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INTERICTAL SPECT IN THE PRESURGICAL EVALUATION IN EPILEPTIC PATIENTS WITH NORMAL MRI OR BILATERAL MESIAL TEMPORAL SCLEROSIS

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Abstract – The aim of this study was to evaluate the sensitivity of interictal compared to ictal SPECT in the lateralization of the epileptogenic focus in refractory temporal lobe epilepsy (TLE) patients that present with normal magnetic resonance imaging (MRI) or bilateral mesial temporal sclerosis (MTS). Thirty patients with TLE, for whom MRI examinations were normal or who presented with bilateral MTS, were retrospectively studied. Using a confidence interval of 95% and a level of significance for p-value <0.05, an estimated agreement rate of 73% with a minimum agreement rate of 57% was calculated comparing interictal and ictal SPECTs. In conclusion the interictal SPECT is only useful when associated with the ictal SPECT and does not substitute it in the localization of epileptogenic areas in patients with normal MRI or bilateral MTS.

KEY WORDS: epilepsy, SPECT, magnetic resonance imaging.

SPECT intercrítico na avaliação pré-cirúrgica de pacientes epiléticos com ressonância magnética normal ou esclerose mesial temporal bilateral

Resumo – O objetivo deste estudo foi avaliar a sensibilidade do SPECT interictal, em relação ao ictal, na lateralização do foco epileptogênico, de pacientes com epilepsia refratária de lobo temporal (ELT) que apresentam ressonância magnética (RM) normal ou esclerose mesial temporal (EMT) bilateral. Foram estudados retrospectivamente 30 pacientes com ELT, nos quais os exames de RM eram normais ou apresentavam EMT bilateral. Avaliada a sensibilidade do SPECT interictal em relação ao ictal, obtivemos taxa estimada de acerto de 73% com taxa mínima de acerto de 57%, adotando intervalo de confiança de 95% e índice de significância p<0,05. Conclui-se que o SPECT interictal é necessário apenas quando associado ao SPECT ictal, e não substitui a realização do ictal na localização da AE em pacientes com RM normal ou EMT bilateral.

PALAVRAS-CHAVE: epilepsia, SPECT, ressonância magnética.

Epilepsy is a chronic neurological disorder that affects from 1% to 3% of the worldwide population[1]. It is a syndrome defined by seizures that are the result of a disturbance in the brain's electrical activity. The treatment of epilepsy is, in general, symptomatic[2]. The use of medications provides complete control of seizures in around 80% of patients[3] and epilepsy surgery can be indicated for refractory cases[4]. Anterior temporal lobectomy with selective amygdalohippocampectomy, the commonest surgical intervention employed, provides good results in 90% of cases with total remission of the seizures in 66% of patients and a significant reduction in the frequency of seizures in the other 24%[5,6]. The success of surgery depends on the identification of the epileptogenic area (EA). Thus, examinations that enable the localization of the EA are necessary. Magnetic resonance imaging (MRI) is the most sensitive examination in the diagnosis of brain structure abnormalities[7] and is the first-line imaging technique in

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the presurgical evaluation of patients indicated for epilepsy surgery[8]. However there are temporal lobe epilepsy (TLE) patients who present with normal MRI or MRI demonstrating unilateral or bilateral temporal lesions[9]. In these cases other examinations are associated in order to identify the EA, including SPECT (Single Photon Emission Computed Tomography) and Prolonged Electroencephalographic and Video Monitoring (EEG monitoring).

SPECT identifies focal alterations in regional brain blood flow by the endovenous administration of ECD-^{99m}Tc (ethyl cysteinate dimer marked with technetium-^{99m}), followed by 3-dimension mapping of the distribution of this agent in the brain[10] performed in two phases; in the ictal and interictal periods. Refractory epilepsy patients generally present with a scintigraphic pattern of cerebral hypoperfusion[11,12], normal cerebral perfusion[13] or, infrequently, hyperperfusion[14] during the interictal period (outside of seizure) and cerebral hyperperfusion[11,15-17] of the same area during the ictal period (during the seizures).

