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Review

Headache associated with ischemic stroke: a narrative review

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Background
Headache is a common symptom in acute ischemic stroke, with an average prevalence of approximately 14%. Its occurence involves neurovascular dysfunction, meningeal inflammation, and posterior circulation compromise. It is more common in women and in individuals with a history of primary headache. This review aims to describe the clinical, pathophysiological mechanisms, therapeutic considerations and prognostic implications of headache associated with ischemic stroke.

Methods
A narrative review of literature was conducted, using Pubmed/MEDLINE, Scopus, and SciELO databases. Observational studies, secondary literature (systematic reviews and meta-analyses), and international consensus statements published between 2013 and 2025 were included.

Results
Headache occurs in approximately 14% of patients with ischemic stroke, particularly in women, patients with posterior circulation infarcts and those with a history of migraine. Its characterized by moderate to intensity pain, gradual onset, frontal or temporal location, and presents tension-type or migraine-like pattern. Involves meningeal irritation, endothelial dysfunction, alterations in cerebral autoregulation, and activation of the trigeminovascular system. The SNNOOOP10 scale is useful for detecting warning signs and guiding the need for neuroimaging. Paracetamol is the safest analgesic option, NSAIDs, triptans and ergot derivatives should be avoided, CGRP antagonists appear safe, although long-term evidence is limited.

Conclusion
Headache associated with ischemic stroke is a relevant clinical manifestation with diagnostic and prognostic implications. Its recognition and appropriate management require a careful balance between analgesic efficacy and vascular safety.

Keywords:
Headache
Ischemic stroke
Migraine, Analgesics
Calcitonin gene-related peptide

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Introduction

Headache is a frequent manifestation in the context of acute cerebrovascular disease, particularly in ischemic stroke, although its clinical recognition is usually underestimated. Various studies suggest that between 6% and 44% of stroke patients have headaches temporally associated with the event, with a pooled prevalence close to 14% (1).

Recent research proposes that this symptom may reflect alterations in cerebral hemodynamics, meningeal inflammation, or neurovascular dysfunction rather than an incidental phenomenon (2).

Methods

A narrative review was carried out using the PubMed/MEDLINE, Scopus and SciELO databases. We included articles published between January 2013 and December 2025.The search strategy combined controlled vocabulary and free-text terms using Boolean operators, as follows: ("headache" OR "cephalalgia") AND ("ischemic stroke" OR "cerebral infarction" AND "cerebrovascular disease").

Inclusion criteria were: Observational studies, systematic reviews, meta-analyses and international statements addressing headache attributed to ischemic stroke; studies published in English, Portuguese or Spanish; and studies involving adult populations. Exclusion criteria included case reports, conference abstracts, editorials, letters to editor and non peer-reviewed sources.

The selection of studies was based on relevance to the objectives of this review, focusing on epidemiology, clinical manifestations, pathophysiology, diagnosis, treatment, and prognosis of headache associated with ischemic stroke.

Results

The literature search initially identified approximately 102 articles across the three databases(PubMed/MEDLINE,Scopus, and SciELO). After removal of duplicates and screening of titles and abstracts, 36 articles were assessed for eligibility. Following the application of inclusion and exclusion criteria a total of 14 publications were included in the narrative synthesis.

Epidemiology

The meta-analysis by Harriot et al.(1) reported a combined prevalence of 14% of headaches in ischemic stroke, with greater frequency in women and posterior circulation infarcts. A systemic review conducted in China, which included 98 studies and 34,460 patients, estimated a prevalence of 18.9% with increased risk in women (OR2.06), history of headache (OR 3.24), and posterior circulation compromise (OR 2.13) (3). In Latin America, a Brazilian study of 303 patients observed headache attributable to stroke in 42.6% of cases (4). The data suggests regional heterogeneity influenced by methodological differences, diagnostic definitions, and population characteristics.

Clinical manifestations

Headache associated with cerebrovascular disease presents variable characteristics, although certain patterns are recognizable. Its appearance usually coincides with the onset of the neurological deficit or occurs within the first hours after the event (3). In clinical studies, the onset was gradual in more than 80% of patients, with moderate intensity, average duration of 20 hours, preferential frontal or temporal location and bilateral predominance in more than 50% (4). The morphology of the pain is mainly described as oppressive or throbbing, similar to tension or migraine headaches.

Autonomic symptoms (tearing, nasal congestion, or facial sweating) are reported in less than 20% of cases (5) . The coexistence of a history of migraine with or without aura is a predisposing factor, although the aura itself does not characteristically occur during stroke. Persistent headache attributed to stroke can persist in approximately 10% of patients a year after the event, with a tendency to become chronic in a migraine pattern (6).

Pathophysiology

Headache in stroke reflects multiple interrelated mechanisms. Meningeal irritation secondary to cortical ischemia, endothelial dysfunction, alterations in cerebrovascular autoregulation and the release of inflammatory mediators contribute to its genesis (2). Compromise of the posterior circulation and brainstem is particularly associated with a higher incidence of pain due to activation of the trigeminal vascular system. These observations support the interpretation of headache not only as an accompanying symptom, but as an indirect marker of active vascular involvement.

