Abstract

Objective: during the second half of 1996, the municipalities of Londrina and Curitiba (State of Paraná, Brazil) included Haemophilus influenzae type b (Hib) vaccine into their routine vaccination regimen, approximately 30 months before its introduction into the National Immunization Program. The present study aimed at verifying the incidence of meningitis caused by Hib among children in Londrina, Curitiba, and in the remaining municipalities of the State, before and after the introduction of this vaccine into the immunization program.

Methods: an observational and retrospective study was carried out. The study included all cases of Haemophilus influenzae type b meningitis recorded by the epidemiological surveillance system in Londrina and by the State of Paraná Health Secretariat between 1992 and 1999 among children aged less than 5 years. The incidence rates of Hib meningitis were calculated per 100,000 children aged less than five years.

Results: after the introduction of Hib vaccine, an important reduction in the incidence rate of Haemophilus influenzae type b meningitis was observed in Londrina (from 23.91 in 1996 to 2.79 in 1999). A similar decrease was observed in Curitiba. In the remaining localities of the state, which had not introduced the vaccine till mid-1999, the incidence rate remained almost unchanged.

Conclusion: regular vaccination against Hib was effective in reducing the incidence rate of meningitis amongst children younger than five years in Londrina and Curitiba. In order to maintain this low incidence rate, adequate vaccination coverage and strict epidemiological surveillance should be guaranteed.

Introduction

In September of 1997, the Pan American Health Organization (PAHO) recommended the governments of the region to adopt routine vaccination campaigns against diseases caused by the Haemophilus influenzae type b (Hib). This recommendation followed the successful decrease in Hib-related diseases in several countries after introduction of the Hib vaccine in immunization campaigns. Up until 1998, 48% of livebirths in the American continent and 29% of livebirths in Latin America and the Caribbean were being administered the vaccine in routine immunization programs. It was estimated that in December of 1999, the referred Hib vaccine coverage would increase to 81% and 75%, respectively.1
In Latin America, Uruguay and Chile were the first to administer Hib vaccines in routine immunization programs for children; consequently, these countries reported a significant decrease in the incidence of Hib-related diseases, especially Hib meningitis.2,3

In Brazil, the Hib vaccine was introduced only circa 1999.4 However, two Brazilian cities, namely Curitiba and Londrina, located in the state of Paraná, started administering the vaccine at public healthcare services in September and December of 1996, respectively. Similar procedures were observed in both cities. First, the project was presented to the City Health Council, indicating the epidemiological relevance of Hib meningitis for children aged less than five years, and the operational costs for acquisition of the vaccine using City Healthcare Fund resources. Second, after the approval by the pertinent Councils and acquisition of the vaccines, routine vaccination campaigns were started on the basic healthcare services network of the cities. The Hib vaccine was administered using a combination of Haemophilus influenzae type b-tetanus toxoid conjugate (PRP-T) and diphtheria-tetanus-pertussis (DTP) in both cities, though with differentiated vaccination schemes.5,6

In the city of Londrina, the vaccination campaign started on December 1st 1996 covering the new cohorts of children born after October 1st 1996, living in the city and aged two months at that time. The scheme included vaccinations at two, four, and six months of age with reinforcement at 18 months. Vaccines were administered in single doses.6 In the city of Curitiba, in turn, the vaccination campaign started on September 17, 1996 covering all children aged up to 24 months. The vaccination campaign followed a scheme recommended by the City Health Department based on the previous vaccinations of DTP.5

In 1999, the Brazilian Ministry of Health indicated the possibility of including the Hib vaccine in the National Immunization Program. Consequently, the City Health Department of Londrina stopped purchasing the PRP-T/DTP vaccine and, after a four-month shortage of the vaccine, started using the vaccine purchased by the Ministry (not combined with DTP). The new vaccination scheme included all children aged up to 24 months.7 In the year of 1999, probably due to the shortage of the vaccine at city healthcare units, the coverage was of only 73.2% in comparison to approximately 97% in previous years - according to data from the epidemiological surveillance services of Londrina. In Curitiba, the vaccine coverage was approximately 92% and 99% on the first two full years of vaccination.5

