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. \( p \leq 0.05 \) 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) | No headache patients (n=100) |
|------------------------------------------|--------------------------|-----------------------------|
|                                          | n (%)                    | 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
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.

Table 3 Clinical state of the patients

| Condition                        | 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%)                       |

*0.05 p=0.05

Table 4 Characteristics of the pain and accompanying symptoms

| Location                          | Patients with headache (n=54) | Patients without headache (n=100) |
|-----------------------------------|-------------------------------|----------------------------------|
| 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.

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

| Condition                        | 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%)                       |

*0.05 p=0.05

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 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.

References

1. Mohr JP, Caplan LR, Melski JW, Goldstein RJ, Duncan GW, Kistler JP, Pessin MS, Bleich HL (1979) The Harvard Cooperative Stroke Registry: a prospective registry. Neurology 28:754–757
2. Edmeads J (1979) The headache of migraine episodes. J Neurol Neurosurg Psychiatry 42:282–285
3. Portonoy RK, Abissi CJ, Lipton RB, Berger AR, Mebler MF, Baglivo J, Solomon S (1984) Headache in cerebrovascular disease. Stroke 15:1009–1012
4. Gorelick PB, Hier DB, Caplan LR, Langenberg P (1986) Headache in acute cerebrovascular disease. Neurology 36:1445–1450
5. Koudstaal PJ, Van Gijn J, Kappelle LJ (1991) Headache in transient or permanent cerebral ischemia. Stroke 22:754–759
6. Mitsias P, Ramadan NM (1992) Headache in ischemic cerebrovascular disease. I. Clinical features. Cephalalgia 12:269–274
7. Mitsias P, Ramadan NM (1992) Headache in ischemic cerebrovascular disease. II. Mechanisms and predictive value. Cephalalgia 12:341–344
8. Vestergaard K, Andersen G, Nielsen MI, Jensen TS (1993) Headache in stroke. Stroke 24:1621–1624
9. Arboix A, Massons J, Oliveres M, Arribas MP, Titus P (1994) Headache in acute cerebrovascular disease: a prospective clinical study in 240 patients. Cephalalgia 14:37–40
10. Gorelick PB (1993) The secondary headaches. Ischemic stroke and intracranial hematomas. In: Olesen J, Tfelt-Hansen P, Welch KMA (eds) The headaches. Raven, New York, pp. 639–646
11. Ferro JM, Melo TP, Oliveira V, Salgado AV, Crespo M, Canhao P, Pinto AN (1995) A multivariate study of headache associated with ischemic stroke. Headache 35:315–319
12. Kumral E, Bogousslavsky J, Van Melle G, Regli F, Pierre P (1995) Headache at stroke onset: the Lausanne Stroke Registry. J Neurol Neurosurg Psychiatry 58:490–492
13. Adams HP, Benedixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, Marsh EE (1993) TOAST investigators. Classification of subtype of acute ischemic stroke: definition for use in a multicenter clinical trial. Stroke 24:35–41
14. Eliasziw M, Rankin RN, Fox AJ, Haynes RB, Barnett HJ for the North American Symptomatic Carotid Endarterectomy Trial (NASCET) (1995) Accuracy and prognostic consequences of ultrasonography in identifying severe carotid artery stenosis. Stroke 26:1747–1752
15. Fox AJ (1993) How to measure carotid stenosis. Radiology 186:316–318
16. Bamford JM (2000) The role of the clinical examination in the subclassification of stroke. Cerebrovasc Dis 10[Suppl 4]:2–4
17. Headache Classification Committee of the International Headache Society (IHS) (1988) Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. Cephalalgia 8[Suppl 7]:1–96
18. Moskowitz MA (1984) Neurobiology of vascular headache. Ann Neurol 16:157–162
19. Edmeads J, Barnett HJM (1973) La cephalia en las afecciones cerebrovasculares occlusivas. In: Friedman AP, Poch GF (eds) Cephalaeas y jacquecas. Eudeba, Buenos Aires, pp 89–100
20. Silbert PL, Mokri B, Schievink WI (1995) Headache and neck pain in spontaneous internal carotid and vertebral artery dissections. Neurology 45:1517–1522
21. Olsen J, Friberg L, Olsen TS, Andersen AR, Lassen NA, Hansen PE, Karle A (1993) Ischemia-induced (symptomatic) migraine attacks may be more frequent than migraine-induced ischemic insults. Brain 116:187–202
22. Edmeads J (1983) Complicated migraine and headache in cerebrovascular disease. Neurol Clin 1:385–397
23. Jensen R (1999) The tension-type headache alternative. Peripheral pathophysiological mechanisms. Cephalalgia 19[Suppl 25]:9–10
24. Castillo J, Martinez F, Corredera E, Aldrey JM, Noya M (1995) Amino acids transmitters in patients with headache during the acute phase of cerebrovascular ischemic disease. Stroke 26:2035–2039
25. Marinkovic SV, Gibo H (1995) The blood supply of the trigeminal nerve root, with special reference to the trigeminocerebellar artery. Neurosurgery 37:309–317
26. O’Connor TP, van der Kooy D (1986) Pattern of intracranial and extracranial projection of trigeminal ganglion cells. J Neurosci 6:2200–2207