VII

Headaches in Children

CQ VII-1

What types of headache are common in children?

Recommendation

The representative primary headaches in children are migraine and tension-type headache. The prevalence of migraine in children in population-based surveys conducted in various countries worldwide is 3.8 to 13.5% and the prevalence in school-based (number of students) surveys is 1.7 to 21.3%, while the prevalence of tension-type headache is 17.4% and 0.7 to 27.6%, respectively. According to Japanese data, the prevalence of migraine in children is 4.8% (boys 3.3%, girls 6.5%) among junior high school students and 15.6% (boys 13.7%, girls 17.5%) among senior high school students, while the prevalence of tension-type headache is 26.8% (boys 23.0%, girls 30.6%) among senior high school students. **Grade B**

Background and Objective

Most of the reports on headache prevalence in children were on migraine, but since 2005, the number of reports on headaches other than migraine has increased. Most of them reported prevalence of headaches diagnosed according to the diagnostic criteria of the first edition of the International Classification of Headache Disorders (IHS classification, 1988) or the International Classification of Headache Disorders 2nd Edition (ICHD-II, 2004). Some studies are based on population, some are based on the number of students in schools, and some are based on the number of outpatients attending headache clinics. The Japanese data are from two articles only,[19)23)] and further accumulation of research data is anticipated.

Comments and Evidence

The prevalence and the basic data of statistical analyses extracted from the references are shown in **Tables 1** to **3**. **Table 1** lists the population-based studies;[1)-7)] **Table 2** shows the school (number of students)-based studies;[8)-25)] and **Table 3** presents the outpatient-based studies.[26)-29)]

The numbers and ages of subjects included in the statistical data and countries of the studies are shown below (the numbers refer to the numbers in the reference list).

1. Review: 50 articles, ages below 20 years
2. Review: 36,000 subjects for migraine (children and youth), 25,000 subjects for tension-type headache (children and youth)
3. 30,636 subjects (3-17 years) (Serbia)
4. 1,679 subjects (11-18 years) (Nigeria)
5. 1,856 subjects (5-11 years) (Brazil)
6. 1,994 subjects (5-12 years) (Brazil)
7. 2,114 subjects (12-14 years) (Denmark)
8. Review: 13 articles
9. 1,385 subjects (11-18 years) (Turkey)
10. 953 subjects (mean 13.2 years) (Thailand)
11. 3,963 subjects (13-15 years) (Taiwan)
12. 2,235 subjects (grades 9-12) (India)
13. 2,669 subjects (mean 8.2±2.4 years) (Turkey)
14. 2,384 subjects (14-18 years) (Turkey)
15. 1,789 subjects (12-15 years) (Thailand)
16. 76,333 subjects (9-17 years) (Turkey)
17. 3,324 subjects (12-15 years) (Germany)
18. Unknown, 8 schools randomly selected from 9 districts (Turkey)
19. 6,472 subjects (12-15 years) (Japan)
20. 1,259 subjects (7-12 years) (Serbia)
21. 2,226 subjects (6-13 years) (Iran)

22. 1,270 subjects (12-14 years), 1,117 subjects (15-17 years) (Turkey)
23. 2,462 subjects (senior high school) (Japan)
24. 13,426 subjects (13-15 years) (Taiwan)
25. 5,777 subjects (grades 2-5) (Turkey)
26. 87 subjects (12-17 years, selected after interview at school) (Turkey)
27. 375 subjects (Thailand)
28. 124 subjects (≤18 years) (Hong Kong)
29. 105 subjects (≤6 years) (Italy)

Table 1. Population-based studies on prevalence of headache in children.

Author	Year	Country	Age (yr)	Prevalence of migraine (%)			Prevalence of tension-type headache (%)		
				Boy	Girl	Total	Boy	Girl	Total
Knezevic-Pogancev et al	2010	Serbia	3-17	8.0	9.6	8.6			—
			3-7	4.2	3.6	3.9			—
Ofovwe et al	2010	Nigeria	11-18			13.5			—
Arruda et al	2010	Brazil	5-12	3.9	3.6	3.8	17.0	17.7	17.4
Russell et al*	2006	Denmark	12-14	7.0	8.2	7.6	78.6	84.5	79.5
Abu-Arafeh et al	2010	review	3-19	6.0	9.7	7.7			—
Stovner et al	2010	review	5-21	5.6	8.2	8.3	10.9	16.1	14.0

*Since data are those for adolescents (12-14 years) from a large-scale study of 33,764 twins aged 12-41 years, we excluded the data of this article from calculation of average age.

