

IMPACT OF A MASS IMMUNIZATION CAMPAIGN TO CONTROL AN OUTBREAK OF SEVERE RESPIRATORY INFECTIONS IN NUNAVIK, NORTHERN CANADA

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ABSTRACT

Objectives. In spring 2002, a mass immunization campaign using a 23-valent pneumococcal polysaccharide vaccine (23-PPV) was launched in order to control an outbreak of severe pneumonia caused by a virulent clone of serotype 1 *Streptococcus pneumoniae* in Nunavik, Quebec, Canada. The objective of the study was to evaluate the impact of this campaign on the incidence of invasive pneumococcal disease (IPD) and hospitalizations possibly associated with pneumococcal infections (HPAPI) in the mostly Inuit population aged 10 to 64 years.

Study design. Retrospective analysis of surveillance and administrative data.

Methods. Multivariate Poisson model comparing the frequency rates of selected outcomes before the outbreak, during the outbreak, and after implementation of the mass immunization program.

Results. The reported incidence of serotype 1 IPD decreased markedly after the implementation of the vaccination campaign (rate ratio = 0.16; $p < 0.002$). The frequency of HPAPI and the mean duration of hospital stay also decreased. However, vaccine failures were documented and the HPAPI rate remained higher than in the period prior to the outbreak.

Conclusions. Although 23-PPV contributed to control the outbreak, better vaccines are needed for the prevention of infections caused by serotype 1 *S. pneumoniae*.

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Key words: pneumococcus, polysaccharide vaccine, immunization, outbreak

INTRODUCTION

Nunavik is the most northerly region of the province of Quebec, Canada. Approximately 90% of the population of about 10 000 is Inuit and inhabitants are spread over 14 communities. In late August 2000, an outbreak of severe pneumonia caused by a virulent clone of serotype 1 *Streptococcus pneumoniae* began in one community and other communities were affected in the following two years (1). An unusual proportion of cases occurred in adults aged 20 to 64 years. In order to control this outbreak, a mass immunization campaign using a 23-valent pneumococcal polysaccharide vaccine (23-PPV) was launched in 2002, targeting the whole population between the ages of 5 and 64 years. This vaccine was already recommended for persons aged 65 years or more and for younger high risk individuals (2). The mass campaign started in February and was completed by the end of June 2002. The vaccine coverage of the target population was estimated to be 83.7%. In February 2002, a 7-valent pneumococcal conjugate vaccine was also introduced in the routine immunization program of infants, along with a catch-up vaccination for children aged between 4 months and less than 5 years. The 7-valent conjugate vaccine, however, does not contain the serotype 1 pneumococcal polysaccharide. Nine- and eleven-valent pneumococcal conjugate vaccines containing the serotype 1 polysaccharide are in development, but not yet licensed for use in Canada.

An evaluation of the impact of the mass 23-PPV campaign was requested by the Quebec Ministry of Health. The objective of the present study was to compare the frequency of invasive pneumococcal diseases (IPD) and of

hospitalizations possibly associated with pneumococcal infections (HPAPI) in the population of Nunavik before the outbreak, during the outbreak, and after the implementation of the immunization campaign.

MATERIAL AND METHODS

The study population was restricted to residents in Nunavik aged 10 to 64 years, as younger persons may have been vaccinated with the 7-valent pneumococcal conjugate vaccine not containing the serotype 1 pneumococcal polysaccharide. Denominator figures were provided by the Quebec Statistics Office, increasing from 5 722 in 1994 to 7 350 in 2004. Three epidemiologic periods were arbitrarily defined: before the outbreak (up to August 31, 2000), during the outbreak (September 1st, 2000, to April 30, 2002), and after the mass immunization campaign (May 1st, 2002 and after).

In 1997, IPD was included in the list of notifiable diseases in Quebec. IPD is defined as a clinical presentation compatible with a pneumococcal infection and isolation of *S. pneumoniae* from a normally sterile site or specimen. A vaccine failure is defined as IPD in a patient who received a pneumococcal vaccine more than 10 days prior to disease onset. Epidemiologic information on IPD cases is collected by the regional public health services and recorded in the provincial registry of notifiable diseases (MADO). Strains of *S. pneumoniae* isolated from a normally sterile site or fluid in public hospital laboratories are transmitted to the Quebec Public Health Laboratory for characterization, including serotyping. Identification of isolates is confirmed by colony

morphology, susceptibility to ethylhydrocuprein, and a Quellung reaction, while serotyping is performed by the capsular swelling method using specific antisera (3). Information on serotypes is transmitted to the regional public health services to be included in the MADO database. Anonymous information on IPD cases occurring in Nunavik residents from 1997 to 2004 was obtained from the Nunavik Public Health Directorate.