Consequently, considering that Londrina and Curitiba started Hib vaccination routines around 30 months before the national vaccination campaign, our objective was to assess incidence of Hib in children aged less than five years and residing in Londrina before and after implementation of the campaigns; to compare the incidence to that of Curitiba, where vaccination started around the same time; and, finally, to that of the remaining cities in the state of Paraná, which did not include the Hib vaccine in their routine immunization programs until circa 1999.

Patients and methods

We carried out an observational, retrospective study using data on reported cases of Hib meningitis in children aged less than five years and residing in the city of Londrina, northern Paraná from 1992 to 1999. The 17th Regional Department of Health, a branch of the State Health Department of Paraná is located in Londrina. This regional department is responsible for advising and supervising statewide healthcare measures of 20 cities located in the northern region of Paraná. According to the last census, Londrina has 446,849 inhabitants out of which 97% reside in urban areas.8 Londrina is the third most populated city in Southern Brazil. The municipalization of the responsibility for epidemiological surveillance measures occurred in the beginning of 1994. From that point on, cities had to start carrying out all measures of collection of data, investigation, and control related to each case of diseases that are mandatorily notified to the local authorities.9

In this sense, the 17th Regional Department of Health was our source of data on Hib meningitis cases of children aged less than five years, from the city of Londrina, and for the years of 1992 and 1993. After the municipalization of healthcare measures, the Epidemiology Management of the City Healthcare Services of Londrina was our source for the years of 1994 to 1999.

We also collected data on cases of Hib meningitis in children aged less than five years for the city of Curitiba and the remaining cities in the state of Paraná for comparison purposes. Data were obtained from the State Department of Health, located in Curitiba.

For calculation of incidence ratios per 100,000 children aged less than five years, we collected population data according to age group and city of residence from the 1991 census and 1996 Brazilian Institute of Geography and Statistics (IBGE) population census; the latter obtained from the Londrina and Curitiba IBGE branches. The population of children aged less than five years was estimated, for the middle of the year (July 1st), by arithmetic progression10 for all years included in our study and for the cities of Londrina, Curitiba, and the remaining cities of Paraná.

Considering that decrease in incidence of Hib meningitis can occur due to poor quality of epidemiological surveillance,11 we also collected data on cases of meningococcal disease (meningococcal meningitis, meningococcal meningitis with meningococcemia, and meningococcemia) and of pneumococcal meningitis involving patients aged less than five years and from the city of Londrina. These data were collected for comparison with incidence of Hib meningitis. The comparison was carried
out in relation to two periods of reference from 1992 to 1996 (prevaccination period) and from 1997 to 1999 (postvaccination period). The average incidence of the diseases were calculated for patients aged less than five years and residing in Londrina.

All cases of Hib meningitis included in the City Healthcare Services database of Londrina were confirmed by laboratory exams of cerebrospinal fluid (CSF) bacterioscopy and culture and/or latex agglutination (latex particles sensitized with antiserum) and/or counterimmunoelectrophoresis. The same laboratory criteria were employed for meningococcal, meningococcal and meningococcemia, and pneumococcal meningitis. The cases of meningococcemia were diagnosed by petechiae in patients and/or by hemoculture. The Paraná State Department of Health employs and recommends these same criteria for confirming diagnosis of meningitis in all cities within the state; the criteria, in turn, are recommended and distributed by the Brazilian Ministry of Health.12

In accordance with the resolution number 196/96 of the National Health Council, our study was approved by the Research Ethics Committee of the Universidade Estadual de Londrina.