Table 2. School (number of students)-based studies on prevalence of headache in children.

Author	Year	Country	Age (yr)	Prevalence of migraine (%)			Prevalence of tension-type headache (%)		
				Boy	Girl	Total	Boy	Girl	Total
Alp et al*		Turkey	11-18			14.3	4.4	4.2	8.6
Including probable migraine				23.0	29.5	25.5			
Visudtibhan et al	2010	Thailand	12-14			12.1			0.7
Fuh et al	2010	Taiwan	13-15			12.2			27.6
Gupta et al	2010	India	16-18			17.2			11.0
Igik et al	2009	Turkey	5-10			3.4			—
Unalp et al	2009	Turkey	14-18			21.3			5.1
Visudtibhan et al	2006	Thailand	12-15	11.7	16.2	13.8			—
Akyol et al	2007	Turkey	9-17	7.8	11.7	9.7			—
Fendrich et al	2007	Germany	12-15	4.4	9.3	6.9	19.1	21.2	20.2
Ando et al	2007	Japan	12-15	3.3	6.5	4.8			—
Milovanovi. et al	2007	Serbia	7-12	2.1	4.6	3.3	0.9	1.7	1.3
Ayatollahi et al	2007	Iran	6-13			1.7	5.5		—
Karli et al	2006	Turkey	12-17			14.5			—
Suzuki et al	2006	Japan	16-18	13.7	17.5	15.6	23.0	30.6	26.8
Wang et al	2005	Taiwan	13-15			5.9			6.3
Bugdayci et al	2005	Turkey	8-16			10.4			24.7
Lewis	2007	Review					Preschool; 3%, primary school; 4-11%, senior high school; 8-23%		

Table 3. Outpatient-based studies on prevalence of headache in children.

Author	Year	Country	Age (yr)	Prevalence of migraine (%)	Prevalence of tension-type headache (%)
Karli et al	2010	Turkey	12-17	57.5	27.6
Ruangsuwan et al	2007	Thailand	3-16	35.2	12.5
Chan et al	2006	Hong Kong	≤18	5.6	24.2
Raieli et al	2005	Italy	≤6	35.2	18.0
Mean				33.4	20.6

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• Search terms and secondary sources

- Search database: PubMed (2011/10/12) The number of articles is shown in parentheses.
  #6Search #4 or #5 Limits: Humans, English, Japanese, All Child: 0-18 years, Publication Date from 2005 to 2011 (476)
  #5Search headache disorders/epidemiology Limits: Humans, English, Japanese, All Child: 0-18 years, Publication Date from 2005 to 2011 (429)
  #4Search Headache Disorders/classification Limits: Humans, English, Japanese, All Child: 0-18 years, Publication Date from 2005 to 2011 (87)
  #3Search Headache Disorders/classification Limits: Humans, English, Japanese, All Child: 0-18 years (241)
  #2Search Headache Disorders/classification (866)
  #1Search Headache Disorders

CQ VII-2

How is migraine in children diagnosed?

Recommendation

Migraine and tension-type headache, which are representative primary headaches in children, are diagnosed according to the International Classification of Headache Disorders, 3rd edition (beta version). **Grade A**

Background and Objective

In the past, migraine in children was diagnosed mainly according to the Vahlquist criteria. Since the publication of the first edition of the International Classification of Headache Disorders (IHS classification, 1988), the diagnostic criteria of the IHS classification began to be used. However, the IHS classification was developed mainly for headaches in adults. Reports appeared pointing out that the migraine duration and headache location provided by the IHS classification could not be applied directly to diagnose migraine in children. In the International Classification of Headache Disorders 2nd Edition (ICHD-II),[1)2)] the criteria for diagnosing migraine in children, which are different from those used in adults, were added. Then, in the International Classification of Headache Disorders, 3rd edition (beta version)[3)] the headache duration for migraine in children has been changed.

Comments and Evidence

According to the International Classification of Headache Disorders, 3rd edition (beta version) (ICHD-3beta), migraine in children is under "1.1 *migraine without aura*" and "1.2 *migraine with aura*". The diagnostic criteria for "1.2 *migraine with aura*" are not different between adults and children, and hence are not described here. The diagnostic criteria for "1.1 *migraine without aura*" are shown below. However, there are differences when these criteria are applied to children, and these are described in Note 3.

