J Headache Pain (2003) 4:132–137
DOI 10.1007/s10194-003-0047-4

ORIGINAL

# Cluster headache in childhood and adolescence: one-year prevalence in an out-patient population

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Received: 5 February 2003
Accepted in revised form: 7 April 2003

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**Abstract** A multicenter one-year study was carried out on 6629 headache patients under 18 years of age, attending 27 centers and clinics devoted to headache in Italy to identify the prevalence of cluster headache (CH) in childhood and adolescence. Two male CH patients aged 9 and 17 years were identified. Their attacks fulfilled the IHS criteria for CH, and they were classified as having cluster headache with undetermined periodicity and episodic cluster headache, respectively. The one-year prevalence in this headache out-patient population under 18 years of age was calculated to be 0.03%. This value is smaller than that derived in the general population. This finding further confirms the rarity of early diagnosis of this primary disorder in childhood and adolescence, as demonstrated in other studies.

**Key words** Cluster headache • Childhood • Adolescence • Prevalence • Headache centers

## Introduction

Despite the clinical picture being extremely characteristic, cluster headache (CH) has been underestimated in the past. In most of the cases, the patients were diagnosed as being affected by other painful conditions such as trigeminal neuralgia, sinusitis and dental diseases.

The prevalence of cluster headache is still a controversial matter, both because the existing epidemiological studies had not been carried out on homogeneous population, and because the inclusion criteria and the personnel devoted to collecting clinical data and to recording methodology differed [1–4].

Only after the introduction of the classification of the International Headache Society (IHS) in 1988 [5] have more precise clinical criteria been available for this primary headache and more detailed epidemiological data have been obtained [6–10].

The mean age at onset of CH, as derived from several epidemiological studies is generally between 20 and 40 years, although in large studies the age at onset widely varies, for instance, between 12–15 and 68–71 years [11, 12]. Moreover, the first cluster attack may also occur in early childhood and at a later age [13–21].

With the aim to verify the occurrence of CH in childhood and adolescence, we investigated in the present study the one-year prevalence of this primary headache in out-patients under 18 years of age attending 27 headache centers in Italy.

## Subjects and methods

A multicenter study was carried out in 27 headache centers, 18 of which are exclusively devoted to juvenile headache. The centers participating in the study are listed at the end of the paper. A specific sheet was sent to all centers in order to register the total num-

ber of new headache patients under 18 years of age attending for a period of 12 months. This was accompanied by an additional sheet in which the clinical history of the patients, the characteristics of the headache, the results of general and neurological examinations and the complementary investigations needed for the differential diagnosis were recorded. This sheet was structured to include any clinical characteristics which would allow the diagnosis of cluster headache to be made according to the IHS classification [5] and was completed when a case of CH was suspected.

Two semesters of recording were chosen: the first period lasted from 1 November 2000 to 30 April, 2001; the second period was from 1 May 2001 to 31 October 2001. After these two periods of recording, the sheets for the recording of all examined patients and, in the case of suspicion of cluster headache, the clinical sheets of the patients were sent to the Reference Center of Perugia, where the diagnosis was reconfirmed according to the 1988 IHS criteria [5].

## Results

We examined 6629 subjects under 18 years of age suffering from headache and attending for the first time one of the 27 headache centers. Of these, 3102 (46.8%) were boys and 3527 (53.2%) were girls .

Three boys were suspected as having CH on the basis of the clinical characteristics: two were examined in the first period of the study while the other was examined in the second period. One case was excluded because the cluster-like symptoms were due to chronic inflammation of the paranasal sinuses; the headache receded after adequate anti-inflammatory and antibiotic treatments.

Only two cases were, therefore, diagnosed as having cluster headache on the basis of the clinical history; the diagnosis was confirmed, according to the 1988 IHS criteria [20], at the Reference Center. Both cases fulfilled the criteria of cluster headache. One patient was classified as having CH with undetermined periodicity while the other had episodic CH. The two cases are described in more detail in the following paragraphs.

The prevalence of cluster headache in the 6629 children and adolescents examined affected by a headache disorder was calculated to be 0.03%.

