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Original Research Article

CLINICAL FEATURES AND MANAGEMENT OF NYSTAGMUS AMONG CHILDREN AT TERTIARY CARE

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Abstract

Background: Nystagmus is defined as an involuntary rhythmic oscillation of the eyes, and it can be confirmed relatively easily through direct observation of eyes and/or eye movement recordings. Nystagmus is commonly encountered in clinical practice and leads to reduced visual acuity due to the excessive motion of images on the retina, and also the movement of images away from the fovea. The prevalence of nystagmus in the general population is estimated to be 24 per 10,000 population with a slight predilection toward European ancestry. **Material and Methods:** This prospective, Single-centre cohort study was conducted in the Tertiary Care Teaching Hospital. Medical charts were selected by searching the keyword "nystagmus" in the fields "history," "clinical examination," and "diagnosis" of the electronic notes. Potential case patients were manually screened by medical chart review. We included all patients referred to the Pigment epithelial detachments (PED) with a history of 30 days of an ocular movement abnormality in whom a diagnosis of nystagmus was confirmed. Exclusion criteria were (1) abnormal eye movements other than nystagmus (such as ocular flutter, opsoclonus, and/or supranuclear gaze disturbances), (2) patients attending the PED because of head injury or (3) epileptic seizures, and (4) patients affected by an already known neurologic condition explaining the nystagmus. **Results:** In 77 cases (37%), patients attended the PED complaining of abnormal eye movements. In the remaining cases, nystagmus was detected during clinical examination in patients with other complaints. The mean time from symptoms onset to admission to the PED was 5 days, with 68% of the whole cohort reporting the onset of symptoms within 3 days before admission (median: 2 days). The Nystagmus plane was horizontal in the vast majority of cases (71.4%). Less frequently, vertical (6.8%), torsional (1%), or combined (3.4%) nystagmus was reported. Nevertheless, in a significant proportion of patients, the oscillation plane was not reported in clinical records (17.4%). **Conclusion:** Since nystagmus has negative psychosocial and functional consequences as discussed earlier, there is a great deal of interest in its treatment. Intervention should be individualized based on the patient's age, function, needs, and concerns. The first step in intervention is the provision of optimal refractive correction, possibly with the inclusion of a prism to stimulate convergence or correct an AHP. If this does not meet the patient's needs, then pharmacological or surgical intervention should be considered.

INTRODUCTION

Nystagmus is defined as an involuntary rhythmic oscillation of the eyes, and it can be confirmed relatively easily through direct observation of eyes and/or eye movement recordings. Nystagmus is commonly encountered in clinical practice and leads to reduced visual acuity due to the excessive motion of images on the retina, and also the movement of images away from the fovea.[1] The prevalence of nystagmus in the general population is estimated to be 24 per 10,000 population with a slight predilection toward European ancestry. The prevalence of infantile nystagmus is 14 per 10,000.[2]

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Nystagmus can be grouped into infantile nystagmus (IN), which usually appears in the first 3–6 months of life, and acquired nystagmus (AN), which appears later. For those who have infantile nystagmus (IN), this can be idiopathic or associated with another eye disease, such as retinal disease, albinism, low vision, or visual deprivation in early life (due, for example, to congenital cataracts or optic nerve hypoplasia). Nystagmus can also be part of neurological syndromes and neurologic diseases.[3]

In association with other eye diseases, vision is not only affected by the excessive motion of the image on the retina caused by the nystagmus but also by a defective visual system.[4] Mechanisms underlying IN are not very clear. Numerous hypotheses and models have been proposed to explain the ocular oscillations observed in IN, usually highlighting various elements of the ocular motor circuitry as the direct cause.[5] However, the clear association between IN and the many sensory anomalies that lead to sight loss during visual development imply an afferent cause to many IN forms.[6]

MATERIALS AND METHODS

This prospective, Single-centre cohort study was conducted in the Tertiary Care Teaching Hospital. Medical charts were selected by searching the keyword "nystagmus" in the fields "history," "clinical examination," and "diagnosis" of the electronic notes. Potential case patients were manually screened by medical chart review. We included all patients referred to the PED with a history of 30 days of an ocular movement abnormality in whom a diagnosis of nystagmus was confirmed. Exclusion criteria were (1) abnormal eye movements other than nystagmus (such as ocular flutter, opsoclonus, and/or supranuclear gaze disturbances), (2) patients attending the PED because of head injury or (3) epileptic seizures, and (4) patients affected by an already known neurologic condition explaining the nystagmus.

