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Chronic daily headache

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Abstract Chronic daily headache relates to the daily or almost daily occurrence of headache in a non-paroxysmal pattern. In this review, I discuss the presentation, development, outcome, and treatment of chronic daily headache. In the context of the development of chronic daily headache, a headache continuum is presented along with its underlying pathophysiology. The treatment section covers rebound headache, analgesic and vasoconstrictor withdrawal, and the use of long-acting

opioids in intractable patients. The review concludes with a discussion of hemicrania continua, an indomethacin-responsive headache syndrome.

Key words Daily headache • Chronic daily headache • Presentation • Development • Tension-type headache • Migraine • Headache continuum • Outcome • Treatment • Rebound headache • Hemicrania continua

Introduction

Chronic daily headache refers to the daily or almost daily occurrence of headache. However, not all daily or almost daily headaches fall under this denominator, as is the case with the daily or almost daily headaches of (chronic) cluster headache and (chronic) paroxysmal hemicrania. These conditions are referred to as *paroxysmal* daily headaches, in which the headaches occur in well-defined attack patterns. In cluster headache, the attack pattern is that of headaches occurring once or twice per day, lasting for one-half to 2 hours; in paroxysmal hemicrania, it is that of headaches occurring 5–15 times per day, lasting for 10–30 minutes.

Of the *non-paroxysmal* daily headaches, *hemicrania continua* is a condition that does not fall under the denominator of chronic daily headache either. However, it is discussed in this review because it is difficult, if not impossi-

ble, to distinguish from chronic daily headache on the basis of its presentation alone. It differs from chronic daily headache in the somewhat more consistent and less variable intensity of the headache *and* in the absolute response to preventive treatment with indomethacin.

Presentation

In a study of 258 patients from my private headache practice with chronic daily headache, defined as headaches occurring at least 5 days per week for at least 1 year, my colleagues and I characterized the presentation of the headache condition [1]. We excluded only those patients with daily headaches who described well-established paroxysmal headache syndromes, in order to capture as much of the clinical features of the condition as possible. Of the 258

patients, 19% were men and 81% women; their average age at the time of consultation was 42 years. The distribution of the age at onset of (any) headache for the men and women separately is shown in Fig. 1: 77% of all patients (69% of men and 79% of women) experienced the onset of headache before the age of 30 years. The onset of headache occurred in the second decade of life in 36% of the women, as opposed to 24% of the men. The peak of headache onset in the second decade in women is indicative of the importance of the menstrual cycle in the development of headache in women.

With regard to diurnal pattern, the daily headaches were present on awakening or came on in the course of the morning in 79% of the patients, came on in the afternoon or evening in 6%, and had a variable time of onset in 15% (Fig. 2). In 25%, the headaches were worst on awakening or in the course of the morning; in 53% they were worst in the afternoon or evening, and in 22% they were worst at a variable time of the day. The results agree with my clinical observation that daily headaches come in two distinct diurnal pat-

terns. The most common pattern is that in which the headaches gradually increase in intensity as the day progresses, to be worst in the afternoon or evening. According to the results of the study, this is the pattern in more than half of the patients with chronic daily headache. The less common pattern, which I refer to as the “reversed diurnal pattern”, is that in which the headaches are worst on awakening in the morning and gradually improve as the day progresses. This was the case in one-quarter of the patients while in the remaining quarter, the diurnal course of the headaches was variable.

The reversed diurnal pattern is associated with the most frequent nighttime awakenings with headache. In the study, nocturnal awakening by headache occurred at least once per week in 36% of the patients. Of the patients who were woken up by headache at least once per week, 48% experienced the worst headache on awakening or in the course of the morning, as opposed to 22% of the patients who were woken up by headache less than once per week.

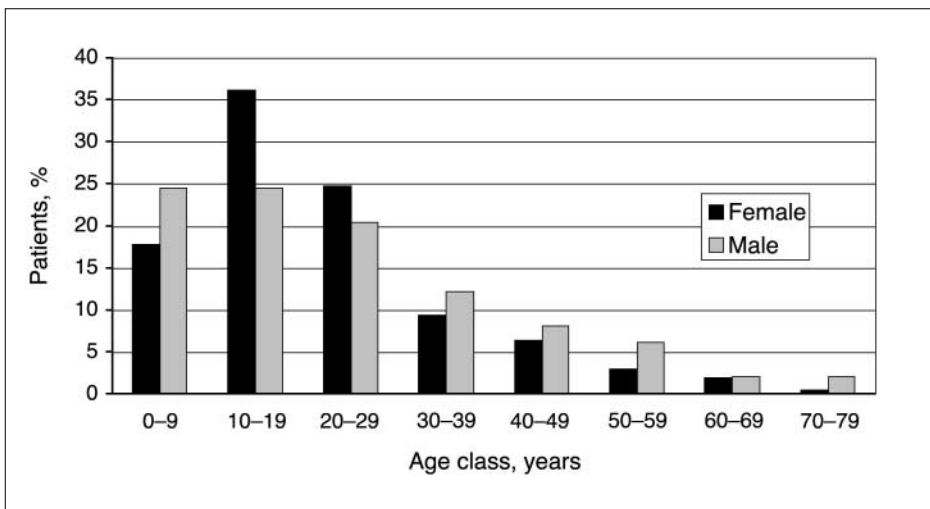


Fig. 1 Age at onset of (any) headache, by gender (n=251). (From [1] with permission)

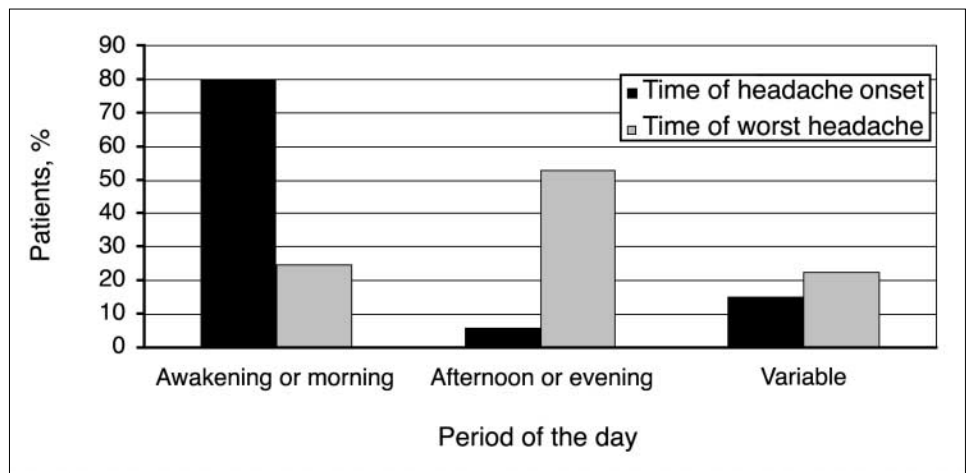


Fig. 2 Diurnal pattern of the daily headaches (n=214). (From [1] with permission)

With regard to associated symptoms, the daily headaches were at least twice per week associated with nausea in 35% and with vomiting in 9%. With regard to the laterality of the daily headaches, 36% were unilateral, 50% bilateral, and 14% either unilateral or bilateral. The unilateral headaches had a fixed lateralization in 83% and alternated between the left and right sides in 17%. The aggravating factors of the daily headaches are shown in Table 1. Apart from light and noise, most common were physical activity, bending over, stress or tension, and menstruation.