Results

Comparison of incidence of Hib meningitis in subjects aged less than five years from the city of Londrina to that of other cities in the state of Paraná (excluding Londrina and Curitiba) indicated that incidence in Londrina peaked in 1995, which is before introduction of the Hib vaccine (Figure 1). The increase in incidence was abrupt and coincides with the period following municipalization of the epidemiology services, which occurred in the beginning of 1994.

In other cities of Paraná, we observed that there were no significant oscillations on the incidence of Hib meningitis during the study period. During the period prior to introduction of the Hib vaccine in Londrina (prevaccination), the coefficients of Hib incidence for the other cities were, in general, lower than that of Londrina, with the exception of the 1994 incidence values.

From 1997 onwards, which was the year immediately after introduction of the vaccine (postvaccination), this pattern is inverted, with Londrina presenting lower coefficients than those in other cities of Paraná. The values observed after 1997 were the lowest ever, especially for the last year of the study period, when they fell to a coefficient of 2.79 per 100,000 children aged less than five years. This fall represents an 88.3% decrease in relation to the 1996 coefficient (last year prior to the first full year of vaccination).

Comparison of incidence of Hib meningitis in subjects aged less than five years from the cities of Londrina and Curitiba indicated that the latter also presented peak incidences. Conversely to Londrina, however, peak incidence in Curitiba followed a gradual increase starting in 1994 and culminating in 1996.

After introduction of the vaccine in both cities, it is also possible to observe a decrease in Hib meningitis incidence for Curitiba; however, the decrease bottomed out between 1998 and 1999. In the city of Curitiba, on the third full year of vaccination (1999) the coefficient of incidence indicated an 84.0% decrease in relation to that of 1996.

In order to verify possible changes in the standards of epidemiological surveillance for the city of Londrina, we compared the incidence of Hib meningitis with that of meningococcal and pneumococcal meningitis during the prevaccination (1992 to 1996) and postvaccination (1997 to 1999) periods, for subjects aged less than five years. Figure 3 presents average incidences of meningococcal disease, where it is possible to observe that they were practically identical for both the pre- and postvaccination periods. In turn, the incidence of pneumococcal meningitis presented a slight decrease (from 12.0 to 9.3 per 100,000 children aged < 5 years), whereas the decrease in incidence of Hib meningitis was more significant (from 20.4 to 6.4 per 100,000 children aged < 5 years).

Discussion

Our results indicate that introduction of the Hib vaccine noticeably decreased incidence of Hib meningitis in children aged less than five years residing in Londrina and Curitiba; the same was not observed for the remaining cities in the state of Paraná, for the same period. The aim of the vaccination campaigns was not of covering all children aged less five years, but rather, for the city of Curitiba, of covering all children aged less than 24 months and, for the city of Londrina, of covering all new cohorts of children.
born after October 1996. In this sense, the decrease observed in the two cities already in the first full year of vaccination is probably due to the ability of routine vaccination procedures of decreasing number of Haemophilus influenza type b carriers and, thus, reducing the risk for transmission to nonimmunized subjects.5,13

Though both cities employed different immunization strategies, there were no significant differences on absolute values of incidence during the first three full years of vaccination. Londrina presented values slightly higher than those of Curitiba for 1997 and 1998, and lower for 1999. As a result, the impact of vaccination routines was similar for both cities; this is probably a consequence of the efficacy and effectiveness of the vaccine and of the decrease in prevalence of carriers of the bacteria.13,14 It is estimated that efficacy of the Hib vaccine is high (95 to 100%); effectiveness, however, depends on the vaccine coverage.14

The Hib vaccine coverage rates, for children aged less than one year and residing in Londrina, were high in 1997 and 1998 (96.4% and 97%, respectively). In 1999, however, due to a shortage of vaccines at city healthcare units, the coverage fell to 73.2%.15 Despite this fact, the incidence of Hib meningitis during the year of 1999 remained low.