We included both patients attending the PED complaining of eye movement abnormality and patients complaining about other symptoms whose nystagmus was detected during the clinical examination. In the latter case, nystagmus was considered a new onset when it was reasonably linked with the same pathologic process causing the acutely presenting symptoms (eg, ataxia, vertigo, headache, altered mental status), it had neither been noticed before nor mentioned in medical records, and it was not explained by any of the known preexisting medical problems.

From each medical record, information about demographic features, clinical history, examination findings, investigations performed, hospital admission, and length of stay (as applicable) was extracted. Accordant with Italian National Health Service guidelines, the priority of consultation on PED admission was based on a 4-color triage coding scale:

- Red code: critical medical state, vital signs alteration needing immediate life-saving intervention, high-priority access to urgent care;
- Yellow code: serious state, risk of evolution into critical conditions, intermediate-priority access and re-evaluation needed in 5 to 15 minutes;
- Green code: fair state, stable vital signs, medical consultation postponable without risk, low priority access and re-evaluation needed in 30 to 60 minutes; and
- White code: good state, nonurgent consultation.

The triage code has to be assigned by a trained triage nurse at the entrance of the emergency department and is periodically reevaluated during the waiting time. This system was enforced during the entire study period, which was conducted after the Italian Ministry of Health agreement with all Italian regions in 2001.

The clinical and demographic features were described in the overall cohort and the 2 subgroups (patients with and without UCs). Each variable was compared between the 2 subgroups to identify significant differences. After reviewing for appropriateness, x2 and Student's t-tests were used for statistical comparison of categorical and continuous variables, respectively.

To detect predictive variables associated with a higher risk of UCs in patients with AN, a logistic regression analysis model was applied. Clinical features revealing significant differences on x2 and t-tests were selected as independent variables. Sex and age were included a priori to adjust the effect of each independent variable for the demographic characteristics of the cohort. Variables with extremely unbalanced distribution in the 2 groups (frequency 0% in 1 group) were excluded.

Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were used as measures of effect. The statistical significance was set at P, .05 for all analyses. SPSS Statistics software package (IBM SPSS Statistics, IBM Corporation) was used to perform all statistical analyses.

RESULTS

A total of 100 patients meeting the inclusion criteria were identified (48 male patients; male-to-female ratio: 1.01). Demographic and clinical features of the whole cohort and the 2 subgroups with and without severe UCs are summarized in Table 1. The mean age at PED attendance was 8 years 11 months. Thirty-seven patients (33%) were, 2 years of age (25 of 37 were, 6 months), 34 children (38%) were aged between 2 and 12 years, and 82 (40%) were .12 years. In 77 cases (37%), patients attended the PED complaining of abnormal eye movements. In the remaining cases, nystagmus was detected during clinical examination in patients with other

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complaints. The mean time from symptoms onset to admission to the PED was 5 days, with 68% of the whole cohort reporting the onset of symptoms within 3 days before admission (median: 2 days). The Nystagmus plane was horizontal in the vast majority of cases (71.4%). Less frequently, vertical (6.8%), torsional (1%), or combined (3.4%) nystagmus was reported. Nevertheless, in a significant proportion of patients, the oscillation plane was not reported in clinical records (17.4%). The symptoms most commonly referred to during PED consultation were headache (43.2%) and vertigo and/or dizziness (42.2%), followed by nausea and vomiting (25.7%) and visual disturbances (16.02%). Many patients presented with a constellation of associated symptoms. Clinical findings most commonly reported during examination included ataxia (18.45%), strabismus (13.1%), or a decreased level of consciousness (6.3%). Sixteen patients (7.8%) were febrile at PED admission (Table 2). In 54.9% of the cases, nystagmus was the only neurologic abnormality reported.