1.1 *Migraine without aura*

A. At least five attacks[Note 1] fulfilling criteria B-D

B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)[Notes 2,3]

C. Headache has at least two of the following four characteristics:

1. unilateral location
2. pulsating quality
3. moderate or severe pain intensity
4. aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs)

D. During headache at least one of the following:

1. nausea and/or vomiting
2. photophobia and phonophobia

E. Not better accounted for by another ICHD-3 diagnosis

• Notes

1. One or a few migraine attacks may be difficult to distinguish from symptomatic migraine-like attacks. Furthermore, the nature of a single or a few attacks may be difficult to understand. Therefore, at least five attacks are required. Individuals who otherwise meet criteria for 1.1 Migraine without aura but have had fewer than five attacks, should be coded 1.5.1 *Probable migraine without aura*.
2. When the patient falls asleep during a migraine attack and wakes up without it, duration of the attack is reckoned until the time of awakening.
3. In children and adolescents (aged under 18 years), attacks may last 2-72 hours (the evidence for untreated durations of less than 2 hours in children has not been substantiated).

• Comments

Migraine headache in children and adolescents (aged under 18 years) is more often bilateral than is the case in adults; unilateral pain usually emerges in late adolescence or early adult life. Migraine headache is usually frontotemporal. Occipital

headache in children is rare and calls for diagnostic caution. In young children, photophobia and phonophobia may be inferred from their behavior.

In ICHD-3beta, "1.6 *Episodic syndromes that may be associated with migraine*" has been added. This group of disorders occurs in patients who also have 1.1 *migraine without aura* or 1.2 *migraine with aura*, or who have an increased likelihood to develop either of these disorders. Although historically noted to occur in childhood, they may also occur in adults.

1.6.1.1 *Cyclic vomiting syndrome*

A. At least five attacks of intense nausea and vomiting, fulfilling criteria B and C
B. Stereotypical in the individual patient and recurring with predictable periodicity
C. All of the following:
  1. nausea and vomiting occur at least four times per hour
  2. attacks last ≥1 hour and up to 10 days
  3. attacks occur ≥1 week apart
D. Complete freedom from symptoms between attacks
E. Not attributed to another disorder[Note 1]
• Note
  1. In particular, history and physical examination do not show signs of gastrointestinal disease.

1.6.1.2 *Abdominal migraine*

A. At least five attacks of abdominal pain, fulfilling criteria B-D
B. Pain has at least two of the following three characteristics:
  1. midline location, periumbilical or poorly localized
  2. dull or 'just sore' quality
  3. moderate or severe intensity
C. During attacks, at least two of the following:
  1. anorexia
  2. nausea
  3. vomiting
  4. pallor
D. Attacks last 2-72 hours when untreated or unsuccessfully treated
E. Complete freedom from symptoms between attacks
F. Not attributed to another disorder[Note 1]
• Note:
  1. In particular, history and physical examination do not show signs of gastrointestinal or renal disease, or such disease has been ruled out by appropriate investigations.

1.6.2 *Benign paroxysmal vertigo*

A. At least five attacks fulfilling criteria B and C
B. Vertigo[Note 1] occurring without warning, maximal at onset and resolving spontaneously after minutes to hours without loss of consciousness
C. At least one of the following associated symptoms or signs:
  1. nystagmus
  2. ataxia
  3. vomiting
  4. pallor
  5. fearfulness
D. Normal neurological examination and audiometric and vestibular functions between attacks
E. Not attributed to another disorder
• Note:
  1. Young children with vertigo may not be able to describe vertiginous symptoms. Parental observation of episodic periods of unsteadiness may be interpreted as vertigo in young children.

1.6.3 *Benign paroxysmal torticollis*

A. Recurrent attacks[Note 1] in a young child, fulfilling criteria B and C

B. Tilt of the head to either side, with or without slight rotation, remitting spontaneously after minutes to days

C. At least one of the following associated symptoms or signs:

1. pallor
2. irritability
3. malaise
4. vomiting
5. ataxia[Note 2]

D. Normal neurological examination between attacks

E. Not attributed to another disorder.

• Notes:

1. Attacks tend to recur monthly.
2. Ataxia is more likely in older children within the affected age group.

Appendix

A1.6.4 *Infantile colic*

A. Recurrent episodes of irritability, fussing or crying from birth to 4 months of age, fulfilling criterion B

B. Both of the following:

1. episodes last for ≥3 hours per day
2. episodes occur on ≥ days per week for ≥3 weeks

