Original Research Article

Radiological study of MR spectroscopy parameters in temporal lobe epilepsy patients at a tertiary hospital

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Abstract

Background: Temporal lobe epilepsy (TLE) is the most common form of partial epilepsy. MRS (MR spectroscopy) is a noninvasive technique capable of providing metabolic information about different tissues; also it enables tissue characterization on a biochemical level surpassing that of conventional magnetic resonance imaging (MRI). It detects abnormalities that are invisible to MRI because metabolic abnormalities often precede structural changes. In present study we evaluated MR spectroscopy parameters in patients with temporal lobe epilepsy at a tertiary hospital. **Material and Methods:** Present observational, prospective study was done in patients 19-60 years, with clinical diagnosis of Temporal lobe epilepsy (TLE) had been made neurologist by previous clinical and EEG records. Mean age was 36.6 ± 5.6 years. 60 % patients were uncontrolled epilepsy, even on medications. Clinical and EEG diagnosis related to temporal lobe epileptic activity suggestive of right-side involvement (60%), left side involvement (27%) and bilateral involvement (13%). The mean values of both NAA/Cr and Cho/Cr of the bilateral hippocampus of Temporal Lobe Epilepsy (TLE) patients were minimally reduced in compared to the reference mean value of NAA/Cr and Cho/Cr respectively. The mean NAA/Cho value of right hippocampus of Temporal Lobe Epilepsy (TLE) patients was significantly reduced and that of left hippocampus was minimally increased when compared to that of the reference mean values. On MRS, right side temporal lobe epilepsy (53%), left side temporal lobe epilepsy (33%), bilateral temporal lobe epilepsy (10%) and normal (3%) findings were noted. **Conclusion:** MR spectroscopy has demonstrated consistent metabolic abnormalities in temporal lobe epilepsy by detecting abnormal spectra of various brain metabolites. The side of maximum reduced NAA/Cho + Cr ratio often coincides with the side of EEG abnormality.

Keywords: MR spectroscopy, temporal lobe epilepsy, NAA/Cr, NAA/Cho.

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INTRODUCTION

Seizure is defined as a paroxysmal alteration in neurologic function resulting from abnormal excessive neuronal electrical activity and usually a symptom of focal or generalized brain abnormality.[1] Epilepsy is a common chronic neurological disorder that is characterized by recurrent unprovoked seizures. These seizures are transient signs and/or symptoms due to abnormal, excessive or synchronous neuronal activity in the brain.[2] Temporal lobe epilepsy (TLE) is the most common form of partial epilepsy. Two types of non-lesional medial TLE are TLE with mesial temporal lobe sclerosis (60–70% ,

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characterized by an atrophied hippocampus with MR signal abnormalities and severe neuronal loss in the histological examination), and TLE with a normal appearing hippocampus on the MRI (30–40%, no or mild neuronal loss in the histological examination.[2,3] Various pathologies of epilepsy include: inflammatory/ infectious, hippocampal sclerosis, malformations of cortical development, tumors and tumor- like conditions, prenatal and perinatal destructive injury, vascular malformations, neurocutaneous disorders, metabolic disorders, trauma and degenerative disorders.[4] Magnetic resonance imaging (MRI) gives precise localization and histological nature of lesions and subsequently, this is of immense help to both clinicians as well as neurosurgeons in their attempt to achieve a faster and more accurate method of discovering the nature of the pathologies.[5] MRS (MR spectroscopy) is a noninvasive technique capable of providing metabolic information about different tissues; also it enables tissue characterization on a biochemical level surpassing that of conventional magnetic resonance imaging (MRI). It detects abnormalities that are invisible to MRI because metabolic abnormalities often precede structural changes.[6] In present study we evaluated MR spectroscopy parameters in patients with temporal lobe epilepsy at a tertiary hospital.

