Tr. J. of Medical Sciences
29 (1999) 31–35

Meral MİRZA[1]
Ahmet TUTUŞ[2]
Füsun ERDOĞAN[1]
Mustafa KULA[2]
Ali TOMAR[1]
Güler SİLOV[2]
Emel KÖSEOĞLU[1]

Interictal Spect With Tc 99m-HM PAO in Migraine Patients

Received: February, 05, 1997

Departments of [1]Neurology [2]Nuclear Medicine
University of Erciyes, Kayseri-Turkey

Abstract: Migraine is considered to be a functional neurological disorder. For several years cerebral blood flow studies have been fueling the controversy surrounding the pathophysiology of migraine headache. Tc 99m-HM PAO SPECT brain imaging was performed during the headache-free period of 29 migraine sufferers (24 without aura, 5 with aura). The findings were compared with those of an age-and sex-matched control group of 17 people. The SPECT images revealed clear interhemispheric asymmetry in the right frontal, temporal and occipital lobes of the brain in the study group. Slight hypoperfusion was observed in patients who had interictal EEG abnormalities.

Key Words: Migraine, Single Photon Emission Computed Tomography.

Introduction

Migraine is a familial disorder characterized by periodic, commonly unilateral throbbing headaches which frequently begin in childhood or after the start puberty. However, its onset may occur at any time from early childhood. Migraine is associated with disturbances of neuronal function and reduced perfusion (1–4). It has been reported that migraine attacks occur in connection with exacerbations of preexisting changes in cerebral autoregulation due to endogenous or exogenous factors (5). Olesen et al. (6) described cerebral blood flow (CBF) asymmetries during acute attacks of migraine with aura.

The aim of this study was to assess the presence of cerebral perfusion abnormalities using Tc 99m–HM PAO as a tracer during the interictal phase.

Material and Methods

Twenty–nine patients (26F, 3M) with a mean age of 34.0±9.1 (range 18–54) were studied during headache–free period. The patients were diagnosed according to the criteria of the International Headache Society (IHS). Twenty–four suffered from migraine without aura and 5 from migraine with aura. The mean duration of their diseases was 9.8±12.4 years. A group of 17 age–matched healthy individuals (15F, 2M) was also studied. The subjects were patients at the Department of Neurology, Faculty of Medicine, Erciyes University, between February and September 1996.

The patients underwent Electroencephalography (EEG), Computed Tomography (CT) and Single Photon Emission Tomography (SPECT) with Tc 99m–HM PAO. In the control group, only SPECT analysis was performed.

The SPECT study was performed, 10 to 60 minutes after the injection of 550 m Bq of Tc 99m–HM PAO, with a 360° rotating single–head gamma camera system (Toshiba GCA602A/5A, Japan) equipped with a LEAP collimator interfaced to a Toshiba computer system. Data were obtained in a 64x64 pixel matrix through 360° rotation at 6° intervals, for 30s per arc interval. The images were reoriented to obtain transaxial slices parallel to the orbitometal (OM) line. The transaxial slices were approximately 0 mm (orbitomeatal line), 33 mm, 49.5 mm and 66 mm above the orbitomeatal plane. The rectangular regions of interest (ROI), 5x5 pixels, were set on the SPECT images in the upper and lower frontal, temporal, parietal and occipital regions and cerebellar hemispheres. The mean values of two or three ROIs in five regions were calculated. The raw data were reconstructed by filtered back projection using a Butterworth (8/0.25) and Ramp filter. No attenuation or scatter correction was applied. Studies were interpreted to obtain activity ratios in axial slices taking cerebellum as reference as previously described by Hoshi et al (7). Mean

cortico/cerebellar ratios were computed for each ROI in both the patient and control groups. The values were estimated in the form: mean±SD. The SPECT findings for the migraine sufferers were compared with those for the controls. For statistical analysis the paired and unpaired Student's t test and Kruskal–Wallis analysis of variance were used when appropriate.

A schematic illustration of transaxial SPECT slices is shown in (Fig.1).