Overall, 94% of the patients experienced severe headaches in addition to the daily headaches (Fig. 3). Twenty-six percent of the patients experienced severe headaches more than 15 days per month, while the majority (63%) experienced severe headaches 10 days per month or less. The results suggest that the majority of the patients with

Table 1 Aggravating factors of the daily headaches (n=258). (From [1] with permission)

	Patients, %
Light	40
Physical activity	33
Bending over	33
Noise	30
Stress or tension	29
Menstruation ^a	28
Alcohol	20
Coughing or sneezing	15
Foods or drinks	13
Lack of sleep	12
Not eating on time	11
Straining	10
Weather changes	10
Exhaustion	10

^a For women only; n=208

chronic daily headache who seek specialty care for their headaches do *not* have chronic tension-type headache. They have chronic tension-type headache combined with migraine or, as I prefer to call it, tension-type vascular headache. This conclusion is based on the view that, with regard to clinical presentation, intensity is the predominant distinguishing feature between migraine and tension-type headache.

With regard to laterality, the severe headaches were unilateral in 43%, bilateral in 42%, and either unilateral or bilateral in 15%. The unilateral headaches had a fixed lateralization in 79% and alternated between the left and right sides in 21%. One would expect the severe headaches to be lateralized more often than the daily headaches, but this was not the case. With regard to associated symptoms, the severe headaches were at least twice per month associated with nausea in 76% and with vomiting in 38%.

In the development of chronic daily headache, medication intake is considered to play an important role, in particular the intake of analgesic and vasoconstrictor medications [2]. A widely used vasoconstrictor for the abortive treatment of headache is caffeine, in beverages, especially coffee, but also in prescription and non-prescription medications. Therefore, we measured the caffeine intake of our patients with chronic daily headache, by looking at their coffee and medication intakes. A cup of coffee was considered to contain 100 mg caffeine. We found that 43% of the patients used less than 100 mg caffeine per day, 35% between 100 and 300 mg, and 22% more than 300 mg. The average caffeine intake was 170 mg per day, which is approximately the equivalent of two cups of coffee. This is less than what was found in the population of Sydney, Australia, where the average caffeine intake was 240 mg per day, with 30% consuming more than 300 mg [3].

With regard to analgesic use, we only considered the non-opioid medications because opioids were hardly used by the patients for the treatment of headaches. Furthermore,

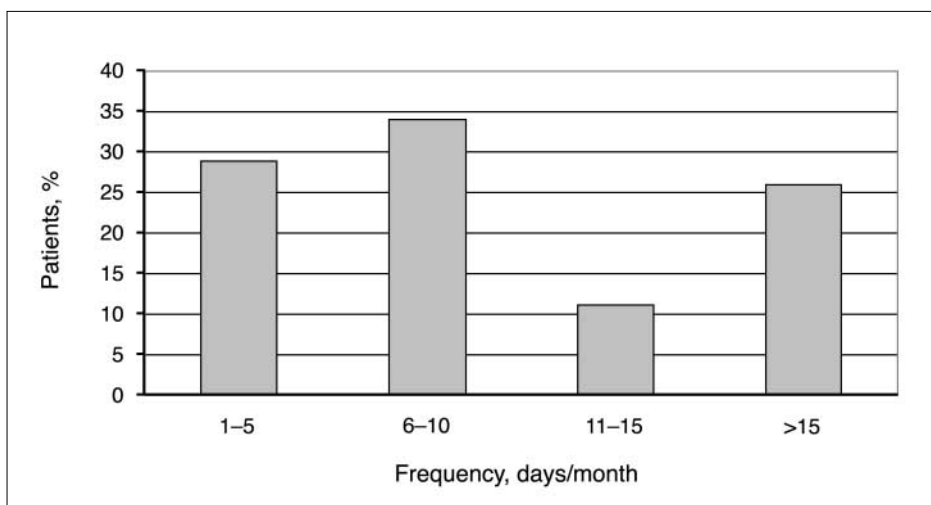


Fig. 3 Frequency of severe headaches in days per month (n=197). (From [1] with permission)

of the barbiturate-containing medications, we did *not* take into account the barbiturate component because it is not strictly an analgesic. With these limitations, we found that 26% of the patients used less than 500 mg aspirin-equivalents per day and 48% less than 1500 mg. The average analgesic intake was 1860 mg aspirin-equivalents per day, which is roughly the same as that found by Mathew et al. [4] in their patients with chronic daily headache. However, it is about half that reported by Kudrow [5] in his landmark paper on the paradoxical effects of frequent analgesic use on headache.

The preceding information on caffeine and analgesic intake only serves to describe, from this perspective, the patient population studied. Conclusions with regard to a possible causative role in the development of chronic daily headache can only be derived from prospective, discontinuation studies.

Development

Of the 230 patients in the study for whom information was available regarding the onset of headaches, 22% experienced daily headaches from the onset [6]. This can be called *primary* chronic daily headache, in the same way as we speak of primary and secondary chronic cluster headache. The remaining 78% initially experienced intermittent headaches, that is, they had *secondary* chronic daily headache. The distribution of the age at onset of the headaches in those 50 patients with daily headaches from the onset (primary chronic daily headache) is shown in Fig. 4. Sixty-six percent of the patients experienced the onset of the daily headaches between the ages of 10 and 39 years.

Of the 179 patients with daily headaches but who initially had intermittent headaches, that is, of those with secondary chronic daily headache, 34 (19%) experienced an

abrupt onset of the daily headaches and 145 (81%) a *gradual* onset. The distribution of the age at onset of the daily headaches in those patients with abrupt-onset secondary chronic daily headache is shown in Fig. 5. There is no difference between this distribution and that of the patients with primary chronic daily headache, as shown in Fig. 4.