Specialist consultations were requested for 83.5% of the patients, mainly neurologic (61.2%) or ophthalmologic (35.4%) consultations. Approximately one-half of the patients underwent neuroimaging tests (53.9%); 60.4% of them performed the test directly in the PED (Table 3).

A total of 118 patients (57.3%) were hospitalized after PED consultation. Migraine was the most common cause of AN (accounting for 25.7% of all cases), followed by vestibular disorders (14.1%). Transient, not otherwise identified vertigo accounted for 12.6% of the cases. Idiopathic infantile nystagmus (IIN) was responsible for 6.8% of the AN cases, representing the first cause of PED consultation for nystagmus in the first year of life. Other rarer causes of AN included toxic ingestion, post infectious cerebellar ataxia, and periodic syndromes. Thirty-nine patients were diagnosed with a UC (18.9%). Brain tumours were the first UC-causing AN (17 cases; 8.3% of the whole cohort). Other causes included idiopathic intracranial hypertension, demyelinating disorders, degenerative conditions, and CNS infections or malformations.

Patients with UCs were found to be significantly younger than non-UC patients (mean age: 6 years and 11 months versus 12 years and 4 months), with the highest frequency of UC cases occurring in children between 1 and 6 years of age. The time delay from symptoms onset to PED presentation was significantly longer in UC compared with non-UC patients (Table 1). Diplopia, blurred vision, strabismus, cranial nerve palsy, ataxic gait, dysmetria, pyramidal weakness, and papilledema, as well as the absence of accompanying symptoms, were significantly more frequent in patients with UCs (Table 2). In contrast, vertigo and the absence of any neurologic sign were more commonly found in non-UC patients (Table 2), as well as the attribution of a nonurgent (green or white) triage code.

On this basis, 14 variables were selected for the logistic regression model (Table 4), including 199 patients (96.6%). According to our model, the presence of cranial nerve deficits, ataxia, or strabismus was strongly associated with an underlying UC, increasing its risk by 46.82-, 9.29, and 9.17-fold, respectively (P, .02) (Table 4). Though not reaching statistical significance, the presence of pyramidal weakness and abnormal head postures were also associated with an increased risk of UC (with an OR of 8.59 and 7.18, respectively). A longer time from symptoms onset to PED referral was found to raise the odds of an underlying UC, with a 9% increase of the risk by each day from nystagmus onset (OR = 1.09; P, .01). Despite the younger age at admission of patients with UCs, this variable was not associated with a greater risk of UC when adjusted for other variables in the logistic regression model (Table 4).

On the other hand, the occurrence of vertigo was found to reduce the odds of an underlying UC (OR = 0.17; P, .01), as well as the attribution of a green or white triage code (OR = 0.30; P = .01).

Table 1: Demographic Overview

	Non-UC (*n* = 60)	UC (*n* = 30)	Whole Cohort (*n* = 90)	p-value
Sex, *n* (%)				.6
Male	32 (53.3)	16 (53.3)	48 (53.3)	—
Female	28 (46.7)	14 (46.7)	42 (46.7)	—
Triage code,[a] *n* (%)				.02
Red	1 (1.7)	1 (3.3)	2 (2.2)	—
Yellow	16 (26.6)	15 (50)	31 (34.5)	—
Green	42 (70)	14 (46.74)	56 (62.2)	—
White	1 (1.7)	0 (0.00)	1 (1.1)	
The main reason for consultation, *n* (%)				.27
Nystagmus	20 (33.3)	13 (43.3)	33 (36.7)	—
Other symptom	28 (46.7)	17 (56.7)	45 (50)	—
Hospitalization after PED consultation, *n* (%)	12 (20)	30 (100.00)	42 (46.7)	,.01[b]
Age at admission, mo, mean (6SD); median	114.78 (666.75); 132.00	85.51 (669.38); 70.00	109.25 (668.34); 122.00	.01[b]
Time from symptoms onset, d, mean (6SD); median	6.23 (68.06); 2.00	10.15 (70.99); 5.00	5.95 (68.88); 4.00	,.01[b]

