

## Improving the Care of the Migrainous Women: A Focus on Cardiovascular Prevention

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Migraine is one of the most prevalent forms of headache in the general population, and is particularly common among subjects seeking medical advice for their head pain. The prevalence of migraine is three times higher in women than in men and peaks in the age group, 30-39 years [1]. Migraine is characterized by recurrent attacks of head pain, often unilateral, pulsating, of an intensity mild to severe, worsened by physical activity and lasting from 4 up to 72 hours [2]. The attacks are often accompanied by neurovegetative symptoms such as nausea, vomiting, photophobia and phonophobia [2]. In one third of migrainous patients, the attacks are preceded by an aura, characterized by reversible focal neurological symptoms that usually develop gradually over 5-20 minutes, and lasts for less than 60 minutes [2].

Attacks of migraine vary widely in intensity, duration and frequency across patients, and also in the same patient over time. In some cases, migraine may present as a very disabling condition, able to impair working and social activities, but aside from that the disease has been long considered as benign. Starting from the end of last century, an association between migraine and ischemic stroke was reported [3-5]. The relationship between the two conditions is complex and bidirectional [6]. Migraine may be causally related to ischemic stroke occurrence (migrainous infarction, an infarction that occurs during the aura phase), or may represent a risk factor for the condition (an infarction that occurs remotely from the aura in a subject with a history of migraine) [7,8]. In addition, migraine-like symptoms may be caused by cerebral ischemia, migraine may mimic cerebral ischemia and viceversa, migraine and cerebral ischemia may share a common cause, and migraine may be also associated with subclinical vascular brain lesions [7-11].

After the pioneer papers showing an increased stroke risk in migraineurs [3-5], numerous data have confirmed the association and have added support toward an increased overall risk of cardiovascular diseases in migraineurs [12]. Available data indicate an increased risk of ischemic stroke in subjects with migraine with aura, while in subjects with migraine without aura, the increase in the risk is non significant [12]. Besides, evidences point toward a possible association between migraine with aura and cardiac disease, intracerebral hemorrhage, retinal vasculopathy, peripheral artery disease, and mortality [12]. As most of the studies included only women, there exists a huge body of evidence linking ischemic stroke with migraine in the female gender, while data on migraine in men are scarce, lack in details referring to migraine type, hindering any definite conclusion about the possible association between migraine and ischemic stroke in the male gender. Up to date, migraine with aura has been categorized among the less well-documented or potentially modifiable risk factors for ischemic stroke, and its population-attributable risk is estimated at 3.5% [13]. The risk of IS in migraineurs is magnified in the presence of some acknowledged vascular risk factors [12]. In fact, in the presence of cigarette smoking, the risk of IS in migraineurs women is increased three- to nine-fold and four- to eight-fold in the presence of oral contraceptive use [12]. The combination in the same subject of smoking and oral contraceptive use

is associated with a ten-fold increase in the risk, with respect to the presence of migraine only [12].

Patients with migraine usually look for the advice of the general physician, the neurologist, and the headache specialist to relieve their pain, or because they are worried about the aura symptoms. Medical consultation for the migrainous patient is usually focused on posing the correct diagnosis by excluding other primary headaches and secondary forms of headache, and on prescribing the most appropriate treatment for the acute phase or for prevention of the attacks, when indicated. Patients are not usually screened for the presence of vascular risk factors, and even in the presence of vascular risk factors, they do not currently receive hints for their management, since this aspect is considered out of the aims of the consultation. I suggest that the opportunity of the visit at the headache center should be for the future, also the occasion to address the cardiovascular risk of the patient. Physicians should screen patients for cigarette smoking, arterial hypertension and use of oral contraceptives. Though subjects suffering from migraine with aura should not be improperly alarmed, anyhow, they should be made aware of their increased risk of ischemic stroke, and of a possible increase of their basic vascular risk in the presence of the mentioned factors. Besides, since migraine without aura is not a definite risk factor for stroke, no specific restrictions are warranted in women suffering from this condition, especially in the absence of vascular risk factors or comorbidities. Cigarette smoking and arterial hypertension represent well documented risk factors for stroke and vascular disease in the general population, and consequently, basic recommendations about their management are almost similar for migraineurs and non migraineurs, while prescription of combined oral contraceptives deserves special caution, even in the absence of evidence-based studies on the prescription of oral contraceptives in migraineurs. Oral contraceptives use should be discouraged in women suffering from migraine with aura, since they may contribute to an unacceptable increased vascular risk. Their prescription is definitely contraindicated in women with migraine with aura and other comorbid vascular risk factors, or congenital or acquired thrombophilia, as well as in those with a family history of cardiovascular diseases in young age. Moreover, an awareness-raising recommendation on this specific issue is needed for gynecologists and general physicians that most likely prescribe oral contraceptives. They should be informed about the increased vascular risk of migraineurs and about the implications of oral contraceptive use. A further difficulty may be represented by the

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lack of capability to reliably identifying migraine by non neurologists or non headache specialists. Efforts should be made to increase the likelihood to correctly diagnose migraine, when present as to solicit for consultations at a specialized headache center where deemed necessary.

An awareness raising campaign toward an increased knowledge of the cardiovascular risk of migraineurs will not have a major impact at the social level, since the overall stroke burden in migraineurs is low. However, the campaign may have important implications at the individual level since migraineurs women, in most of the cases, are in their active age, being workers, mothers and wives. For those same reasons, prevention is mandatory, as the consequences of stroke in this group may be particularly devastating.

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