C. Not attributed to another disorder.

A1.6.5 *Alternating hemiplegia of childhood*

A. Recurrent attacks of hemiplegia alternating between the two sides of the body and fulfilling criteria B and C

B. Onset before the age of 18 months

C. At least one other paroxysmal phenomenon is associated with the bouts of hemiplegia or occurs independently, such as tonic spells, dystonic posturing, choreoathetoid movements, nystagmus or other ocular motor abnormalities and/or autonomic disturbances

D. Evidence of mental and/or neurological deficit(s)

E. Not attributed to another disorder.

In ICHD-II, the diagnostic criteria have been modified to include headache duration from 1 hour and bilateral headache if frontotemporal in location for the diagnosis of migraine in children. Several reports indicated that use of the ICDH-II criteria improved the diagnostic sensitivity of migraine in children.[4)-7)] On the other hand, some reports also pointed out that the sensitivity of 73.9% (53% for migraine without aura and 71.0% for migraine with aura) remained unsatisfactory.[4)5)] Regarding associated symptoms, the proposed revision of considering photophobia and phonophobia as independent diagnostic criteria is regarded not useful at this time.[7)] In ICHD-3beta, the headache duration for migraine in children has been changed from one hour or longer to two hours or longer.

• References

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• Search terms and secondary sources

- Search database: PubMed (2011/10/7)
  migraine & children 2679
  & diagnosis 1538 & ICHD 39
  & ICHD- 217
  pediatric migraine 737
  & ICHD 18
  & diagnosis 494
  cyclical vomiting 61
  & diagnosis 32
  cyclic vomiting 394
  & diagnosis 190
  abdominal migraine 17167 & children 2298
  & diagnosis 1322
  & criteria 378
  benign paroxysmal vertigo & children 100
  & diagnosis 78
  & criteria 9
- Search database: Ichushi Web for articles published in Japan (2011/10/7)
  Children & headache 1491
  & migraine 276
  & secondary 13
  & diagnosis 1061
  & classification 80

CQ VII-3

What types of secondary headache are common in children?

Recommendation

The most common secondary headache in children is headache attributed to infection, followed by traumatic injury to the head. Secondary headaches are not frequently seen at headache clinics. Headaches encountered in pediatric emergency departments are most commonly infections other than neurological diseases, such as viral diseases and sinusitis, followed by traumatic injury to the head. Although serious central nervous system disorders are rare, brain CT or MRI should be conducted in the presence of risk factors. **Grade B**

Background and Objective

There are few reports on the prevalence of secondary headaches in children. Irrespective of general pediatricians, pediatric neurologists and pediatric emergency physicians, diagnosing secondary headaches appropriately is important also from the viewpoint of making an accurate diagnosis of primary headaches (migraine and tension-type headache).

Comments and Evidence

In a population-based study of 2,165 schoolchildren (aged 5 to 15 years) in the community, the prevalence of secondary headache among all children with headache was 42.9%, including infection 30.9%, trauma 5.1%, special illness 2.3%, and poor eyesight 1.3%.[1)]

In a study of 437 patients (aged 3 to 19 years) attending a headache clinic of a university hospital, secondary headache was found in 26 patients (6%). According to the first edition of the International Classification of Headache Disorders (1988), 9 patients were diagnosed with "5. *Headache associated with head trauma*", 1 patient with "6. *Headache associated with vascular disorders*", 1 patient with "7. *Headache associated with non-vascular intracranial disorder*", 8 patients with "9. *Headache associated with non-cephalic infection*", and 7 patients with "11. *Headache or facial pain associated with disorder of cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cranial structures*".[2)]

In a study of 243 patients at the pediatric headache clinic of a university hospital using the International Classification of Headache Disorders 2nd Edition (ICHD-II), 3 patients had "6. *Headache attributed to cranial or cervical vascular disorder*", 1 patient had "7. *Headache attributed to non-vascular intracranial disorder*", 1 patient had "8. *Headache attributed to a substance or its withdrawal*", 4 patients had "11. *Headache or facial pain attributed to disorder of cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cranial structures*", 2 patients had "12. *Headache attributed to psychiatric disorder*", and 17 patients were unclassifiable.[3)]