An anonymous copy of the Quebec hospital administrative database (MedEcho) was available for the period 1993-2003. Discharge summary records with a diagnostic code possibly associated with a pneumococcal infection were retrieved. Diagnostic categories and ICD-9 codes of interest were: pneumococcal septicemia (038.2), pneumococcal meningitis (320.1), pneumococcal peritonitis (567.1), pneumococcal pleuresy (511.1), pneumococcal pneumonia (481.-), pneumococcal infection in condition classified elsewhere and of unspecified site (041.2), bacterial pneumonia unspecified (482.9), bronchopneumonia, organism unspecified (485.-), and pneumonia, organism unspecified (486.-). Standard rules are applied for extracting information from hospital records and coding. The main and secondary diagnoses are determined from the medical discharge note and from the results of diagnostic investigations, including X-rays and cultures. When a lobar pneumonia is mentioned, the ICD-9 481 code has to be used. This code is also used for any lower tract respiratory infection with a positive culture for *S. pneumoniae* but this is not frequent. Any other type of pneumonia has to be coded as ICD-9 486 unless another specific pathogen is isolated. During the period April 1996 to March 1997, the recording of hospital

discharge summaries in one of the two hospitals in Nunavik was incomplete and the corresponding monthly frequencies were corrected using a month-specific average for the period April 1993 to March 2000, excluding April 1996 to March 1997.

Statistical analyses

Monthly frequencies were calculated for IPD and HPAPI. For the latter category, transfers from one hospital to another were excluded from the numerators. Frequency rates were computed using person-months at risk in the denominator. Frequency rates during different periods were compared using a multivariate Poisson model, adjusting for monthly variation and secular trends in hospitalizations. As there was no significant interdependency between successive monthly observations, an autoregressive model was not considered. Proportions in different groups were compared using a Chi-square test, and means were compared using an analysis of variance.

RESULTS

During the years 1997 to 2004, a total of 24 IPD cases were identified in the Nunavik population aged 10 to 64 years, representing an average incidence rate of 3.7 per 100 000 person-months. The distribution of cases by serotype and by period is indicated in Table I. Not one IPD case caused by serotype 1 was diagnosed prior to September 2000, while 11 cases were observed during the epidemic period of September 2000 to April 2002. The reported incidence of serotype 1 IPD decreased markedly after the implementation of the mass vaccination campaign (rate

ratio = 0.16; $p < 0.002$). Three vaccine failures were observed among vaccinated individuals: one serotype 1 (female patient aged 63 years) and another serotype 4 IPD case (male patient aged 28 years) during the outbreak period, and one serotype 1 IPD case (male patient aged 33 years) after the mass campaign. The incidence of vaccine-type IPD decreased from 11.0/100 000 during the outbreak to 1.3/100 000 after the mass immunization campaign, which corresponds to a 88% decline (95%CI: 59% to 97%).

During the years 1994 to 2003, a total of 400 HPAPI records were identified, the code of interest being the primary diagnosis in 276 records (including 8 transfers) and a secondary diagnosis in 124 records (including 5 transfers). The distribution of cases according to diagnostic category is indicated in Table II. Pneumococcal pneumonia (including lobar pneumonia, organism unspecified) and pneumonia, organism unspecified were the two most frequent conditions reported (91% of all cases).

Table I. Number (and incidence rate per 100 000 per month) of laboratory-confirmed invasive pneumococcal infections in persons aged 10 to 64 years in Nunavik, Quebec, Canada, 1997-2004.

Serotype	Period		
	January 1st, 1997 to August 31, 2000	September 1st, 2000 to April 30, 2002	May 1st, 2002 to December 31, 2004
Serotype 1	0 (0.0)	11 (8.0)	3 (1.3)
Other serotypes included in 23-PPV*	4 (1.4)	4 (2.9)	0 (0.0)
Other serotypes not included in 23-PPV*	1 (0.4)	0 (0.0)	1 (0.4)
All serotypes	5 (1.8)	15 (11.0)	4 (1.7)

* 23-valent pneumococcal polysaccharide vaccine

Table II. Frequency of hospitalizations possibly associated with pneumococcal infections in persons aged 10 to 64 years in Nunavik, Quebec, Canada, 1994-2003.