Hence, this study aimed at evaluating the sensitivity of interictal SPECT compared with ictal SPECT in refractory TLE patients with normal MRI or bilateral MTS.

METHOD

Thirty patients (22 women and 8 men) with refractory TLE submitted to a presurgical assessment for epilepsy (PSAE) in the Epilepsy Surgical Center of Hospital de Base/FAMERP were included in this retrospective study. The mean age at the time of the surgery was 37.4 years (range: 22 to 58 years old). The MRI examinations of the patients were normal, that is, they did not demonstrate any structural alterations (11 patients) or demonstrated bilateral mesial temporal sclerosis (19 patients). The research Ethics Committee of Hospital de Base/FAMERP approved the study and all patients signed consent forms.

The brain MRI examination was performed using a 1.5T Philips Gyroscan Intera apparatus employing axial, coronal and sagittal plane sequences in FLAIR, T2 TSE, T1 SE and T1 FFE.

EEG monitoring consisted in the simultaneous registration of brain electrical activity with images acquired by video camera. The 64-channel Stellate system that performs this examination enables reformulation of images and prolonged recording of brain electrical activity.

The brain SPECT was performed after a venous injection of 740 to 1480 Mbq (20 to 40 mCi) of 99mTc-ethyl cysteinate dimer (ECD). In the critical study the injection was applied when patients were being monitored by prolonged EEG and presenting with clinical and electroencephalographic manifestations of epileptic seizures. In the intercritical examinations, the radioisotope was injected at least 24 hours after the last ictal activity documented by EEG monitoring. Images were acquired in a computed head scintillation camera (Elscient SP-4), equipped with a low-energy and highly-sensitive colimeter, using a 360° acquisition protocol with 6° intervals and scanning times of 30 seconds. The images were reconstructed with the use of filtered back projection followed by attenuation correction (1st order Chang method). Finally transaxial, coronal, temporal and sagital views were obtained, which were qualitatively evaluated, that is, assessed by SPECT color map changes by a specialist in nuclear medicine. The interictal SPECT was initially evaluated in isolation and then in association with the images of the ictal SPECT, with the lateralization of this latter analysis being considered the gold standard and thus employed in the surgical approach of the EA.

Using the normal MRI images or those with signs of bilateral hippocampal sclerosis, the interictal SPECT examinations were analyzed to provide an assessment of the sensitivity of this examination compared to the ictal SPECT. The unilateral test of proportions was applied with a confidence interval of 95% and a level of significance for p-value <0.05.

Table 1. Localization of interictal SPECT vs. ictal SPECT.

SPECT	Consistent	Inconsistent
Nº patients	22	8
%	73.33	26.67

RESULTS

Of the 30 patients who had normal MRI or signs of bilateral mesial temporal sclerosis, 29 had lateralization of EA and only one patient had bilateral EA identified by ictal SPECT.

For 22 patients, the interictal SPECT presented hypoperfusion in the temporal region coinciding with the area that demonstrated hyperperfusion in the ictal study (Table 1). Of the remaining eight patients, the interictal SPECT demonstrated: bilateral hypoperfusion and unilateral hyperperfusion in the ictal study in 2 cases; unilateral hyperperfusion associated with ipsilateral hyperperfusion in the ictal SPECT in 1 case and contralateral hyperperfusion in the ictal SPECT in another case. In 3 cases, the hypoperfusion in the interictal study was associated with contralateral hyperperfusion in the ictal SPECT. Only one case showed bilateral hyperperfusion in the ictal SPECT and unilateral hypoperfusion in the interictal SPECT (Table 2).

The statistical evaluation of the sensitivity of the interictal SPECT when compared to the ictal SPECT showed an estimated agreement rate of 73%, varying between 54% and 88% (p-value=0.016) and a minimum agreement rate of 57% (p-value=0.008).

