International Journal of Biomedicine 14(1) (2024) 88-92
http://dx.doi.org/10.21103/Article14(1)_OA13

ORIGINAL ARTICLE

Radiology

INTERNATIONAL JOURNAL OF BIOMEDICINE

Comparison of Ictal SPECT with ^{99m}Tc-HMPAO versus MRI for the Epileptic Seizure Onset Zone Detection in Saudi Patients

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Abstract

Background: In the presurgical evaluation of patients with drug-resistant epilepsy, magnetic resonance imaging (MRI) and ictal brain perfusion SPECT with the chemical microspheres ^{99m}Tc-HMPAO are widely used for diagnosing the seizure onset zone (SOZ). For both modalities, there is theoretical controversy over favoring one over the other. This study aimed to compare the performance of ^{99m}Tc-HMPAO SPECT with MRI for SOZ identification in EEG-proved epileptic Saudi patients.

Methods and Results: For this observational retrospective study, the database of the nuclear medicine departments at the Prince Sultan Military Medical City (PSMMC) and King Abdullah bin Abdulaziz University Hospital (KAAUH) were searched for male and female patients with suspected unifocal epilepsy in whom ictal brain perfusion SPECT and MRI had been performed for presurgical evaluation. A total of 14 adult epileptic patients above 18 years were included who have undergone SPECT scans using 99mTc-HMPAO and MRI between Jan 2014 and Dec 2021. ^{99m}Tc-HMPAO SPECT and MRI scans were performed simultaneously for each patient, and there was almost general agreement that ^{99m}Tc-HMPAO SPECT accurately localized and detected the SOZ in 12/14 patients (sensitivity 85.71%). It was superior to MRI, which detected and localized the SOZ in only 7/14 patients (sensitivity 50.0%). Unfortunately, the specificity of ictal brain perfusion SPECT, by using ^{99m}Tc-HMPAO in seizure localization in epileptic patients, was not detected due to the shortage of data that led to all the EEG findings being 100% positive.

Conclusion: This study reported that ictal SPECT using ^{99m}Tc-HMPAO provides more valuable information about SOZ localization than MRI. However, future studies with a larger sample size are needed to assess the specificity of ^{99m}Tc-HMPAO SPECT in detecting the SOZ.**(International Journal of Biomedicine. 2024;14(1):88-92.)**

Keywords: epilepsy • seizure• perfusion • ^{99m}Tc-HMPAO • ictal SPECT

For citation: Mansour S, Algaloud G, Aldhawi M, Alamri M, Baghdadi R, Alhoshan S, Khayyat S, Alsuhibani W, Alamri R, Faqeeh G. Comparison of Ictal SPECT with ^{99m}Tc-HMPAO versus MRI for the Epileptic Seizure Onset Zone Detection in Saudi Patients. International Journal of Biomedicine. 2024;14(1):88-92. doi:10.21103/Article14(1)_OA13

Abbreviations

EEG, electroencephalography; **ETE**, extratemporal epilepsy; **EZ**, epileptogenic zone; **MRI**, magnetic resonance imaging; **NE**, neocortical epilepsy; **SPECT**, single photon emission computed tomography; **SOZ**, seizure onset zone; **^{99m}Tc-HMPAO,** ^{99m}Tc-labeled tracers hexamethyl propyleneamine oxim; **TLE**, temporal lobe epilepsy.

Introduction

Epilepsy is a chronic medical disorder or condition characterized by unprovoked recurrence of seizures, which are paroxysmal events owing to neuron hyperexcitability with synchronicity or abnormal neuronal discharges.[1,2] This neurological disease results in abnormal elevations of brain activity, unusual behaviors and sensations, loss of

consciousness, and repetitive seizures.[3] Globally, with no socio-demographic boundary, it affects about 50 million individuals, and former reports have estimated epilepsy point prevalence to be 4-10/1000 individuals.[4,5]