Diagnostic evaluation and usefulness of the Snoop 10 scale

The Snoop 10 scale constitutes a useful clinical screening tool to identify alarm signs ("red flags") in secondary headaches. Its sensitivity close to 100% makes it an appropriate instrument for the early detection of vascular causes (7). In the context of stroke, the sudden appearance of headache accompanied by focal deficit, advanced age or change in pattern should motivate immediate neuroimaging study. Although it does not discriminate between types of secondary headache, its application

guides the differential diagnosis and favors the timely identification of an underlying stroke.

Pharmacological treatment, therapeutic considerations and precautions

Therapeutic management of headache in patients with cerebrovascular disease should focus on vascular safety and prevention of complications. Paracetamol continues to be the analgesic drug of choice due to its effectiveness and low risk of interfering with coagulation or blood pressure.

The use of nonsteroidal anti-inflammatory drugs (NSAIDs) requires caution, since several studies have shown their association with an increased risk of stroke and major cardiovascular events. Among them, diclofenac and selective cyclooxygenase-2 inhibitors, such as rofecoxib and celecoxib, have the highest relative risk (8). This risk increases when combined with antiplatelet agents or anticoagulants, given the potential to increase the risk of intracranial or gastrointestinal bleeding.

Triptans, widely used in the acute treatment of migraine, exert arterial vasoconstriction through the stimulation of serotonergic 5-HT1B/1D receptors. Due to this, they are formally contraindicated in patients with a history of ischemic stroke, coronary heart disease, peripheral arterial disease or uncontrolled hypertension (9). Likewise, ergot derivatives such as ergotamine and dihydroergotamine, due to their powerful vasoconstrictive action, increase the risk of cerebral or coronary artery disease and should be avoided in any patient with previous cerebrovascular disease or high vascular risk.

Regarding the preventive treatment of migraine, a possible increase in vascular risk with certain drugs has been described. Combined hormonal contraceptives, frequently used in young women with migraine with aura, are associated with a significantly increased risk of ischemic stroke, particularly in the presence of smoking or hypertension (10). The calcitonin gene-related peptide CGRP has a neuroprotective function during stroke by improving collateral circulation and reducing damage due to ischemia reperfusion, therefore it was proposed that blocking its function could worsen stroke patients; However, it has been observed that CGRP receptor antagonists, including monoclonal antibodies and oral antagonists, do not show an increased risk of stroke in recent clinical studies and present a favorable safety profile in patients with cerebrovascular comorbidities, although long-term evidence remains limited (11). On the contrary, beta blockers such as propranolol and metoprolol, used in migraine prophylaxis, are considered safe and could exert a certain protective effect in hemodynamic terms.

The use of tricyclic antidepressants or anticonvulsants (amitriptyline, topiramate, valproate) has not been consistently linked to an increased risk of developing cerebrovascular disease; however, they should be used with caution for their effects on body weight, blood pressure, or liver function, depending on the patient's clinical condition.

Long-term follow-up should include control of vascular factors, blood pressure monitoring, and education on the rational use of analgesics. Medication overuse headache can develop in up to a third of patients with persistent post-stroke headache (12), reinforcing the need to periodically re-evaluate the indication and frequency of analgesic or prophylactic drugs.

In summary, treatment should be individualized, prioritizing hemodynamic stability and avoiding medications with vasoconstrictor or proaggregant potential, while promoting the control of comorbidities that may increase the risk of recurrence or cerebrovascular complications.

Prognosis and correlation with severity

The relationship between headache and stroke severity continues to be a matter of debate. In a registry of more than 11,000 patients, headache at baseline was associated with better functional outcome and less disability within the first month after stroke (13). Other studies confirm its greater presence in less severe strokes, with lower NIHSS scores and smaller infarct extent (14). On the other hand, there has been no evidence of a significant relationship with mortality or persistent long-term disability (4).

Recent evidence suggests that headache in the context of ischemic stroke may be more commonly observed in milder clinical presentations. A contemporary narrative review by Im and Kingston (7) emphasizes that post-stroke headache is frequently reported in patients with less severe neurological deficits and may reflect preserved nociceptive and neurovascular pathways rather than extensive cerebral injury. This observation could partially explain the association between headache and more favorable short-term functional outcomes reported in several cohorts.

In Latin America, data is limited. A Brazilian study found an absence of a relationship between headache and adverse functional outcomes (14). These observations suggest that headache could be linked to a less severe stroke phenotype, although methodological heterogeneity precludes definitive conclusions.

Conclusions

Headache associated with cerebrovascular disease is a common clinical symptom that can occur before, during or immediately after the ischemic event. Its appearance is

usually related to posterior circulation infarctions, a history of primary headache, and female sex. The predominant characteristics are gradual onset, moderate pain, and a tension-like or migraine pattern. The persistence of pain in the chronic phase occurs in a minority of patients and requires therapeutic monitoring.

There is no solid evidence that headache correlates with increased mortality or disability; On the contrary, it could correspond to less severe ischemic events. Clinical management should focus on early detection, differentiation using the SNNOOOP10 scale, and judicious use of safe analgesics. Future research, especially in Latin America, should address its prognostic impact and long-term functional evolution with homogeneous methodologies.

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