Canadian Nosocomial Infection Surveillance Program

Final

Ongoing Surveillance for *Clostridium difficile* associated diarrhea (CDAD) within Acute-Care Institutions

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Canadian Nosocomial Infections Surveillance Program (CNISP)

Project Protocol for Surveillance for *Clostridium difficile* associated diarrhea

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1. INTRODUCTION

Clostridium difficile associated diarrhea (CDAD) is the most frequent cause of nosocomial infectious diarrhea in industrialized countries[1-3], affecting more than 300,000 hospitalized patients yearly in the United States[4, 5]. Clinical manifestations range from asymptomatic colonization, to severe diarrhea, pseudomembranous colitis (PMC), toxic megacolon and death[6].

Since the last half of 2002, several hospitals in Quebec have experienced a dramatic increase in the incidence, severity and number of relapses associated with CDAD[7-10]. In this context, we propose an ongoing prospective surveillance system of patients admitted to hospitals participating in the CNISP network to determine the incidence of CDAD. This surveillance project will be mandatory for all CNISP hospitals.

1.1 BACKGROUND

Increase in incidence, severity and relapse in Canadian hospitals

Recent reports have suggested an increase in incidence, severity and/or risk of relapse of CDAD in Canada[7]. Several health-care institutions in Quebec (located mostly in the southern region of the St-Lawrence River, Montreal and the Eastern Townships) are reporting increased incidence of nosocomial cases, with average rates of 25 cases/1000 admissions[8].

An increase in the frequency of *C.difficile* toxin-producing strains at the Centre Hospitalier Universitaire de Sherbrooke lead to a 13 year review (January 1991-December 2003) of 1721 cases of CDAD in the Eastern Townships of Quebec[11] . From 1991/92 to 2001/02, the overall annual incidence of CDAD was stable with rates of 35 per 100,000 to 50 per 100,000. However, in 2003 the incidence increased to 160 per 100,000 with a rate of almost 900 per 100,000 for adults older than 65 in 2003. This represents a total of 390 new cases in 2003.

Severity of colitis was defined as perforation, toxic megacolon, shock or death within 30 days of diagnosis. Using this definition, in 2003, an increase in the incidence of severe colitis when compared to previous years 1991-2002 [adjusted OR 2.2; 95% CI, 1.0-4.9] was

reported.

1997 N-CDAD Point Prevalence Surveillance Project

In 1997, the Canadian Nosocomial Infections Surveillance Program conducted a six week prospective surveillance study within 19 health care facilities in 8 Canadian provinces[12]. During this period, the participating CHEC sites tested all diarrheal stools from hospitalized patients for *C.difficile* toxin detection. Questionnaires were completed for patients with positive assays who met eligibility criteria (diarrhea >2 days, symptoms occurred 3 days or more after admission, or symptoms causing readmission within one month of the current admission).

Among inpatients with diarrheal stools, 13% were caused by *C.difficile*. The mean number of N-CDAD cases was 66.3 cases/100,000 patient days (95% CI 37.5-95.1) and 5.9 cases/1000 patient admissions (95% CI 3.4-8.4). N-CDAD was found most frequently in older patients and those hospitalized > 2 weeks in medical or surgical wards.

A sub-section of the initial project addressed morbidity, mortality and healthcare burden of N-CDAD in the same centers[13]. Of the 269 patients that satisfied the N-CDAD case definition, 41 (15.2%) died, 4 (1.5%) of these were directly attributable to CDAD. The annual cost of N-CDAD readmission for each centre was estimated to be at least of $128,200.

These reports were pivotal since they provided baseline rates to which other Canadian hospitals could compare. As well, they provided the only available information on healthcare burden of CDAD on Canadian hospitals.

2004-2005 CDAD Prospective Surveillance Project

Over the course of the 2005 surveillance period, we identified 1847 patients with CDAD. 45% were male. The vast majority, 95% were adults 19 years of age and older with a mean age of 69 years. There are 101 children with CDAD identified in 8 of the 34 participating hospitals.

The number of patients with CDAD per 1000 admissions was 2.2 times higher in Quebec than the rest of the country. Patients examined in this study were in major teaching hospitals and so likely not entirely representative of all hospitalized patients in Canada. Also,

we did not evaluate acuity of patients between hospitals which may account for the variability in rates.