Results

The characteristics of the groups are listed in Table 1.

Table 1. Characteristics of Groups.

	Patients (n: 29)	Controls (n: 17)
Sex F/M	26/3	15/2
Age (years)	34.0±9.1	30.2±12.2
Duration of history (years)	9.8±12.4	
Migraine with aura	5	
Migraine without aura	24	
Headache localization		
• Unilateral	20	
• Bilateral	9	

In the EEG tracing, increased β activity was observed in 9 (31.0%) of the 29 patients, slow wave activity in the temporal and posterior cerebral regions in 5 (17.2%) patients and normal EEG in the remaining 15 (51.7%) patients (Table II).

Table 2. EEG Findings For the Patients.

EEG State	n	%
Normal	15	51.7
β activity	9	31.0
Slow wave activity in the temporal and posterior cerebral regions	5	17.2

The CT scans of the patients were found to be normal.

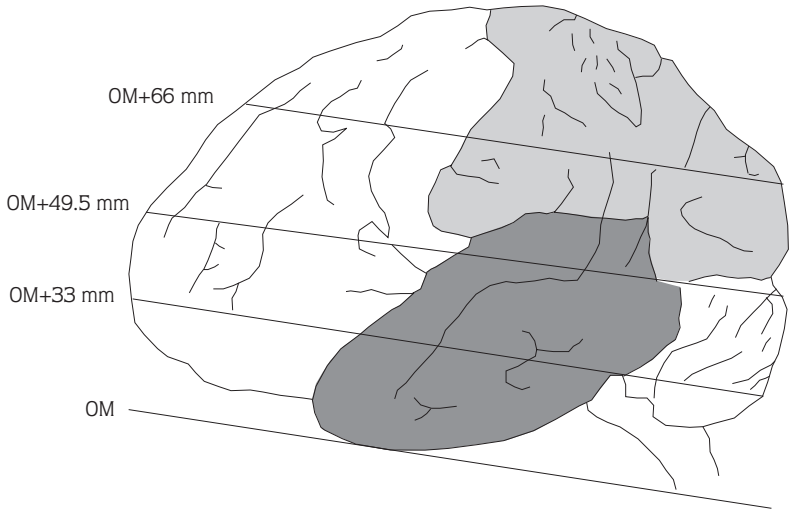
The data obtained from the groups compared are shown in Table III. No differences were detected in left and right cortex Tc 99m–HM PAO uptake values between the patient and control groups.

The interhemispheric SPECT findings for the groups are shown in Table IV.

As shown in Table IV, migraine patients exhibited significantly reduced Tc 99m–HM PAO uptake in the right lower frontal, temporal, upper frontal and occipital regions. There was no correlation between the side of the pain and hemispheric impairment. There were no significant interhemispheric differences in Tc 99m–HM PAO uptake in control the group.

Discussion

Although the existence of migraine has been known for nearly 2000 years, its cause is not completely understood. According to vascular theory, vasoconstriction of cerebral arteries leads to neurological symptoms and rebound vasodilatation of either



OM: Orbitomeatal line

Figure 1. Schematic illustration of transaxial SPECT slices parallel to orbitomeatal line.

Table 3. Comparison of the Tc 99m-HM Pao Uptake Ratios for the Groups.

		PATIENTS (n: 29)				CONTROLS (n: 17)		
		(M+A)		(M–A)				
REGİONS		mean	min–max	mean	min–max	mean	min–max	h
Lower frontal	L	0.89	0.75–1.08	0.95	0.83–1.14	0.95	0.92–1.00	0.63*
	R	0.88	0.74–1.03	0.93	0.82–1.14	0.96	0.91–1.00	1.48*
Temporal	L	0.97	0.85–1.09	0.99	0.89–1.23	1.03	0.96–1.10	1.67*
	R	0.94	0.82–1.11	0.98	0.87–1.22	1.02	0.95–1.08	2.91*
Parietal	L	0.87	0.78–1.07	0.93	0.78–1.12	0.96	0.91–1.06	1.84*
	R	0.85	0.77–1.05	0.93	0.78–1.11	0.96	0.91–1.05	1.55*
Upper Frontal	L	0.97	0.77–1.03	0.94	0.76–1.13	0.93	0.89–1.88	0.12*
	R	0.92	0.76–1.03	0.91	0.76–1.12	0.94	0.89–1.01	0.93*
Occipital	L	0.88	0.80–1.05	0.97	0.80–1.16	0.99	0.92–1.10	1.94*
	R	0.88	0.77–1.03	0.94	0.82–1.15	0.99	0.94–1.12	4.02*