The circumstances related to the onset of the daily headaches in the patients with primary chronic daily headache and in those with abrupt-onset secondary chronic daily headache are shown in Table 2. The table also shows the circumstances of daily headache onset for the two groups combined, as there was no difference in distribution of the circumstances between the two groups. The most common circumstance of daily headache onset in the two groups combined was head, neck, or back injury, caused by a motor-vehicle accident in 61%. Flu-like illness/sinusitis and medical illness/surgical procedure follow it as causes of daily headache onset. Examples of medical illness associated with the (abrupt) onset of chronic daily headache are colitis, fibromyalgia, vertigo, encephalitis, and meningitis.

There were also no differences between the patients with primary chronic daily headache and those with abrupt-onset secondary chronic daily headache with regard to the following features: gender distribution, time of daily headache occurrence, worst headache time daily, nocturnal awakening, laterality of the daily headaches, occurrence and frequency of severe headaches, laterality of the severe headaches, and parental occurrence of headache. The *only* difference between the two groups was the association of the daily *and* severe headaches with nausea. Nausea was more common in the patients with abrupt-onset secondary chronic daily headache than in those with primary chronic daily headache. The difference is probably due to the fact that 57% of the patients in the abrupt-onset group had a history of severe headaches, which tend to be associated with gastrointestinal symptoms.

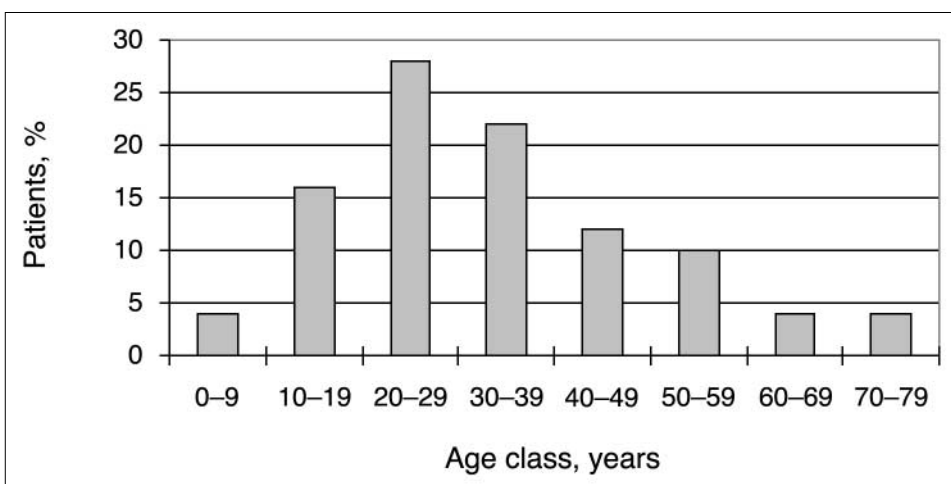


Fig. 4 Age at onset of daily headache, in the patients with primary chronic daily headache (n=50). (From [6] with permission)

Fig. 5 Age at onset of (daily) headache, in the patients with abrupt-onset secondary chronic daily headache (n=32). (From [6] with permission)

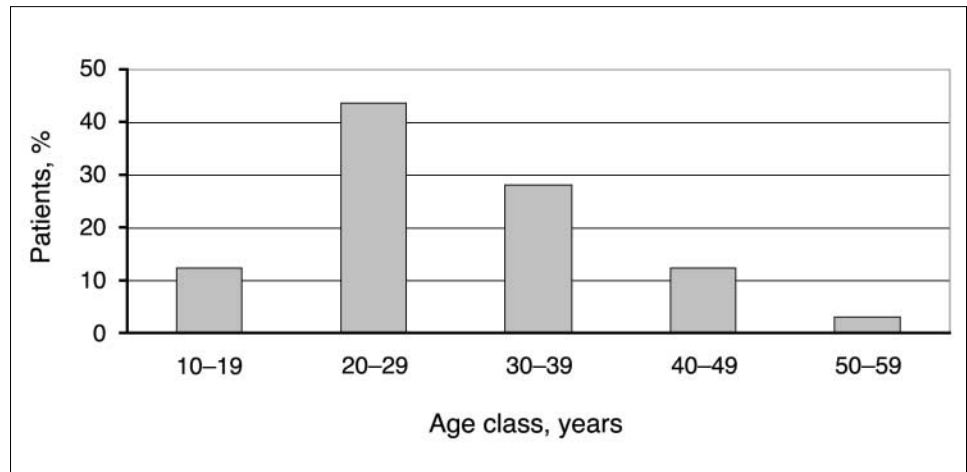


Table 2 Circumstances of (abrupt) onset of the daily headaches. Values are percent of patients. (From [6] with permission)

	Primary chronic daily headache (n=51)	Abrupt-onset secondary chronic daily headache (n=34)	Combined group (n=85)
Head, neck, or back injury	25	29	27
Flu-like illness or sinusitis	12	18	14
Medical illness or surgical procedure	14	15	14
Miscellaneous	18	12	15
No apparent reason	31	26	30

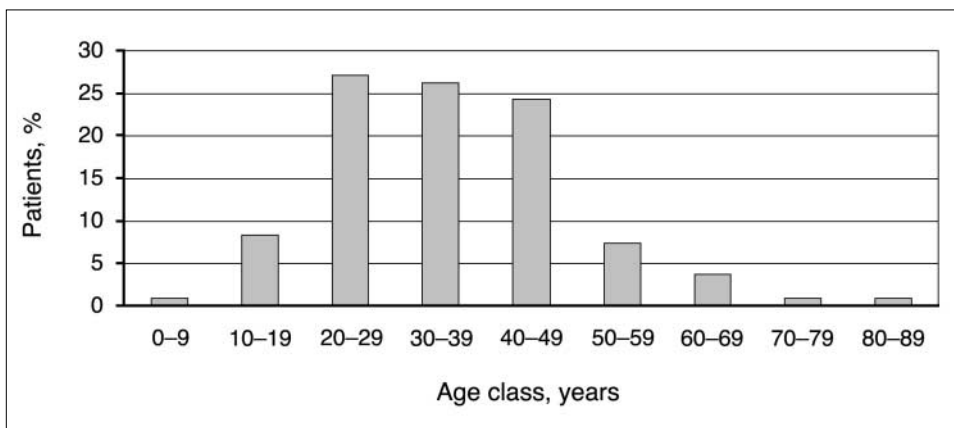


Fig. 6 Age at onset of *daily* headache, in the patients with gradual-onset secondary chronic daily headache (n=106). (From [6] with permission)

The distribution of the age at onset of the daily headaches in those patients with gradual-onset secondary chronic daily headache is shown in Fig. 6. Seventy-eight percent of the patients experienced the onset of daily headaches between the ages of 20 and 49 years. The distribution of the age at onset of the initial, intermittent headaches in this group is shown in Fig. 7. The two figures are combined in Fig. 8, which shows the distribution of the age at initial *and* daily headache onset in the patients with gradual-onset secondary chronic daily headache. The average duration of the transition of the headaches from intermittent to

daily was 11 years, which is reflected in the figure by the separation of the two distributions by approximately a decade.