Category	ICD-9 code	Main diagnosis	Secondary diagnosis	Main or secondary diagnosis
Pneumococcal pneumoniae (including lobar pneumonia, organism unspecified)	481.-	112	32	144
Pneumococcal septicemia	038.2	1	3	4
Pneumococcal peritonitis	567.1	0	1	1
Other bacterial disease caused by pneumococcus	041.2	0	2	2
Bacterial pneumonia, unspecified	482.9	5	2	7
Pneumonia, organism unspecified	486.-	144	76	220
Bronchopneumonia, organism unspecified	485.-	14	8	22
Total		276	124	400

The monthly distribution of hospitalizations associated with pneumococcal infections is shown in Figure 1. The baseline frequency increased in late summer 2000 and there was a peak during the winter 2001-2002. The implementation of the mass immunization campaign in February 2002 was associated with an apparent reduction in the frequency of hospitalizations, but the baseline tended to remain higher than before the outbreak.

The frequency rates of hospitalizations corrected for under-registration during the period April 1996 to March 1997 are presented in Table III. Results confirmed the pattern observed in the figure. In multivariate analyses focusing on HPAPI as the main diagnosis which best represents community-acquired infections, the rate ratio before the outbreak/during the outbreak was statistically

significant ($RR = 0.41$; $p < 0.001$), while the rate ratio during the outbreak/after the mass campaign was of borderline significance ($RR = 1.45$; $p = 0.07$). Interestingly, the rate ratio before the outbreak/after the mass campaign was also significant ($RR = 0.55$; $p < 0.05$), indicating a continuation of the increased frequency of HPAPI after the mass campaign. When the analysis is restricted to pneumococcal pneumoniae (ICD9 481.-) including lobar pneumoniae, organism unspecified, the magnitude of the outbreak and the impact of the mass campaign are more evident. The frequency of hospitalizations with this code as a primary diagnosis, increased from 9.5/100 000 before the outbreak to 29.9/100 000 during the outbreak, and decreased to 9.1/100 000 after the campaign ($RR = 0.44$; $p < 0.01$).

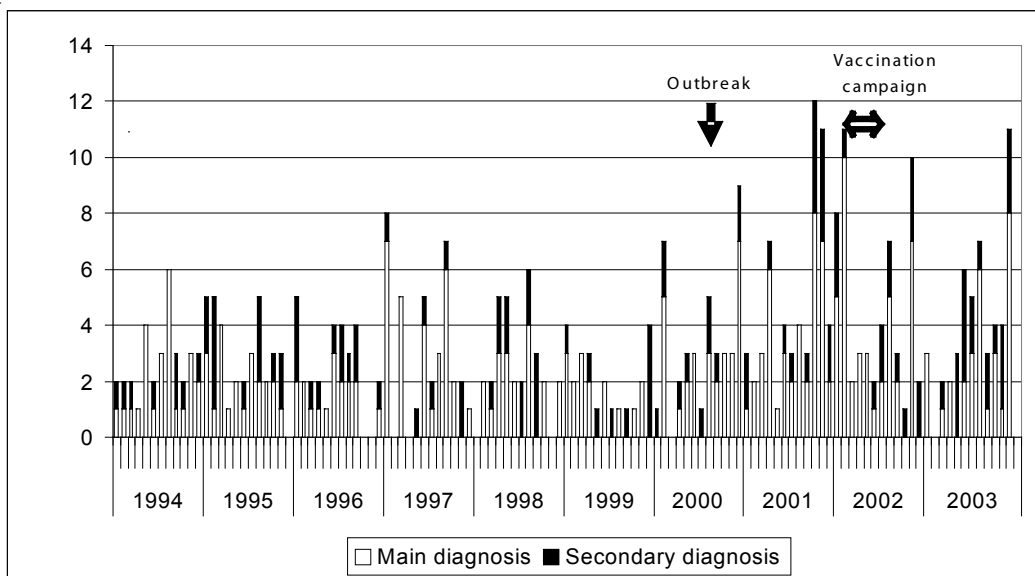


Figure 1. Monthly frequency of hospitalizations possibly associated with pneumococcal infections in Nunavik, Quebec, Canada, 1994-2003 (an outbreak caused by serotype I *S. pneumoniae* began in late August 2000, and a mass immunization campaign using a 23-valent polysaccharide vaccine was implemented in the period February-June 2002).