L : Left
R : Right
M+A : Migraine with aura
M–A : Migrine without aura
* P>0.05, Kruskal–Wallis analysis of variance

Table 4. Interhemispheric Spect Findings for the Groups.

Regions	PATIENTS (n: 29)		CONTROLS (n: 17)	
	Left	Right	Left	Right
	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Lower frontal	0.96±0.096	0.936±0.097*	0.96±0.03	0.96±0.03
Temporal	1.008±0.91	0.994±0.97*	1.03±0.04	1.02±0.04
Parietal	0.943±0.102	0.939±0.102	0.98±0.04	0.97±0.04
Upper frontal	0.93±0.102	0.921±0.1*	0.94±0.03	0.94±0.03
Occipital	0.972±0.101	0.959±0.98**	1.00±0.04	1.00±0.05

* P<0.05, **P<0.01; paired t test.

extracranial or intracranial vessels causes the headache (8). There appear to be many neurogenic and humoral factors that contribute to the disorder of cerebrovascular control (9).

The EEG is usually normal, but sometimes nonspecific EEG abnormalities can be found in migraine sufferers. Computed tomography has shown cerebral edema in patients with migraine, particularly during an attack. Cerebral infarction and cortical atrophy may be observed during migraine attacks and between attacks, although the majority of patients have normal CT scans (10, 11). In the present study, normal EEG tracing was observed in 15 patients, increased β activity in 9, and slow wave activity in the temporal and posterior cerebral regions in the other. 5. CT scans were normal in all patients.

Most studies using SPECT with Tc 99m–HM PAO as the tracer have demonstrated CBF abnormalities during migraine attacks and pain–free periods (8, 12–17).

In this study, the semiquantitative analysis of SPECT images revealed clear interhemispheric asymmetry, especially in the right frontal, temporal and occipital parts of the brain in the patient group. Many studies have reported interhemispheric asymmetry during interictal periods in migraine sufferers (15, 16, 18, 19). The cortical hypoperfusion is probably caused by local disturbance of vasomotor regulation.

According to the studies of Battistella et al. (20) and Friberg et al. (21), impaired regional cerebral vascular autoregulation may exist during migraine and headache–free periods in patients suffering from classical and hemiplegic migraine. However, Olesen et al. (22) concluded that common migraine attacks were not initiated by reduced cerebral blood flow and, therefore, they differed pathophysiologically from classical migraine attacks.

In the present study there were no regional correlations found between hypoperfusion areas and clinical presentation. Bes et al. (8) also observed this lack of correlation. However, a positive correlation between clinical presentation and hemispheric impairment has been determined (5, 13, 14, 16).

SPECT revealed slight unilateral hypoperfision in the posterior cerebral regions in migraine sufferers with interictal EEG abnormalities. Neuronal dysfunction may play a role in this.

Previous studies of patients suffering from migraine have revealed oligaemic changes, especially in the posterior cerebral regions. The present study has provided additional information, in that the SPECT with Tc 99m–HM PAO revealed right frontal temporal and occipital decrease in CBF in the interictal phase. We think that many factors may contribute to the development of migraine and it may be that migraine is not a single pathogenic entity. Neural and vascular mechanisms play a role in migraine.

Our data indicate that Tc 99m–HM PAO brain SPECT is a useful technique for detecting alterations in cerebral perfusion in migraine sufferers. CT and EEG abnormalities are not frequently encountered in migraine patients.

