Migraine in a pediatric population: a clinical study in children younger than 7 years of age

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AIM Migraines in children younger than 7 years of age have received limited attention in the published literature. The aim of this study is to describe the characteristics of migraine phenotypes in children younger than 7 years, and to compare them with migraines in children older than 7 years of age.
METHOD We reviewed all standard clinical files, collected over 4 years, related to children with a diagnosis of primary headache. We included all children younger than 7 years diagnosed with migraine in our study.
RESULTS A total of 374 children (188 males, 186 females) were affected by migraine with/without aura: 40 of these patients (10.7%; 20 males, 20 females; mean age 5y 7mo, SD 1y 2mo) where younger than 7 years old. The frequencies of the main migraine features in the younger age group were similar to those of children older than 7 years, with the exception of a shorter duration of migraine and reduced frequency of attacks.
INTERPRETATION In children younger than 7 years of age, the clinical phenotype of migraine is similar to that seen in older children. We propose that there is a general genetic migraine susceptibility that, in the presence of activating environmental factors, may induce typical attacks of migraine in individuals already predisposed to migraine attacks. Therefore, different modules induce different clinical features within the different age groups, but there is no difference in the frequencies of clinical phenotypes between the two age groups.

Although migraine is a common and crippling neurological disorder in pediatric populations,[1,2] it has not received much attention in children younger than 7 years of age,[3] with only a limited number of published studies describing the clinical and therapeutic features of migraine in this younger age group.[4–11] Furthermore, symptoms with possible clinical and therapeutic implications such as osmophobia,[12] allodynia,[13] and cranial autonomic signs[14,15] have not been reported in these studies.[4–11] The aim of this study is to describe some characteristics of migraine phenotypes in children younger than 7 years of age and make a comparison with those symptoms seen in children older than 7 years of age with migraines.

METHOD

The standard clinical files of children diagnosed and treated for headaches between 1 April 2010 and 1 April 2014 at the outpatient service at the Child and Adolescent Neuropsychiatry Department, Di Cristina Hospital, Palermo, Italy were reviewed. All patients were classified according to the 2004 International Headache Society criteria[16] and diagnosed with primary headache. All children younger than 7 years old and diagnosed with migraine were included in the study. We used a semi-structured interview,[17] routinely adopted for clinical purposes, to collect information on demographic and headache characteristics. These were categorized as follows: age, sex, family migraine history (presence/absence), frequency (<4≥ attacks for month), duration of the attacks (<4≥h for attack), duration of migraine disorder (<1y≥), quality, intensity, lateralization and localization of the pain, the influence of physical activity (yes/no), occurrence of nausea (yes/no), emesis (yes/no), photophobia (yes/no), phonophobia (yes/no), osmophobia (yes/no), occurrence of aura (yes/no), allodynia (yes/no), presence of cranial autonomic symptoms during migraine attacks (conjunctival injection, lacrimation, nasal congestion, eyelid oedema, forehead/facial sweating, flushing facial, rhinorrhoea, red ear, ptosis, and miosis), and the use of symptomatic and prophylactic drugs.

General and neurological examinations were carried out for all children. Other diagnostic investigations (e.g. blood tests, neurophysiological and neuroimaging studies, other specialist visits) were performed if required.

Informed consent was obtained from parents of all children. All the data were part of the patient's standard medical files. According to local ethical policies, no formal approval by the Hospital Ethics Committee was necessary or required.

Statistics

Chi-squared and Student's *t*-tests were used to compare nominal and continuous variables respectively. A *p* value less than 0.05 was considered statistically significant. Data were processed using SAS software (version 9.1.3 for Windows; SAS Inc., Cary, NC, USA).

