Arq Neuropsiquiatr 2002;60(4):912-916

CLINICAL FEATURES OF EPISODIC MIGRAINE AND TRANSFORMED MIGRAINE

A comparative study

José Carlos Busto Galego[1], José Paulo Cipullo[2], José Antonio Cordeiro[3], Waldir Antonio Tognola[2]

ABSTRACT - Transformed migraine (TM) is one of the most frequent types of chronic daily headache. Eighty patients: 40 with episodic migraine (EM) and 40 with TM with ages ranging from 18 to 60 years old were studied. Females were the majority. At first examination, the mean age was similar in both groups. The initial age of migraine attacks was significantly smaller in the TM group. Time history of episodic attacks was similar in both groups. In the EM group, the headache was predominantly located on only one side of the head; whereas in the TM group, on more than one side. There was variation in the character of pain and intensity in the TM group. Nocturnal awakening with headache, aura and family history did not show significant association with EM or TM. The TM was distinguished from the EM in relation to the frequency, location and pain intensity of the headache. Patients with early migraine headache onset may exhibit a further risk of developing TM.

KEY WORDS: transformed migraine, chronic daily headache.

Estudo comparativo entre as características clínicas da migrânea episódica e a migrânea transformada

RESUMO - A migrânea transformada (MT) é apontada como a forma mais frequente de cefaléia crônica diária. Foram estudados 80 pacientes: 40 com ME e 40 com MT entre 18 e 60 anos de idade. As mulheres foram maioria. A idade média na primeira consulta foi semelhante nos 2 grupos. A idade de início das crises migranosas foi significantemente menor no grupo MT. O tempo de história de crises episódicas nos dois grupos foi semelhante. No grupo ME predominou um só local da cefaléia enquanto no MT, mais de um. Houve variação no caráter e intensidade da dor na MT. Despertar noturno com cefaléia, aura e história familiar, não apresentaram associação significante com ME ou MT. A MT se distinguiu da ME quanto à frequência, localização e intensidade dolorosa da cefaléia. O início precoce das crises de migrânea pode sugerir um fator de risco para o desenvolvimento da MT.

PALAVRAS–CHAVE: migrânea transformada, cefaléia crônica diária.

The phenomenon of episodic migraine (EM) transformation into chronic headache was suggested by Mathew et al.[1] in 1982. In this study, the authors investigated 80 patients complaining of daily headache. Out of those, 61 patients (76.25%) have had migraine episodes in their past history, before the onset of daily headache. In 1987, Mathew et al.[2]. used the term of transformed migraine (TM) to describe this daily or almost daily headache with some clinical characteristics between migraine and tension-type headache, and with a particular and natural history. The patients with TM usually experience migraine attacks with or without aura during adolescence or early adult life. The onset over the years has become more frequent. At the same time, these patients developed mild interictal headaches, evolving to chronic daily headache (CDH)[3]. Several studies reported that TM is the most common type of headaches, followed by chronic tension-type headache[4-7]. In 1994, Silberstein et al.[8] proposed some criteria for TM diagnosis (Table 1).

The purpose of this study was to compare clinical characteristics between the EM and the TM.

METHOD

Eighty patients, both sexes, the ages ranging from 18 to 60 years old were studied. They were examined at the headache outpatient service of Hospital de Base, Medical

Departamento de Ciências Neurológicas da Faculdade de Medicina de São José do Rio Preto (FAMERP), São José do Rio Preto SP, Brasil: [1]Professor Assistente Mestre; [2]Professor Adjunto Doutor; [3]Professor Adjunto Livre Docente.

Received 26 November 2001, received in final form 22 May 2002. Accepted 6 June 2002

Dr. José Carlos Busto Galego – Rua Professor Nelson Bento Lutaif 145 - 15091-550 São José do Rio Preto SP - Brasil. E-mail: jcgalego@uol.com.br

School of São José do Rio Preto, SP. In this clinical prospective study, the patients were consecutively admitted and divided into two groups. The first, 40 patients with EM diagnosis, according to the International Headache Society 's criteria[9]. The second, 40 patients with TM diagnosis according to Silberstein et al.'s criteria[8]. Patients with some chronic disease were not included in the study.