Finally, is should be noted that no single laboratory procedure –including SPECT– is a reliable marker for migraine, but SPECT is helpful when used in conjunction with a patient's in history and with clinical examinations.

References

1. Raskin NH. Migraine and other headaches. Merritt's textbook of Neurology (Edt LP Rowland) Williams & Wilkins. Baltimore, Philadelphia, 1995, pp: 837–40.
2. Lauritzen M., Olesen J. Leao's spreading depression. Migraine (Edt JN Blau) Chapman & Hall. London, 1987, pp: 387–99.
3. Blau JN. Migraine: theories of pathogenesis. Lancet 339: 1202–7, 1992.
4. Lance JW. Current concepts of migraine pathogenesis. Neurology 43: 11–5, 1993.
5. Schlake HP., Bottger IG., Grotemeyer KH., Husstedt IW. Brain imaging with 1231–IMP–SPECT in migraine between attacks. Headache 29: 344–9, 1989.
6. Olesen J., Friberg L. Timing and topography of cerebral blood flow, aura and headache during migraine attacks. Ann Neurol 28: 791–8, 1990.
7. Hoshi H., Ohnishi T., Jinnouchi S. et al. Cerebral blood flow study in patients with Moyamoya disease evaluated by IMP SPECT. J Nucl Med 35: 44–50, 1994.
8. Bes A., Fabre N. Debit Sanguin cerebral et migraine sans aura. Pathol Biol (Paris) 40: 325–31, 1992.
9. Meyer JJ., Hata T., Imai A. Evidence supporting a vascular pathogenesis of migraine and cluster headache. Migraine (Edt JN Blau) Chapman & Hall. London, 1987, pp: 265–93.
10. Selby G. Investigating migraine: when, why and how. Migraine (Edt JN BLau) Chapman & Hall. London, 1987, pp: 77–89.
11. Messa C., Fazio F., Costa DC., Ell PJ. Clinical brain radionuclide imaging studies. Seminars in Nuclear Medicine Vol XXV: 130–2, 1995.
12. Lauritzen M., Olesen J. Regional cerebral blood flow during migraine attacks by Xenon–133 inhalation and emission tomography. Brain 107: 447–61, 1984.
13. Colamussi P., Giganti M., Cittanti C. et al. Significato ed utilita della SPET con 99m Tc–HM PAO nella diagnostica dell'emicrania con aura. Radiol Med (Torino) 89: 324–9, 1995.
14. Tomaiolo S., Stiglich F., Bonomo F. et al. La SPET con 99 m Tc–HM PAO nello studio dell'emicrania classica. Radiol Med (Torino) 81: 537–41, 1991.
15. Maini CL., Turco GL., Castellano G. et al. Cerebral blood flow and volume in symptom–free migraineurs: a SPECT study. Nuklearmedizin 29: 210–4, 1990.
16. Ramadan NM., Levine SR., Welch KMA. Interictal cerebral blood flow asymmetries in migraine with aura. Cephalalgia Supl 11: 42–43, 1991.
17. Gilkey S., Welch KMA, Ramadan NM. Major hemispheric flow asymmetry measured interictally differentiates migraine with and without aura. Cephalalgia Supl 13: 16, 1993.

18. Levin SR., Welch KMA. Cerebral blood flow asymmetries in headache–free migraineurs. Stroke 18: 1164–5, 1987.

19. İdiman F., Baklan B., Durak H. et al. Migrenli olgularda interiktal ve iktal Tc 99m–HM PAO SPECT ve EEG Brain Mapping. Neurol Bil D 12: 29–36, 1995.

20. Battistella PA., Ruffili R., Della RF. et al. 99m–Tc HM PAO SPECT in pediatric migraine. Headache 30: 646–9, 1990.

21. Friberg L., Olsen TS., Roland PE., Lassen NA. Focal ischaemia caused by instability of cerebrovascular tone during attacks of hemiplegic migraine. A regional cerebral blood flow study. Brain 110: 917–34, 1987.

22. Olesen J. The common migraine attack may not be initiated by cerebral ischaemia. Lancet 438–40, 1981.