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ORIGINAL ARTICLE

Resurgence of pertussis at the age of vaccination: clinical, epidemiological, and molecular aspects☆

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KEYWORDS
Whooping cough;
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Abstract
Objective: Report the incidence, epidemiology, clinical features, death, and vaccination status of patients with whooping cough and perform genotypic characterization of isolates of *B. pertussis* identified in the state of Paraná, during January 2007 to December 2013.
Methods: Cross-sectional study including 1,209 patients with pertussis. Data were obtained through the Notifiable Diseases Information System (Sistema de Informação de Agravos de Notificação – SINAN) and molecular epidemiology was performed by repetitive sequence-based polymerase chain reaction (rep-PCR; DiversiLab®, bioMerieux, France).
Results: The incidence of pertussis in the state of Paraná increased sharply from 0.15-0.76 per 100,000 habitants between 2007-2010 to 1.7-4.28 per 100,000 between 2011-2013. Patients with less than 1 year of age were more stricken (67.5%). Fifty-nine children (5%) developed pertussis even after receiving three doses and two diphtheria-tetanus-pertussis (DTP) boosters vaccine. The most common complications were pneumonia (14.5%), otitis (0.9%), and encephalopathy (0.7%). Isolates of *B. pertussis* were grouped into two groups (G1 and G2) and eight distinct patterns (G1: P1-P5 and G2: P6-P8).
Conclusion: The resurgence of pertussis should stimulate new research to develop vaccines with greater capacity of protection against current clones and also encourage implementation of new strategies for vaccination in order to reduce the risk of disease in infants.

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PALAVRAS-CHAVE
Coqueluche;
Clones;
Bordetella pertussis;
Rep-PCR;
Vacinas;
Incidência

Ressurgimento da coqueluche na era vacinal: aspectos clínicos, epidemiológicos e moleculares

Resumo

Objetivo: Relatar a incidência, aspectos epidemiológicos, clínicos, morte e a vacinação de pacientes com coqueluche e realizar a caracterização genotípica de isolados de *B. pertussis* identificados no estado do Paraná, de janeiro de 2007 a dezembro de 2013.

Métodos: Estudo transversal, incluindo 1.209 pacientes com coqueluche. Os dados foram obtidos através do Sistema de Informação de Agravos de Notificação (SINAN) e a epidemiologia molecular foi realizada por PCR baseada em sequências repetitivas (rep-PCR; DiversiLab®, bioMerieux, France).

Resultados: A incidência de coqueluche no Estado do Paraná aumentou acentuadamente de 0,15-0,76 por 100.000 habitantes entre 2007-2010 para 1,7-4,28 por 100.000 habitantes entre 2011-2013. Os pacientes com menos de um ano de idade foram os mais afetados (67,5%). Cinquenta e nove crianças (5%) desenvolveram coqueluche mesmo depois de receber três doses da vacina e dois reforços com a vacina tríplice DTP. As complicações mais comuns foram pneumonia (14,5%), otite (0,9%) e encefalopatia (0,7%). Isolados de *B. pertussis* foram agrupados em dois grupos (G1 e G2) e oito padrões distintos (G1: P1-P5 e G2: P6-P8).

Conclusão: O ressurgimento da coqueluche vem para sugerir novas pesquisas com o objetivo se desenvolver vacinas com maior capacidade de proteção contra os clones atuais e também implementar novas estratégias de vacinação, a fim de reduzir o risco de doenças em lactentes.

Introduction

Pertussis, commonly known as whooping cough, is a severe, highly contagious disease of the human respiratory tract, caused by *Bordetella pertussis*.[1] The disease is characterized by uncontrollable coughing fits, accompanied by inspiratory stridor.[2] Children and adults of any age can develop the disease; however, it is more severe in infants, especially up to 6 months of age.[3] Despite good vaccination coverage, it is estimated that 50 million cases occur each year, with approximately 300,000 deaths annually, 90% of them in developing countries.[1,4]

The last decade showed a surprising increase in incidence rates of pertussis in several regions of the world. The causes of this disease resurgence are still unclear. Some hypotheses raised were post-vaccine immunity loss; implementation of molecular methods for diagnosis; improvement of epidemiological surveillance systems; reduction of the vaccine efficacy; or even genetic changes in the pathogen.[5,6]

In Brazil, pertussis was included in the notifiable diseases list in 1975, with the recommendation to investigate all disease outbreaks. In the early 1980s, there were more than 40,000 cases a year and the incidence rate was > 30/100,000 inhabitants. This number has decreased sharply since 1983, with the introduction of the diphtheria-tetanus-pertussis (DTP) vaccine in the Brazilian childhood vaccination schedule; since then, it has shown a downward trend. Evidence of pertussis resurgence in Brazil was demonstrated by the detection of some outbreaks in 2010, followed by an increase in the number of cases in several Brazilian capitals.[7]

The monitoring of *B. pertussis* circulation is being performed in the Brazilian states, with the implementation of surveillance services and qualified laboratories for the isolation of the etiological agent. The methods used in the laboratory diagnosis of pertussis include culture and real time polymerase chain reaction (RT-PCR). The diagnosis of pertussis by laboratory testing was implemented in the Central Laboratory of the state of Paraná (Lacen-PR) in 2005. The test (culture) was first made available for three sentinel hospitals; two implemented in the capital city of Curitiba and another in the city of Londrina.

The first isolation of *B. pertussis* occurred only in 2007, in a family contact with cough, from a child with the disease symptoms. In 2011, the survey was expanded to all Basic Health Units (BHUs) and other hospitals in the city of Curitiba and the metropolitan area. These services received training that addressed clinical diagnosis, epidemiological behavior, and biological sample collection. Recently, some studies have reported the use of repetitive element sequence-based PCR (rep-PCR; DiversiLab®, bioMerieux, France) for molecular typing of microorganisms. This method uses oligonucleotide primers complementary to repetitive highly conserved DNA sequences present at numerous copies in the bacterial genome. It allows genotypic characterization, clone differentiation, and their dispersion in the community.[8]

The objective of this study was to describe the incidence, epidemiological and clinical characteristics, number of deaths and vaccination status, of patients with pertussis, and to perform the genotypic characterization of isolates of *B. pertussis* circulating in the state of Paraná, Brazil, from January of 2007 to December of 2013.