Case 1

The patient is a 17-year-old boy who experienced the first and only cluster headache episode when he was 16 years old. The attacks were of severe intensity, with unilateral, orbital and supraorbital locations on the right side, lasting 15 minutes; the frequency was 2–3 attacks per day with onset at different times of the day. Headache was associated with conjunctival injection, nasal congestion, rhinorrhea, miosis, ptosis and eyelid edema. Other autonomic symptoms included pallor and palpitations. The clinical history and the general and neurological examinations excluded secondary headache disorders listed in groups 5–11 of the 1988 IHS classification. To treat the attacks, the patient used sumatriptan nasal spray (one puff per nostril), and this was moderately effective, reducing the intensity of the attacks or stopping them in a few minutes. He was preventively treated with verapamil per os at the dosage of 120 mg for two months with satisfactory results. No family history emerged for CH or for other primary headache disorders.

Case 2

This 9-year-old boy had his first cluster headache episode when he was 7,5 years old. He presented attacks of severe intensity of unilateral pain on the right side, with an orbital location. The cluster period lasted 7 days with a frequency of one attack per day. The duration of the attacks varied from 30 to 60 minutes and he was treated with 500 mg acetylsalicylic acid per os with no efficacy. The time of onset for all episodes was around 10:30 in the morning. The attacks were associated with the following symptoms: conjunctival injection, nasal congestion and rhinorrhea. Pallor was also present. Even in this case, the clinical history and the general and neurological examinations excluded secondary headache disorders listed in groups 5–11 of the 1988 IHS classification. Up to 31 October 2001, the child had a total of three cluster headache periods. Family history was not remarkable.

**Table 1** Patients attending the 27 headache centers and clinics in the one-year study period

| Headache centers and clinics | All patients, n | Boys, n | Girls, n |
|---|---|---|---|
| Alessandria | 167 | 87 | 80 |
| Ancona | 143 | 62 | 81 |
| Bari | 93 | 30 | 63 |
| Bergamo | 169 | 93 | 76 |
| Biella | 101 | 55 (1 case)[a] | 46 |
| Chieti | 120 | 55 (1 case)[b] | 65 |
| Fano | 97 | 53 | 44 |

*Cont.* →

**Cont. Table 1**

| Headache centers and clinics | All patients, n | Boys, n | Girls, n |
|---|---|---|---|
| Florence | 446 | 225 | 221 |
| San Giovanni Rotondo (FG) | 231 | 111 | 120 |
| Foggia | 540 | 232 | 308 |
| Genoa | 205 | 77 | 128 |
| Ivrea | 140 | 59 | 81 |
| L'Aquila | 307 | 165 | 142 |
| Mestre (VE) | 37 | 16 | 21 |
| Milan | 81 | 35 | 46 |
| Naples | 97 | 36 | 61 |
| Padua | 677 | 336 | 341 |
| Palermo: Aiuto Materno Hospital | 561 | 270 | 291 |
| Palermo: Ingrassia Hospital | 201 | 122 (1 case)[c] | 79 |
| Pavia | 720 | 306 | 414 |
| Perugia | 64 | 31 | 33 |
| Rome: La Cattolica | 76 | 37 | 39 |
| Rome: S. Carlo Hospital | 337 | 157 | 180 |
| Sassari | 192 | 81 | 111 |
| Turin: Molinette Hospital | 59 | 25 | 34 |
| Turin: S. Anna Hospital | 97 | 33 | 64 |
| Trieste | 671 | 313 | 358 |
| Total | 6629 | 3102 | 3527 |

[a] Cluster headache with undetermined periodicity (3.1.1)

[b] Episodic cluster headache (3.1.2)

[c] Excluded because the cluster-like clinical symptoms were secondary to at paranasal sinusitis

## Discussion

Several studies have investigated the prevalence of cluster headache in the general population and in out-patients attending centers and clinics devoted to headache disorders.

A lifetime prevalence between 0.07% and 0.14% emerged in population-based studies [6–10] with a clear male preponderance which seems to decrease in the last decades [8, 9]. This was attributed to changes in lifestyle factors over the years (such as employment rate and smoking habits), but this finding was not recently confirmed [22].

Typically, the mean age at onset of cluster headache is around 28–30 years, even if CH is believed to begin at any age up to around 70 years.

With regards to the onset of headache in childhood, Lance and Anthony [14] reported one patient that had isolated episodes of retro-orbital pain and lacrimation at the age of 8 years which recurred twice each year until typical bouts occurred in his second decade.