In a study of 478 patients (aged 2 to 15 years) with chronic and recurrent headache attending the pediatric outpatient clinic of a general hospital, 13 patients (3%) had secondary headaches. According to the IHS classification (1988), 3 patients had "6. *Headache associated with vascular disorders*" (1 patient each with intracranial hemorrhage, moyamoya disease, and hypertension due to renin-producing tumor) and 6 patients had "7. *Headache associated with non-vascular intracranial disorder*" (3 patients with intracranial neoplasm, 1 with high cerebrospinal fluid pressure/hydrocephalus, and 2 with headache associated with other intracranial disorder). In addition, 4 patients had "11. *Headache or facial pain associated with disorder of facial or cranial structures*" (1 patient with eosinophilic granuloma of cranial bone, 1 with hyperopic astigmatism, and 2 with acute sinusitis).[4)]

A total of six articles on secondary headaches in pediatric emergency department were identified.[5)-10)] The most common secondary headache is headache attributed to infection, represented by viral diseases, with frequencies of 14.8 to 61.0%.[5)-10)] This was followed by headache attributed to head and/or neck trauma with frequencies of 6.6 to 20.0%,[5)6)9)10)] and headache attributed to sinusitis with frequencies of 9.0 to 16.7%.[5)6)10)] The frequencies of headache attributed to viral meningitis were 0.4 to 9.0%,[5)-10)] and the frequencies of headache attributed to VP shunt problem were 0.3 to 11.5%.[5)-10)] The frequencies of headache attributed to intracranial neoplasm were 0.4 to 2.6%.[6)8)-10)] Although there are no reports of prevalence according to age, approximately 70% of secondary headaches are attributed to infections especially in young children aged 2 to 5 years[9)] (**Table 1**).

Head CT should be performed in patients who have recent onset headache with unexplained etiology and in patients who

have underlying diseases.[7] On the other hand, for young children presenting with headache but no abnormal neurological findings and no remarkable history, head CT seldom contributed to diagnosis and early intervention.[9] In another study, when neuroimaging was performed upon requests from patients or their parents or when there were changes in headache properties, none of those patients required surgical treatment.[11]

Table 1. Etiologies of secondary headaches

	Burton[5] (1997)	Lewis[6] (2000)	Kan[7] (2000)	Scagni[8] (2008)	Lateef[9] (2009)	Conicella[10] (2008)
Age (yr.)	2-18	2-18	0-18	0-16	2-5	2-18
No. of patients	288	150	130	526	364	432
% secondary headaches				42.0	84.3	55.0
Viral disease	39.2	39.0	28.5	38.0	61.0	14.8
Sinusitis	16.0	9.0				16.7
Traumatic head injury	6.6	20.0		—*	13.0	8.7
Beta hemolytic streptococcal pharyngitis	4.9	9.0				
Viral meningitis	5.2	9.0	2.3	0.4	1.1**	2.5
VP shunt problem	0.3	2.0	11.5	0.4	3.8	1.8
Brain tumor		2.6		0.4	1.9	1.1
Post-convulsion		1.3		0.9	0.5	
Cerebrovascular disease				0.5	0.3***	

Data are percentage relative to all headaches.
*: Excluding headache attributed to head trauma and headache attributed to bacterial meningitis
**: Bacterial meningitis or viral meningitis
***: Cerebral infarction or ADEM

• References

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• Search terms and secondary sources

- Search database: PubMed (2011/10/7)
  Headache & Children (6566)
  & Secondary (392)
  & emergency (277)
  & infection (770) & emergency (39)
  & meningitis (343) & emergency (30)
  & head trauma (277) & emergency (61)
  & brain tumor (561) & emergency (17)
  & brain hematoma (73) & emergency (13)
  & brain hemorrhage (317) & emergency (30)
  & VP shunt (13) & emergency (1)
  Secondary headache (2895)
  & prevalence (412)
  & children (393) & epidemiology (99)
  & children (393) & prevalence (107)

- Search database: Ichushi Web for articles published in Japan (2011/10/7)
  Children & headache 1491
  & migraine 276
  & secondary 13
  & diagnosis 1061
  & classification 80

CQ VII-4

What kinds of acute and prophylactic medications are available for the treatment of migraine in children, and how effective are they?

Recommendation

As first-choice acute medications for migraine in children, ibuprofen and acetaminophen are effective, safe and low-cost drugs, and ibuprofen exhibits the best analgesic effect. Among triptans, sumatriptan nasal spray is effect and safe for migraine in children, and rizatriptan tablet is also effective and safe. The recommended strategy is to start acute medication as early as possible after onset of headache and at an adequate dose. For prophylactic treatment of migraine in children, the anti-epileptic drug topiramate is effective and well tolerated, but is currently not covered by health insurance in Japan. **Grade A**

Background and Objective

In children also, pharmacotherapy is necessary when migraine causes a high degree of disability in daily living. This section examines whether ibuprofen and acetaminophen are superior acute medications for migraine in children, and whether triptans are effective and tolerable for children. In children with frequent severe migraine attacks, prophylactic therapy should be considered. This section also investigates the types, efficacy and safety of prophylactic medications.