During the entire study period, the proportion of hospitalizations in tertiary care hospitals in Montreal was 19.0% (63/400). There was no statistically significant difference in this proportion according to the epidemic period: 23.0% before the outbreak, 16.3% during the outbreak, and 21.2% after the mass immunization campaign. The mean duration of hospital stay according to the diagnostic category and the epidemic period is indicated in Table IV. Hospital stays tended to be of longer duration during the outbreak than before or after ($p = 0.06$ for HPAPI as main diagnosis; $p = 0.44$ for HPAPI as secondary diagnosis).

DISCUSSION

This study relied on surveillance and administrative data collected in a population of small size in an Arctic region and the interpretation of results should be made with great care. Obviously, the rate of invasive pneumococcal infections is influenced by the frequency and timing of blood cultures. In Nunavik, antibiotics are rapidly prescribed for suspected respiratory infection. In nursing stations, antibiotics are given to any patient being transferred to a hospital facility and no specimen is taken for bacteriologic examination. Blood cultures are

Table III. Frequency rate (per 100 000 per month) of hospitalizations possibly associated with pneumococcal infections in persons aged 10 to 64 years in Nunavik, Quebec, Canada, 1994-2003.

Diagnostic category	Period		
	January 1 st , 1997 to August 31, 2002	September 1 st , 2000 to April 30, 2002	May 1 st , 2002 to December 31, 2004
All categories*			
Main diagnosis	38.8	55.5	35.0
Secondary diagnosis	15.4	13.9	22.4
Main or secondary diagnosis	46.2	69.4	57.4
Pneumococcal pneumoniae**			
Main diagnosis	9.5	29.9	9.1
Secondary diagnosis	2.8	8.8	3.0
Main or secondary diagnosis	12.3	38.7	12.1

* ICD9 codes: 481.-, 038.2, 567.1, 041.2, 482.9, 486.-, 485.-

**ICD9 code: 481.-

Table IV. Mean duration (in days) of hospitalizations possibly associated with pneumococcal infections* in persons aged 10 to 64 years in Nunavik, Quebec, Canada, 1994-2003.

	Period		
	January 1 st , 1997 to August 31, 2000	September 1 st , 2000 to April 30, 2002	May 1 st , 2002 to December 31, 2004
Main diagnosis	4.9	5.1	3.4
Secondary diagnosis	7.5	10.6	7.9
Main or secondary diagnosis	5.6	7.0	5.1

* ICD9 codes: 481.-, 038.2, 567.1, 041.2, 482.9, 486.-, 485.-

available in the two regional hospitals only. Culture of sputum is almost never done in case of acute respiratory infection. As a consequence, reported IPD are gross underestimates of the true frequency of bacteremic pneumococcal pneumoniae in the study population. Following the identification of the outbreak of severe pneumonia in the fall of 2000, a recommendation for an increased use of blood culture was issued and this was not modified thereafter. It is thus unlikely that the rapid decrease in the incidence of serotype 1 IPD observed following the mass campaign could be due to a change in diagnostic practice. For our study, an authorization was received to use anonymous databases, and it was not possible to perform a validation study linking the hospital discharge database with patients' records. During the study period, however, there was no significant change in the processing of hospital discharge summaries, beyond the problem experienced during the period April 1996 to March 1997 and for which appropriate corrections were made. However, changes in the criteria used for hospital admission and discharge are difficult to identify, and the introduction of a variable representing a secular trend in the model is an imperfect solution to control this factor.

The real effectiveness of polysaccharide pneumococcal vaccines is still a matter of controversy (4-7). In the most comprehensive meta-analysis of randomized trials in immunocompetent adults (8), vaccine efficacy was 82% (95%CI: 42% to 95%) for the prevention of definitive vaccine-type pneumococcal pneumonia, and was 23% (95%CI: -2% to 42%) for all causes pneumonia. Our results showing a 88% decrease in the incidence of vaccine-type IPD and a 37% decrease in the frequency of hospitalizations following the mass immu-

nization campaign are consistent with these estimates, knowing that the proportion of community acquired pneumonia which are attributable to *S. pneumoniae* may be much higher in the Inuit population in the Arctic than among Caucasians living in a temperate climate in Europe or North America (9). In Nunavik, the 7-valent pneumococcal conjugate vaccine was introduced for children at the time of the mass campaign and this factor may have contributed to the overall reduction of all causes pneumonia in the adult population through herd immunity. In the U.S., however, this effect was gradual and restricted to vaccine-type IPDs (10).

