancy, has undergone great changes due to the better living conditions and health care, but above all following the introduction of vaccination [1].
These diseases, in fact, whilst no longer representing, in our area, a fundamental health problem of importance, are still included amongst the avoidable causes of death and to be aware of their effective behaviour and distribution, besides indicating the state of health of the population, is essential in order to be able to effectively combat them.
Aim of the present study was to analyse the course of infectious diseases, preventable by means of vaccinations in the developmental age reported between 1995 and 2003 in the area surrounding the town of Frosinone and Province, and to compare the data related to measles, rubella, epidemic mumps and pertussis, with those published following the monitoring of diseases preventable by vaccine, based upon the findings of Paediatric Sentinel Surveillance System (SPES).

Material and methods

Data, in this study, were collected directly from the report forms collected, during the period 1st January, 1995-31st December, 2003, by the Hygiene and Public Health Service of the Local Health Agency (LHA) of the province of Frosinone, comprising 4 health districts accounting for approximately 490,000 inhabitants. In two of the districts, the report forms related to 1995 and 2000 were not available for consultation.
The population residing in the Frosinone Province, analysed to elaborate the incidence rates for the period under consideration, was provided by the ISTAT data bank (demo.istat.it).
Taken into consideration were infectious diseases preventable with the use of vaccinations (both compulsory and recommended) included in the infant vaccination calendar (measles, mumps, rubella, hepatitis B, pertussis, invasive infections due to *haemophilus influenzae* type *b* [Hib] and tetanus) for which the temporal course has been analysed from 1995 to 2003 and for which the incidence rates, classified according to age group and year, have been calculated. Data referring to the morbidity incidence were analysed within the reference residential population per 100,000 inhabitants. In the comparison with the SPES incidence rates, the population taken into consideration was aged 0-14 years. An ACCESS format database was set up and the Epiinfo 3.2.2 statistics programme was used in the elaboration of the data. Differences and associations between variables were evaluated by means of χ^2 with a p value < 0.05 being considered significant.

Results

A total of 2,323 reports were received by the Frosinone LHA during the period under consideration (Tab. I).
An analysis of the distribution of the 185 cases of hepatitis B showed that the mean age, in 1995, was 26.5 ± 9.4 but 41.1 ± 12.2 in 2003, predominantly involving the male sex (74.1%). The highest percentage of cases of hepatitis B (16.8%) was recorded in 1995 and primarily affected subjects aged between 20 and 24 years, while in the last year under consideration, the age group most affected referred to subjects aged 35-39 years (Tab. II). The only case reported in a subject less than 14 years old, as well as 9/10 of the age group 15-19 years and 70.5% of the total number of reports received, refer to cases in which the subject had not been vaccinated, while 27.7% of the subjects were unaware of their vaccination status.
The 5 cases of tetanus concerned 3 females over 70 years old, only one of whom vaccinated, and 2 males aged 54 and 77 years with an unknown vaccination history.
The reports received concerning invasive disease due to Hib refer exclusively to 13 cases of meningitis (median age 5.0 years, mode 1.0).
The most representative year was 1996 with 6 cases, including 4 children under 10 years of age; 2 cases were reported in 2003, in children aged 1-4 years. In 45.5% of the reports, no information was available regarding the vaccination status, whilst the remainder were not vaccinated.
With regard to pertussis, from 1995 to 2003, 119 cases (median age 4.0, mode 1.0) were reported, 4 of which in vaccinated subjects. The distribution according to age revealed a larger number of reports related to cases under 15 years of age involving, in particular, in 1995, children aged 1-4 years and, in 2003, infants under 12 months of age, 75% of whom within the first 2 months after birth (Tab. II).
Of the 850 cases of measles (median age 7.0, mode 5.0), the highest number of reports was recorded in 1997 (349 cases: median age 7.0, mode 5.0) and in 2002 (199 cases: median age 8.0, mode 8.0); 1.8% in vaccinated subjects (Fig. 1).
In both these years, the 5-9 years age group was the most affected, but, in 2002, an increase was observed in the percentage of subjects aged 10-14 years (Tab. III).
The number of reported cases of rubella reached 411 (median age 12.0, mode 11.0), 53.3% referring to females and 1.7% vaccinated. The highest number was reported in 1997 (45.5%, median age 12.0, mode 5.0) involving primarily children aged 5-9 years. Cases of rubella were recorded also in adults, no statistically significant difference being found between males and females. Reports in 2002 (median age 19.0, mode 17.0) concerned primarily subjects aged between 15 and 19 years, again with no significant difference being observed between males and females (Tab. III).
As far as concerns mumps, the last epidemic peak occurred in 2001 (median age 7.0, mode 6.0) with 137 cases being reported *vs*. 285 in 1995 (median age 10.0, mode 7.0). In the years under consideration, the 5-9 years age group was found to be the most involved, also revealing a prevalence of the male sex, 59.3% in 1995 and 54% in 2001; 9.3% of the cases had been vaccinated.