Comments and Evidence

The recommended management of migraine in children is first to identify and avoid factors that trigger headache, and to use non-pharmacologic biobehavioral treatments such as regular sleep, dietary modification, exercise, biofeedback and stress management.[1)]

1. Acute medications

Ibuprofen and acetaminophen are effective and safe acute medications for migraine in children.[1)-3)] The recommended strategy is to start treatment at an adequate dose as early as possible after onset of headache.[1)2)] Among the triptans, sumatriptan and zolmitriptan (currently not available in Japan) in nasal spray form, and rizatriptan and almotriptan (currently not available in Japan) in tablet form have been reported to be safe and efficacious.[1)] Three randomized controlled trials (RCT) have demonstrated the efficacy and safety of sumatriptan nasal spray.[2)] It is recommended for children aged 12 years and older, although one RCT in children aged 6 years and older showed no adverse effects except bad taste.[1)2)] In a small-scale Japanese study of sumatriptan nasal spray in 20 patients aged 12 to 17 years with migraine, treatment was effective in 75% of the patients ($p = 0.002$), but only 55% wished to continue the prescription in the future mainly because of the adverse effect of bad taste.[4)] For oral triptan, an RCT studied rizatriptan in 96 children with migraine aged 6 to 17 years using a dose of 5 mg for those weighed 20 to 39 kg, and 10 mg for those weighing 40 kg or more.[5)] In this trial, the primary end point at 2 hours revealed effective rates of 74% after the first dose and 73% after the second dose; both were significantly higher ($p < 0.001$) compared to placebo (36%), with no serious adverse effects. In a large-scale multicenter study of zolmitriptan tablet for migraine in 850 adolescents aged 12 to 17 years, there was no significant improvement between zolmitriptan and placebo. Examination of the study method suggested the high placebo response rate in adolescents.[6)] On the other hand, an RCT of zolmitriptan tablet in an European headache clinic recruiting 29 children with migraine aged 6 to 18 years reported significantly higher ($p < 0.05$) effective rate for zolmitriptan (62%) compared to placebo (28%).[3)] A multicenter RCT of eletriptan in 380 adolescents with migraine aged 12 to 17 years demonstrated no significant difference in response rate between eletriptan and placebo, but eletriptan was significantly superior ($p = 0.028$) to placebo with respect to the reduction of headache recurrence within 24 hours.[7)]

2. Prophylactic medications

For children younger than 10 years of age who have no obesity problem, cyproheptadine at 2 to 4 mg as a single bedtime dose is a simple and safe strategy.[1)] The dose may be increased, but children become sedated at doses higher than 4 to 8 mg/day.

Attention is necessary, because in children with a history of convulsion and/or with fever, cyproheptadine may induce convulsion. Although amitriptyline has not been evaluated by RCT, it is the most widely used medication.[1)2)] The starting dose is 5 to 10 mg at bedtime, and may gradually be increased to 1 mg/kg/day. Since the publication of guideline on treatment of migraine in children in 2004,[2)] the antiepileptic drug topiramate has been shown to achieve good outcome in RCT, and has become the recommended drug. In a multicenter RCT recruiting 32 adolescents with migraine aged 12 to 17 years, treatment with topiramate 50, 100, and 200 mg/day for 26 weeks reduced monthly migraine frequency by 46% (P = 0.07), 63% (P = 0.02), and 65% (P = 0.04), respectively, compared to placebo (16%).[8)] In an RCT conducted at the pediatric outpatient department of a university hospital, the group treated with topiramate 100 mg/day had significantly greater reduction in headache frequency per month compared to the group treated with placebo (p = 0.025), and significantly reduced school absenteeism (p = 0.002).[9)] In a multicenter RCT, topiramate at 100 mg/day, but not 50 mg/day, resulted in a significant reduction in monthly migraine attack rate and a significant decrease in number of days with migraine compared to placebo.[10)] In all these trials, no serious adverse events were observed, but weight loss, lowered concentration, somnolence, and dizziness were found in topiramate-treated patients. The recommended regimen for topiramate is to start from 15 to 25 mg once a day at bedtime, and increase gradually to 50 mg twice a day.[1)]

