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Incidence and Types of Pediatric Nystagmus

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Abstract

Purpose—To report the incidence, prevalent subtypes and clinical characteristics of pediatric nystagmus diagnosed over a 30-year period.

Design—Retrospective, population-based study

Methods—Using the Rochester Epidemiology Project, the medical records of all children (<19 years) diagnosed as residents in Olmsted County, Minnesota with any form of nystagmus from January 1, 1976, through December 31, 2005, were reviewed.

Results—Seventy-one children were diagnosed during the 30-year period, yielding an annual incidence of 6.72 per 100,000 younger than 19 years (95% confidence interval [CI], 5.15–8.28). Infantile nystagmus, onset by 6 months, comprised 62(87.3%) of the study patients, corresponding to a birth prevalence of 1 in 821. The median age at diagnosis for the cohort was 12.7 months (range, 0 days to 18.6 years) and 42(59.2%) were male. The main types of nystagmus, in declining order, were: nystagmus associated with retinal/optic nerve disease in 23(32.4%), idiopathic or congenital motor nystagmus in 22(31.0%), manifest latent nystagmus or latent nystagmus in 17(24.0%), and 2(2.8%) each associated with Chiari malformation, medication use, tumor of the CNS and no diagnosis. Developmental delay was diagnosed in 31(43.6%), strabismus in 25(40.3%), and amblyopia in 10(25.6%). Eighty percent had 20/40 (or equivalent) or better vision at presentation in at least one eye.

Conclusions—This study provides population-based data on incidence and clinical characteristics of childhood nystagmus in North America. Idiopathic and nystagmus associated with retinal/optic nerve disease were the most common presentations with most patients having good vision. Developmental delay, strabismus, and amblyopia were common in this cohort.

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Introduction

Nystagmus is an abnormal rhythmic oscillation of one or both eyes that can occur at birth or any time thereafter. Although there are a number of classifications schemes for childhood nystagmus, most investigators generally define nystagmus diagnosed in the first 6 months of life as infantile nystagmus, which is commonly subdivided into sensory motor nystagmus (which will hereafter be referred to as nystagmus associated with retinal/optic nerve disease), manifest latent nystagmus or latent nystagmus (MLN/LN), spasmus nutans, or idiopathic or congenital motor nystagmus (as also termed idiopathic nystagmus).¹ Less commonly, nystagmus in infants can be associated with conditions such as multiple sclerosis, hydrocephalus, trisomy 21 and a cerebral vascular accident.² Prevalence rates of infantile nystagmus have been reported primarily from Europe and Asia, and ranges widely from 1/1000 to 1/500,000.²⁻⁷ The most recent study providing prevalence data on nystagmus from North America is from a small study in which approximately 2,500 children were screened for ocular abnormalities in which 1 out of 283 had nystagmus.⁸ Estimates of nystagmus incidence are also limited.

The purpose of this study was to identify the incidence, subtypes, and clinical characteristics of pediatric nystagmus in a North American population of children (<19 years of age) diagnosed over a 30-year period using a population-based medical records linkage system.

Methods

This study was comprised of residents of Olmsted County who were <19 years of age when diagnosed with any form of nystagmus from January 1, 1976, through December 31, 2005. Potential causes were retrospectively identified using the resources of the Rochester Epidemiology Project, a medical record linkage system designed to capture data on any patient-physician encounter in Olmsted County, Minnesota.¹⁰ The racial distribution of Olmsted County residents in 1990 was 95.7% white, 3.0% Asian American, 0.7% African American, and 0.3% Native American; the remaining 0.3% were of other race. The population is relatively isolated from other urban areas, and virtually all medical care is provided to its residents by Mayo Clinic, Olmsted Medical Group, and their affiliated hospitals. Patients not residing in Olmsted County at the time of their diagnosis were excluded from the study. Institutional Review Board approval was obtained for this study. The medical records of all potential patients were reviewed by an ophthalmologist. Children with nystagmus were subdivided into idiopathic nystagmus, nystagmus associated with retinal/optic nerve disease, MLN/LN, medication-induced, associated with Chiari malformation or a tumor of the central nervous system (CNS). Demographic information, visual acuity, presence of co-existing ocular disease, causes of nystagmus and treatment, if applicable, were reviewed. The medical records were specifically reviewed for the first complete ocular exam reporting nystagmus, final ocular exam, and the most recent follow-up evaluation in any department.

The overall incidence of infantile nystagmus was estimated using the age- and sex-specific population figures for Olmsted County census data for 1976 through 2005. Yearly incidence rates for age and sex groups were determined by dividing the number of cases with infantile

nystagmus within that group by the estimated total Olmsted County resident population of the group for that given year. Population figures come from the U.S. census data, and population figures for the inter-census years were estimated using linear interpolation. These incidence rates were also age- and sex-adjusted to the 2010 census figures for the U.S. white population. The 95% confidence intervals (CIs) for the rates were calculated assuming Poisson error distribution.