RESULTS

A total of 456 children with primary headaches (216 males, 240 females, mean age 10y 9mo [SD 3y 1mo]) were seen during the study period. Of these patients, 374 (82%; 188 males, 186 females) were affected by migraine with/without aura and 82 (18%) were affected by other primary headaches (six primary stabbing headache, 57 episodic tension headache, and 19 chronic tension headache). Forty (8.7%; 20 males, 20 females; mean age 5y 7mo [SD 1y 2mo]) of the children affected by migraine were younger than 7 years of age; only two of these patients were affected by migraine with aura. The frequency of the main migraine features was similar in both groups of children. Symptoms such as osmophobia, allodynia, and cranial autonomic symptoms were present without significant differences between the two age groups, although there was a discrete group of not defined answers in younger age group.

Demographic characteristics and the main clinical migraine features are reported in Tables I and II, where children are stratified according to age (younger and older than 7y of age). No significant statistical differences were found, except for history of migraine and the frequency and duration of attacks.

DISCUSSION

We observed that there was no significant difference between most migraine features in patients younger than 7 years of age compared to the older age group. Furthermore, no significant differences between the two age groups were observed for migraine features that have recently received great attention such as osmophobia, allodynia, and cranial autonomic symptoms. Similar frequencies of these symptoms have been reported in older age groups and in different countries.[12–15] The

main differences between the two age groups in our study is the shorter history of disease (70% of older children had a migraine history longer than 1y compared to 50% of younger children), the reduced frequency of attacks, and the shorter duration of episodes. A limited number of studies have been conducted in young children, and these are generally based on small sample sizes. Two studies comparing migraines in preschool- versus school-age children[8,10] noted the following differences between the two groups: lower frequency of phonophobia and photophobia[8] and a higher frequency of emesis in the younger population, and a higher frequency of aura in the older group.[10]

For other studies that include the younger age group used in our study, while they do not compare the younger and older migraine population groups they do show a similar prevalence and distribution of clinical migraine phenotypes noted in our sample. However, some studies were published before the primary or secondary International Headache Society classification so it is difficult to establish a comparison.

According to a previous study that included a younger population group,[7] there was lower frequency of typical migraine features than reported in our current sample population. However, the duration of attacks was similar between the two populations, showing about 80% attacks lasted less than 4 hours. The clinical history of migraine and reduced frequency of attacks are probably due to a selection bias, because at this younger age the onset of recurrent headaches causes alarm and fear in doctors and parents of a more serious illness and that could result in a more likely referral to headache centre. As other studies[8] also show the same results, cross-sectional longitudinal studies performed on the general population may resolve this selection bias.

The shorter duration of migraine attacks in the younger age group cannot be explained by selection bias as this bias would have more easily selected children with longer painful attacks. The shorter duration of headaches in younger children was also reported by Battistella et al.[8] Their study comprised a younger group of children

Table I: Migraine characteristics in children under/over 7y

Variable	Younger children		Older children		
	<7y of age; *n*=40	Min–max	≥7y of age; *n*=334	Min–max	*p*
Age at interview, y (SD)	5.7 (1.2)	3.6–6.11	11.3 (3.1)	7.0–17.7	<0.001
Duration disease, mo (SD)	10.7 (7.8)	3–30	12.3 (8.6)	4–48	0.262
Duration attacks, h (SD)	2.6 (2.7)	0.5–8	3.8 (2.5)	0.5–20	0.005
Frequency of attacks per month	5.8 (5.7)	2–20	7 (4.7)	2–30	0.137