In cases with suspected focal epilepsy, brain surgery is a therapeutic choice for patients who do not respond efficiently to drug treatment.[6,7] To all patients with focal epilepsy, it was concluded that "assessment for surgical selection should be offered where the first 2 antiepileptic drugs have failed."[7,8] The aim of epilepsy surgery is to remove the epileptogenic zone (EZ), defined as the cortex area that needs to be disconnected or removed to completely abolish seizures.[9] For surgery planning, since the EZ clearly is not an operational concept, the combination of 5 varied operationally detected cortical zones based on noninvasive tools is usually used in presurgical evaluation:[10] 1) the "functional deficit zone" that is not functioning normally in the interictal period and can be derived by neuropsychological and neurological evaluation, 2) the "epileptogenic lesion" defined as a single discrete macroscopic lesion causing the seizures that is visible on the structural MRI, 3) the "symptomatogenic zone" that can be localized by initial seizure semiology and that causes the initial ictal symptoms, 4) the "irritative zone" that generates interictal spikes and can be localized by interictal scalp-EEG, and 5) the SOZ that initiates seizures and can be localized by ictal scalp-EEG.(7) If all 5 zones can be reliably delineated and all point to the same brain region as EZ, additional presurgical investigation is usually not required.[2] If one or more of the zones point to different brain regions or cannot be reliably detected, more investigations might be helpful, including nuclear imaging,[11,12] to localize the SOZ or to plan the placement of intracranial EEG electrodes to achieve this aim.[7]

^{99m}Tc-HMPAO brain SPECT is a nuclear imaging tool commonly used in epilepsy cases for presurgical evaluation with discrepant or uncertain standard pointers.[13,14] ^{99m}Tc-HMPAO, after intravenous injection, is fully extracted from arterial blood (like a chemical microsphere) to tissue through a single capillary passage and then is locally retained in the tissue.[7] In tissue, its fixation is because of glutathione-dependent metabolism to hydrophilic forms and binding to non-diffusible cell components.[15] The aim of the ictal brain SPECT is to detect SOZ by its regional hyperperfusion.[16] Compared to regional hypoperfusion between seizures, regional hyperperfusion is not only more sensitive for SOZ detection, but is also more specific, specifically in cases with any lesion types (including non-epileptogenic lesions) that may, independent of epileptic activity, cause regional hypoperfusion.[7,17]

Against this introduction, the aim of the current study was to evaluate and compare the performance, effectiveness, and diagnostic accuracy of ictal brain perfusion SPECT with ^{99m}Tc-HMPAO and MRI in localizing the SOZ in epileptic Saudi patients.

Materials and Methods

For this observational retrospective study, the database of the nuclear medicine departments at the Prince Sultan Military Medical City (PSMMC) and King Abdullah bin Abdulaziz University Hospital (KAAUH) were searched for male and female patients with suspected unifocal epilepsy in whom ictal brain perfusion SPECT and MRI had been performed for presurgical evaluation. All patients were diagnosed with EEG, and patients were excluded when the tracer injection latency, after electrical seizure onset, was >120 seconds.[18] Also, any adolescent or pediatric epileptic patients and any patients who have had SPECT scans without MRI scans were excluded. A total of 14 adult epileptic patients above 18 years were included who have undergone SPECT scans using ^{99m}Tc-HMPAO and MRI between Jan 2014 and Dec 2021.

Sample size

The statistical calculation was done by using an online calculator.[19] The obtained theoretical sample size, a 95% confidence interval, and a total population size of 30 from multiple hospitals were inserted in the online calculator. Therefore, according to the online calculator, the theoretical sample size is 28 epileptic patients who have undergone a brain perfusion Ictal ^{99m}Tc-HMPAO SPECT