With regard to parental occurrence, headache in the father or mother was more common in the patients with gradual-onset secondary chronic daily headache than in the combined group of those with primary chronic daily headache and abrupt-onset secondary chronic daily headache (69% vs. 45%). This observation is interesting because conditions that develop abruptly generally have less of a genetic involvement than do those that develop gradu-

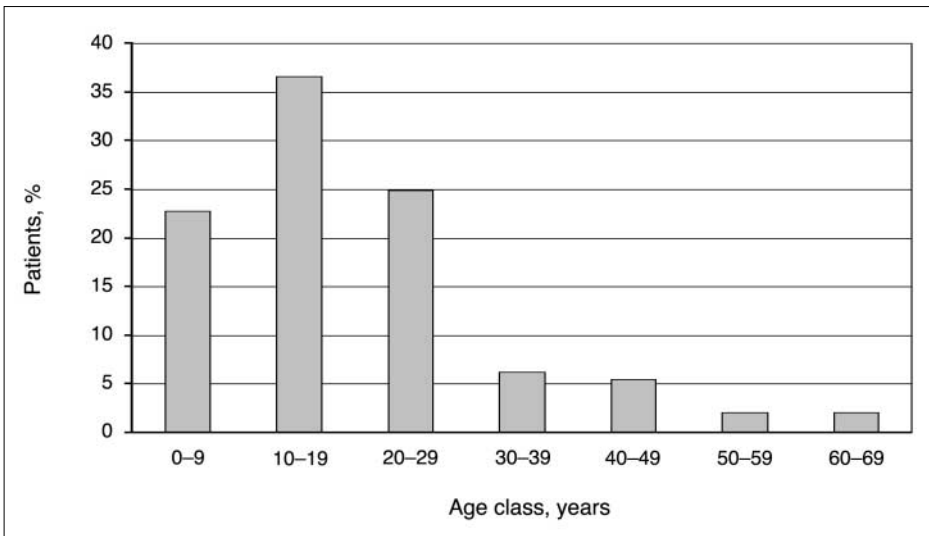


Fig. 7 Age at onset of *initial* headache, in the patients with gradual-onset secondary chronic daily headache (n=145). (From [6] with permission)



Fig. 8 Age at onset of initial *and* daily headache, in the patients with gradual-onset secondary chronic daily headache (n=145 and 106, respectively). (From [6] with permission)

ally. On the basis of the information gathered on parental headache occurrence, this also seems to be the case in chronic daily headache.

With regard to the intensity of the initial headaches, in the 145 patients with gradual-onset secondary chronic daily headache, the headaches were mild in 33% and severe in 67% (Table 3) [7]. The mild headaches were associated with nausea in 25% and vomiting in 0%, as opposed to the severe headaches, which were associated with nausea in 84% and vomiting in 72%. With regard to the frequency of the initial headaches, there was no difference between the mild and severe headaches: The mild headaches occurred less than twice per week in 88% and the severe headaches in 91%.

Table 4 shows the features of the *daily* headaches separately for those patients whose initial headaches were mild and for those whose initial headaches were severe. There were no differences between the two groups with regard to

any of the features studied. The two groups also did not differ significantly from each other with regard to the age at onset of the (initial) headaches (Fig. 9).

Table 3 Features of the initial headaches in the patients with gradual-onset secondary chronic daily headache

	Mild	Severe
Headache intensity (n=112)	33%	67%
Associated symptoms	n=12	n=61
Nausea	25%	84%
Vomiting	0%	72%
Headache frequency	n=25	n=60
≤4 per month	60%	73%
5-9 per month	28%	18%
10-19 per month	8%	7%
≥20 per month	4%	2%

Table 4 Features of the daily headaches in the patients with gradual-onset secondary chronic daily headache, according to the initial intensity of the headaches. (From [11] with permission)

	Mild	Severe
Gender	n=37	n=75
Women, (%)	84	80
Men, (%)	16	20
Diurnal headache pattern ^a		
Time of headache onset	n=36	n=75
Awakening or morning, (%)	83	69
Afternoon or evening, (%)	3	9
Variable, (%)	14	22
Time of worst headache	n=33	n=67
Awakening or morning, (%)	39	18
Afternoon or evening, (%)	39	55
Variable, (%)	22	27
Nocturnal headache awakening	n=34	n=70
At least once/week, (%)	29	39
Associated symptoms	n=37	n=70
Nausea, (%)	41	43
Vomiting, (%)	8	13
Laterality	n=37	n=75
Unilateral, (%)	32	48
Bilateral, (%)	57	39
Uni/bilateral, (%)	11	13
Occurrence of severe headaches, (%)	97 (n=36)	96 (n=74)
Associated symptoms of severe headaches	n=36	n=69
Nausea, (%)	75	87
Vomiting, (%)	37	48
Frequency of the severe headaches	n=29	n=62
1–5 days/month, (%)	35	31
6–10 days/month, (%)	31	31
11–15 days/month, (%)	14	19
16–20 days/month, (%)	3	8
>20 days/month, (%)	17	11
Laterality of the severe headaches	n=35	n=70
Unilateral, (%)	43	53
Bilateral, (%)	49	33
Unilateral or bilateral, (%)	8	14

From a classification perspective, does it make sense to distinguish between primary and secondary chronic daily headaches as we did and, within the latter group, between abrupt and gradual onset? Judging from the age at onset of the daily headaches, gender distribution, headache presentation, circumstances of headache onset, and parental headache

occurrence, there does not seem to be a reason for the distinction between primary chronic daily headache and secondary chronic daily headache *with* abrupt onset. The two groups should probably be considered as having one and the same chronic daily headache condition, which could be referred to as *abrupt-onset chronic daily headache*, represent-