For divalproex sodium, an RCT on migraine prophylaxis conduced in adolescents aged 12 to 17 years was available.[11)] No significant difference in migraine prophylactic effect was observed between any dose of divalproex sodium (250 mg/day, 500 mg/day or 1,000 mg/day) and placebo, but the drug was well-tolerated. In a single-center open-label study, after 4 months treatment with divalproex sodium, 50% headache reduction was achieved in 78.5% of patients, 75% reduction in 14.2% of patients, and 9.5% of patients became headache-free.[12)] Two open-label studies of levetiracetam showed some efficacy of levetiracetam for migraine prevention, and concluded that this drug seemed to be a promising candidate. In a small-scale open-label study of zonisamide, reduction in headache frequency was observed.[1)]

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• Search terms and secondary sources

- Search database: PubMed (2011/11/17)
  Migraine treatment 13921
  & children 1602 & adolescents 2376
  & children adolescents 1002
  OR analgesics 236 OR triptan 23 OR acetaminophen 31 OR ibuprofen 28
  OR preventive 60 OR prophylactic 106 OR antiepileptic 145
- Search database: Ichushi Web for articles published in Japan (20/11/17)
  migraine treatment (excluding proceedings) 1832
  & children 189 OR adolescent 11
  & children adolescent 9

CQ VII-5

What is the prevalence of chronic daily headache in children, and how is the headache diagnosed and treated?

Recommendation

According to population-based surveys, the prevalence of chronic daily headache (CDH) was 1.68% in children aged 5 to 12-years, 1.5% in those aged 12 to 14 years, and 3.5% in those aged 12 to 17 years. The prevalence of CDH in headache centers was variable, ranging from 5.9 to 38.0% in patients aged 6 to 18 years. The diagnostic criteria of CDH require the presence of headache on 15 or more days per month, for a duration of 1 month in two sets of population-based survey and more than 3 months in the data of all headache centers. The duration of headache per day was often not included in the diagnostic criteria. There is no randomized controlled trial on the treatment of CDH in children, and is an issue for future study. **Grades B and C** (prevalence and diagnosis: B, treatment: C)

Background and Objective

In headache clinics, children and adolescent sometimes present with chronic daily headache (CDH) that impairs daily living. The CDH in this age group does not respond well to analgesics and often becomes refractory to treatment. To find out the prevalence of CDH in children and adolescents and how this headache is diagnosed and treated, this section reviews population-based studies and data from various headache clinics to identify the prevalence and appropriate diagnosis and treatment of CDH in children and adolescents.

Comments and Evidence

1. Prevalence of CDH in children (using the International Classification of Headache Disorders 2nd Edition: ICHD-II)

(1) Population-based prevalence and headache types

The prevalence of CDH among adolescents age 12 to 17 years was 3.5%, and the prevalence by headache type was chronic migraine (CM) 20.9% and chronic tension-type headache (CTTH) 2.8%. Consequently, 76.3% of the cases could not be diagnosed as CM or CTTH, 27.5% of which fulfilled the diagnostic criteria for medication overuse headache (MOH). In a US study of adolescents aged 12 to 17 years, the prevalence of CM without MOH was 0.79% and that of CM with MOH was 1.75%, and was higher in females than in males.[1] In a Brazilian study, the prevalence of CDH among children aged 5 to 12 years was 1.68% (girls 2.09%, boys 1.33%), and was significantly higher in girls.[2] In a report from Taiwan, the prevalence of CDH in adolescents aged 12 to 14 years was 1.5% (girls 2.4%, boys 0.8%), and was significantly higher in girls. By type of CDH, the prevalence of CM was 6.6% and that of CTTH was 65.5%, and was significantly higher for CTTH. Twenty percent of the cases were suspected of medication overuse (Taiwan).[3] In summary, CDH was more prevalent in girls among primary school and also junior and senior high school students, and medication overuse or suspected overuse was found in more than 20% of senior high school students with CDH.

(2) Prevalence in pediatric headache center or outpatient clinic and headache types

The prevalence of CDH among children with headache attending pediatric headache outpatient departments reported from various countries was: 24% (mean age: 11.8 years, 70% girls) from Japan,[4] 31.7% (6 to 18 years, 68.6% girls) from Canada,[5] 16.5% (mean age: 10.5 years, 61.8% girls) from France,[6] prevalence unknown due to no data of total number (mean age: 12.8 years, 70% girls) from the United States,[7] 5.9% (mean age: 13.5 years, 69.6% girls) from Italy,[8] 38.0% (mean age: 10, 59.5% girls) from Holland,[9] and 18.9% (mean age: 11.2 years, 62.7% girls) from Italy.[10] From these studies, the prevalence varied between 5.9 and 38.0%, but it was higher in girls than in boys.