A total of 1331 patients or 72% met the case definition for hospital-acquired CDAD. The percentage of patients with hospital-acquired CDAD in each of the 4 regions (Western, Ontario, Quebec and Maritimes) was similar ranging from 70% in Ontario to 80% in Quebec.

In conclusion, this study demonstrates that CDAD is a common and serious hospital-acquired infection in Canada and is associated with substantial morbidity and mortality. Despite the limitations, the study provides useful "benchmark" data for Canadian health care facilities, and in understanding the impact of CDAD in Canadian patients.

Canadian Nosocomial Infection Surveillance Program

The Canadian Nosocomial Infection Surveillance Program (CNISP) is a collaborative effort of the Canadian Hospital Epidemiology Committee (CHEC), a subcommittee of the Association of Medical Microbiologists and Infectious Disease (AMMI) and the Centre for Infectious Diseases Prevention and Control (CIDPC) of the Public Health Agency of Canada.

Established in 1994, the objectives of CNISP are to provide rates and trends on nosocomial infections at Canadian health care facilities thus enabling comparison of rates (bench-marks), and providing evidence-based data that can be used in the development of national guidelines on clinical issues related to nosocomial infections. At present, 48 sentinel hospitals from 9 provinces (representing all the major teaching hospitals) participate in the CNISP network.

CHEC members participate in CNISP by working on sub-committees that direct the development, implementation and analysis of surveillance projects in CNISP. CHEC members participate voluntarily in CNISP projects by collecting standardized, case-by-case, non-nominal data on hospitalized patients at risk of nosocomial infection. The data is submitted to CNISP for compilation and analysis. All data is analyzed by region or larger geographical area. At no time is submitted data analyzed by individual facility or site.

1.2 GOALS AND OBJECTIVES

1. To determine the incidence and burden of illness associated with CDAD in CNISP hospitals.
2. To determine the incidence of nosocomially-acquired CDAD in CNISP hospitals.
3. To describe the epidemiology of CDAD.
4. To characterize susceptibility profile of *C.difficile* strains
5. To characterize molecular subtype/toxinotype of *C.difficile* strains in different provinces and correlate if certain strains are associated with different outcomes.
6. To determine the adverse outcomes (mortality and morbidity) associated with CDAD.

2. METHODOLOGY

2. 1 *Surveillance Design*

As of January 1st, 2007, surveillance for CDAD will be ongoing and mandatory in all hospitals participating in CNISP. CDAD surveillance will consist of: 1) monthly reporting of incidence rates, and 2) an annual two-month targeted surveillance for patient outcomes and laboratory characterization of *C.difficile*.

***Ongoing surveillance for CDAD*:** all hospitals will provide monthly incidence rates for CDAD starting in January 2007. Patients with CDAD will be identified through review of toxin positive stool samples from the microbiology laboratory. A chart (health record) review will be conducted to determine if the patient meets the case definition for CDAD. Number of cases of CDAD will be recorded. A patient collection form will not be completed for ongoing surveillance for CDAD. Patients can be enrolled more than once.

The total number of monthly CDAD cases and denominator will be provided quarterly to PHAC. Denominator information will include total patient days, patient admissions, and total number of liquid stools submitted to microbiology laboratory. Whenever possible, denominator information will be obtained separately for pediatric and adult patients. The surveillance information will be forwarded to PHAC every three months by email.

Annual targeted surveillance for CDAD: Once a year over a two-month consecutive period, patient data will be collected on all patients meeting the case definition for CDAD. The annual period for the targeted surveillance will be determined each year at the CNISP meeting for the next calendar year. The targeted surveillance for 2007 will be from March 1st to April 30th. Patient information will include: basic demographic data including age and sex, admission date, and type of patient ward where the patient is located on the day CDAD is identified. Information about CDAD will include date of onset of diarrhea or date of the first positive specimen submission. Data will be recorded for each CDAD episode. An episode is defined as the time from onset of symptoms until the last day of antibiotic treatment. Episodes which do not meet the criteria for disease (i.e., positive test, but criteria for diarrhea or other symptoms not met) will not be included.

Adverse Outcomes

Data regarding adverse events will be collected 30 days after the diagnosis of a positive case, and will include death (all cause, and attributable to CDAD), ICU admission, and colectomy.