The statistical analyses were performed by means of Analysis of Variance, Student's t and Kruskal-Wallis' tests, and the crossed frequencies tables by means of Dependence Analysis[10].

RESULTS

There were 33 females (82.5%) and 7 males (17.5%) in the EM group; 38 females (95%) and 2 males (5%) in the TM group. At first examination, the mean age was similar in both groups ($p = 0.95$) (Table 2). The mean duration of years of the episodic attacks was also similar in both groups ($p = 0.34$) (Table 3), although the mean age at the beginning of the migraine attacks was significantly lower in the TM group ($p = 0.022$) (Table 4). In the TM group, the mean age at which the transformation occurred to CDH was 34.8 ± 11.6 years and the mean duration after transformation was 2.24 ± 1.72 years. In the EM group, 75% of the patients reported hemicrania headache (37.5% alternanting, 25% right-sided and 12.5% left-sided); 20% frontal, 10% difuse, 5% occiptal and 5% in the vertex. In the TM group, 80% reported hemicrania headache (45% alternanting, 20% right-sided and 15% left sided), 42.5 frontal, 30% occiptal, 30% diffuse and 7.5% in the vertex. In the EM group, headaches were predominantly one-sided location; whereas in TM, on more than one location ($p < 0.005$).

All patients from the EM group complained of only pulsating pain; whereas the patients from TM group, 57.5% pulsating pain, 40% pulsating and non-pulsating pain, and 2.5% non-pulsating pain. In the EM group, 72.5% of the patients described attacks of severe intensity, and 27.5% moderate. In the TM group, 62.5% described variation of intensity between moderate and severe; 37,5% between mild and severe. This showed that the variation of pain intensity was more frequent in MT group ($p < 0.0005$).

The majority of patients in EM group (65%) reported attacks occurring fortnightly to monthly, 15% weekly, 12.5% weekly to fortnightly, and 7.5% bimonthly , quarterly and yearly. In the TM group, 80% of the patients reported daily occurrence of headaches and 20% almost daily (always more than 15 days). In the EM group, 40% of the patients reported the headache lasting from 1 to 3 days, 27.5% 1 day, 22.5% 1 to 2 days, 5% 5 days (attacks evolved into status migrainosus) and 5% 4 to 8 hours. In this same group, 90% of the migraine attacks lasted up to 3 days ($p < 0.0005$).

All patients from the TM group reported headache with a mean duration over four hours per day, according to the adopted criteria. There was a significant association between migraines and the number of associated symptoms ($p < 0.0005$) (Fig 1).

In both migraine types, 2 or more symptoms occurred in the majority of the cases, although in the episodic, the frequency of less than two symptoms was rare. The existence or non-existence of triggering factors (Fig 2) is related to the migraine type ($p = 0.006$); more than 85% of the TM group presented a continuous headache intensified by trigger factor ($p = 0.049$). In the EM group, 55% of the patients reported the worsening of the headache with head movements (to bend down and to raise), 40% with physical activity; 37.5% with coughing; 32.5% with odours and 17.5% with sneezing. Head movements were reported as a worsening factor by 52.5% of the patients in the TM group, 40% reported physical activity; 12.5% odours; 10% coughing; and 5% sneezing. We found that no worsening factor is greatly related with TM ($p < 0.0005$), according to the number of worsening factors in the EM and TM groups.

In the EM group, 37.5% reported resting in a dark room as an improving factor; 30% resting; 22.5% the

Table 1. Proposed criteria for transformed migraine (Silberstein et al.[8]).

A.	History of episodic migraine meeting any IHS criteria 1.1 to 1.6
B.	Daily or almost daily (> 15 days/month) head pain for >1 month
C.	Average headache duration of 4 hours/day (if untreated)
D.	History of increasing headache frequency with decreasing severity of migrainous features over at least 3 months*
E.	At least one of the following:
	1. There is no suggestion of one of the disorders listed in groups 5 – 11
	2. Such a disorder is suggested, but it is ruled out by appropriate investigations
	3. Such disorder is present, but first migraine attacks do not occur in close temporal relation to the disorder

*Methods must be developed and validated for measuring this characteristic.