Results

A total of 71 children were diagnosed in Olmsted County, Minnesota during the 30-year period. The annual age- and gender-adjusted incidence of all forms of pediatric nystagmus was 6.72 per 100,000 residents less than 19 years (95% confidence interval [CI], 5.15–8.28). Among those with infantile nystagmus (onset by 6 months of age), diagnosed in 62(87.3%), the birth prevalence was 1 in 821 live births. The specific types of nystagmus observed (Table 1), in declining order, were: nystagmus associated with retinal/optic nerve disease in 23(32.4%), idiopathic nystagmus in 22(31.0%), MLN or LN in 17(24.0%), and 2(2.8%) each associated with Chiari malformation, medication use, tumor of the CNS and no given diagnosis (CI 0.3–9.8). There was one case of neurologic nystagmus and no cases of spasmus nutans (0 in 71, CI 0.0–5.1).

The median age at diagnosis was 12.7 months (range, 0 days to 18 years) and 42(59.2%) were male. Presenting complaints included abnormal eye movements (17(24.3%)), abnormal head posture (5(7.1%)), night blindness (1(1.4%)) and photophobia (1(1.4%)). Nystagmus occurred bilaterally in 64(92.8%), in the right eye only in 2(2.9%), and in the left eye in 3(4.4%). Fifty-six (78.9%) patients had no torticollis, 8(11.2%) predominately had a left face turn, 3(4.2%) had a right face turn, 2(2.8%) had a chin down position and one case was unknown.

Sixty (84%) of the 71 had an assessment of visual acuity at presentation, of which 48(80%) had 20/40 (or central, steady, maintained or fix and follow for pre verbal children) or better vision at presentation in at least one eye. Exotropia or esotropia was present in 25(40.3%) patients while amblyopia was documented in 10(25.6%). Abnormal anterior segment findings were present in 5(7.9%) and abnormal posterior segment findings in 20(33.3%). The most common ocular abnormalities of nystagmus associated with retinal/optic nerve disease patients were albinism (7(30.4%)), optic nerve hypoplasia (3(13.0%)), Lebers Congenital Amaurosis (2(8.7%)) and congenital cataract (2(8.7%)) as shown in Table 2.

Developmental delay was diagnosed in 31(43.6%) of the 71 children with nystagmus. Among these 31 delayed patients, nystagmus associated with retinal/optic nerve disease occurred in 11(35.5%), idiopathic in 6(19.6%), MLN/LN in 9(29%), 2 with no diagnosis, and one each with neurologic nystagmus, medication-induced, and Chiari malformation. The most commonly diagnosed developmental abnormalities noted in these patients were nonspecific “delay” in 18(58.1%), cerebral palsy in 6(19.4%) and Down syndrome in 3(9.7%).

Discussion

Infantile nystagmus, comprising approximately half of the children diagnosed in this cohort over a 30-year period, occurred in 1 in 821 live births. Nystagmus associated with retinal/optic nerve disease, idiopathic nystagmus and manifest latent nystagmus or latent nystagmus (MLN/LN) made up nearly 90% of the 71 study patients while only 2 were associated with a malignancy of the central nervous system (CNS). Of the patients with visual assessment at presentation, 80% had 20/40 (or equivalent) or better and torticollis occurred in approximately 20%. Developmental delay, as well as strabismus and amblyopia, were commonly encountered in this study cohort.

While prevalence data is readily available for nystagmus, incidence data is more variable and difficult to identify. Previous estimates of idiopathic nystagmus incidence range widely but are suggested to be 1/6,550.¹¹ This is in contrast to the incidence of 6.72 per 100,000 live births (or 1/14881) from our study. However, given the potential variability in age at diagnosis as well as differences in classifications systems, it is reasonable to expect some variation in this relatively rare condition. In 1964, Norn estimated the incidence of idiopathic nystagmus to be 1/20000 based on a cohort spanning 1927–1963 of partially sighted or blind children in Denmark. The author acknowledged, however, that the incidence was based on patients referred for low vision and was likely to be an overestimate.⁴ This referral bias is in contrast to the findings of this study in which the diagnosis of nystagmus was made within a well-established population cohort. Unlike incidence, the birth prevalence of 1 in 821 in our study was similar to the Leicestershire study which identified a prevalence of 1 in 588.²

Idiopathic nystagmus and nystagmus associated with retinal/optic nerve disease made up the majority of children with nystagmus and were found to occur in equal measure. This finding is in contrast to a previous report in which the nystagmus associated with retinal/optic nerve disease form of nystagmus predominates in infants presenting before 6 months of age.¹² Albinism and optic nerve hypoplasia made up slightly more than half of the causes of nystagmus associated with retinal/optic nerve disease in this cohort (Table 2), similar to published studies.^{1,2} MLN/LN accounted for 1 of 4 patients in this study. In the Leicestershire hospital-based survey, 11.8% of patients with nystagmus had MLN or LN.² Since LN is, by definition, absent until the eye is occluded, this form of nystagmus is likely to be uncommonly observed and underreported.