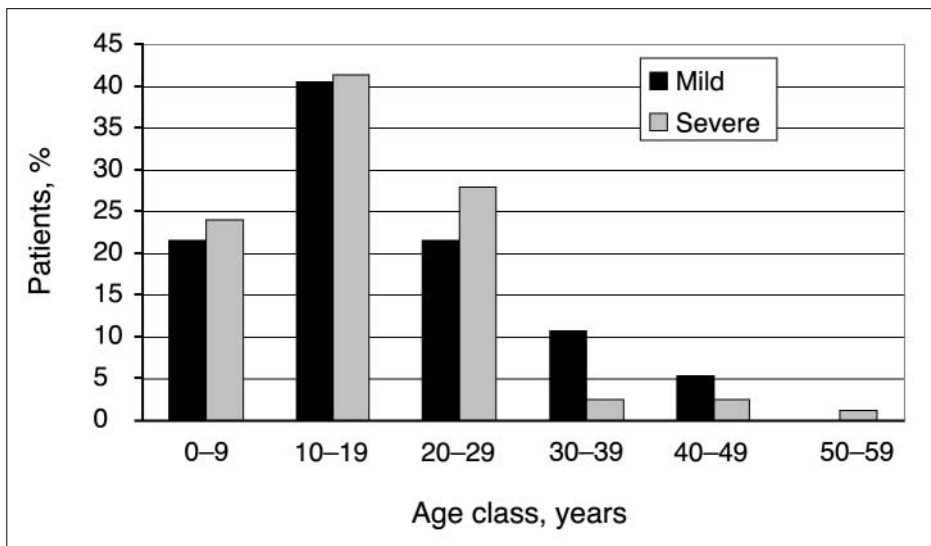


Fig. 9 Age at onset of headache, in the patients with gradual-onset secondary chronic daily headache, separately for those with initially mild headaches (n=37) and those with initially severe headaches (n=75). (From [6] with permission)

ing 37% of our study group. However, this group should probably be distinguished from the one with chronic daily headache with gradual onset because of the very different development of the daily headaches and the difference in parental headache occurrence. The latter group could be referred to as *gradual-onset chronic daily headache*. Future studies will have to decide whether the distinction is meaningful in terms of predicting treatment and/or outcome.

Headache continuum

The previously described findings with regard to the development of chronic daily headache support the concept of headache continuum as I originally proposed (Fig. 10) [8–11]. The headache continuum includes episodic and chronic tension-type headache, migraine headache, and tension-type vascular headache. Tension-type headache and migraine are the two most common headache presentations. Episodic tension-type headache is almost universally experienced, while migraine headaches affect 10%–15% of the population. The major clinical distinction between the two, in my opinion and as mentioned previously, is the intensity of the headaches. Headache intensity is traditionally divided into three categories, that is, mild, moderate, and severe, depending on the extent to which the headache affects the ability to function. A mild headache does not affect the ability to function, a moderate headache affects the ability to function but does not necessitate bed rest, and a severe headache is incapacitating and requires bed rest. Tension-type headaches are typically mild or moderate in intensity while migraine headaches tend to be moderate or severe.

Related to the (peripheral) mechanisms involved in causing the pain, the migraine headache is localized while

the tension-type headache is more diffuse in location. The migraine headache is localized not only to one side of the head but within the side of the head, to areas such as the temple or eye. The pain tends to be throbbing or sharp, steady in nature, while the pain of tension-type headache is more dull and steady. Also related to the mechanisms involved in causing the pain, the migraine headache is affected by movement and activity, which is not typically the case with tension-type headache. The migraine headache often develops during the night and is present on awakening in the morning or wakes the patient up out of sleep at night, usually between 4 and 6 AM. Episodic tension-type headache, on the other hand, generally comes on during the day, often in the late afternoon, that is, between 4 and 6 PM. The episodic tension-type headache lasts for a couple of hours, whereas the migraine headache lasts from part of a day to several days. Related to the generally low intensity of the pain, tension-type headache has few, if any, symptoms associated with it and when symptoms are present, they are mild in intensity. The migraine headache, on the other hand, has intense associated symptoms related to the generally high intensity of the pain. Almost universally present in migraine are photophobia and phonophobia; however, nausea is also common and with the most intense migraine headaches, vomiting occurs as well.

There is ongoing debate with regard to the mechanisms involved in causing the pain of tension-type headache and migraine. It is my belief that peripheral mechanisms are important in both headache presentations, although the present thinking is more oriented toward central mechanisms, including central sensitization. Central sensitization relates to the lowering of the activation threshold of central, sensory neurons to peripheral stimulation. The mechanism by which this occurs, if it does, is not known.

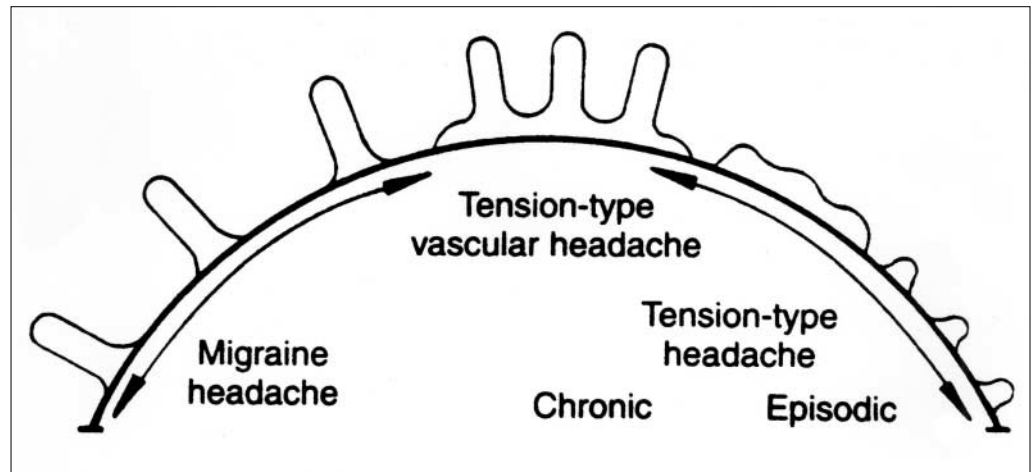


Fig. 10 The continuum of headache syndromes, which includes episodic and chronic tension-type headache, migraine headache, and tension-type vascular headache

In tension-type headache, the *peripheral* mechanism is that of sustained contraction of the craniocervical muscles; in migraine headache it is that of *extracranial* arterial vasodilation. The arterial vasodilation in migraine activates a secondary mechanism, which is known as neurogenic inflammation. Stretching of the nerve fibers involved in pain transmission (C and A δ) surrounding the blood vessels causes the neurogenic inflammation. The stretching causes the nerve fibers to depolarize, which, on the one hand, generates the action potentials that are transmitted to the central nervous system. On the other hand, it causes the release of inflammatory chemicals into the peripheral tissues, such as substance P, calcitonin gene-related peptide, and neurokinin A. The inflammatory chemicals act to further dilate the arteries and also lower the pain threshold locally in the peripheral tissues. Thus, a vicious cycle is created in which vasodilation causes inflammation that, in turn, accentuates the vasodilation and renders it extremely painful.