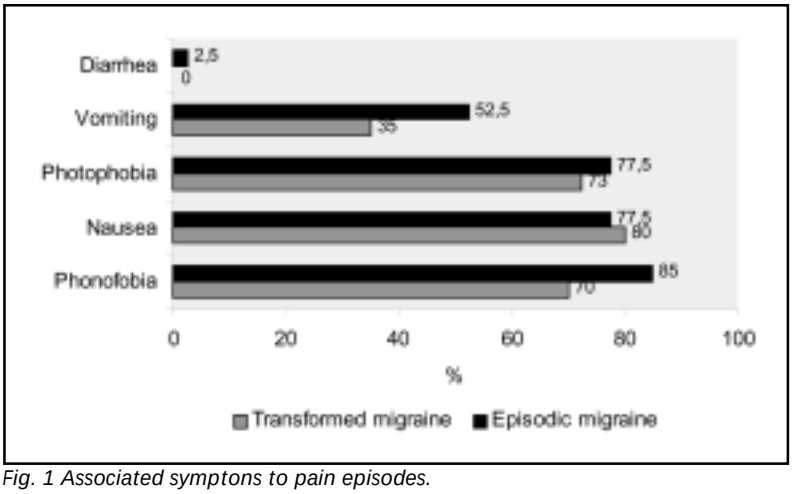

Fig. 1 Associated symptons to pain episodes.

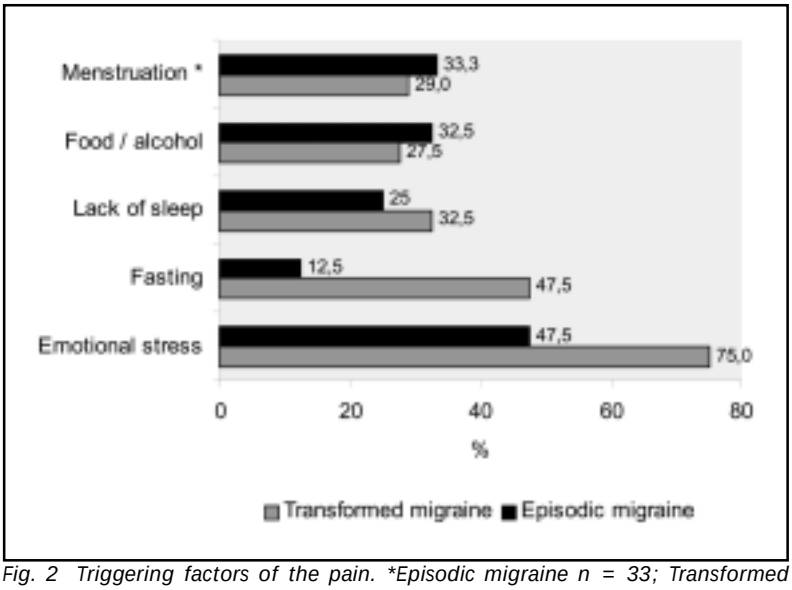

*Fig. 2 Triggering factors of the pain. *Episodic migraine n = 33; Transformed migraine n = 38.*

use of pain relievers, and 17.5% sleep. In the TM group, the use of pain relievers (dipyrone or associations with ergotamine) as an improving factor was reported by 62.5% of our patients; 40% resting in a dark room; 20% resting; 5% sleep and 5% leisure activities. Fifty five percent of patients from the EM group and 62.5% from the TM group reported waking up in the morning or being woken up very early in the morning with headache.

To wake up with headache was not seen as a significant association between both groups (p=0.12). Aura was reported by 20% of the patients from EM group; 33% in the TM group. There was no significant association between the presence of aura and the type of migraine (p=0.133). History of headache similar to migraine as occurring in first degree relatives was reported by 48% of the patients from EM group, and 55% from the TM group. There was no significant association between the migraine type and family history (p=0.37).

DISCUSSION

EM and TM most commonly occur in women[2,5-7,11-14]. Our results support these findings; they also showed that in the TM group, the women percentage (95%) was higher than the one in EM group (82.5%).