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Length of hospitalization (*n* = 114), mean (6SD); median	6.95 (66.20); 6.00	17.89 (629.55); 12.00	10.48 (619.28); 7.00	,.01

Table 2: Frequencies of Signs and Symptoms Associated with Nystagmus in the Whole Cohort and in the 2 Subgroups

	Non-UC (*n* = 60), *n* (%)	UC (*n* = 30), *n* (%)	Whole Cohort (*n* = 90), *n* (%)	p-value
Diplopia	5 (8.3)	7 (23.3)	12 (13.3)	.01[a]
Blurred vision	3 (5)	4 (13.3)	7 (7.8)	.04[a]
Photophobia	2 (3.3)	1 (3.3)	4 (4.4)	.75
Headache	25 (41.7)	12 (40)	37 (41.1)	.76
Vertigo	27 (45)	7 (23.3)	34 (37.8)	,.01[a]
Hearing loss	2 (3.3)	2 (6.7)	4 (4.4)	.36
Tinnitus	2 (3.3)	1 (3.3)	3 (3.3)	.89
Vomiting	14 (23.3)	10 (33.3)	24 (26.7)	.42
No associated symptom	7 (11.7)	9 (30)	16 (17.8)	.01[a]
Abnormal head posture	2 (3.3)	2 (6.7)	4 (4.4)	.049[a]
Strabismus	5 (8.3)	12 (40)	17 (18.9)	,.01[a]
Ptosis	1 (1.7)	0 (0.00)	1 (1.1)	.492
Pupillary defects	2 (3.3)	2 (6.7)	4 (4.4)	.26
Cranial nerve palsy	1 (1.7)	4 (13.3)	5 (5.6)	,.01[a]
Hypotonia	3 (5)	2 (6.7)	5 (5.6)	.84
Hypertonia	1 (1.7)	0 (0.00)	1 (1.1)	.4
Ataxic gait	10 (16.7)	10 (33.3)	20 (22.2)	.02[a]
Tremor	2 (3.3)	2 (6.7)	4 (4.4)	.17
Dysarthric speech	1 (1.7)	1 (3.3)	2 (2.2)	.52
Dysmetria	2 (3.3)	3(10)	5 (5.6)	.01[a]
Paresthesia	3 (5)	1 (3.3)	4 (4.4)	.89
Consciousness impairment	5 (8.3)	2 (6.7)	7 (7.8)	.69
Pyramidal weakness	2 (3.3)	3 (10)	5 (5.6)	.01[a]
Sensory loss	1 (1.7)	1 (3.3)	2 (2.2)	.26
Papilledema	0 (0.00)	2 (6.7)	2 (2.2)	,.01[a]
No associated neurologic abnormality	40 (66.7)	10 (33.3)	50 (55.6)	,.01[a]
Fever	5 (8.3)	4 (13.3)	9 (10)	.19

Table 3: Investigations Performed in the Whole Cohort and the 2 Subgroups

Non-UC (*n* = 60), *n* (%)		UC (*n* = 30), *n* (%)	Whole Cohort (*n* = 90), *n* (%)	*P*
Blood test	25 (41.7)	16 (53.3)	41 (45.6)	.288
Neuroimaging				,.001[a]
No imaging	32 (53.3)	1 (3.3)	33 (36.7)	—
CT	10 (16.7)	2 (6.7)	12 (13.3)	—
MRI	12 (20)	12 (40)	24 (26.7)	—
CT 1 MRI Specialist consultation	6 (10)	15 (50)	21 (23.3)	—
Neurologist	33 (55)	16 (53.3)	49 (54.4)	.3
Neurosurgeon	2 (3.3)	11 (36.7)	13 (14.4)	,.01[a]
Ophthalmologist	20 (33.3)	10 (33.3)	30 (33.3)	.95
Otorhinolaryngologist	12 (20)	2 (6.7)	14 (15.6)	.03
Toxicology screen	3 (5)	1 (3.3)	4 (4.4)	.5
EEG	15 (25)	4 (13.3)	19 (21.1)	.27
SSEP and/or MEP	2 (3.3)	4 (13.3)	6 (6.7)	.07
VEP	15 (25)	8 (26.7)	23 (25.6)	.82
ERG	9 (15)	2 (6.7)	11 (12.2)	.2
BAEP	2 (3.3)	2 (6.7)	4 (4.4)	.57
OCT	1 (1.7)	1 (3.3)	2 (2.2)	.45
Fundus oculi	17 (28.3)	10 (33.3)	27 (30)	.99
Vestibular tests	6 (10)	1 (3.3)	7 (7.8)	.62
CSF sampling	2 (3.3)	8 (26.7)	10 (11.1)	,.01[a]

