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Preventing chronicity of migraine

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Abstract Chronic migraine and transformed migraine are conditions with a progression from episodic to chronic headache, a disabling stage. During attack, cutaneous allodynia frequently occurs: it reflects sensitisation of the central neurons of the trigeminovascular system. Early triptan therapy (prior to the development of central sensitisation) may protect from the chronicisation of migraine. In addition, early recognition of non-headache changes in neurologic function between episodes of headache offers a sensitive indicator of headache transfor-

mation. Attack frequency is the stronger predictor for migraine progression: prophylactic agents could be administered to patients with a high number of attacks. Medication overuse is the most important iatrogenic risk factor for the acceleration of disease and it must be prevented; other important risk factors are female sex, obesity and stressful life events.

Key words Chronic migraine • Central sensitisation • Disease progression • Risk factor • Medication overuse

Introduction

A subgroup of migraine patients have a clinical disorder that results in headaches that occur on more than 15 days per month, thus indicating the evolution of episodic migraine into a chronic form [1]. The International Headache Society Classification includes the operational diagnostic criteria for the diagnosis of chronic migraine. This is considered a complication of migraine without aura with 15 or more migraine days per month. Headache syndromes that occur 15 or more days per month also include transformed migraine. The term “transformed” implies a process of change over time with a history of transformation from episodic to chronic migraine. Transformed migraine seems to be a clinical form that has a clinical usefulness in recognition of the migraine subgroup who have had a chronic evolution from episodic migraine.

Intervention strategies on disease progression are paramount goals for the prevention of chronicity of migraine [2]. Prevention must be carried out against the main modifiable risk factors that are currently known.

Progression during attacks

Allodynia, pain resulting from application of a non-noxious stimulus to normal skin, is a recently described symptom of migraine [3]. In fact clinically detectable allodynia, a manifestation of central sensitisation, occurs with high frequency during migraine attacks. Migraine pain progresses along the neural pathway with throbbing head pain occurring early in the attack (sensitisation of first-order neurons), followed by central sensitisation and cutaneous allodynia within the

referred pain area (second order) and finally extracephalic allodynia (third order). When central sensitisation occurs, central trigeminal vascular neurons that receive conveying sensory input from the meninges as well as from scalp and facial skin can propagate information about pain process without the need for further external stimuli. Manifestation of cutaneous allodynia include discomfort when combing hair, shaving and wearing glasses, contact lenses, earrings or tight clothing. Sometimes muscle and extracephalic allodynia may lead respectively to muscle tenderness and hypersensitivity of fingertips and/or forearms and toes. Repeated episodes of migraine with central sensitisation may contribute to disease progression: correlation in fact was found between the duration of illness as well as frequency of migraine and allodynia. It seems reasonable to infer from current knowledge that, in the subset of patients who report symptoms of cutaneous allodynia during migraine attacks, treatment designed to prevent the initiation of central sensitisation can be the best intervention to prevent the development of chronicity of migraine. Early diagnosis of migraine could permit the application of a treatment affecting the initiation of central sensitisation during the attack. Thus a first migraine attack in a high-risk patient may be viewed as a signal to begin protective therapy, with the aim of altering the course of the disease.

Triptans can abort pain prior to the development of central sensitisation, but not after allodynia has been established [4]. Unfortunately, when central sensitisation and allodynia are established, pharmacological agents only attenuate migraine symptoms but do not stop the underlying pathophysiological process. Early initiation of triptan therapy is currently the best intervention to achieve rapid, complete and sustained pain relief and to prevent central sensitisation during migraine attack. Therefore protective benefits against migraine progression can derive from scrupulous management of individual attacks with triptans.

The evolution from episodic to chronic headache may reflect the neurologic disruption observed during the progression of an acute migraine attack and those changes in neurologic function between episodes of headache may be a sensitive indicator of headache transformation [5]. Early recognition of nonheadache changes in nervous system function may offer a sensitive and specific approach to prevention of chronicity. From this perspective the evaluation shifts from attack to a more global assessment of neurological function of the patient with migraine.

Attack frequency

The strongest predictor for migraine progression is attack frequency. Frequently recurring migraine episodes may predispose a person to disease chronicity through a permanent status of central sensitisation. Neuroimaging studies showed

that brain white matter lesions increased with episode frequency, possibly demonstrating progression of the disease [6]. In addition, repetitive attacks may lead to chronic headache through a progressive impairment of the central antinociceptive system in the periaqueductal grey matter that controls activity of the trigeminovascular system [7]. In this context, prophylactic medication that acts to reduce the number of migraine attacks, more likely than abortive agents, might have a long-term effect on the natural evolutive history of migraine. Prophylactic agents could be administered over a long enough period to truly affect disease progression. Long duration prophylaxis (greater than 6 months) could be recommended for patients with high attack frequency and other risk factors for migraine progression. Drugs providing a large decrease in attack frequency will have a corresponding positive effect on disease progression.

Medication overuse

Medication overuse is commonly identified as the most important iatrogenic risk factor for the acceleration of disease which leads to chronicity of migraine. Migraine patients are particularly predisposed to develop chronic headache in association with medication overuse [8]. The regular use of symptomatic medications is associated with the development of chronic headache in individuals who have an existing history of migraine; medication overuse *per se* did not cause the development of headache *de novo* in patients without previous headache history. Analgesics and other antimigraine drugs may be a cofactor in the development of chronicity in a genetically vulnerable individual. The best strategy against medication overuse includes several aspects but awareness and prevention are the most important. This may be accomplished by setting limits to abortive medication overuse, in particular anticipatory medication use should be discouraged, improving utilisation of prophylactic medication, behavioural modification and nonpharmacological approaches to headache control earlier in the natural history of migraine, without resorting to medication overuse.

Other risk factors for progression

Other risk factors for migraine progression are not readily modifiable factors such as female sex, low education/socioeconomic status, head injury and modifiable factors such as obesity, stressful life events, snoring and sleep disturbances [9].

Nonpharmacological intervention addressing the stressful life events may also have an important protective action on the development of chronicity of migraine. Cognitive-

behavioural strategies aimed at reducing illness behaviour such as biofeedback have demonstrated efficacy in reducing the frequency and/or severity of migraine attacks.

Conclusions

The increasing recognition of migraine as a disorder that is sometimes progressive creates opportunities for

intervention to prevent migraine progression. Emerging treatment strategies to prevent disease progression include risk factor modification, and possibly the use of triptans as early as possible in the course of a migraine episode and at the onset of the disease. A more aggressive multidisciplinary approach to the treatment of migraine is certainly warranted for many patients at high risk of chronicity. The benefits of prospective strategies to prevent migraine progression await testing in well-designed studies.

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