

# Are Menstrual and Nonmenstrual Migraine Attacks Different?

Kjersti Grøtta Vetvik · Michael Bjørn Russell

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**Abstract** Migraine is the second most common headache condition next to tension-type headache. Up to one fourth of all women have migraine, and 20% of them experience migraine without aura attack in at least two thirds of their menstrual cycles. The current literature is analyzed in response to the question of whether menstrual and nonmenstrual migraine attacks are different. The different studies provide conflicting results, so it is not possible to answer the question firmly. Future studies should be based on the general population. Collection of both prospective and retrospective data is warranted, and headache diagnosis base on interviews by physicians with interest in headache are more precise than lay interviews or questionnaires.

**Keywords** Menstrual migraine · Symptomatology · Disability and treatment · Perimenstrual headache · Nonmenstrual migraine · Attacks · Rizatriptan · Almotriptan

## Introduction

The appendix of the second edition of the International Classification of Headache Disorders (ICHD-2) from 2004 describes two types of migraine without aura (MO) related to menstruation: pure menstrual migraine (PMM) and

menstrually related migraine (MRM) [1]. Those with PMM have MO attacks exclusively in relation to at least two thirds of their menstrual periods, while those with MRM additionally experience MO attacks outside the menstrual period. Before the ICHD-2 classification, researchers had no specific guidelines for the definition of menstrual migraine. The first classification of the International Headache Society from 1988 did not classify menstrual migraine as a specific type of headache, but had a comment in relation to MO: “Migraine without aura may occur almost exclusively at a particular time of the menstrual cycle—so-called menstrual migraine. Generally accepted criteria for this entity are not available. It seems reasonable to demand that 90% of attacks should occur between 2 days before menses and the last day of menses, but further epidemiological knowledge is needed” [2]. The latter definition encompasses only a few of those with MRM. A recent epidemiological survey suggests that 21% of women with migraine have menstrual migraine, and about two thirds have MRM [3]. These circumstances make the literature on menstrual migraine heterogenous, which one should bear in mind in the current analysis of symptomatology of menstrual and nonmenstrual migraine attacks. To complicate matters, what about migraine with aura (MA)? About one third of all migraineurs have MA [4]. An epidemiological survey implies that headache in attacks of MO may be slightly more severe than headache in attacks of MA [5], but it seems that MA is not associated with menstruation on the same scale as MO. In fact, MA may be unrelated to menstruation [6].

The most precise information on migraine attacks is ascertained from prospective recording (ie, headache diaries with detailed information about pain characteristics, accompanying symptoms, duration, and treatment). Such data may not be generalizable because keeping a headache diary for a longer period is not applicable for a large population

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K. G. Vetvik · M. B. Russell (✉)  
Head and Neck Research Group, Research Centre,  
Akershus University Hospital,  
1478 Lørenskog, Oslo, Norway  
e-mail: m.b.russell@medisin.uio.no

K. G. Vetvik · M. B. Russell  
Institute of Clinical medicine, Campus Akershus University  
Hospital, University of Oslo,  
1478 Lørenskog, Oslo, Norway

due to low compliance. In contrast, retrospective data from large population-based studies may be generalizable, but the detailed information about migraine attacks is subject to memory bias. Thus, a combination of prospective and retrospective data is likely to give the most precise description of the migraine attacks.

This review analyzes the literature to enlighten whether menstrual and nonmenstrual migraine attacks are different, given the methodological challenges mentioned above.

## Menstrual Versus Nonmenstrual Migraine Attacks

### Attack Frequency

A Danish epidemiological survey based on 18– to 65-year-old people from the general population, including a direct clinical interview and a physical and neurological examination by a physician, found that less than 10% of women with MO had more than one MO attack per month [5].

Thus, the vast majority (ie,  $\geq 90\%$ ) of all women with migraine have 1 or fewer MO attacks per month. Some of those with PMM will have 1 MO attack per month, while most patients with MRM have more than 1 MO attack per month. Thus, the MO attack frequency is much higher in most women with PMM or MRM than in those with nonmenstrual MO. Although this does not address whether menstrual and nonmenstrual MO attacks are different, it indicates that those with menstrual MO are likely to have a higher disease burden than most women with nonmenstrual MO.

### Attack Severity

#### *Pain Characteristics*

Table 1 shows attack characteristics of menstrual migraine in relation to nonmenstrual migraine. Two studies from the general population suggest that the pain intensity is higher in menstrual than nonmenstrual MO [7, 8]. Studies on clinic populations provide conflicting results; four studies are in support of the findings in the general population, while four studies suggest similar pain intensity and one study missed information on pain intensity [9–15, 16•, 17•].