DISCUSSION

In cases of obvious head turn, eye muscle surgery can be performed to shift the null zone of nystagmus into the primary position. The procedure is performed not only for cosmetic reasons but also to alleviate neck problems that can arise due to an abnormal head posture. There may also be improvement in visual acuity in some patients. For example, surgically correcting the head position in patients who wear glasses can enable them to view through their glasses centrally and achieve better

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optical correction Several attempts have also been made to improve visual acuity.[7-13]

The recession of all four horizontal muscles and, more recently, tenotomy (disinsertion and reattachment on the original insertion) of the four horizontal muscles have been reported to improve visual function and eye movements in IIN.[14] However, there are no randomized controlled studies to confirm these results. Surgeries used to treat nystagmus and anomalous head postures associated with IIN have also been used to treat albinism and other nystagmus forms.69, 70 Although improvements in the intensity of nystagmus are effective using surgical intervention, improvements in visual acuity are limited by the underdeveloped fovea and other afferent deficits in these patients.[15]

Although drugs have been administered for some time in AN, the pharmacological treatment for IN has not been explored until recently. Gabapentin and memantine, drugs which may have an anti-glutaminergic action, both showed a positive effect in patients with IIN (i.e., unassociated with other visual deficits) and patients with IN associated with other visual deficits (albinism, achromatopsia, optic atrophy, optic nerve hypoplasia, and congenital cataracts). The tolerability of the drugs was good and only mild side effects were noted, such as dizziness and tiredness.[16] Treatment for IN was trailed in a dosage of either up to 2400 mg gabapentin per day in three divided doses or 20–40 mg of memantine. The mechanism behind how these interventions improve nystagmus is unclear. No trials have been done on children.[17]

Refractive error in nystagmus is often high and it is therefore important that refractive error is examined for and appropriately prescribed for if required.[18] As many of these children have strabismus, occlusion, and other strabismus management is important. There has been some controversy about the use of contact lenses in nystagmus; there are reports that contact lenses improve visual acuity and reduce nystagmus, particularly in IN.[19] The improvements in visual acuity with the use of contact lenses compared to spectacles may be attributed to reduced optical aberrations, enlarged retinal image, and increased peripheral visual field.[20] A recent randomized trial assessing the use of hard and soft contact lenses in infantile nystagmus showed that neither hard nor soft lenses dampen nystagmus as compared to wearing glasses. Visual acuity with soft contact lens wear in this study was worse than with both hard lenses and glasses.

Prisms can also be used to dampen nystagmus. In some occurrences of IN, where the amplitude of nystagmus is smaller in convergence, prisms can be introduced if the patient has binocular vision. The prisms create an artificial divergence that the patient is required to overcome by converging the eyes even when looking at distance.

CONCLUSION

Since nystagmus has negative psychosocial and functional consequences as discussed earlier, there is a great deal of interest in its treatment. Intervention should be individualized based on the patient's age, function, needs, and concerns. The first step in intervention is the provision of optimal refractive correction, possibly with the inclusion of a prism to stimulate convergence or correct an AHP. If this does not meet the patient's needs, then pharmacological or surgical intervention should be considered. The decision on which treatment is best suited for a particular patient lies with the patient and his or her physician. While treatments are focused on decreasing nystagmus intensity and improving acuity, vision habilitation should also be recommended for those with vision impairment that affects the ability to perform everyday tasks.

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