Ekbom et al. [2], identified well-defined cases of cluster headache in young Swedish 18-year-old males, and already in 1970 the same authors described 8 cases of cluster headache in a total of 105 patients affected by the same disorder who presented their first episode at an age ranging from 10 to 15 years [3].

Kudrow [16] described in detail, in his monograph *Cluster headache. Mechanisms and management*, a "three–year, two month old girl having a history of headache since age one. The major characteristics of her headache disorder were consistent with the diagnosis of cluster headache and, more specifically, with primary chronic cluster headache.

A study carried out by Swanson et al. [13] confirmed the onset of cluster headache before age 40 years and identified this primary headache disorder in only two boys aged 15 and 19 years, respectively, whereas they did not find cluster headache in patients under the age of 15 years. A recent study including 554 patients with episodic and chronic cluster headache examined between 1963 and 1997 showed 125 cases with an age at onset of CH from 10 to 19 years, with a clear prevalence in males (male-to-female ratio, 3.6:1) [22]. Furthermore, Garrido et al. [23] reported a 5-year-old child with cluster headache starting at age 3 years. There are also additional reports in the literature of onset in early childhood with the youngest patients being 3 and 4 years old [24, 25].

Based on these findings, the present one-year study was aimed at verifying the occurrence of this primary disorder in

children and adolescents with compelling headache and attending headache centers in Italy. Among the 6629 outpatients with headache under 18 years of age, two cases of CH were diagnosed: boys aged 9 and 17 years with ages of CH onset of 7 and 16 years, respectively. For both patients the diagnostic criteria for single CH attacks were fulfilled. They were diagnosed, on the basis of the presentation of the cluster periods over time, as having episodic CH and CH with undetermined periodicity, respectively.

In the older patient some doubt can be expressed regarding the efficacy of sumatriptan for cluster attacks because of the brief duration of the attacks (15 minutes) and the formulation used (intranasal, which is certainly not the first choice treatment and not as fast as subcutaneous injection). This observation makes the hypothesis of spontaneous recovery from the attack plausible. On the other hand the efficacy of verapamil as prophylactic treatment seems to support the diagnosis, although a spontaneous relief of cluster period cannot be excluded.

For the younger patient, treatment had some limitations because both sumatriptan and verapamil were contraindicated. In any case, the use of the latter prophylactic drug was not taken into consideration independently of age, due to the shorter duration of the cluster periods. In this patient, the inefficacy of acetylsalicylic acid for cluster attacks should be emphasised, in agreement with a previous report of two cases of childhood cluster headache [18]. One of the few treatment options in this case could be oxygen, which sufficiently controlled CH attacks in an affected child [24]. The younger CH patient identified in our study did not use oxygen, and therefore its efficacy could not be verified.

Indomethacin, a first choice treatment for chronic paroxysmal migraine in adults, has been demonstrated to be effective in relieving attacks in 2 cases of childhood headache [26]. Indomethacin should be mentioned as an alternative treatment.

No family history emerged for either patient, although a genetic risk for cluster headache has been described [27, 28].

On the basis of our results, the one-year prevalence of cluster headache in our out- patients affected by headache under age 18 years attending specialized centers and clinics was 0.03%. This value is smaller than that derived in the general population of all ages, and this finding further confirms the rarity of early diagnosis of this primary disorder in childhood and adolescence, at least as previously reported [3, 4].

The more brief duration of the attacks (as observed in both patients identified in our study) can partially explain the rarity of childhood cluster headache diagnosis, particularly among young patients selected from headache centers. It is also possible that childhood-onset cases may not be referred to a specialized tertiary headache or neuropsychiatric center due to the brief duration and low frequency per year of the cluster periods with spontaneous recovery [16].

Cases of CH with onset in childhood and adolescence should, in any case, be carefully followed to observe the course of the disease and the effects of therapeutic approaches. Finally, considering the rarity of cluster headache in childhood and adolescence and the frequent atypical clinical pattern in children and adolescents compared to adults (less and shorter duration of attacks, sometimes very short cluster periods), it is recommendable that appropriate neuroimaging examinations be carried out in young cluster headache patients to exclude organic disorders responsible for cluster-like attacks, such as arteriovenous malformations, endosellar or cervical spinal cord tumors, and paranasal sinus diseases, as suggested by previous studies [29, 30].

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