J Headache Pain (2001) 2:25–29

ORIGINAL ARTICLE

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Headache associated with acute ischemic stroke

Received: 5 January 2001
Accepted in revised form: 6 April 2001

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Abstract Headache occurs frequently in acute ischemic stroke, but its frequency varies widely among different studies. We have prospectively studied headache features in patients with first-ever ischemic acute stroke and assessed the relationship between headache, stroke location, and etiology. The study included consecutive patients admitted to our Stroke Unit for a first-ever ischemic acute stroke. The study included 154 consecutive patients with ischemic stroke, and 54 of these (35.1%) had headache during stroke onset. Twelve patients (22.2%) with headache during stroke had history of headache; no patients without headache had history of headache. Headache was present in 25.8% (32/124) of the patients with anterior circulation stroke and in 73.3% (22/30) of the patients with posterior circulation stroke (p=0.001). Large artery disease was more frequent with than without headache (40.7% versus 14.0%, p=0.04). Headache was present in more than one-third of the patients with ischemic stroke. All patients with positive history for headache had headache during stroke onset. The cephalic pain was much more common among patients with infarcts in the posterior circulation than in patients in whom the anterior circulation was involved. Headache was more common when the cause of stroke was large artery disease.

Key words Headache • Acute stroke • Vascular risk factors • Cephalic pain

Introduction

Headache occurs frequently in acute ischemic stroke, but its frequency varies widely among different studies, ranging from 18% to 41% depending on data sources [1–12]. Few reports [5, 9–12] have prospectively analyzed the incidence, nature, and type of headache in stroke of diverse pathogenesis and location.

We have prospectively studied headache features in patients with first-ever ischemic acute stroke and assessed the relationship between headache, stroke location, and etiology. The findings were compared with those in patients without headache.

Patients and methods

The study included all consecutive patients admitted to the Stroke Unit of Department of Neurology of University of Perugia for a first-ever ischemic acute stroke in a period of 6 months. Hemorrhages, transient ischemic attacks, artery dissections, and unconscious, confused and/or aphasic patients were not included in the present study. We investigated all patients using a standard protocol including demographic characteristics, vascular risk factors, previous history of headache, clinical signs and symptoms, electrocardiography, computed tomographic scan, duplex and transcranial Doppler, and magnetic resonance imaging, and/or angiography in selected cases. We considered the main etiology for brain infarction according to previous

defined criteria: large artery disease, cardioembolism, small vessel disease, and other or undetermined causes [13]. We classified infarcts in the anterior circulation or in the posterior circulation according to the anatomical and vascular locations (anterior in the territory of internal carotid artery and posterior in the vertebro-basilar territory).

The presence of carotid atherosclerosis was defined as a stenosis ≥50% or occlusion of internal carotid artery on Doppler ultrasonography [14] and/or angiography according to previous criteria [15]. Occlusion of internal carotid artery was defined as flow absent on Doppler ultrasonography at carotid bifurcation.

Headache was defined as cephalic pain appearing before or after other stroke symptoms. Headache features studied included side of headache (unilateral, unilateral alternating, or bilateral), severity of headache (mild, moderate, or severe), location of headache [diffuse; anterior (frontal, temporal, and parietal); posterior (occipital)], pain quality (pulsating or stabbing), duration of headache (<30 min, 30 min-4 h, 4–72 h, >72 h), accompanying symptoms of headache (nausea, vomiting, photophobia, and phonophobia), and aggravation by routine physical activity.

"Sentinel headache" was defined as headache noted by the patient in the 7 days before stroke onset, "onset headache" as headache reported by the patient at stroke onset or on the same day as the stroke onset, "sentinel-onset headache" as headache reported by the patients before and during the stroke onset, and "late-onset headache" as headache reported by the patient 2 or more (≤7) days after stroke onset.

To detect potential differences between patients with headache and those without , we compared risk factors, clinical state (according to OCSP criteria) [16], and type, causes, and location of stroke in these two groups. Statistical analysis was carried out by chi-squared test and Fisher's exact test when appropriate. $p<0.05$ was considered statistically significant.