When headaches occur regularly, they lead, through an involuntary reflex mechanism, to progressive tightening of the craniocervical muscles. The greater intensity of the pain makes this effect more pronounced in migraine than in tension-type headache. Hence, temporal and cervical electromyographical activity is higher in migraine patients than it is in those with tension headache [12]. Likely contributing factors to the process of tightening of the craniocervical muscles are treatment of tension-type headaches with analgesics (as opposed to efforts to relax the muscles) and lack of effective abortive treatment in migraine.

In tension-type headache, the progressive increase in tightness of the craniocervical muscles leads, over time, to an increase in frequency of the headaches. It also leads to a progressive earlier occurrence of the headaches during the day. Ultimately, a daily or almost daily headache condition develops in which the headaches are present on awakening or come on shortly after getting up. As long as

the headaches remain mild or moderate in intensity, the condition can be referred to as chronic tension-type headache. However, once the headaches have taken up all available time, they tend to increase in intensity to create "migraine headaches". The condition is then referred to as migraine with chronic tension-type headache. However, a better term would be tension-type vascular headache, emphasizing the existence of one single headache condition, rather than suggesting the presence of two separate conditions.

When the regular occurrence of migraine headaches leads to a progressive increase in tightness of the craniocervical muscles, a gradual increase in frequency of the headaches occurs, as well as a progressive interposition of the migraine headaches with tension-type headaches. The increase in frequency of the migraine headaches, I propose, is due to the fact that the muscle tightness, in and by itself, becomes a trigger of migraine headaches. As the muscles become tighter, they begin to interfere mechanically with their own circulation, creating a stimulus for dilation of the feeding arteries. One such feeding artery is the frontal branch of the superficial temporal artery, which overlies the powerful temporalis muscle. This is also the artery that is involved, preferentially, in the process of migrainous vasodilation, causing the throbbing or sharp, steady pain in the temple so characteristic of the condition [13]. Ultimately, the migraine and tension-type headaches merge into daily or almost daily headaches, with frequently occurring migraine headaches. A condition is, thus, created that is identical to what has been described previously as migraine with chronic tension-type headache or tension-type vascular headache. However, the difference is that here it developed out of migraine ("transformed" or "chronic migraine"), while the condition described before developed, through chronic tension-type headache, out of episodic tension-type headache.

Outcome

Of the 145 patients in our study with gradual-onset (secondary) chronic daily headache, we were able to contact 91 (63%) [7]. Seven patients refused to participate in the follow-up telephone interview, and eleven no longer remembered the nature of their initial headaches. One patient was excluded from the analysis because of the absence of headaches at the time of contact and three patients because of missing data. The remaining 69 patients (77%) were able to provide adequate information to classify their initial *and* present headaches as tension-type headache or migraine according to International Headache Society (IHS) criteria [14].

Of the 69 patients, 23 (33%) still had daily headaches, while the remaining 46 (67%) again experienced intermittent headaches. Of the latter 46 patients, the initial headaches were classified as migraine in 39 (85%) and tension-type in 7 (15%) (Table 5). Their present headaches were classified as migraine in 34 (74%) and tension-type in 12 (26%). Thus, over time a slight shift had occurred from migraine to tension-type headache. Similar shifts over time from migraine to tension-type headache have been observed in children and adolescents by Dooley and Bagnell [15] and Guidetti and Galli [16]. Dooley and Bagnell conducted a 10-year follow-up study of 77 children and adolescents. At the initial evaluation, they found 83% to have migraine and 17% tension-type headache, while at follow-up these numbers were 60% and 40%, respectively [15]. Guidetti and Galli conducted an 8-year follow-up study of a random sample of 100 children and adolescents, out of a total group of 240 with migraine or tension-type headache, diagnosed according to IHS criteria. At the initial evaluation, they found 79% of the patients to have migraine and 21% episodic tension-type headache, while at follow-up these numbers were 55% and 45%, respectively [16].

However, the question that we wanted to address in our study was not whether the patients with intermittent headaches had improved in comparison to their initial headaches, but whether the patients with gradual-onset chronic

daily headache reverted back to their initial headache condition, once the headaches had become intermittent again. In the study, of the 39 patients whose initial headaches were classified as migraine, 30 (77%) also had migraine at follow-up and nine (23%) had tension-type headache (Table 5). Of the seven patients whose initial headaches were classified as tension-type, three (43%) had tension-type headache at follow-up and four (57%) had migraine. Therefore, it seems that after going through daily headaches, migraine patients as a rule revert back to migraine, although some find their headaches changed to episodic tension-type headache. However, the situation is different for those patients who initially had episodic tension-type headache. They seem to come out worse after having experienced daily headaches, with some left with headaches that have features and associated symptoms categorized as migraine in the IHS classification. While we found that 57% of our patients who initially had episodic tension-type headaches had evolved into migraine, Dooley and Bagnell [15] found this to be the case in 11% of their children and adolescents, and Guidetti and Galli [16] observed this in 25%. Apart from the age difference, however, there is also the fact that in our study all patients had progressed, at one point in time, to daily headaches, which was not the case in the pediatric studies. In addition, the number of patients in the tension-type headache group in our study is small, making it difficult to draw a reliable conclusion.

Treatment

The first step in the treatment of chronic daily headache is the accurate establishment of the use of analgesic and vasoconstrictor medications, prescription *and* non-prescription. It is important to establish their use in terms of the number of tablets or capsules taken per day and the number of days of use per week or month. Patients tend to be notoriously vague about their intake of medications that they take as needed only. They also often have to be reminded specifically with regard to the use of non-prescription medications. Once the exact intake of analgesic and vasoconstrictor medications has been established, it should be determined whether there is "overuse". Overuse is defined as medication intake for headache that is detrimental rather than beneficial to the headaches. It is use that promotes the occurrence of headaches long-term rather than providing headache relief. Analgesic and vasoconstrictor medications promote headache if they are taken at time intervals shorter than their duration of action, which means that frequency of intake is more important than quantity. Hence, when these medications are allowed to accumulate in the system, they bring on headache when their effect wears off, a phenomenon that has become known as "rebound".