More serious disorders associated with childhood nystagmus in this cohort included Chiari malformation, medication use and central nervous system malignancies. Chiari malformation is well known to be associated with various presentations of nystagmus, although it is most commonly associated with the downbeat form.¹³ In this cohort, there was one type 1 and one type 3 Chiari malformation. The two medications associated with nystagmus in this group were phenytoin and carbamazepine, both of which are documented to cause nystagmus.^{14,15} Of the 2 of 71 (2.8%) patients in this study with CNS tumors, both were pilocytic astrocytomas of the posterior fossa, and both acquired unilateral nystagmus at 13 years of age. Although tumors of the CNS can have diverse clinical presentations, nystagmus can be the initial presenting sign.¹⁶ Central nervous system malignancies encompassed a minority of the cases seen in the present study. Appropriate consideration for

this cause of nystagmus should be made when examining a new patient. A full history and examination is necessary to identify findings suggesting a cause other than idiopathic nystagmus, nystagmus associated with retinal/optic nerve disease or MLN/LN which might indicate the need for an electroretinogram (ERG) or magnetic resonance imaging (MRI).

Two additional patients, not included in this study, were diagnosed with spasmus nutans by their primary care provider. However, neither of these patients was examined by an eye care provider, and there was no mention of nystagmus within the medical record. If true and none of the 71 patients diagnosed with nystagmus over the 30-year period were found to have spasmus nutans, the confidence interval for its occurrence in this population still reaches as high as 5%.

Some form of developmental delay was diagnosed in 31(43.6%) of the 71 children with nystagmus. The only other study reporting on the prevalence of developmental delay in childhood nystagmus was a review of 25 patients with congenital nystagmus from a single practice in which two thirds of their patients had developmental delay.¹⁷ A specific reason for this association is unknown and is likely to be multifactorial; however, an insult to the CNS of children that results in nystagmus may simultaneously affect regions governing development. Most of these patients had either idiopathic nystagmus, nystagmus associated with retinal/optic nerve disease or MLN/LN and carried diagnoses ranging from cerebral palsy, Down syndrome, Asperger's syndrome, or simply mention of developmental delay without further description. Regardless of the cause, and given the high risk of developmental delay among these patients, children with nystagmus should be carefully monitored to maximize their ophthalmic and developmental progress.

There is considerable controversy regarding nomenclature and classification of childhood nystagmus. As such, the Committee for the Classification of Eye Movement Abnormalities and Strabismus (CEMAS) endeavored to clarify and update the nomenclature of nystagmus.¹⁸ (Complete classification available at <https://nei.nih.gov/sites/default/files/nei-pdfs/cemas.pdf>) A key factor in this classification system is the utilization of eye movement recordings to classify the nystagmus. None of the patients in this review had eye movement recordings making CEMAS reclassification difficult. Furthermore, some of the patients in this study could not be organized according to the CEMAS classification. The incidence of nystagmus in this cohort, based on the CEMAS classification scheme, is 1 in 1131 births (n = 45) for Infantile Nystagmus Syndrome (the combination of nystagmus associated with retinal/optic nerve disease and idiopathic nystagmus) and 1 in 2994 births (n = 17) for Fusion Maldevelopment Nystagmus Syndrome (formerly the MLN/LN group). In the two patients with no specific nystagmus diagnosis, one had a history of cerebral palsy while the other had a history of an occipital lobe lesion noted at birth leading to delayed visual maturation.

There are several limitations to the findings in this study. This retrospective study is limited by incomplete data and irregular follow-up. Additionally, the ability to generalize the findings from this population-based data to other populations is limited by the lack of diversity of the population in Olmsted County during the study years of the project. In this regard, the study population may be somewhat similar to the previous studies from Europe

(United Kingdom, Denmark, Netherlands, and Sweden). It also may be difficult to directly compare results from this study to the BPEDS report because of potentially different racial demographics.⁸

In this population-based study of childhood nystagmus, nystagmus associated with retinal/optic nerve disease, idiopathic nystagmus, and manifest latent or latent nystagmus comprised nearly 90% of the study patients. Nystagmus associated with a malignancy of the central nervous system was uncommon and nearly half of the patients had some form of developmental delay. Although most patients had relatively good vision, strabismus and amblyopia were common in this cohort.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Types of childhood nystagmus diagnosed from 1976 to 2005 in Olmsted County, Minnesota (N=71)

Type of Nystagmus	n	%
Associated with retinal/optic nerve disease	23	32.4
Idiopathic/Congenital	22	31.0
Manifest Latent/Latent	17	24.0
Chiari Malformation	2	2.8
CNS Tumor	2	2.8
Medication Induced	2	2.8
No Diagnosis	2	2.8
Neurologic	1	1.4
Overall	71	100.0

Table 2

Diagnoses in nystagmus group associated with retinal/optic nerve disease

Type	n	%
Albinism	7	30.4
Optic Nerve Hypoplasia	3	13.0
Lebers Congenital Amaurosis	2	8.7
Congenital Cataracts	2	8.7
Foveal Hypoplasia	2	8.7
Achromatopsia	1	4.3
Persistent Fetal Vasculature	1	4.3
Presumed Retinal Dystrophy	1	4.3
Optic Nerve Pallor from Hypoxic Encephalopathy	1	4.3
cerebral palsy, cortical blindness	1	4.3
neonatal hydrocephalus, cerebral palsy	1	4.3
None recorded	1	4.3
Overall	23	100