Results

The study included 154 consecutive patients with first-ever ischemic stroke (80 male, 74 female; mean age 70.98±10 years, range 45–86 years), 124 with anterior circulation stroke and 30 with posterior circulation stroke. Headache was reported in 54 patients (35.1%) [13 sentinel headache (mean time 2.24 days before stroke onset), 21 onset headache, 20 sentinel-onset headache; no patients had late-onset headache]. Baseline characteristics of the patients with and without headache are summarized in Table 1. History of headache was present only in stroke patients with headache. All the patients with history of headache had headache during the year before the stroke. Carotid atherosclerosis was also significantly more frequent in the patients with headache. Six patients (11%) with headache had internal carotid artery occlusion versus 9 (9%) without headache.

Headache was present in 25.8% (32/124) of the patients with anterior circulation stroke and in 73.3% (22/30) of the patients with posterior circulation stroke (p=0.001).

Large artery disease was more frequent with than without headache (40.7% versus 14.0%, p=0.04); occlusion of internal carotid artery was present in 16.6% of patients with headache and 6.0% of patients without headache. Small vessel disease, potential cardiac sources of emboli, and undetermined stroke were similar in patients with or without headache (Table 2).

There were no differences in blood pressure values between patients with or without headache.

Table 1 Baseline characteristics of the patients

Risk factors	Headache patients (n=54) n (%)	No headache patients (n=100) n (%)
Sex (male/female)	26 (48.1)/28 (51.9)	54 (54.0)/46 (46.0)
Age (years)	69.2±10	71.9±10
Hypertension	37 (68.5)	71 (71.0)
Smoking	21 (38.9)	38 (38.0)
Diabetes mellitus	7 (12.9)	22 (22.0)
Impaired glucose tolerance	2 (3.7)	1 (1.0)
Obesity	7 (12.9)	8 (8.0)
Ischemic heart disease	37 (68.5)	83 (83.0)*
Hyperlipidemia	26 (48.1)	36 (36.0)
Family history of cerebrovascular disease	17 (31.4)	34 (34.0)
Previous TIA	2 (3.7)	6 (6.0)
Carotid atherosclerosis	32 (59.1)	41 (41.0)**
History of headache	12 (22.2)	0***

*p=0.03; **p=0.02; ***p=0.001
TIA, transient ischemic attack

Table 2 Etiology of stroke and headache

Etiology	Patients with headache (n=54)	Patients without headache (n=100)
Large artery disease	22 (40.7%)	14 (14.0%)*
Small vessel disease	7 (12.9%)	23 (23.0%)
Cardioembolism	8 (14.9%)	21 (21.0%)
Undetermined or other causes	17 (31.5%)	42 (42.0%)

*p=0.04

Table 3 Clinical state of the patients

	Patients with headache (n=54)	Patients without headache (n=100)
Total anterior circulation infarct	4 (7.4%)	14 (14.0%)
Partial anterior circulation infarct	19 (39.2%)	43 (43.0%)
Lacunar infarct	7 (12.9%)	25 (25.0%)
Posterior circulation infarct	22 (40.7%)	18 (18.0%)*

*0p=0.05

Table 4 Characteristics of the pain and accompanying symptoms

Location		
Anterior (frontal, temporal or parietal)	32	(59.2%)
Posterior (occipital)	10	(18.5%)
Diffuse	12	(22.2%)
Side		
Unilateral (ipsilateral to ischemia)	7	(13.0%)
Unilateral (contralateral to ischemia)	2	(3.7%)
Unilateral alternating	1	(1.8%)
Bilateral	44	(81.5%)
Severity		
Mild	11	(20.4%)
Moderate	34	(63.0%)
Severe	9	(16.6%)
Pain quality		
Pulsating	9	(16.6%)
Stabbing	45	(83.4%)
Duration of headache		
<30 min	5	(9.3%)
30 min–4 h	25	(46.3%)
4–72 h	16	(29.6%)
>72 h	8	(14.8%)
Accompanying symptoms		
Nausea	8	(14.8%)
Vomiting	8	(14.8%)
Photophobia	7	(13.0%)
Phonophobia	8	(14.8%)
Without accompanying symptoms	23	(42.6%)
Aggravation by physical activity		
Yes	8	(14.8%)
No	46	(85.2%)

The clinical status of the patients with and without headache is summarized in Table 3.