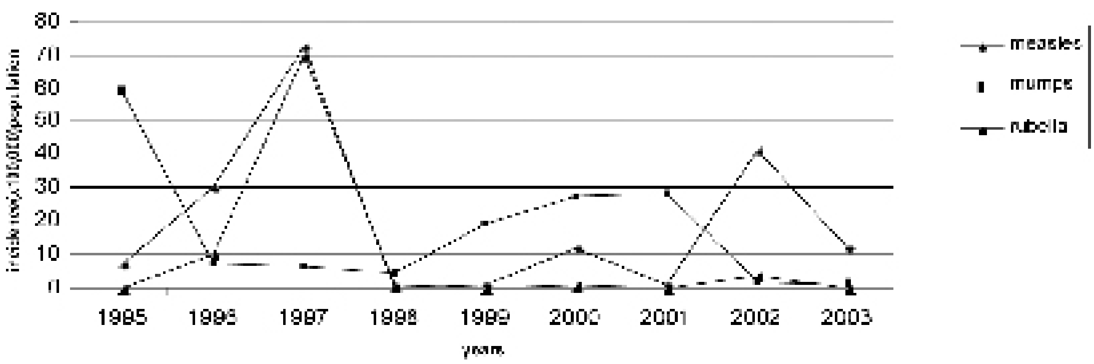
Tab. I. Cases and Incidence (x 100,000 inhabitants/year) Province of Frosinone (1995-2003).

Year		Hib invasive disease	Tetanus	Rubella	Mumps	Measles	Pertussis	Hepatitis B	Tot. cases/year
1995	Cases	1	1	1	285	37	35	31	391
	Incidence	0	0	0	59	8	7	6	
1996	Cases	6	0	46	34	143	18	27	274
	Incidence	1	0	10	7	30	4	6	
1997	Cases	2	0	337	29	349	9	15	741
	Incidence	0	0	70	6	72	2	3	
1998	Cases	2	0	6	20	1	18	20	67
	Incidence	0	0	1	4	0	4	4	
1999	Cases	0	1	2	90	3	17	7	120
	Incidence	0	0	0	19	1	4	1	
2000	Cases	0	0	4	129	56	3	26	218
	Incidence	0	0	1	27	12	1	5	
2001	Cases	0	0	1	137	3	4	21	166
	Incidence	0	0	0	28	1	1	4	
2002	Cases	0	0	14	10	199	2	19	244
	Incidence	0	0	3	2	41	0	4	
2003	Cases	2	3	0	6	59	13	19	102
	Incidence	0	1	0	1	12	3	4	
Tot. cases of disease		13	5	411	740	850	119	185	2323

Tab. II. Comparison of cases of pertussis and hepatitis B in 1995 and 2003.

Age bracket (yrs)	Pertussis 1995	Pertussis 2003	Hepatitis B 1995	Hepatitis B 2003
< 1	3 (8.6%)	4 (30.8%)	0	0
1-4	18 (51.4%)	1 (7.7%)	0	0
5-9	6 (17.1%)	4 (30.8%)	0	0
10-14	3 (8.6%)	3 (23.1%)	0	0
15-19	1 (2.9%)	0	5 (16.1%)	0
20-24	2 (5.7%)	1 (7.7%)	13 (41.9%)	0
25-29	1 (2.9%)	0	8 (25.8%)	3 (15.8%)
30-34	0	0	1 (3.2%)	1 (5.3%)
35-39	0	0	0	9 (47.4%)
> 40	1 (2.9%)	0	4 (12.9%)	6 (31.6%)
Total	35	13	31	19

Fig. 1. MMR incidence reported by Frosinone LHA 1995-2003.