We did not find significant difference in relation to the mean age at first examination in both groups: EM (37.25±10.32 years old) and TM (37.1±11.71 years old). This may suggest that the age is not a factor related with chronic migraine type. In our patients, the mean duration of EM before the transformation was 16.25±12.26 years. Baldrati et al.[15] reported a mean duration of 19.3 years in EM; Mathew et al.[2] found 16±11 years; Jevoux et al.[7] 9.6±6.3 years and Sandrini et al.[16] 17.3±1.9 years.

Table 2. Age in both groups at first examination.

Statistic	Episodic migraine	Transformed migraine
Mean (SD)	37.25 (10.32)	37.1 (11.71)
Median	35.5	34
Range	18 – 55	19 – 59

SD, standard deviation; values in years.

Table 3. Time history of episodic attacks.

Statistic	Episodic migraine	Transformed migraine
Mean (SD)	13.88 (9.68)	16.25 (12.26)
Median	10.5	12
Range	1 – 35	2 – 46

SD, standard deviation; values in years.

Table 4. Age at beginning of the migraine attacks.

Statistic	Episodic migraine	Transformed migraine
Mean (SD)	23.37 (10.0)	18.75 (10.16)
Median	23.5	16
Range	7 – 45	7 – 48

SD, standard deviation; values in years.

In our study, we did not find significant difference when we compared the mean duration in years of the episodic attacks between the EM group and TM group.

There are few studies comparing the patients' age at the beginning of EM, before the development to the chronic type with the initial age of migraine attacks in patients with episodic type. Baldrati et al.[15] compared 50 patients with "chronic migraine" and 90 patients with EM. They found the mean age of 19.5 years old at the beginning of EM in the patients with chronic migraine; however, it was not reported the initial mean age of the episodic attacks in the EM group.

The study of 489 patients with TM by Mathew et al.[2] showed the mean age of 22±9.2 years old at the beginning of migraine attacks. In 39 patients, Jevoux et al.[7] found the mean age at the beginning, 21.3±8.7 years old. Sandrini et al.[16] evaluated 90 patients with CDH, out of them, 68 had an initial history of EM. In these patients, the mean age at the beginning of the episodic attacks was 19.4±10.8 years old. In the TM group, we found initial mean age of the episodic attacks 18.75±10.6 years old. Comparing the mean age at beginning of episodic attacks in the EM group (23.37±10.0 years old) with the TM group (18.75±10.16 years old), we found an initial age significantly smaller in the TM group. Considering the time of evolution of the episodic type of migraine was similar in both groups as well as the mean age of the patients at the time of study, this may suggest that an early beginning of migraine attacks is a further risk factor to the development of TM. In the study of Solomon et al.[4], patients had reported the beginning of headache in childhood and adolescence, however there is no report regarding initial headache type.

Mathew et al.[2] reported a mean age of transformation to CDH of 39±11.2 years; Jevoux et al.[7] 31.1±9.5 years. We found this mean age to CDH of 34.8±11.6 years. Mathew et al.[2] reported a mean duration after transformation to CDH of 6±5 years; Jevoux et al.[7] 3.96±3.95 years. At first examination, we found in the TM group a mean duration after transformation to CDH of 2.24±1.72 years.

The location mainly unilateral was found by Mathew et al.[2] in 58% of patients in the TM group, and in 54% frontal or frontal temporal. Jevoux et al.[7] reported the unilateral location in 82% of the patients, and in 61.5% frontal, temporal and frontal-temporal. The association between more than one location was reported by 48.75 of the patients. Krymchantowski et al.[13] found bilateral frontal-temporal location in 22.8% of the patients; hemicrania non-alternating in 20.9%, bitemporal in 15.3%; diffuse pain in 12.1%; unilateral alternating frontal-temporal headache in 8.8%; bifrontal headache in 8.4%; unilateral per orbital pain in 7.4%, and other location in 26.5%. In our study, comparing the location of the beginning of EM and TM we found mainly one location in the episodic type (unilateral or frontal or occipital); in the transformed, more than one location of the beginning of the headache (unilateral, bilateral, frontal, occipital and vertex). Jevoux et al.[7] found association of pulsating and non-pulsating pain in 66.7%; pulsating in 33.3%. Krymchantowski et al.[13] reported throbbing pain in 37.2% of the patients; pressing pain in 36.2%; 17.2% association of pressing and throbbing pain, and 7.4% other types. Our results showed this variation of pain character in TM group.