Table II: Migraine characteristics according to categorization used

Variable	Younger children (<7y of age; n=40) (%)	Older children (≥7y of age; n=334) (%)	p
Sex			
Males	20 (50.0)	168 (50.0)	
Females	20 (50.0)	166 (50.0)	
Duration disease			
1y	21 (52.5)	100 (29.9)	
≥1y	19 (47.5)	234 (70.1)	0.004
Duration attacks			
4h	33 (82.5)	202 (60.4)	
≥4h	7 (17.5)	132 (39.6)	0.006
Frequency attacks for months			
4 attacks	19 (50.0)	114 (35.4)	
≥4 attacks	21 (50.0)	220 (64.6)	0.02
Family migraine history			
Yes	39 (97.5)	300 (89.8)	
No	1 (2.5)	34 (10.2)	ns
Aura			
Yes	2 (5.0)	46 (13.8)	
No	38 (95.0)	288 (86.2)	ns
Unilaterality pain			
Yes	9 (22.5)	112 (33.5)	
No	31 (77.5)	222 (66.5)	ns
Quality of pain			
Throbbing	25 (62.5)	234 (70)	
Gravative	6 (15)	98 (29.5)	
Not described	9 (22.5)	2 (0.5)	ns
Physical activity			
Yes	24 (60.0)	203 (60.7)	
No	16 (40.0)	131 (39.3)	ns
Intensity pain			
Yes	30 (75.0)	242 (72.4)	
No	10 (25.0)	92 27.6)	ns
Emesis			
Yes	18 (45.0)	115 (34.4)	
No	22 (55.0)	219 (65.6)	ns
Nausea			
Yes	21 (52.5)	188 (56.3)	
No	19 (47.5)	146 (43.7)	ns
Phonophobia			
Yes	31 (77.5)	247 (74.0)	
No	9 (22.5)	87 (26.0)	ns
Photophobia			
Yes	29 (72.5)	248 (74.3)	
No	11 (27.5)	86 (25.7)	ns
Cranial allodynia			
Yes	8 (20.0)	104 (31.1)	
No	25 (62.5)	230 (68.9)	
Not defined	7 (17.5)		ns
Cranial autonomic symptoms			
Yes	22 (55.0)	170 (51.0)	
No	18 (45.0)	164 (49.0)	ns
Osmophobia			
Yes	10 (25.0)	86 (25.7)	
No	11 (52.5)	248 (74.3)	
Not defined	9 (22.5)	–	ns

ns, not significant.

presenting with an onset of headache before the age of 6 years and a second group of randomized patients aged between 12 years and 18 years with headache onset after the age of 12 years.

Researchers have recently focused their attention on mechanisms that stop migraine attacks, suggesting that these are active rather than passive (physiological) mechanisms.[18] According to this assumption, the shorter attacks reported in the younger age group could be explained by active mechanisms (e.g. sleeping), rather than physiological pain mechanisms. Sleep has often been used to stop the pain phase of headache attacks, and when sleep is altered it might increase or provoke headache but it may also stop the attack. Preschool-age children, especially under 6 years of age, have longer sleep durations and they often sleep more easily during the day.[19] It is therefore possible that the shorter attacks depend on easier initiation of active mechanisms such as sleep stopping the pain phase. It would be interesting to verify if children with shorter duration of migraine attacks are able to sleep during the daytime so they can use activation of sleep to resolve the painful attack.

Another important factor to note from our data and in general from all literature is that the clinical migraine phenotype appears to be similar in both the younger and older age groups. This is contrary to expectations given that the different brain maturation stages (e.g. neuromediators, peptides, maturation of cortex) between the two age groups would provoke different clinical features. Given that the prevalence of migraine increases as children get older, we propose that there is a general migraine genetic susceptibility that, in the presence of activating environmental factors, may induce migraines in those individuals already predisposed to typical migraine attacks. Therefore, different modules (see modular theory of migraine[20]) may result in unique clinical features within age groups (i.e. intra-age differences), but the overall key clinical symptoms are the same in both age groups (i.e. inter-age similarities).

The main limitations of our study, like others cited, are probably related to its retrospective nature, the small sample size, and that the clinical population may underestimate or overestimate the occurrence of some clinical manifestations. However, as our service is one of the only two outpatient services for the diagnosis and treatment of headaches within the Palermo catchment area, the likelihood of the patients enrolled in this study being characterized by more severe symptoms or more difficult headache diagnosis is low. Prospective studies based on general pediatric population could help to better define the headache in the preschool-age population.

CONCLUSION

Children younger than 7 years old present with a clinical migraine phenotype that appears to be similar to that seen in older children. We propose that there is a general genetic migraine susceptibility that, in presence of activating environmental factors, may induce typical attacks of migraine in individuals already predisposed. Therefore, different modules result in intra-age differences in clinical expressions of migraines, but inter-age similarities are observed for key clinical symptoms.

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