Tab. III. Cases of MMR according to age.

Age (yrs)	Measles 1997	Measles 2002	Mumps 1995	Mumps 2001	Rubella 1997	Rubella 2002
< 1	5 (1.4%)	3 (1.5%)	1 (0.3%)	0	2 (0.6%)	0
1-4	68 (19.5%)	26 (13.1%)	34 (11.9%)	26 (19.0%)	39 (11.6%)	2 (14.3%)
5-9	157 (45.0%)	92 (46.2%)	104 (36.5%)	73 (53.3%)	91 (27.0%)	0
10-14	50 (14.3%)	38 (19.1%)	44 (15.4%)	17 (12.4%)	71 (21.1%)	1 (7.1%)
15-19	29 (8.3%)	12 (6.0%)	24 (8.4%)	3 (2.2%)	37 (11.0%)	5 (35.7%)
20-24	22 (6.3%)	8 (4.0%)	17 (6.0%)	3 (2.2%)	30 (8.9%)	3 (21.4%)
25-29	6 (1.7%)	7 (3.5%)	15 (5.3%)	3 (2.2%)	19 (5.6%)	1 (7.1%)
30-34	2 (0.6%)	4 (2.0%)	27 (9.5%)	3 (2.2%)	13 (3.9%)	0
35-39	1 (0.3%)	5 (2.5%)	8 (2.8%)	2 (1.4%)	17 (5.0%)	0
> 40	6 (1.7%)	3 (1.5%)	8 (2.8%)	7 (5.1%)	13 (3.9%)	2 (14.2%)
n.a.*	3 (0.9)	1 (0.5%)	3 (1.0%)	0	5 (1.5%)	0
Total	349	199	285	137	337	14

*n.a. = not available

Discussion and conclusions

Data emerging from this study reveal a reduction over time in the number of reports for almost all the diseases under consideration.

The distribution of cases of hepatitis B confirms the high protection offered by the vaccination strategy commenced in 1991 with the introduction of compulsory hepatitis B vaccination. In fact, a coverage rate of 95% with three doses of HB vaccine in newborns in the year

2000 was recorded in the province of Frosinone [2] and 4,617 complete cycles of three doses of vaccine were administered on a total of 5,525 twelve-year-old children in the year 2001 [3]. The implementation of the routine immunization program to a double cohort, infant and 12-year-old adolescents showed absence of no reported case of hepatitis B in the age cohorts covered by immunization and the age shift of its incidence. The greater involvement of male subjects results from their poor perception of risk, revealed by the habit of indiscreet sexual behaviour [4-8].

Despite the high rate of vaccinations achieved and the resulting decrease in the incidence, sero-epidemiological studies should now be carried out to analyse the prevalence of HBV markers in the various age groups.

For tetanus, as throughout Italy, advanced age and female sex are the main characteristics in these cases and reflect the history of the vaccination campaign; the cases of disease act, in fact, as spies regarding the existence of members of the population who have never been vaccinated or have not been adequately vaccinated, thus stressing the need to support attempts to ensure vaccination reaches this age group [9-11].

The course of Hib meningitis has decreased with time probably on account of the larger number of subjects taking advantage of the vaccination programme over the years [12-14] and which, in our Region, has increased from 7.8% in 1997 to 88.4% in 2004 [3].

The distribution of cases of pertussis probably reflects not only the greater attention focused on the disease by paediatricians but also the greater difficulty in diagnosing the condition in adults. The real decrease observed in the number of cases has to be attributed to the high levels reached in vaccination coverage, which would also explain, in agreement with reports in the literature, the cases which occurred before the beginning of the early vaccination campaign [2, 3, 11, 15-17].

Measles, mumps and rubella (MMR) were the diseases presenting the greatest morbidity and are also those that in the Lazio Region, in 2003, reached 83% vaccination coverage [3].