Among the 54 stroke patients with headache, the location of pain was anterior in 59.3% of patients, posterior in 18.6%, and diffuse in 22.2%. Frontal, temporal, or parietal headache was present in 71.9% of patients with anterior circulation infarct and in 40.9% of patients with posterior circulation infarct, whereas occipital headache was present in 31.8% of patients with posterior circulation infarct and in 9.4% of patients with anterior circulation infarct. Diffuse headache was present in 18.7% of patients with anterior circulation infarction versus 27.3% of patients with posterior circulation infarction. The characteristics of the pain and the accompanying symptoms are shown in Table 4. Among 10 patients with unilateral pain, headache was ipsilateral to the ischemic lesion in 8 patients. Considering the IHS 1988 criteria [17], among 54 patients with headache, 45 (83.3%) had headache with clinical characteristics of tension-type headache and 9 (16.7%) of migraine. These patients had not had a sufficient number of crises to consider headache-like episodic tension-type headache or migraine without aura.

Discussion

Headache is one of the primary features of acute cerebrovascular disease especially in patients with hemorrhagic stroke or subarachnoid hemorrhage. In this report, consider-

ing patients with ischemic stroke, headache was present in more than one-third of the patients and was much more common among patients with infarcts in the posterior circulation than in patients in whom the anterior circulation was involved. Several authors have reported that the vessels in the posterior circulation are more richly innervated by nociceptive afferents than in the anterior circulation [8, 18].

In our series, stroke-related headache was frequently associated with large artery disease, being uncommon in patients with lacunar infarctions. The frequency of headache was higher in patients with carotid artery occlusion, but this was not significant compared with patients without headache. Similar results have been obtained by other authors, headache frequency ranging from 26% to 35% of patients with symptomatic carotid artery disease [2, 4, 19]. In the presence of the occlusion of carotid artery, the headache is more important when the cause of occlusion is the dissection of the vessel [20], but in our report, patients with artery dissection were not included.

Headache during stroke seems to be induced through the activation of the trigemino-vascular system [18]. A previous history of headache was related to the presence of headache during stroke, probably because ischemia can trigger a flurry of migraine episodes [21], but in our report the prevalent type of headache was pain with clinical characteristics of tension-type headache. Previous reports [2, 22] suggested that headache during stroke may be caused by a release of vasoactive substances (like during migraine attacks) in the trigemino-vascular system, but the same release of these vasoactive substances seems to have an important role in the multifactorial pathogenesis of tension-type headache [23]. Also the release of amino acid neurotransmitters [24] and platelet activation [2, 22] may play a role in the pathogenesis of headache occurring at the onset of ischemic stroke. Forty-one percent of the patients with posterior circulation infarct had frontal, temporal, or parietal headache. This can be explained by the anatomical connection between the posterior circulation and the trigeminal system by means of trigemino-cerebellar artery [25]. Among 10 patients with unilateral pain, headache was contralateral to ischemic lesion in 2 patients. We can explain this strange phenomenon by considering the anatomical organization of the trigemino-vascular system. In fact, some intracranial vessels have contralateral trigeminal innervation and single trigeminal neurons have large receptive fields and provide fibers to more than one vessel [26].

In conclusion, headache was present in more than one-third of patients with ischemic stroke; all patients with positive history for headache had headache during stroke onset; the cephalic pain was much more common among patients with infarcts in the posterior circulation than in patients in whom the anterior circulation was involved; headache was more common when the cause of stroke was large artery disease; the prevalent type of headache was pain with clinical characteristics of tension-type headache present in more than 80% of patients.

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