Ictal brain perfusion SPECT

While the patient was undergoing video-EEG monitoring, ictal tracer injections were administered during a seizure in the inpatient epilepsy unit. The patient was transported to a quiet and dimly lit room. Within one hour, patients were positioned supine and their heads secured to the table to ensure all the brain and cerebellum were included in the image.[20] SPECT was acquired with a double-head gamma camera (Siemens Symbia T2, Germany) equipped with low-energy ultra-high-resolution collimators and angular steps of 2.8-3.0°. The total acquisition time was around 30 minutes, and the rotation radius was 15.3±1.6cm. Five million count events, or more, should be detected. Furthermore, SPECT images are reconstructed by iterative reconstruction using a low pass (e.g. Butterworth) filter with the brain processing protocol, generating the trans-axial, sagittal, and coronal slices.[20] The resulting SPECT images were normalized stereotactically using the statistical parametric mapping software (version SPM12). All images were interpreted twice.

Magnetic resonance imaging

This study used MRI as another non-invasive method to detect epilepsy. Sequences of MRI images were combined to enhance sensitivity and specificity in identifying probable anatomical abnormalities that are caused by seizure disorders. MRI protocol, along with the procedures for adults with epilepsy, was done at 3T. If the physicians viewed the tumor, they gave contrast and did pre- and post-T1 AX (COR T2 / FLAIR perpendicular to the long axis of the hippocampus). Pulse sequence was: 1) Coronal T2 whole brain 2mm/0.4, 2) Coronal FLAIR, 3) Axial T1 3D with reformats, 4) Axial DWI, 5) Axial GRE (SWI), 6) Axial T2, 7) Axial FLAIR and 8) Coronal (optionally).

Statistical analysis was performed using statistical software package SPSS version 21.0 (Armonk, NY: IBM Corp.). Baseline characteristics were summarized as frequencies and percentages for categorical variables. For the descriptive analysis, results are presented as mean (M) ± standard deviation (SD). Sensitivity, Specificity, and Predictive Values for the study tests were calculated.

Results

Baseline characteristics of the study cases are presented in Table 1. ^{99m}Tc-HMPAO SPECT and MRI scans were performed simultaneously for each patient, and there was almost general agreement that ^{99m}Tc-HMPAO SPECT accurately localized and detected the SOZ in 12/14 patients (sensitivity 85.71%; Table 2). It was superior to MRI, which detected and localized the SOZ in only 7/14 patients (sensitivity 50.0%; Table 3).

Table 1.

Baseline characteristics of the study patients.

Variable	Value
Total number of patients	14
Gender (male/female)	8/6
Age	32.57±14.86
Height (cm)	160.14±8.97
Weight (kg)	71.54±17.03
Positive EEG (number/percentage)	14 (100%)

Table 2.

Cross-tabulation of the EEG × ^{99m}Tc-HMPAO SPECT results

			^{99m}Tc-HMPAO SPECT	
			Positive	Negative
			n=12	n=2
EEG	Positive	n=14	12	2
	Negative	n=0	0	0

Table 3.

Cross-tabulation of the EEG × MRI scan results.

			MRI	
			Positive	Negative
			n=7	n=7
EEG	Positive	n=14	7	7
	Negative	n=0	0	0

Most of the patients (6/7) detected by MRI were also detected accurately by ^{99m}Tc-HMPAO SPECT. But ^{99m}Tc-HMPAO SPECT detected 6/7 cases that MRI did not detect (Table 4).

Table 4.

Cross-tabulation of the ^{99m}Tc-HMPAO SPECT × MRI scan results.

			^{99m}Tc-HMPAO SPECT	
			Positive	Negative
			n=12	n=2
MRI	Positive	n=7	6	1
	Negative	n=7	6	1

Discussion

In the epileptic brain, SPECT, PET, and MRI are all used to image abnormalities.[21,22] Comparison of these modalities is difficult because they assess different aspects of the epileptic process, perfusion, metabolism, and structure.[23] In the localization of epileptogenic foci, these methods have been studied extensively as individual techniques, but only a few comparative studies have been performed.[24] Few studies have been conducted to compare these techniques in the presurgical diagnosis of lesional and nonlesional epilepsy.[21,25,26] SPECT with ^{99m}Tc-HMPAO can help in localizing the SOZ, as epileptic activity is related to a significant elevation in blood flow in affected cortical areas.[27] This study aimed to compare the diagnostic performance and clinical utility of ^{99m}Tc-HMPAO SPECT with MRI in localizing the SOZ in epileptic Saudi patients, all of which are positive (100%) epileptic diagnosis and verified by EEG.