The prevalence of subtypes of CDH was 6%,[5][9] 10%,[7] 17.9%,[8] and 50%[6] for CM; 16%,[5] 22%,[9] 30%,[7] 34% (IHS),[10] and 64.3%,[8] for CTTH; and 47% (IHS)[10] and 53%[5] for concurrent CM and CTTH. The prevalence of CDH with school phobia was 5% for CM, 46% for CTTH, and 50% for co-occurrence of CM and CTTH.[4] Analgesic overuse was found in 22.8%,[9] 52.9%,[6] and 60% (36% with suspected CM, 24% with CTTH).[7] Some reported no overuse,[4][8] while one report mentioned that analgesic overuse is not involved in the chronicization process.[10]

2. Diagnosis of CDH in children

As for the diagnostic criteria of CDH, the required headache frequency was more than 15 days per month in most references,[1)-10)] or more than 8 days per month according to the ICHD-II diagnostic criteria for migraine in children; the required duration was 3 months or longer[3)-10)] or for the past one month.[1)2)] The duration of a headache episode was variable: more than 4 hours,[5)9)] more than 2 hours,[3)] more than 1 hour,[4)] or not stated.[1)2)6)-8)10)] The headache types were diagnosed according to the ICHD-II,[1)-9)] or the first edition of International Classification of Headache Disorders (IHS classification 1988). New criteria for the diagnosis of CDH in children have been proposed.[11)]

3. Disability and comorbidities of CDH in children

(1) In children, CDH causes a high degree of disability in daily living, and should be considered.[1)-10)]

(2) Coexistence of psychiatric disorders

In the literature, CDH coexisted with psychiatric disorders (anxiety disorders,[4)5)7)10)] mood disorders,[5)7)] adjustment disorders,[4)] somatoform disorders,[4)5)] sleep disorders[9)10)]), stressors,[5)6)] and school absenteeism.[4)9)]

4. Treatment of CDH in children

There is no randomized controlled trial for the treatment of CDH in children.[11)12)] The information presented here are extracted from two review articles published by pediatric headache experts.[11)12)] Both articles described that control of CDH takes several months.

(1) Non-pharmacotherapy[11)]

Relaxation training, biofeedback, and counseling for mood disorders and anxiety disorders provided by clinical psychologists, as well as exercises such as aerobic exercise (starting from 10 minutes a day) are recommended. Environmental factors play an important role in CDH. Many children are well during summer holiday and deteriorate as school starts. Factors such as stress, lack of sleep, bright light in school, decreased access to exercise, less time for relaxation, and a tendency to skip breakfast may be associated. School absenteeism is a significant problem. Once children have been out of school, it is difficult for them to return to school schedule. Many of these children have sleep disturbances, and find it difficult to start off with early morning classes. Therefore, starting with one or two class periods around lunch time should be considered.

(2) Pharmacotherapy[11)]

The goals of pharmacotherapy for CDH are to reduce the frequency of migraine headache and to reduce the severity of the headache that persists all day. The following prophylactic medications have been proven by RCT in adults.

- Amitriptyline (decrease in headache frequency)
- Topiramate (decrease in headache days)
- Gabapetin (increase in headache-free days)
- Valproic acid (reduction in maximal pain levels and frequency)

However, there are limitations to use valproic acid in adolescent females due to the potential for weight gain, possible risk of polycystic ovary syndrome and teratogenicity.[12)]

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• Search terms and secondary sources

- Search database: PubMed (2011/10/6)
  Chronic daily headache 30373
  & {Children} 4096
  & (Children and adolescents) 2709 & {Prevalence} 815
  OR {epidemiology} 719 OR {diagnosis} 1664 OR (treatment) 1357
  OR {psychological factor} 375 OR {anxiety disorders} 154
  OR {depression} 168 OR {mood disorders} 94
  OR {somatoform disorders} 37 OR {phobia} 14
  OR {conversion} 8
  Articles with large number of cases and using ICHD-II criteria were selected.
- Search database: Ichushi Web for articles published in Japan (2011/10/29)
  Chronic daily headache 3135 (excluding proceedings)
  & children 259
  & children adolescents 9
  All were case reports with only comments. There were no high quality original articles