Jevoux et al.[7] classified the headache of TM as severe in 10.3%; moderate in 28.2%, and between severe and mild, mainly mild, in 61.5%. Krymchantowski et al.[13] reported all patients with moderate daily headache, and in 40.5% intermittent attacks of pulsating pain aggravated by routine physical activities, nausea and/or vomiting, photo and phonophobia. Our study showed a great association bet-

ween the migraine types and the pain intensity. The combined types of the intensity (severe, moderate and mild) were more frequent in TM; moderate or severe in EM ($p<0.0005$). Krymchantowski et al.[13] reported their patients with daily moderate pain. Our patients with TM presented a frequency longer than 15 days per month, and in 80%, the headache was daily. In the episodic type, 65% of the attacks were fortnightly and monthly.

Mathew et al.[2] found 76% of patients with gastrointestinal disorders such as nausea, vomiting and diarrhea; however, they did not point out the percentage of these symptoms; whereas, visual disturbances and "neurological symptoms" in 36% of the patients. Jevoux et al.[7] reported phonophobia in 82% of the patients; 77% photophobia; 51.2% nausea and 10.2% vomiting.

We found a significant association between migraine and the number of associated symptoms. The frequency of less than 2 associated symptoms is rare in the episodic migraine.

Mathew et al.[2] found triggering factors of headache in 88% of the patients; however, they were not distinguished. Jevoux et al.[7] identified triggering factors in 76.9% of the patients with TM. The most common were emotional disturbances in 64.1%; lack of sleep in 41%; fasting in 30.7%, and sensitivity to light and smell 48.7% and 51.2%, respectively. Krymchantowski et al.[13] reported 76.2% of the patients with triggering factors such as menstrual period, long fasting, and stress; however, the percentage of frequency of these factors was not distinguished. Our results showed that the presence or absence of triggering factors is related with the type of migraine; more than 85% of the patients from the TM had any triggering factor.

Jevoux et al.[7] found worsening factors in 92.3% of the patients; mainly by physical activities reported by 76.9%, up and down head moving in 25.6%, lying down in 7.7%, sensibility to light, sound and odours in 7.7%. According to our results, no worsening factor was more common in the TM group. This may suggest that those patients are more bearable to the worsening factors reported by the patients of EM type.

In the series of patients studied by Mathew et al.[2], Jevoux et al.[7] and Krymchantwski et al.[13], there is not any improving factor reported in the TM. Our results showed that in the TM, the use of pain-relieving medications provided to be the main improvement factor (62.5%). This may suggest a high addict of this medication by this group of patients.

Mathew et al.[2] reported 73.6% of patients with TM, with headache in the first hours of the day. Jevoux et al.[7] series of patients, 69% waking up early in the morning with headache. Krymchantowski et al.[13] reported 64.6% with some sleep symptoms such as: insomnia, interrupted sleep , nocturnal or awakening headache, and asthenia. We did not find any significant association of nocturnal or awakening headache between TM and EM groups**.**

Mathew et al. reported 90.8% of the patients with migraine without aura, and 9.2% with aura before the TM development. Krymchantowski et al.[13] described the initial diagnosis in 167 patients (77.7%) of migraine without aura , and in 48 (22.3%) migraine with and without aura, before the development to daily headache. Our results showed that there is no significant association between aura and migraine type.

Positive family history of headache was in 73.5% of TM cases studied by Mathew et al.[2] . Jevoux et al.[7] reported in 64.1% of the patients. We did not find significant association of family history in both types of migraine.

CONCLUSION

The TM showed some distinguished clinical characteristics of the episodic migraine type according to the frequency, location and pain intensity of the headache. Earlier beginning of migraine attacks may be a further risk factor for TM development.

Acknowledgements – We are grateful to Adília M. Pires Sciarra for the help in the English version.

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