In Uruguay, only 76.6% of children aged two months to four years and 80% of livebirths received the vaccine during the first five months of routine vaccinations. This allowed for a 99.8% decrease in incidence of Hib meningitis - from 15.6 to 0.03 per 100,000 children aged less than five years, respectively, in 1993 and 1996 (second full year of vaccination).3 It is important to underscore, however, that vaccination in Uruguay was introduced in a widespread manner and administered simultaneously to all children aged less than five years. This fact may have contributed to a more marked decrease in incidence in comparison to that observed in Chile, for example, where the vaccine was introduced only to new cohorts of livebirths,2 much similarly to the case of Londrina.

Other have also shown the effectiveness of routine vaccination campaigns on decreasing Hib meningitis.16-19 In Sweden, the vaccine was introduced in 1991 when the incidence of Hib meningitis was 34.4 per 100,000 children aged less than five years. The vaccine coverage attained was 90% and three years after introduction of the vaccine, the incidence of Hib meningitis decreased 89.8%.16

Other studies have also reported the impact of introduction of the Hib vaccine on the diagnosis of other invasive disease caused by Hib.20,21 We limited our study to incidence of meningitis since other invasive, Hib-related diseases are not mandatorily notified to authorities in Brazil and since there is a difficulty in obtaining reliable data on incidence of other diseases, such as pneumonia.4 However, it is highly possible that other Hib-related diseases also decreased in Londrina and Curitiba; in this sense, further studies are needed to assess effect of the vaccine on diseases other than Hib meningitis.

When analyzing trends of diseases mandatorily notified to authorities, it is important to assess the quality of the epidemiological surveillance services. Included in the numerous factors that can influence quality of these services are coverage of the service, adequate laboratory support, collection of samples or specimens for culture, access to healthcare services, and indiscriminate use of antibiotics.4,22,23 In Brazil, there are data indicating undernotification and underestimation of cases of bacterial meningitis. This undernotification and underestimation is, however, less important in southern and southeastern states, which provide better access to healthcare services. In this sense, we believe that the decrease in incidence of Hib meningitis...
meningitis observed in the city of Londrina, located in southern Brazil, was not due to changes in standards of epidemiological surveillance. This is corroborated by the fact that incidence of meningococcal disease remained similar for both the pre- and postvaccination periods, and, also, by the fact that despite the slight decrease in incidence of pneumococcal meningitis, this decrease was not as significant as that in Hib meningitis. These findings are similar to those observed in Colombia.11 Still, it is important to emphasize that, contrarily to the situation in a significant number of cities of the state of Paraná, all general hospitals in Londrina are backed up by appropriately-quipped laboratory services for etiological diagnosis and management of meningitis.

In this context, routine Hib vaccination is greatly responsible for the change in the epidemiological profile of Hib meningitis. According to data from the City Healthcare Services, there were no more reported cases of Hib meningitis in Londrina children born after October 1996;15 in other words, in children in the target population. In Curitiba, the decrease in incidence of meningitis and in prevalence of Hib carriers was also attributed to introduction of the vaccine in that same year.5,13

The low incidence observed in the two cities will be maintained as long as adequate vaccine coverage rates are ensured. Thus, it is important to maintain an adequate surveillance of meningitis and enhance epidemiological surveillance measures especially as to what concerns laboratory diagnosis. The PAHO understands that well-structured epidemiological surveillance systems will allow for valuable information on introduction and impact assessment of new vaccines in routine programs in the Americas, as in the case of the Hib vaccine.24

Finally, in addition to underscoring the importance of aiming at enhanced coverage and quality of surveillance and immunization measures, it is also important to understand that combined use of Hib vaccine with other vaccines such as DTP would allow for a decrease in the number of injections administered to children. As a result, this may allow for increases in coverage and adhesion to this type of measure.25 Considering that in Londrina, in 1999, there was a change in the type of vaccine administered (from combined PRP-T/DPT to separate vaccines), further studies are needed in that city to assess possible changes on vaccine coverage and causes of possible nonimmunization of children.

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References


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