MATERIAL AND METHODS

Present observational, prospective study was done at Department of Radiodiagnosis, XXX medical college and hospital, XXX. Study was conducted between July 2018 to June 2020 (18 months).

Inclusion criteria

Patients 19-60 years, with clinical diagnosis of Temporal lobe epilepsy (TLE) had been made neurologist by previous clinical and EEG records

Exclusion criteria

- Patients with contraindications to MRI like cardiac pacemakers, cochlear implants etc.
- Pregnancy
- Abnormalities in brain
- Claustrophobic patients

The initial evaluation included detailed history of the present and past, general and systemic examination, relevant laboratory and biochemical tests. EEG examination was done in all patients.

The patients underwent MR imaging in Symphony Maestro 1.5 T MR scanner from Siemens Ltd. The examination was performed with a dedicated head coil. Sedation or general anesthesia was used for uncooperative patients. Spectroscopic evaluation was done as follows. Two-dimensional fast low angle shot (FLASH) images (200/6) were acquired in coronal, sagittal and oblique transverse planes for localisations of epileptic focus. Single voxel Proton MR Spectra were obtained with an 8 ml voxel (20x20x20 mm3) in each of the medial temporal lobes including a part of the hippocampus. Attention was kept on the reproducibility of the voxel position with respect to the brain stem and hippocampus. Water suppression was effected by a 90-degree Gaussian pulse. An interactive shimming was subsequently performed to obtain a least FHWM (6-8) and the highest possible integral value. Spectra were acquired using a spin echo sequence with an echo time (TE) of 135 msec and a Repetition Time (TR) of 1365 ms and number of excitation as 256. To compensate for eddy current artefacts, we obtained a reference scan with the same scan parameters but with eight acquisitions and with no water suppression. Automatic phase correction was done. Three resonances of importance could be identified, viz NAA at 2 ppm, Cr at 3 ppm and Cho at 3.2 ppm. These peaks were quantified by simple triangulation as well as automatic calculation using the proprietary software. Metabolite signal intensities and metabolite ratios like NAA/ (Cho+Cr), NAA/Cr, NAA/Cho were calculated and analyzed in reference to the standard values. Radiological diagnoses were made based on cumulative findings. Statistical analysis was done using descriptive statistics.

All abnormal patients were followed up by clinical examination, response to medical or surgical treatment, histopathology or by follow up scans.

RESULTS

During study period 30 patients with temporal lobe epilepsy were studied. Female patients were 63%. Mean age was 36.6 ± 5.6 years. 60 % patients were uncontrolled epilepsy, even on medications. Clinical and EEG diagnosis related to temporal lobe epileptic activity suggestive of right-side involvement (60%), left side involvement (27%) and bilateral involvement (13%).

Table 1: Baseline clinical data.

Characteristic	Number of patients (%) / Mean ± SD
Gender	
Male	11 (37%)
Female	19 (63%)
Age in years (Mean ± SD)	36.6 ± 5.6
The duration of the disease illness at time of MRS studies in years (Mean ± SD)	6.5 ± 4.3

Medication	
Controlled	12 (40%)
Uncontrolled	18 (60%)
Clinical and EEG diagnosis related to temporal lobe epileptic activity	
Right side	18 (60%)
Left side	8 (27%)
Bilateral	4 (13%)

The mean values of both NAA/Cr and Cho/Cr of the bilateral hippocampus of Temporal Lobe Epilepsy (TLE) patients were minimally reduced in compared to the reference mean value of NAA/Cr and Cho/Cr respectively. The mean NAA/Cho value of right hippocampus of Temporal Lobe Epilepsy (TLE) patients was significantly reduced and that of left hippocampus was minimally increased when compared to that of the reference mean values.