CDAD attributable death: All cases of death within 30 days of diagnosis of a CDAD episode will be assessed by the CHEC member to determine if the death was attributable to CDAD. Cause of death will be determined by the following criteria:

1. CDAD directly related to the death of this patient, that is, the patient had no underlying condition that would have caused death during this hospitalization.
2. CDAD indirectly related to death: CDAD contributed to death, but was not the primary cause, that is, the CDAD exacerbated an existing disease condition that led to the patient's death.
3. CDAD not related to death: The patient died from causes unrelated to CDAD.

Information may be obtained from patient hospital charts, nurses' logs, laboratory reports, nursing/medical staff, etc. Investigators will be encouraged to participate in medical

rounds to facilitate data collection. The data will be entered on manually-completed patient questionnaire forms (Appendix A). Each site will retain a copy of the patient questionnaires. Patient forms will be forwarded to NML along with the corresponding stool samples. The patient forms do not need to be complete when forwarded to NML. At the end of the two-month targeted surveillance period and the 30-day patient follow-up, patient forms, if not previously complete, may be forwarded to NML with a note indicated that the form is a revision. PHAC will be responsible for all data entry, validation and analysis.

2.2 *Case Definition for Clostridium difficile-associated diarrhea*

CDAD surveillance will include Laboratory, Gastroenterology and Pathology involvement at each hospital site. The charts of patients with positive stool samples for *C.difficile* toxin will be examined in order to determine whether the patient meets the case definition for CDAD.

The following definition will be used for CDAD:

1. Diarrhea* or fever, abdominal pain and/or ileus AND laboratory confirmation of a positive toxin assay for *C.difficile*;

OR

2. Diagnosis of pseudomembranes on sigmoidoscopy or colonoscopy, or histological/pathological diagnosis of CDAD.

*Diarrhea will be defined as one of the following:

- 6 watery stools in past 36 hours
- 3 unformed stools in 24 hours for 2 days
- 8 unformed stools over 48 hours

In the event that information regarding the frequency of diarrhea is not available, the Infection Control Professional will determine if this patient has CDAD based on his/her best judgment.

Once a patient has been included in the surveillance project, the infection will be considered hospital-acquired if it meets the following criteria:

1. Patient's symptoms occur at least 72 hours after current admission;

OR

2. Symptoms cause readmission in a patient who had been hospitalized within the previous two months of the current admission date, and who is not resident in a chronic care hospital or nursing home.

2.3 *Eligible Patients*

All hospitalized patients meeting the case definition for CDAD will be enrolled in the surveillance project except for neonates under 1 month of age and patients residing on psychiatric and long-term care or awaiting placement units. Long-term care and awaiting placement patients who are on acute-care wards during the surveillance period will be included. Eligible subjects will be identified by daily review of stool *C.difficile* toxin assay results in the clinical microbiology laboratory. All hospitalized patients with CDAD will be included, both community-acquired and hospital-acquired cases of CDAD.

C.difficile Strains Identification Procedures – See Laboratory Surveillance Protocol, Appendix D

2.4 *Statistical Analysis and Evaluation*

Information from the patient questionnaire will be entered and verified by PHAC on a customized database mirroring the data collection form (MS Access version 2002). Data will analyzed using SAS version 8.2 (SAS Institute, Cary NC) or compatible statistical software.

The CDAD subcommittee will review the data in order to describe the incidence of hospital-acquired CDAD among hospitalized patients and to examine the burden of this disease on health care facilities.

Summary data providing descriptive epidemiology will include but not limited to:

- Number of CDAD cases
- Incidence of nosocomial vs. community-acquired cases
- Incidence of CDAD cases by geographic region
- Location (Ward) of cases
- Severe outcomes

Patient information will be merged with laboratory data, i.e. molecular characterization of patient stool specimens. Genmod logistic regression technique will be used to determine if there is a correlation between certain strain types and severe outcome.

3. ETHICS

While this surveillance project is observational and does not involve any alteration in patient care, ethics approval may be sought at some hospital sites. Surveillance for nosocomial infections is a routine component of quality assurance and patient care in Canadian health care institutions and therefore informed consent will not be required. A unique identifier linked to patient name will only identify patients at the local CHEC site and ill not be transmitted to the PHAC. All data will be strictly confidential.

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