Chronobiological features in episodic and chronic migraine

Aspectos cronobiológicos na enxaqueca episódica e crônica

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ABSTRACT

Altered melatonin secretion and circadian, seasonal variations have been shown in migraine patients, but little is known about migraine chronobiological features. Two hundred migraine patients were studied. Headaches were reported to occur after changes in patients sleep schedule (46%), shift work (86%) and traveling across time zones (79%). Patients significantly delayed their sleep phase, 54% shifted their sleep phase. Chronobiology is a relevant aspect in migraine patients.

Key words: Melatonin; migraine; chronobiology.

RESUMO

Secreção alterada de melatonina e as variações sazonais têm sido demonstrado em pacientes com enxaqueca, mas pouco é sabido sobre as características cronobiológicas na enxaqueca. Duzentos pacientes com enxaqueca foram estudados. Dores de cabeça foram relatadas ocorrer após as alterações do horário do sono em pacientes (46%), trabalho por turnos trocados (86%) e viajar através dos fusos horários (79%). Pacientes atrasaram significativamente a fase do sono, 54% alteraram a fase de sono. Cronobiologia é um aspecto relevante em pacientes com enxaqueca.

Palavras-chave: Melatonina; enxaqueca; cronobiologia.

INTRODUCTION

The nervous system evolved to meet the demands of environmental conditions, including the light-dark cycle, in order to assure survival and reproduction of living organisms. A synchronization system to adapt the internal to the external environment is one of the key elements of the central nervous system to maintain life. It has been demonstrated in the past decades that the circadian biological rhythm is not only the response to the 24-hour day night environment but in fact is due to a system in the brain.[1]

Chronobiological disorders occurring in human being can be divided in two types. 1) the environmental or external variety, due to the life style and environment, as in shift workers, individuals crossing time zones in the jet lag syndrome, and in maladaptation to daylight savings. 2) the endogenous or internal type, including the delayed and advanced sleep phase syndromes, and the non-24-hour sleep -wake disorder with free-running circadian rhythm.[2] It has been proposed the endogenous type may underlie many conditions including depression, chronic fatigue, fibromyalgia, and migraine.[3]

Chronobiology is connected to headache disorders in many ways, from experimental models[4] to clinical settings and treatment.[5] Increasing evidence links melatonin secretion and pineal function with cluster headache, hypnic headache, hemicranias continua, migraine and its

comorbid conditions.[5-14] Pineal cysts have been found to be linked with headache disorders.[11]

Melatonin secretion has been studied in menstrual migraine,[15] chronic migraine,[1] acute migraine,[8] migraine status,[16] and migraine comorbid disorders.[7] All studies found altered levels of melatonin in plasma or urine.

Clinical symptoms may fluctuate over time, in menstrual migraine a cycle is evident, but headaches may vary according to circadian and circannual variation. Many migraine patients work in shift hours and travel across time zones but it is unknown whether these could be aggravating factors. Chronobiological features have not been studied in detail.

We aimed in this study to evaluate clinical features of chronic and episodic migraine patients regarding chronobiological aspects.

PATIENTS AND METHODS

We included 200 consecutive migraine patients, men or women, episodic or chronic migraine according to the International Classification of Headache Disorders, 2nd edition. Informed consents were obtained, the local ethics committee approved the study. Patients filled out a questionnaire about their headache and sleep features, including chronobiological issues. Patients were asked if headaches were aggravated when they changed their sleep schedule, went to shift work or after traveling across time zones. Time patients went to bed, time they slept, and their preferred time to sleep were ascertained. A shift of patients sleep cycle was then calculated subtracting the time they really went to bed to the time they preferred go to bed. Number of patients who delayed or advanced their sleep phase (stayed up too late or went to bed too soon) was calculated, based on more than 2 hours of shift.

Chi square and Student t-test were applied for sleep features comparisons between chronic versus episodic migraine, with a $p<0.05$ considered statistically significant. No missing data was observed in our sample.

RESULTS

Two hundred patients were studied, 162 (81%) women and 38 (19%) men, 72 episodic migraine (36%), and 128 chronic migraine (64%) patients. Ninety-three patients (46.5%) reported headaches after changing their sleep schedule. Chronic migraineurs had more headaches after changing sleep schedule than episodic migraine patients, $p < 0.05$. Twenty-eight patients (14%) reported shift work. 86% of them reported having worse headaches after shift work. Eighty six patients (43%) reported frequent traveling across time zones, and 79% had worsening of headaches when traveling. Patients significantly delayed their sleep phase (22:46 h±01:20 h) vs. (22:22 h±01:17 h) $p<0.001$, 108 patients (54%) shifted their sleep phase ranging from -2:30 h to+05:00 h. Most of them – 75 (69%) delayed the sleep phase (stayed up too late), as opposed to 33 (31%) that advanced it (went to bed too soon). Patients shifting more than 02:00 h in both directions represented 12.5% of migraineurs.

DISCUSSION

Chronobiological parameters have been studied in several neurological disorders and have been implicated in migraine mechanisms and treatment. Our data suggest the presence of chronobiological dysfunction in migraine patients. Our sample is from a tertiary headache center, therefore a more severe patient population. In the general population, with less severe migraine individuals, chronobiological issues could be less relevant, but, on the other hand, migraine patients sensitive to time changes may not look for treatment. A study on chronobiological features in the general population would solve this question.

Migraine patients should be systematically asked about their sleep patterns including other chronobiological aspects, and should be managed accordingly. Severe cases should avoid when possible travels across many time zones, or take short term preventives, such as long acting triptans or NSAIDs before the trip. Migraine patients should avoid shift work when possible, or short term prevention should also be considered.

More than 10% of patients shifted their cycle more than 2 hours, most of them delayed their sleep phase. Delayed sleep phase syndrome (DSPS) could be the cause or consequence of migraine. The suprachiasmatic nuclei and an altered melatonin secretion are probably behind this clinical feature, but other neuropeptides may also be involved including orexin, adiponectin, and others.[1] Melatonin supplementation is the first line choice for this patients (migraine + DSPS).[17] Patients who shifted less than 2 hours may also benefit from melatonin supplementation. Melatonin analogues such as ramelteon and agomelatin should be tested.

Since migraine with comorbid conditions, including depression, anxiety, fatigue and fibromyalgia, have decreased melatonin levels[7, 18] (i.e. a well known internal synchronizer of the central and peripheral biological clocks)19, chronobiological features may particularly be implicated in those patients, a special attention to those aspects is important in migraine patients.

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