#### *Associated Symptoms*

The study based on prospective filled-in diaries from the general population suggests no significant difference in associated symptoms in attacks of menstrual and nonmenstrual migraine [7]. This is supported by three studies based on clinic populations [10, 15, 16•]. However, two

clinic studies based on prospective filled-in diaries suggest that menstrual migraine attacks are accompanied by more nausea and vomiting than nonmenstrual attacks [11, 14].

#### *Duration*

The study based on prospective filled-in diaries from the general population suggests that attacks of menstrual and nonmenstrual migraine have similar duration [7]. In contrast, all the other studies suggest that attacks of menstrual migraine are longer than attacks of nonmenstrual migraine, including data based on prospective filled-in diaries [8, 10, 16•, 17•].

#### *Disability*

The study based on prospective filled-in diaries from the general population and one clinic study suggest that attacks of menstrual and nonmenstrual migraine have similar disability [7, 15]. In contrast, all the other studies suggest that attacks of menstrual migraine are more disabling than attacks of nonmenstrual migraine, including data based on prospective filled-in diaries [8, 10, 12, 13, 16•, 17•].

#### *Treatment*

Two clinical trials on rizatriptan and almotriptan suggest equal efficacy on pain relief 2 h post-treatment of menstrual and nonmenstrual migraine attacks [9, 15]. Other studies suggest that attacks of menstrual migraine are more treatment resistant than attacks of nonmenstrual migraine [8, 10, 16•] or that menstrual migraine attacks are more likely to relapse [17•].

## Conclusions

The question whether menstrual and nonmenstrual migraine attacks are different unfortunately cannot be answered unambiguously because previous studies provide conflicting results. This is mainly due to different patient populations, unequal definitions of menstrual migraine, and different methods employed.

Future studies should focus on the general population to provide generalizable data, in contrast to possibly skewed data from selected clinic populations. Prospective recordings should be employed, combined with retrospective data on the headache history. To provide precise headache diagnoses, interviews by a trained physician or neurologist with special interest in headache is the gold standard. Such a study is likely to more firmly answer whether menstrual and nonmenstrual migraine attacks are different.

**Table 1** Attack characteristics of menstrual migraine in relation to nonmenstrual migraine

Study	Population	Country, Year	Design	Pain intensity	Associated symptoms	Duration	Disability	Treatment
Stewart et al. [7]	General	USA, 2000	81 women filled in diary for 98 days	Slightly higher pain intensity during the first 2 days of menstruation	No difference	Similar duration	Equally disabling	NR
Couturier et al. [8]	General	The Netherlands, 2002	1,181 women (13–55 y) replied on a questionnaire	More painful	NR	Longer duration	More disabling	More treatment resistant
Silberstein et al. [9]	Clinic	USA, 2002	95 women	Similar pain intensity	NR	NR	NR	Rizatriptan gave equal pain relief (78%) after 2 h
Granello et al. [10]	Clinic	Italy, 2004	64 women filled in diary for 2 months	Similar pain intensity	No difference	Significantly longer duration, more frequent status migrainosus	Significant higher work-related disability	More treatment resistant (lower 2-hour pain-free response, lower sustained pain-free response, higher recurrence)
MacGregor et al. [11]	Clinic	UK, 2004	155 women (15–58 y) filled in diary	More painful	More nausea and vomiting	NR	NR	NR
Martin et al. [12]	Clinic	USA, 2005	21 women filled in diary for 3 menstrual cycles	Significant higher headache index during menstruation	NR	NR	Higher disability index	NR
Dowson et al. [13]	Clinic	UK, 2005	30 women from general practices filled in a questionnaire	NR	NR	NR	Significant more time with <50% productivity	NR
MacGregor et al. [14]	Clinic	UK, 2006	38 women (29–50 y) filled in a diary	More painful	More nausea and vomiting	NR	NR	NR
Diamond et al. [15]	Clinic	USA, 2008	190 women in a multicenter, double-blind, parallel-group trial (post hoc analysis)	Similar pretreatment pain intensity	No difference	NR	Similar pretreatment disability	Almogran gave similar pain relief after 2 h, pain-free response after 2 h, and sustained pain-free
Pinkerman et al. [16•]	Clinic	USA, 2010	107 women not receiving migraine prophylaxis filled in a diary	More painful	No difference	Longer duration higher recurrence within 24 h. Attacks >72 h were twice as frequent	More disabling	Less pain-free response at 2 h; higher recurrence within 24 h; used more doses of triptans per migraine attack and rescue medication required more often
MacGregor et al. [17•]	Clinic	USA, 2010	153 women (>18 y) in a 2-month multicenter, open-label study (post hoc analysis)	Similar pain intensity	NR	Longer duration	Higher functional impairment	More likely to relapse

NR not reported

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