DISCUSSION

SPECT, in particular during the ictal phase, is considered an important method in the detection of the EA[17]. A systematic review of the efficacy of neuroimaging techniques to locate the EA published in 2006 reported that the ictal SPECT was the most efficacious to locate the EA

Table 2. Identification, MRI, EEG monitoring, ictal SPECT, interictal SPECT.

Case	Gender	Age at surgery	MRI	EEG monitoring	Ictal SPECT	Interictal SPECT
1	F	40	R/L	R	R	R
2	F	45	R/L	R	R	R/L
3	F	36	R/L	L	L	Hyper L
4	F	39	R/L	L	L	L
5	F	37	R/L	R	L	L
6	M	54	R/L	R	R	R
7	F	28	R/L	L	L	L
8	F	53	R/L	L	L	L
9	F	36	R/L	R	R	R
10	F	31	R/L	R	R	L
11	M	27	R/L	R	R	R
12	F	22	R/L	L	L	L
13	F	33	R/L	R	R	R
14	F	34	R/L	R	R	R
15	M	53	R/L	R	R	Hyper L
16	F	58	R/L	R	R	R/L
17	F	31	R/L	R	R	R
18	F	57	R/L	R	R	L
19	F	45	R/L	R	R	R
20	M	28	No	R	R	L
21	F	42	No	L	L	L
22	F	42	No	L	L	L
23	M	23	No	R	R	R
24	F	43	No	R	R	R
25	F	31	No	R	R/L	L
26	M	30	No	R	R	R
27	M	20	No	R	R	R
28	M	24	No	R	R	R
29	F	39	No	L	L	L
30	F	43	No	L	L	L

F: female; M: male; MRI: magnetic resonance imaging; EEG monitoring: prolonged video electroencephalographic monitoring; R: right; L: left; Hyper: hyperperfusion; No: normal.

in patients with TLE[17]. In a meta-analysis of the sensitivity of SPECTs and their diagnostic value in the detection of EAs in patients with TLE, a greater sensitivity was observed for the ictal SPECT (97%), followed by the post-ictal (75%) and interictal (44%) SPECTs[18].

Despite of the great variation reported in the literature about the sensitivity of the interictal SPECT in identifying lateralization of the EA (35–80% – with a mean value of 50%)[19], this examination is frequently used in epilepsy treatment centers as it is a simple technique that is readily available with less necessity of specialized staff when compared to the ictal study[20].

An association between hypoperfusion in the interictal SPECT and hyperperfusion in the ictal SPECT was the commonest finding during the PSAE[16]. However we found variations such as hyperperfusion in the interictal SPECT, even when no seizures were identified within the previous 24 hours or of Periodic Lateralized Epileptiform Discharges (PLED), which may be responsible for this change in the scintigraphic pattern as has been reported in publications in approximately 5% of interictal studies[14]. The finding of interictal study images with bilateral hypoperfusion and hypoperfusion contralateral to ictal hyperperfusion demonstrate the necessity of other diagnostic approaches in

dubious cases. Hence, the best option in these cases is the use of ictal EEG for the preoperative location of EAs[21].

In respect to the ictal SPECT, bilateral hyperperfusion was found in only one patient and interestingly this patient's interictal SPECT demonstrated hypoperfusion contralateral to the EEG monitoring findings and normal MRI. This fact may be explained by the hypothesis that the interictal SPECT can evidence dysfunctional areas related to the EA, which do not always represent the primary focus[22].

The ictal SPECT is the best technique of functional imaging when the MRI does not define the EA[19]. Thus, we should consider that the high rate of correct lateralization of this technique contributes to the interictal SPECT evaluation as, the result of the ictal SPECT is obtained after a combined analysis with interictal SPECT images[23].

In spite of the advantages inherent in interictal SPECT evaluations and the good results in sensitivity, as seen in this study, we can not consider this approach in isolation as there is discordance when compared with the ictal examination and due to its considerably lower sensitivity in TLE patients.

Hence, the interictal SPECT is more specific to locate EAs in patients that present with a normal MRI or bilateral MTS only when evaluated in association with the ictal SPECT and so in these cases it can not substitute the ictal SPECT.

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