Table 5 Present and initial headaches in the 46 patients (36 women and 10 men) who initially had intermittent headaches, developed daily headaches through a gradual transition, and again have intermittent headaches. Values are numbers of patients

Initial headaches	Present headaches		Total
	Migraine	Tension-type	
Migraine	30	9	39
Tension-type	4	3	7
Total	34	12	46

Rebound headache generally occurs when analgesic or vasoconstrictor medications are taken more often than 2 days per week on the average. This is particularly true for caffeine-containing medications because of the prolonged vasoconstrictor effect of caffeine, which can last up to 60 hours. A higher frequency of intake of analgesic or vasoconstrictor medications can be allowed for simple analgesics and the shorter-acting triptans, such as sumatriptan. A lower frequency of intake has to be considered with the longer-acting ergots, ergotamine and dihydroergotamine. However, it has to be kept in mind that the “rebound threshold” has *not* been determined for any medication or group of medications. Also, the diagnosis of rebound headache can only be made retrospectively, after withdrawal from analgesic or vasoconstrictor medications has been accomplished *and* improvement of headaches has occurred. A *suspicion* of rebound headache can be based not only on the *frequency* of medication intake but also on increased medication usage over time, with decreasing efficacy (Fig. 11). The decreasing efficacy is often attributed to the development of tolerance but, in my opinion, it is more a manifestation of worsening of the headaches and an indication that use has become overuse.

If it is suspected that medication overuse and rebound headache are present, this needs to be addressed next. However, it can only be addressed after the patient has been given insight into the situation. With regard to vasoconstrictor medications, reference can be made to the vascular mechanism of headache. The vascular mechanism is antagonized by the vasoconstrictor medications, resulting in rebound vasodilation and headache recurrence when the vasoconstrictor effect wears off. Analgesic medications only

address the pain of the headache and *not* the underlying mechanisms. Consequently – and as with symptomatic treatment in general – the underlying mechanisms deteriorate, resulting in worsening of the headaches.

The withdrawal of analgesic and vasoconstrictor medications is generally best accomplished abruptly. However, whether this is possible also depends on the kind and quantity of medications taken. When specific quantities of barbiturate-containing or opioid medications are involved, withdrawal may require hospitalization for close monitoring of withdrawal symptoms and intravenous administration of medications. The withdrawal of a significant amount of barbiturate-containing medications also requires a barbiturate taper to prevent the occurrence of seizures. The withdrawal of a significant amount of opioid medications requires expertise in addiction medicine and may have to be done in a detoxification center. Otherwise, it can often be accomplished on an outpatient basis, and several protocols have been developed to assist the patient with the withdrawal.

A recent protocol employs sumatriptan for withdrawal headache after abrupt discontinuation of the rebound-causing medications [17]. The sumatriptan is given in a dose of 25 mg orally, three times per day for 10 days, or until the patient is headache-free for 24 hours. After that, it is only used as needed for the abortive treatment of moderate and severe headaches. Of the 35 sequentially selected patients to be enrolled in a study using this particular protocol, nine left the clinic and 26 were actually treated. They had suffered from daily headaches for an average of 8.2 years. Of the 26 patients treated, 58% no longer experienced daily headaches after 1 month, and 69% had reverted back to intermittent headaches after 6 months.

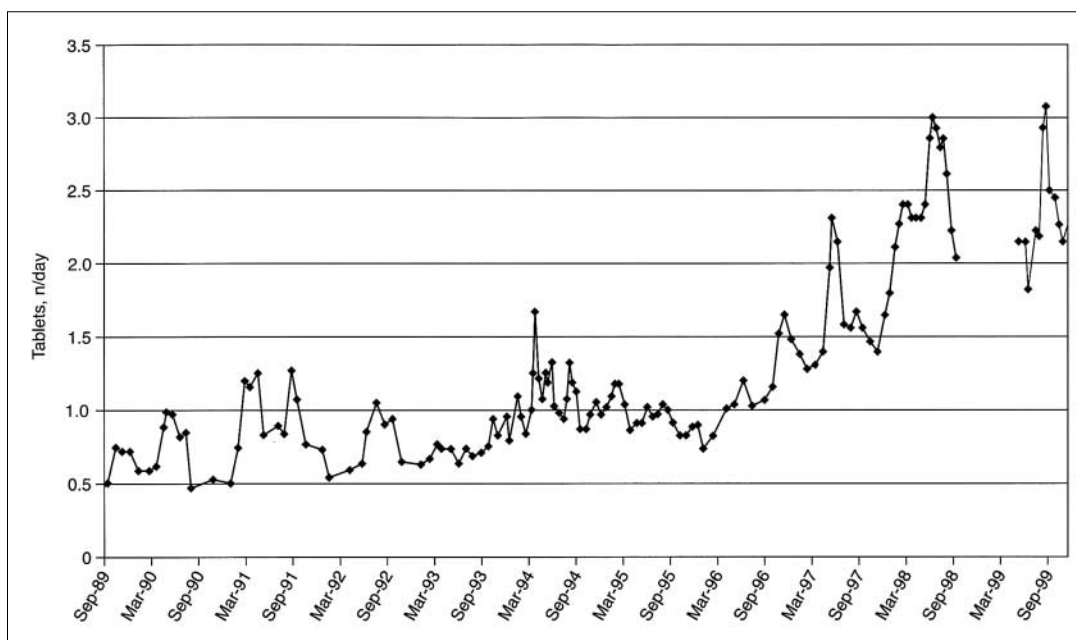


Fig. 11 Example of the increase in intake of a caffeine containing analgesic medication for headache, in number of tablets per day, over a period of 10 years

An out-patient protocol that I myself have used successfully for the last 20 years to withdraw patients with daily headaches from the daily or almost daily use of abortive medications is that utilizing a short course of prednisone. Depending on the kind and quantity of the medications that the patient has to be withdrawn from, I give prednisone for 3 or 6 days. The three-day schedule consists of 15 mg prednisone four times per day for 1 day, 10 mg four times per day for 1 day, and 5 mg four times per day for 1 day; the days are doubled in the six-day schedule. If the patient exhibits prominent muscular symptoms, that is, complains of tight or sore neck and shoulder muscles, I add diazepam to the schedule in a dose of 1–5 mg four times per day to help relax the muscles.

I have used a similar schedule for patients admitted to the hospital when outpatient withdrawal was unsuccessful because of the patient's inability to tolerate the withdrawal headache or its association with severe nausea and vomiting. Under these circumstances, I add metoclopramide as an anti-nausea medication, which I give intravenously in a dose of 10 mg four times per day. It is important to start the metoclopramide immediately, that is, before the patient becomes sick, because once vomiting has developed, it is difficult to control even with intravenous administration of the medication. Instead of prednisone orally, dexamethasone can be given intravenously in a dose of 4 mg, four times per day, for a number of consecutive days. The diazepam can then be given every 6 hours but only as needed for severe headache and can also be given intravenously. An alternative to diazepam intravenously is lorazepam intramuscularly in a dose of 1 or 2 mg, as needed every 6 hours.