The primary finding of the current study is that ^{99m}Tc-HMPAO SPECT (sensitivity 85.71%) was superior to MRI (sensitivity 50.0%) in presurgical detecting and localizing of the SOZ in epileptic Saudi patients. Unfortunately, the specificity of ictal brain perfusion SPECT, by using ^{99m}Tc-HMPAO in seizure localization in epileptic patients, was not detected due to the shortage of data that led to all the EEG findings being 100% positive.

Our results agreed with previous studies. Lee et al.[25] evaluated the sensitivity of ^{99m}Tc-HMPAO SPECT for localizing the SOZ among 40 patients (17 with temporal lobe epilepsy (TLE) and 23 with neocortical epilepsy (NE)). They reported that ^{99m}Tc-HMPAO had 89% sensitivity in localizing the TLE and 70% sensitivity among patients with neocortical epilepsy. A review by Spencer et al.[23] suggested that compared to MRI, SPECT has higher sensitivity in extratemporal epilepsy (ETE) detection (60% vs. 43%). Also, SPECT was superior to MRI in TLE diagnosis (66% for SPECT and 55% for MRI).[23] They suggested that the highest diagnostic specificity and sensitivity were obtained by ictal imaging with SPECT (81% in ETE, 90% in TLE). In patients with occipital lobe epilepsy, ^{99m}Tc-HMPAO ictal SPECT was reported to be helpful in lateralizing EZs, even in patients with ambiguous MRI results.[28]

A study by Won et al.[24] included 118 patients who performed surgery for intractable epilepsy, and they retrospectively compared the ability of MRI with ictal ^{99m}Tc-HMPAO SPECT and invasive EEG to localize the epileptogenic focus. Results revealed that MRI was concordant with ictal SPECT in 58% of patients. Using pathologic diagnosis as the standard, MRI and ictal SPECT correctly lateralized the lesion in 72% and 73% of patients, respectively. Among patients who underwent EEG, MRI was concordant with EEG in 47% compared to 58% in the case of ictal SPECT. Among patients with normal MRI results, ictal SPECT accurately lateralized lesions in 55%.[24]

There were some limitations of the study that should be mentioned. This study was retrospective, which led to a lack of data on some patient variables. To avoid retrospective inclusion-related potential selection bias, only very liberal eligibility criteria were applied. Another limitation is the

small number of cases. This is because, in the hospitals of Riyadh, researchers expect that the data will be collected from another ictal detecting technique known as PET. Thus, the data are only collected from one hospital containing a few cases (n=14), which restricted this study from reaching the calculated sample size 28. Finally, the specificity could not be calculated due to the fact that the EEG data did not exhibit negative results for epilepsy, perhaps because of the shortness of sample size.

Conclusion

This study reported that ictal SPECT using ^{99m}Tc-HMPAO provides valuable information about SOZ localization with higher sensitivity, 85.17%, and diagnostic accuracy, 85.17%, compared to MRI. Although invasive EEG detected 100% of patients, ^{99m}Tc-HMPAO SPECT is not a redundant method, and combining refined imaging techniques findings holds great promise in epilepsy diagnosis and localization corresponding to MRI. Future studies with a larger sample size are needed to assess the specificity of ^{99m}Tc-HMPAO SPECT in detecting the SOZ, and more studies should be considered.

Competing Interests

The authors declare that they have no competing interests.

Ethical Considerations

The ethical approval of the study protocol was obtained from the Institutional Review Board (IRB) at Princess Nourah bint Abdulrahman University. All data were gathered from patients' medical records, and all patients' information was confidentially coded.

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