CPSP
CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM

Listeria in the newborn and early infancy

PROTOCOLS

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Background

Listeriosis is associated with high morbidity and mortality, often spread through contaminated food.[1,2] In North America and Europe, more deaths are attributed to Listeria than to any other foodborne infection.[3-6]

Neonatal listeriosis has two distinct clinical patterns, early-onset (during the first seven days of life) and late-onset (>1 week old) infection.[1,2] The epidemiologic factors associated with early-onset infection are well characterized, as outbreaks involving pregnant women and newborn babies are often the first indicator of a foodborne spread of infection; in some outbreaks, over 50% of cases have been diagnosed as early-onset newborn infection.[1,2] The incidence and epidemiological factors contributing to late-onset infection of the newborn are not well defined.[1,2] In other developed countries the incidence of late-onset listeriosis has recently been investigated, with few cases occurring past one month of age.[7] Specifically, in a review of 456 cases of neonatal listeriosis in the UK where the time of onset was captured, 342 (75%) were found to be of early onset (occurring <7 days of age) and 114 (25%) of late onset but presenting <28 days of age. Only five (i.e., ~1%) occurred between one and three months of age. Case fatality rates of neonatal listeriosis range from 14% to 56%; early recognition and empiric treatment has been shown to improve outcome.[1,2] Empiric therapy for

suspected sepsis in newborns in Canada includes use of a broad-spectrum cephalosporin antibiotic, such as cefotaxime, plus ampicillin. Ampicillin is included specifically to target Listeria.[8,9] However, the cutoff age beyond four weeks at which Listeria is no longer a risk, and ampicillin no longer the antibiotic of choice, is not clear.[7] Knowledge of the age of reported cases is thus essential in developing evidence-based treatment guidelines.

In summary, there is little information about Canada-specific incidence and individual-level medical risk factors leading to early-onset vs. late-onset neonatal listeriosis, and the associated outcomes are entirely unknown. This gap in knowledge does not allow an evidence-based design of age-appropriate empiric antibiotic therapy and, with that, prevents optimal support of Canadian newborns and infants at risk.

Methods

Through the Canadian Paediatric Surveillance Program (CPSP), over 2,500 paediatricians and paediatric subspecialists will be actively surveyed to identify new cases of early- and late-onset listeriosis. A short questionnaire designed to capture associated risk factors and clinical course will be provided to CPSP participants who identify a new case. The questionnaire will capture information on the clinical features, such as gestational age, age of onset of signs and symptoms of the infant, as well as relevant data around the birth of the infant. It will also include a brief history of clinical illness during pregnancy.

Case definition

Report any new patient less than six months of age, meeting the following criteria:

1) Definitive

- Positive culture of Listeria from a usually sterile site, such as blood, CSF or pleural fluid; or
- Positive culture of Listeria from the placenta in the presence of compatible clinical features of listeriosis (sepsis, meningitis, respiratory distress, etc.).

2) Probable

- Positive PCR for Listeria from a usually sterile site or the placenta in the presence of compatible clinical features of listeriosis (sepsis, meningitis, respiratory distress, etc.).

Objectives

1) Determine the age-specific incidence of neonatal listeriosis in Canada.
2) Collect information on maternal and perinatal factors associated with early- vs. late-onset listeriosis in Canada.
3) Determine factors associated with more severe outcome (need for intensive care admission, death).

Duration

May 2015 to April 2017

Expected number of cases

Canada has a passive listeriosis surveillance program in place. The Enhanced National Listeriosis Surveillance Program, Public Health Agency of Canada (PHAC), was piloted

in 2010 and implemented as an ongoing surveillance program in 2012. The PHAC program uses a standardized questionnaire to collect case-level information, including demographic, laboratory data and food consumption for invasive listeriosis infections in Canada, and has reported annual national rates (all age groups) of listeriosis between 1.8 and 3.4 per million population.[10] However, based on the reported incidence of neonatal listeriosis in the United Kingdom of 5/100,000 live births, and in the United States of 8.6/100,000 (both of which also have a passive surveillance system),[7] five to eight cases of neonatal listeriosis per 100,000 live births would be expected to occur per year in Canada.[11] With an annual birth cohort of approximately 370,000, this would translate in 19-30 neonatal cases nationally per year.

Ethical approval

- University of British Columbia (BCCH) Research Ethics Board
- Health Canada and the Public Health Agency of Canada's Research Ethics Board

Analysis and publication

Quarterly reports will be provided to the CPSP and PHAC regarding number of cases, geographic distribution of cases, and completion rates of questionnaires. On an annual basis, a summary of data will be provided for inclusion in the *CPSP Results* publication. Interim data will be presented at paediatric meetings. Final results will be published in peer-reviewed journals and presented at conferences.

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