An alternative to this in-patient protocol with metoclopramide, dexamethasone, and diazepam or lorazepam is one involving metoclopramide and dihydroergotamine. In this protocol, both medications are given intravenously on a regular, generally 8-hour, schedule with the metoclopramide administered *before* the dihydroergotamine. The administration sequence prevents the occurrence of nausea and vomiting as a result of the intravenous administration of dihydroergotamine. The dose of metoclopramide is usually 10 mg, while that of dihydroergotamine is gradually increased from 0.25 to 1 mg, depending on the ability of the patient to tolerate the medication, especially in terms of gastrointestinal side effects. A long-term follow-up study of 50 consecutive patients with chronic daily headache treated with an intravenous dihydroergotamine protocol showed 44% to have good or excellent results after 3 months and 59% after 2 years [18].

After withdrawal from analgesic and vasoconstrictor medications, headaches may improve for up to 3 months. Often preventive pharmacologic treatment is initiated immediately after the withdrawal but I generally do not do that. An exception is when the patient has problems sleeping

at night for which I will prescribe amitriptyline, doxepin, or trazodone. These are sedating tri- or tetracyclics of which the first two have been shown to be effective in the preventive treatment of chronic tension headache [19–22]. However, I do recommend that patients get involved immediately with non-pharmacologic treatments, such as using a heating pad daily on the neck and shoulders to help decrease the muscle tightness that many of them have developed over time. At a later stage, I may prescribe more formal physical therapy, consisting of massage, ultrasound, stretching exercises, etc. or do trigger point injections to further help relax the muscles.

For the daily headaches, I allow patients to use muscle relaxants such as metaxalone or carisoprodol. For the severe headaches, 50-mg promethazine suppositories can be helpful, as long as it is judged better for the patient not to use analgesic and vasoconstrictor medications. Once the headaches have become intermittent, I focus with the abortive treatment on the severe headaches for which I try to find effective treatment, relying as much as possible on specific antimigraine medications. I define effective treatment as treatment that provides *full* relief of headache and associated symptoms within 2 hours of initiation. It is important for this treatment to be *consistently* effective as well, which would allow the patient to wait until the headache is severe before initiating it. This is the only way that patients can be prevented from, over time, falling back into the pattern of frequent intake of analgesic or vasoconstrictor medications.

With regard to preventive pharmacologic treatment, a particularly useful combination in patients with frequent *and* severe headaches is that of a tricyclic and a beta-blocker [23]. The tricyclics that I prefer to use are amitriptyline, doxepin, and imipramine. The first two I prescribe when sedation is needed to help the patient fall asleep and sleep through the night. If sleep is not an issue, I prefer imipramine because it has fewer side effects, in particular regarding increased appetite and weight gain. Imipramine has also been shown to be effective in the preventive treatment of chronic tension headache, but only in an open study and with less benefit than amitriptyline [24].

With regard to the beta-blockers, six have been shown in randomized, double-blind, placebo-controlled studies to be effective in migraine prevention [25]. These beta-blockers are: atenolol, bisoprolol, metoprolol, nadolol, propranolol, and timolol. In patients with chronic daily headache, they are often effective in decreasing the intensity of the headaches, while the tricyclics tend to have more of an effect on headache frequency. The calcium-entry blockers, in particular verapamil [26, 27], I have found helpful if after analgesic or vasoconstrictor withdrawal, the headaches continue to frequently wake the patient up out of sleep at night.

Kudrow [5] determined the effects of analgesic withdrawal and preventive treatment with amitriptyline in 200

patients with chronic muscle-contraction headache who used analgesics daily, as documented by one-month pretrial records. He randomly divided the patients into two groups and four subgroups. Half of the patients were prescribed amitriptyline (25 mg per day for 1 week and 50 mg per day thereafter). In each group, half of the patients were allowed to continue taking analgesics without restriction, while the other half was instructed to discontinue these medications. The percentage headache improvement he observed in the four groups is shown in Table 6. Analgesic withdrawal, in and by itself, resulted in a 43% headache improvement 1 month after initiation of treatment. The addition of amitriptyline to the analgesic withdrawal increased the headache improvement to 72%.

Our study suggests that, with the treatment approach outlined above, two-thirds of patients who have daily headaches can be improved to intermittent headaches [7]. Preventive treatment in these patients may make the intermittent headaches somewhat better than what they were initially, as the shift from migraine to tension-type headaches observed in the study suggests, when the present headaches were compared to those that occurred initially.

However, what should be done with the patients who continue to have frequent and severe headaches, despite being off analgesic and vasoconstrictor medications and despite efforts at preventive treatment? It is impossible to let these patients suffer forever and, here, there may be an indication for the use of long-acting opioids, to relieve the pain and allow these patients to function in their professional and personal lives. The long-acting opioids that I have used in

these patients are fentanyl patch, oxycodone, and morphine sulfate. I have found that the medications generally work shorter than the manufacturers indicate and, for example, will use the fentanyl patch every 2 days rather than 3 days. I gradually increase the dose of the medication until *satisfactory* pain control is achieved and the patient is back to a relatively normal level of functioning. I prefer the use of long-acting to short-acting opioids because of much less development of tolerance and addiction. For some reason, rebound headache does not seem to develop with the long-acting opioids, while it is standard to occur with short-acting analgesics, including opioids. The development of tolerance *and* rebound headache both increase the use of opioid analgesics over time and make it difficult, if not impossible, to accomplish adequate pain control.

Hemicrania continua

As far as its presentation is concerned, hemicrania continua [28] can be looked upon as a form of chronic daily headache. It is a non-paroxysmal daily headache, present continuously throughout the day, limited to one side of the head. However, it is different from chronic daily headache in its treatment. Hemicrania continua is treated with indomethacin to which it has an *absolute* response, similar to paroxysmal hemicrania [29]. The different treatment suggests a different etiology, which would preclude the condition from being grouped with chronic daily headache.

Hemicrania continua has been described resistant to preventive treatment with indomethacin [30]. Resistance to treatment with indomethacin, however, by definition means that it is *not* hemicrania continua. This does not mean that there are not many patients who have continuous unilateral headaches with fixed lateralization that do *not* respond preventively to indomethacin. These patients have chronic daily headache and should be treated accordingly. The key to look for in the history is a response to aspirin, which seems to predict the responsiveness of the headaches to indomethacin. This is also the feature that led to the identification of both paroxysmal hemicrania and hemicrania continua as indomethacin-responsive headache syndromes.

Table 6 Headache improvement 1 month after initiation of treatment in 200 patients with chronic muscle-contraction headache who used analgesics daily. (Modified from [5])

	Patients with improvement, %
Treated with amitriptyline	
Analgesics continued (n=50)	30
Analgesics withdrawn (n=50)	72
Not treated with amitriptyline	
Analgesics continued (n=50)	18
Analgesics withdrawn (n=50)	43

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