MIGRAINE AND ISCHAEMIC STROKE

Dr Elliot Shevel
Medical Director, The Headache Clinic, Johannesburg, Durban, Cape Town

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Abstract

In recent years, evidence has been mounting that a relationship exists between migraine and cerebral ischaemia. In this article, four possible mechanisms are discussed by which the two entities may be related. First, is migraine possibly a predisposing factor in ischaemic stroke? Second, can migraine actually cause ischaemic stroke? Third, can ischaemic stroke cause migraine? Fourth, is there a connection between patent foramen ovale (PFO), migraine, and stroke?

Introduction

Many headache sufferers self-medicate and do not seek medical attention; notwithstanding, headache remains the most common complaint seen by neurologists. Migraine, although less prevalent than tension-type headache, is the most common type of primary headache seen in the tertiary care setting, possibly because the intensity of the pain is more severe, and because the associated symptoms such as aura, nausea and vomiting, photophobia and phonophobia are more common among migraineurs.[1,2]

THERE MAY BE A CAUSAL RELATIONSHIP BETWEEN MIGRAINE AND ISCHAEMIC STROKE

The quality of life of migraineurs is worse than that associated with other major conditions, such as arthritis and diabetes; it is comparable to the level of dysfunction seen with recent myocardial infarction or congestive heart failure.[3] Even with this severe impairment in the quality of life, migraine is not generally regarded as a cause of long-term brain damage. New data have emerged however indicating: 1) that there is a disproportionately high incidence of migraine in young individuals with stroke, 2) that there is dysfunction of the cerebral arteries during migraine attacks, and 3) that asymptomatic infarct-like brain lesions are found in migraineurs.[4]

Is migraine a predisposing factor for ischaemic stroke?

The first indication that migraine may be a risk factor for stroke appeared in a study published in the *Journal of the American Medical Association* in 1975. It was reported that young women with migraine, who used oral contraceptives, had double the relative risk of stroke compared with controls.[5] The results of subsequent studies pooled in a meta-analysis showed that the relative risk of stroke in patients with migraine (with and without aura) is 2.16 (95% CI, 1.89 to 2.48). The risk with migraine with aura is 2.27, and with migraine without aura 1.83.[6]

Does migraine cause ischaemic stroke?

Ischaemic stroke is known to occur during the course of a migraine attack, although this is fortunately a rare occurrence. Nevertheless this suggests that there may be a causal relationship between the two conditions. In the International Headache Society classification, stroke occurring during an attack of migraine with aura (MA) has been termed "migrainous infarction".[7] It does not however only occur with MA. Stroke has been reported in two series as occurring more frequently in migraine without aura (MO) than in MA.[8,9] The important predisposing factors in migraineurs who develop stroke during migraine attacks are female sex, mean age of 30-35 years, cigarette smoking, and ischaemic involvement of the territory supplied by the posterior cerebral artery.[10-12] Neuroimaging studies on migraineurs have revealed an increase in the incidence of white matter lesions (WMLs).

These infarct-like lesions are common in the general population, and are present in up to 80% of individuals in their 8th decade.[13] The number of WMLs increased with advancing age, cardiovascular disease, stroke, dementia, and vascular risk factors such as diabetes, tobacco smoking, hypertension and hypercholesterolaemia.[14-17] Patients with migraine also have a significantly higher prevalence of WMLs in the cerebellum than controls (5.4% versus 0.7%), and patients with MA have a 12-fold increased risk

of developing cerebellar infarcts, with the risk of WMLs increasing with increasing attack frequency.[18] If the brain lesions in migraine are of a progressive nature, then an important aim of treatment will be prevention of progressive brain damage. To prevent disease progression, treatment should be directed at preventive therapies rather than abortive therapies.[19,20]

Can migraine be a consequence of ischaemic stroke?

There is clinical and experimental evidence that acute focal cerebral ischaemia can sometimes trigger migraine attacks.[21] The frequency of stroke-related headache is greater in younger females with ischaemic damage in the vertebrobasilar territory, and a history of migraine. The frequency ranges from 7% to 65%.[22,23] Migraine can actually be the presenting symptom of cerebral infarction, but the frequency of this occurrence is unknown because of lack of data.

Is there a connection between PFO, migraine and ischaemic stroke?

The incidence of PFO is significantly higher in MA than in non-migraineurs. Similarly in patients with ischaemic stroke, MA is twice as common in patients with PFO than in those without PFO.[24,25] The interrelationship has been highlighted by the finding that PFO closure reduces the frequency of migraine attacks.[26-33] Although the possibility of a three-way association between migraine, stroke and PFO is still a subject of speculation, the available evidence supports the idea that PFO predisposes to both migraine and ischaemic stroke. It is possible, although the jury is still out on this, that migraine may emerge as an indicator for carrying out diagnostic tests to determine the possible presence of PFO, particularly in those with associated risk factors. Closure of PFO has been suggested as a possible preventive treatment for migraine, but this is at present highly speculative, as there is not yet enough data to draw clear conclusions.

Reducing the risk of ischaemic stroke in migraineurs

The first step towards reducing the risk of stroke is the identification of those migraineurs with the highest risk of stroke. The risk factors in migraineurs are, as in other individuals, cigarette smoking, hypertension, hyperlipidaemia and diabetes mellitus. Although there is no absolute contraindication to the use of combined oral contraceptives in women with migraine, those formulations with low oestrogen formulations are preferred.

In patients with MA together with other risk factors, progestogen-only contraceptives are preferable. With regard to the use of vasoconstrictive migraine-specific drugs such as ergotamine and the triptans, their use is inadvisable for migraineurs with pre-existing cardiac or cerebral ischaemia and other vascular risk factors.

Those migraine sufferers who have in addition recognised stroke risk factors, should be advised to use the available prophylactic migraine treatments in order to reduce the possible added risk of increasing WMLs and of ischaemic stroke during migraine attacks. Pharmacologic migraine preventive therapies, although useful in some patients, are often discontinued because of the frequency of adverse events or poor effectivity,[34] and should be used only as a last resort. In a recent survey, two out of three (67%) migraine patients reported that they had delayed or avoided taking headache prescription medication at some time because of concerns about adverse effects.[35] Botulinum toxin is effective and well-tolerated, but the effect is temporary.[36] Proven non-pharmacologic therapies are the treatments of choice. Muscle tension and tenderness of the craniocervical and craniomandibular muscles is a constant finding during migraine,[37-39] and treatment modalities that reduce this muscle tension are effective in migraine prevention.

MIGRAINE SUFFERERS WITH RECOGNISED STROKE RISK FACTORS SHOULD USE PROPHYLACTIC MIGRAINE TREATMENTS TO REDUCE THE POSSIBLE ADDED RISK OF INCREASING WMLS AND OF ISCHAEMIC STROKE DURING MIGRAINE ATTACKS

These include intra-oral devices,[40-42] physiotherapy, relaxation therapy, biofeedback, and cognitive behavioural training.[43] When the pain is positively diagnosed as originating in the extracranial terminal branches of the external carotid artery, surgical cauterisation of the relevant vessels has a low morbidity and is effective in migraine prevention.[44-46]

Conclusion

The available evidence suggest that there exists a link between migraine and cerebral ischaemia, which appears to be more in evidence in the young. The data suggest that this link is stronger in MA than in MO. It would appear prudent, particularly in individuals with MA together with other risk factors for ischaemic stroke, not only to institute early management of the other risk factors, but also preventive treatment of the migraine.

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