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Original Article

Prevalence of narcolepsy in King County, Washington, USA ☆

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Abstract

Background: Relatively few epidemiologic studies have focused on narcolepsy, a disabling sleep disorder with a strong association with HLA-DQB1*0602.
Methods: We sought to estimate the prevalence of narcolepsy using multiple overlapping techniques to identify residents of King County, WA who were 18 years or older with physician-diagnosed narcolepsy. Patients were entered into a registry and recruited into an epidemiologic study entailing interview and buccal scrapings to determine HLA-DQB1*0602 status. Missing values were imputed to allow prevalence to be estimated based on all 425 patients entered into the registry between 2001 and 2005, whether they were recruited into the epidemiologic study ($n = 279$) or not ($n = 146$).
Results: As of July 01, 2001, estimated prevalence per 100,000 of physician-diagnosed narcolepsy with cataplexy was 21.8 (95% confidence interval (CI): 18.8–24.8), similar to prior studies. The median age of onset was 14 (interquartile range: 10–18). For narcolepsy with HLA-DQB1*0602, prevalence was 15.3 (95% CI: 12.8–17.9). Estimated prevalence was higher in women than men and in African-Americans than other racial groups.
Conclusions: These differences could reflect problems in identification and recruitment or may provide etiologic clues about narcolepsy. This study illustrates the challenges in performing population-based studies of narcolepsy.

Keywords: Narcolepsy; Cataplexy; HLA-DQB1*0602; Epidemiologic studies; Prevalence; Incidence

1. Introduction

Narcolepsy, a disabling sleep disorder characterized by excessive daytime sleepiness and episodic loss of muscle tone triggered by strong emotions (cataplexy), likely results from selective destruction of hypocretin-producing cells in the lateral hypothalamus of genetically susceptible people defined by their carrying human leucocyte antigen (HLA-) DQB1*0602 [1]. We sought to identify all residents of King County, WA with narcolepsy in order to estimate the prevalence of disease, to seek etiologic clues, and to characterize clinical features in a population-based rather than clinic-based series of patients. To allow comparison with the single study that reported incidence [2], we also tried to estimate approximate incidence using recalled year of onset, realizing that study design and data available were not ideal for this purpose.

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2. Methods

2.1. Setting

Our goal was to identify as many residents as possible of Seattle and surrounding King County, WA who were 18 years or older with a physician diagnosis of narcolepsy. Most King County residents seek medical care within the county, which includes 10 sleep disorder centers. The Institutional Review Board at the University of Washington approved the study.

2.2. Case ascertainment

From July 01, 2001 to June 30, 2005 we tried to identify all eligible patients and determine whether they had the onset of their disease before the prevalence date, July 01, 2001. We used multiple overlapping methods directed at clinicians and patients. We met with directors of sleep disorders centers to explain the study and seek their help. We sent monthly letters to clinicians working in sleep disorder centers and to all neurologists in King County asking that they let us know about any patient whom they diagnosed with narcolepsy. We also sent a mailing to the county's family medicine physicians, psychiatrists, and community clinics where patients without financial resources often receive care.

For patients, study fliers were posted in waiting rooms of sleep disorder centers. Presentations about the study were made at the region's support groups and at the Narcolepsy Network's national annual meeting held in King County in 2004. A monthly newsletter was sent to all who had participated in the study hoping to inform others by word of mouth. Pharmacists in King County agreed to include an information sheet about the study with all prescriptions for certain medications commonly used to treat patients with narcolepsy. Advertisements and public service announcements were placed in several newspapers, on county buses, on several radio stations, and on television. All of these sources of information included a contact telephone number and address for the study's web site. The University of Washington also maintained a web site for research volunteers where information about the study was available.

2.3. Data sources

Patients with physician-diagnosed narcolepsy identified by any of these means were entered into a registry and invited to participate in an epidemiologic study of narcolepsy. For those not recruited, information was limited. For those who agreed to participate and who provided written informed consent, a trained professional interviewer asked the patient specific questions about clinical manifestations, onset of disease, and diagnosis. Also in those who agreed, medical records were requested and abstracted by the study neurologist. Information about cataplexy came from interviews and review of medical records. An affirmative response to experiencing muscle weakness when telling or hearing a joke, or when laughing, was considered a positive screen for cataplexy [3]. For this study, we defined cataplexy as present if indicated by medical record review, self-reported cataplexy, or a positive screen.

Because most patients with narcolepsy, especially narcolepsy with cataplexy, have been found in previous studies to carry HLA-DQB1*0602 [1], we were keenly interested in patients' HLA type. After obtaining consent, the interviewer collected buccal specimens, which were used to obtain genomic DNA. Genotyping of HLA-DQB1 entailed quantitative DNA amplification and fluorescence detection with sequence-specific probes, as described previously for HLA-DRB1 alleles [4]. Presence or absence and copy number of DQB1*0602 were scored for each sample.

2.4. Disease definitions

Current definitions distinguish between narcolepsy with and without cataplexy [5]. Sleep studies are required to make the diagnosis in patients without cataplexy and were not always available for patients with a physician diagnosis of narcolepsy. Based on all the information collected on these patients, we estimated the date of onset of narcolepsy symptoms. Using several definitions of narcolepsy, we estimated prevalence under each definition on July 01, 2001 in King County in those 18 years or older (about 1.4 million people). Although current definitions of narcolepsy do not require the patient to carry HLA-DQB1*0602 [5], we also defined a group in which all patients were positive for HLA-DQB1*0602. This group is key for future epidemiologic studies of etiologic risk factors that may only be relevant in susceptible people defined by their carrying HLA-DQB1*0602 [6].

2.5. Statistical analyses

Using information on both recruited and non-recruited cases in our registry, we estimated prevalence for three definitions of narcolepsy: (1) with or without cataplexy, (2) with cataplexy, and (3) with HLA-DQB1*0602. To estimate age, gender, and race-specific prevalences of narcolepsy in King County we imputed key variables for which values were unknown. Our registry included 425 cases, 146 of whom were not recruited for the study. For those not recruited, age was missing for 85; race for 123; and HLA status, cataplexy status and age of onset for all. We multiply imputed age, race, HLA status, cataplexy status and age of onset using the method of chained equations [7] as implemented by the