Serotype 1 *S. pneumoniae* is known to be associated with epidemics and outbreaks of pneumonia (11,12). Also, pneumonia caused by serotype 1 organisms are usually more severe than those caused by more common serotypes (11). Infections caused by serotype 1 *S. pneumoniae* are common in the Inuit population of Canada and Greenland (12-14). This serotype was less frequently isolated in Alaska (15). Experience with the control of community outbreaks caused by serotype 1 *S. pneumoniae* is limited and we could only identify one report of an apparently successful mass vaccination program using the 23-PPV in a small community of African Americans living in southern Israel (16). A before-after comparison without any control group is a far from an ideal design to assess the effectiveness of an intervention. However, there is currently no other option in such a situation. Our results suggest that the control of the serotype 1 outbreak in Nunavik was only partially successful: vaccine failures were documented and the HPAPI rates after the mass campaign were not lower than in the period prior to the outbreak.

Conclusions

The 23-PPV mass immunization campaign implemented in Nunavik in 2002 contributed to the control of an outbreak of severe respiratory infections caused by a virulent clone of serotype 1 *Streptococcus pneumoniae*. However, better vaccines are needed for the primary prevention of outbreaks and of sporadic pneumonia caused by serotype 1 *S. pneumoniae*.

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REFERENCES

1. Proulx JF, Déry S, Jetté LP, Ismaïl J, Libman M, De Wals P. Pneumonia epidemic caused by a virulent strain of *Streptococcus pneumoniae* serotype 1 in Nunavik, Quebec. *Can Commun Dis Rep* 2002;28:124-31.
2. Protocole d'immunisation du Québec. Québec: Ministère de la santé et des services sociaux. (<http://206.167.52.1/fr/document/publication.nsf/4b1768b3f849519c852568fd0061480d/a61341010d1b912885256e82006cc1bc?OpenDocument>).
3. Lund E, Henrichsen J. Laboratory diagnosis, serology and epidemiology of *Streptococcus pneumoniae*. *Methods Microbiol* 1978;12:241-62.
4. Hirschmann JV, Lipsky BA. The pneumococcal vaccine after 15 years of use. *Arch Intern Med* 1994;154:373-77.
5. Fedson DS, Shapiro ED, LaForce FM, Mufson MA, Musher DM, Spika JS et al. Pneumococcal vaccine after 15 years of use. Another view. *Arch Intern Med* 1994;154:2531-35.
6. Fedson DS, Liss C. Precise answers to the wrong question : prospective clinical trials and the meta-analyses of pneumococcal vaccine in elderly and high-risk adults. *Vaccine* 2004;22:927-946.
7. Conaty S, Watson L, Dinnes J, Waugh N. The effectiveness of pneumococcal polysaccharide vaccines in adults : a systematic review of observational studies and comparison with results from randomised controlled trials. *Vaccine* 2004;22:3214-24.
8. Dear K, Holden J, Andrews R, Tatham D. Vaccines for preventing pneumococcal infection in adults (Review). *The Cochrane Database of Systematic Reviews* 2003, Issue 3. Art.No.:CD000422 DOI:10.1002/14651858.CD000422.
10. Musher DM. *Streptococcus pneumoniae*. In : Mandell, Douglas and Bennett eds. *Principles and Practice of Infectious Diseases*. 4th ed. Philadelphia: Churchill Livingstone 2000;Vol. 2:2128-47.
10. McBean AM, Park YT, Caldwell D, Yu X. Declining invasive pneumococcal disease in the U.S. elderly. *Vaccine* 2005;23:5641-45.
11. Hausdorff WP, Feikin DR, Klugman KP. Epidemiological differences among pneumococcal serotypes. *Lancet Infect Dis* 2005;5:83-93.
12. Christiansen J, Paulsen P, Ladefoged K. Invasive pneumococcal disease in Greenland. *Scand J Infect Dis*. 2004;36:325-9.
13. Christiansen J, Paulsen P, Ladefoged K. Invasive pneumococcal disease in Greenland. *Int J Circumpolar Health*. 2004;63 Suppl 2:214-8.
14. Macey JF, Roberts A, Lior L, Tam TW, VanCaeseele P. Outbreak of community acquired pneumonia in Nunavut, October and November, 2000. *Can Commun Dis Rep*. 2002 Aug 15;28(16):131-8.
15. Rudolph KM, Parkinson AJ, Reasonover AL, Bulkow LR, Parks DJ, Butler JC. Serotype distribution and antimicrobial resistance patterns of invasive isolates of *streptococcus pneumoniae*: Alaska, 1991-1998.
16. Dagan D, Gradstein S, Belmaker I, Porat N, Siton Y, Weber G et al. An outbreak of *Streptococcus pneumoniae* serotype 1 in a closed community in southern Israel. *Clin Infect Dis* 2000;30:319-321.

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