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A systematic review and meta-analysis on the epidemiology of Duchenne and Becker muscular dystrophy

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Abstract

The muscular dystrophies are a broad group of hereditary muscle diseases with variable severity. Population-based prevalence estimates have been reported but pooled estimates are not available. We performed a systematic review of worldwide population-based studies reporting muscular dystrophies prevalence and/or incidence using MEDLINE and EMBASE databases. The search strategy included key terms related to muscular dystrophies, incidence, prevalence and epidemiology. Two reviewers independently reviewed all abstracts, full text articles and abstracted data using standardized forms. Pooling of prevalence estimates was performed using random effect models. 1104 abstracts and 167 full text articles were reviewed. Thirty-one studies met all eligibility criteria and were included in the final analysis. The studies differed widely in their approaches to case ascertainment, resulting in significant methodological heterogeneity and varied data quality. The pooled prevalence of DMD and BMD was 4.78 (95% CI 1.94–11.81) and 1.53 (95% CI 0.26–8.94) per 100,000 males respectively. The incidence of DMD ranged from 10.71 to 27.78 per 100,000. This is the first meta-analysis of worldwide prevalence estimates for muscular dystrophies. There is a need for more epidemiological studies addressing global estimates on incidence and prevalence of muscular dystrophies, utilizing standardized diagnostic criteria as well as multiple sources of case ascertainment.

Keywords: Incidence; Prevalence; Epidemiology; Muscular dystrophy; Population-based

1. Introduction

The muscular dystrophies are a broad group of hereditary muscle diseases with variable phenotypes. The molecular causes of the more common types of muscular dystrophies have been identified and research towards effective therapies is ongoing. Duchenne and Becker muscular dystrophy are X-linked recessive allelic disorders caused by mutations of the *dystrophin* gene. Duchenne muscular dystrophy (DMD) is the most common form of inherited muscle disease in childhood, with an estimated incidence of 1 in 3500 boys [1]. The absence of dystrophin protein leads to progressive muscle necrosis, loss of independent ambulation by early

Abbreviations: DMD, Duchenne muscular dystrophy; BMD, Becker muscular dystrophy; CI, confidence interval

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adolescence, cardiomyopathy, respiratory insufficiency, and premature death in affected individuals. Becker muscular dystrophy (BMD) is a generally milder and more variable form of dystrophinopathy, with an incidence of 1 in 18,518 male births [1]. The diagnosis of Duchenne and Becker muscular dystrophy is based on careful review of the clinical features and confirmed by additional investigations including muscle biopsy and/or genetic testing.

Population-based prevalence estimates for the muscular dystrophies exist but more precise pooled estimates are unavailable. Robust pooled estimates are essential to facilitate the interpretation of clinical studies on molecular epidemiology, natural history, and impact of potential treatments. In addition, analysis of economic impact and health care burden are contingent upon precise population-based prevalence estimates. The purpose of this study is to systematically evaluate the worldwide incidence and prevalence of Duchenne and Becker muscular dystrophy. This study was part of a larger initiative funded by the Public Health Agency of Canada to facilitate better understanding of the burden of neurological illnesses in Canada and worldwide.

2. Methods

2.1. Search strategy

We performed a systematic review of worldwide population-based studies reporting the incidence and prevalence of muscular dystrophies using MEDLINE and EMBASE databases. A comprehensive literature search was developed with guidance from a research librarian experienced in systematic reviews. Both MEDLINE and EMBASE were searched for terms related to muscular dystrophy and incidence, prevalence and epidemiology on January 28, 2011 (see Appendix 1 for detailed search strategies).

The diagnosis of DMD and BMD was historically based on the clinical picture of calf hypertrophy and progressive muscular weakness in affected boys, in the presence of a positive family history. Specific clinical criteria for DMD include age of onset under 5 years of age, loss of ambulation by age 15 years without treatment; progressive muscular weakness and atrophy with calves hypertrophy, scoliosis, joint contractures, and respiratory failure prominent before 20 years of age; high serum creatine kinase, dystrophic changes in muscle biopsy with less than 1% dystrophin present; and positive family history with X-linked recessive inheritance [2,3].

Two independent reviewers screened abstracts to determine eligibility for full-text review. Population based studies reporting an incidence and/or prevalence of muscular dystrophies were included. Studies were considered population based if they employed a sampling method meant to be representative of the entire population and/or were completed in a defined geographic area of known population size. Studies were excluded if they did not provide an estimate of incidence or prevalence, collected data before 1985, or reported non-original data (i.e. reviews, letters, or editorials). To identify additional studies the bibliographies of the excluded non-original data studies and the studies that were included in the review were hand searched. Agreement at the abstract review stage was calculated using the Kappa statistic [see http://www.cochrane.org/handbook/726-measuring-agreement].

2.2. Data abstraction

Two independent reviewers extracted data from included studies using standard forms. Demographic data including age characteristics, race, sex, and location were recorded. In addition, the types and sources of data, case definitions, and diagnostic criteria for the disorders were also collected. Prevalence and incidence of the conditions within each study was recorded, and estimates were stratified by age and sex if provided. Disagreements between reviewers during abstract screening, full-text review, and/or data extraction were resolved by consensus and the use of a third reviewer as required.

2.3. Study quality

Two reviewers independently completed a quality review for each study using a modified existing quality assessment tool [4]. Quality scores were determined from eight key questions pertaining to representativeness of the sample, assessment of the neurological condition, and statistical analysis (see Appendix 2).

2.4. Statistical analysis

Depending on the natural history of diseases the estimates of point and period prevalence can vary; however, due to the irreversible nature of muscular dystrophies we chose to consider both forms of prevalence together. The pooled prevalence of DMD, BMD, and combined dystrophies per 100,000 were calculated when appropriate. Estimates using total population (males and females) as the denominator were considered separately from those including only males in the denominator. Also, studies that included only male children were separated from those including males of all ages.

In order to be included in the meta-analysis studies needed to report the number of cases and sample size, an estimate with confidence intervals, or the information needed to calculate the required information. As significant heterogeneity was expected we decided *a priori* to employ random-effects models to complete stratified analyses along with meta-regression to investigate sources of heterogeneity. To assess for significant between-study heterogeneity the Cochrane Q statistic was calculated as

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