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Epidemiology of myasthenia gravis in Ontario, Canada

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Abstract

Incidence and prevalence estimates in myasthenia gravis have varied widely. Recent studies based on administrative health data have large sample sizes but lack rigorous validation of MG cases, and have not examined the North American population. Our aim was to explore trends in MG incidence and prevalence for the years 1996–2013 in the province of Ontario, Canada (population 13.5 million). We employed a previously validated algorithm to identify MG cases. Linking with census data allowed for the calculation of crude- and age/sex-standardized incidence and prevalence rates for the years 1996–2013. The regional distribution of MG cases throughout the province was examined. Mean age at the first myasthenia gravis encounter was 60.2 ± 17.1 years. In 2013, there were 3611 prevalent cases in Ontario, and the crude prevalence rate was 32.0/100,000 population. Age- and sex-standardized prevalence rates rose consistently over time from 16.3/100,000 (15.4–17.1) in 1996 to 26.3/100,000 (25.4–27.3) in 2013. Standardized incidence rates remained stable between 1996 (2.7/100,000; 95% CL 2.3–3.0) and 2013 (2.3/100,000; 2.1–2.6). Incidence was highest in younger women and older men, and geographic variation was evident throughout the province. In conclusion, this large epidemiological study shows rising myasthenia gravis prevalence with stable incidence over time, which is likely reflective of patients living longer, possibly due to improved disease treatment. Our findings provide accurate information on the Canadian epidemiology of myasthenia gravis and burden for health care resources planning for the province, respectively.
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Keywords: Administrative health data; Epidemiology; Incidence; Myasthenia gravis; Prevalence

1. Introduction

Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disorder resulting in ocular and limb muscle weakness, and potential bulbar weakness and respiratory failure [1] . Despite being considered a rare disease, the disease carries a large public health burden due to the presence of chronic muscle weakness and fatigability. The disease has high direct health care costs (including long-term treatment and periodic hospitalizations) and indirect costs such as income loss and reduced caregiver productivity. A US study calculated the mean yearly cost attributable to MG at $15,675 per patient [2]. Therefore, accurate identification of patients with MG and careful epidemiological studies are important for the organization of health care services and for implementation of preventative health measures.

A number of epidemiological studies have been performed in MG since 1950 – principally in Western Europe and Asia – and have reported marked variation in incidence, prevalence, and mortality values. Incidence rates have varied from 1.7 to 30 cases per million person-years [3,4], and prevalence rates have ranged from 7 to 179 cases per million population [5,6]. As a result of this marked variation, a small number of recent studies have explored the use of administrative health data (AHD) to better characterize MG incidence and prevalence in larger populations [7–10]. These studies generated incidence and prevalence estimates on the high end of the reported ranges – likely due to the ability of AHD to capture mild or pure ocular MG managed in a primary care setting. Although these studies cast a broader net, they lack rigorous validation to ensure accurate identification of MG cases within AHD. In addition,

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none of these AHD-based studies were carried out in a North American population.

The single-payer Canadian health care system (providing coverage to 95% of the population) should provide a rich environment for studies of population disease statistics. However, only two prior studies have examined MG epidemiology in Canadian populations – an unpublished chart review from Nova Scotia in the 1950s [5] and a study from British Columbia reporting only acetylcholine-receptor antibody positive cases [11]. Recently, our group validated an algorithm to allow for identification of MG patients using AHD for the province of Ontario, Canada [12]. Therefore, the goal of the current study was to use this validated algorithm to identify trends in MG incidence and prevalence during the years 1996–2013.

2. Methods

The study protocol received ethics approval from the Research Ethics Board of Sunnybrook Health Sciences Centre in Toronto. We performed a population-based epidemiological study in Ontario, Canada's most diverse and populous province. In Ontario, 95% of the population receives health care through a publicly funded health care system (known as the Ontario Health Insurance Plan [OHIP]) which covers physician visits, hospitalizations, surgical procedures, and diagnostic tests [13]. All administrative health databases for the province are housed at the Institute for Clinical Evaluative Sciences (ICES) in Toronto. Statisticians at ICES performed data analysis for this study using SAS version 9.4 software.