This rise, whilst leading to a decrease in the incidence of the 3 diseases, exposed adolescents and young adults, however, to risk of infection. In fact, in agreement with national data, the mean age of the patients presenting measles and rubella has increased [18, 19]. The highest incidence of measles, in 2002, was due to the nationwide epidemic and the geographic location of the Province of Frosinone which borders on the Campania Region, in which, in that same year, 66 epidemic outbreaks occurred [11, 20].

The distribution of the cases of rubella, per year and sex, reflect the lack of success of the earlier vaccination campaigns, in which vaccination was reserved only for females of prepuberal age. Furthermore, the finding of infection in females of fertile age, also in 2002, suggests that campaigns should be encouraged in order to reach those subjects at risk of catching the disease [21]. The number of MMR and pertussis notifications, received in our province, although few, lead to reflection since even if they cannot be considered representative of the entire population of the Frosinone area, do confirm, on the other hand, the important changes that are taking place regarding the epidemiological pattern of almost all the diseases taken into consideration in the present study.

As already pointed out, the number of reports does not coincide, in the least, with the number of cases of the disease that actually occurred [22-24] and quite often lack important information, particularly concerning the vaccination status.

Under-estimation of the reports, even if varying according to the disease, is still very significant. This can clearly be appreciated, for example, when comparing the incidence rate quoted in the surveillance data by the family paediatricians (SPES) for Central Italy, with the incidence data of the Frosinone LHA calculated on 100,000 subjects aged 0-14 years (Tab. IV), and again the differences emerging from the comparison between the number of reports received by the Frosinone LHA and the number of reports from SIMI per year and disease (Tab. V) possibly due to the difficulties encountered in handling the paperwork, incomplete data on the report forms, but also to the differences existing, in some cases, between the data of the LHA where the report was made and those of residence.

There can be no doubt that a well programmed and organized surveillance system offers the opportunity to check the epidemiological peculiarities of an infectious disease thus enabling an evaluation to be made regarding the approach strategy; this is closely correlated with good quality data and the rapidity with which these are transmitted and analysed. Informatization of the flow

Tab. IV. Comparison of incidence (x100,000 subjects aged 0-14 years) of MMR between SPES findings and those of Frosinone LHA.

Year		Measles	Mumps	Rubella	Pertussis
2000	SPES	90	2274	177	379
	FR LHA	57	131	5	3
2001	SPES	19	665	212	122
	FR LHA	4	237	0	4
2002	SPES	304	206	168	176
	FR LHA	223	8	4	3
2003	SPES	156	81	95	139
	FR LHA	64	3	0	17

Tab. V. Comparison between Frosinone LHA and SIMI concerning number of notifications of the various infections.

Year	Hepatitis B		Tetanus		Pertussis		Measles		Rubella		Mumps	
	LHA	SIMI	LHA	SIMI	LHA	SIMI	LHA	SIMI	LHA	SIMI	LHA	SIMI
1996	27	23	0	0	18	28	143	129	46	102	34	111
1997	14	15	0	2	9	11	349	368	337	347	29	30
1998	20	19	0	2	18	22	1	3	6	7	20	24
1999	7	4	1	1	17	17	3	3	2	1	90	101
2001	21	15	0	0	4	3	3	4	1	1	137	145
2002	19	18	0	0	2	1	199	199	14	15	10	10
2003	19	11	3	2	13	10	59	53	0	0	6	8
Total	185	105	5	7	119	92	850	759	411	473	740	429

of information on the reports should have improved the efficacy of the surveillance of infectious diseases but, for as long as the levels reached rely upon the surveillance networks on a voluntary basis and until the flow of information is correctly programmed, it is necessary to continue to sensitize the doctors, offer them the opportunity to become more involved in epidemiological studies in this field, in order to achieve a feedback of their work, complete the improvements/updating of peripheral centres in order to make the procedure easier and stimulate those, for whom a report is still considered merely a bureaucratic nuisance, to report cases in a more rapid and accurate fashion [25].

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■ Correspondence: Dr E. Langiano, Department of Motor Sciences and Health, Local Health Agency, University of Cassino, viale Bonomi s.n.c., 03043 Cassino (FR), Italy - Tel. +39 0776 2993793 - Fax +39 0776 2993839 - E-mail: langiano@unicas.it