2.1. Administrative health data sources

There were 4 administrative health data sources used in this study. (1) The Canadian Institute for Health Information (CIHI) discharge abstracts database contains information on all hospitalizations classified using ICD-9 (until and including 2002) and ICD-10 (after 2002) codes. MG is coded as 358.0, 358.00, or 358.01 in ICD-9; and G70.0, G70.1, or G70.2 in ICD-10. (2) The Ontario Health Insurance Program (OHIP) database contains fee codes and diagnostic codes for outpatient physician visits and procedures. MG is coded as 358, single-fiber electromyography as G458, and Tensilon testing as G419. (3) The Ontario Drug Benefit (ODB) database contains prescription drug information for seniors >65 years old and patients on social assistance. (4) The Ontario Registered Persons Database was used to obtain information about each patient's age, sex, vital status, and location of residence. These data sources are maintained with very high accuracy (little missing data) and patient records are linked between databases via coded health insurance numbers [14].

2.2. MG patient cohort

The criteria for inclusion in the MG Ontario patient cohort were generated based on a previously validated algorithm [12]. The optimal AHD algorithm previously identified was: [1 hospital discharge abstract with MG listed as a primary or secondary diagnosis], *or* [5 outpatient MG visits and 1 relevant diagnostic test within 1 year], *or* [3 pyridostigmine prescriptions within 1 year]. The above algorithm was able to identify MG with sensitivity = 81.6%, specificity = 100%, positive predictive value = 80.0%, and negative predictive value = 100% [12].

2.3. Statistical analyses: incidence and prevalence

Once patients were identified using the validated algorithm, disease onset was defined as the first health care encounter with MG as the recorded diagnosis. As AHD were available from April 1, 1991 to March 31, 2013, we used a 5-year run-in period (from 1991 to 1995) to identify pre-existing MG patients (those diagnosed before the onset of administrative data). This run-in period is required, as all pre-existing MG patients identified in the earliest years of observation would otherwise appear as incident.

Annual crude and standardized incidence and prevalence rates (with corresponding 95% confidence intervals [95% CIs]) were calculated among patients 18 years and older for the years 1996–2013.

Only individuals with no such previous contacts for MG were counted as incident cases for the relevant year, and the incident population at risk was calculated as the census population minus the prevalent cases from the previous year. The numerator represents all MG patients, and the denominator represents all persons aged ≥18 years living in Ontario for the relevant year. Prevalent cases were carried forward for each year, and persons who died or moved out of the province were excluded from the numerator and denominator. Individuals aged <18 years were also excluded from both the numerator and the denominator.

Annual age-specific rates were also computed for 10-year age bins and expressed per 100,000 population. The 1991 Ontario population was used as the standard population for direct age and sex standardization.

The province was divided by administrative health regions (known as Local Health Integration Networks or LHINs) to examine and map the density of MG patients in each region, with the aim to determine whether any regional variation was evident.

3. Results

We identified 6750 incident cases of MG in Ontario over the study period. Of those incident cases, 2252 initially qualified for the MG cohort based on prescription data, 2367 based on hospitalization data, and 2131 based on outpatient MD visits and diagnostic tests. The mean age at first MG encounter was 60.2 ± 17.1 years.

Table 1 displays both the crude and age/sex-standardized incidence and prevalence rates during the years 1996–2013. The crude MG prevalence showed a steady increase over time from 1422 cases (16.6 per 100,000 population) in 1996 to 3611 cases (32.0 per 100,000 population) in 2013. Over the same time period, the crude incidence rates remained essentially stable (2.7 per 100,000 population in 1996; and 2.8 per 100,000 population in 2013), although some year-to-year fluctuations

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