Table 2: Mean values of the metabolites in MRS study

Variables	NAA	CR	Cho	NAA/CR+Cho	NAA/CR	NAA/Cho
Mean ± SD	1.9 ± 0.8	2.9 ± 0.8	2.87 ± 0.8	2.7 ± 0.4	1.7 ± 0.4	1.2 ± 1.84
Right	1.9 ± 0.6	3.1 ± 0.5	2.7 ± 0.4	2.9 ± 0.5	1.3 ± 0.5	1.3 ± 0.3
Left	2.0 ± 0.3	2.8 ± 0.7	2.8 ± 0.7	2.7 ± 0.6	1.2 ± 0.6	0.9 ± 0.4

On MRS, right side temporal lobe epilepsy (53%), left side temporal lobe epilepsy (33%), bilateral temporal lobe epilepsy (10%) and normal (3%) findings were noted.

Table 3: MRS diagnosis related to temporal lobe epileptic activity

Side	Number of patients	Percentage (%)
Right side	16	53%
Left side	10	33%
Bilateral	3	10%
Normal	1	3%

DISCUSSION

The main purposes of neuroimaging in epilepsy patients are to identify underlying structural or metabolic abnormalities that require specific treatment and to aid in formulating a syndromic or etiologic diagnosis. Neuroimaging is even more important for those patients who have medically intractable seizures. The majority of temporal lobe seizures originate in the mesial temporal structures, primarily in the hippocampus, para-hippocampal gyrus and amygdala.[7] The most important tools in the diagnosis of temporal lobe epilepsy are the clinical neurological features and the intensive video-EEG monitoring, neuropsychological evaluation, brain magnetic resonance imaging (MRI), positron emission tomography (PET), magnetic resonance spectroscopy (MRS) and single photon emission computed tomography (SPECT) imaging are diagnostic approaches in the assessment of epileptic foci.[8] Accurate diagnosis of the cause of seizures is crucial for finding an effective treatment. With its high spatial resolution, excellent inherent soft tissue contrast, multiplanar imaging capability, and lack of ionizing radiation, MRI has emerged as a versatile tool in the evaluation of patients with central nervous system disorders.[5] Magnetic resonance spectroscopy (MRS) is an analytical method used for the identification and quantification of metabolites. It differs from conventional magnetic resonance imaging (MRI) since it provides physiological and chemical information instead of only anatomy.[9] Temporal lobe epilepsy (TLE) is the most common cause of focal epilepsy; reduction in NAA concentration and NAA/Cho + Cr ratio is observed in TLE, which reflects the neuronal damage.[9] Proton magnetic resonance spectroscopy (^{1}H-MRS) is a sensitive, non-invasive technique that provides metabolic information on the status of viability of neurons and on the membrane metabolism of the brain. Hydrogen 1 MR spectroscopic imaging depicts the anatomic distribution of metabolite signals from N-acetyl aspartate (NAA), which is a putative neuronal marker, and creatine (Cr) and choline (Cho)-containing compounds. Previous studies have shown that interictal NAA is reduced in the ipsilateral mesial temporal lobe, assisting in the lateralization of TLE even in cases with negative MR images.[10] Use of an asymmetry index improved the lateralizing capacity of the parameter NAA/Cho + Cr derived from the mesial temporal lobes of patients with unilateral temporal lobe epilepsy by means of single voxel proton MR spectroscopy as frequent bilateral temporal lobe involvement was found.[11] Similar findings were noted in present study. Vielhaber *et al*. revealed that decreased NAA peak in MTLE, especially in the hippocampal sclerosis-Ammon's horn sclerosis might be due to the impaired mitochondrial function, not correlated with the neuronal cell losses.[12] In previous studies, most of the authors explained and dedicated on the importance of significantly decreased NAA/Cr and NAA/Cho + Cr ratios

of the epileptic foci in the temporal lobes. They believed that "both ratios were strongly correlated with the lateralization and localization of the epileptogenic area, degree of seizures and epileptic discharges''[8,13,14] Similar findings were noted in present study. Reduced NAA levels probably reflects metabolic impairment due to repeated seizures. Regardless of the origin of the N-acetyl aspartate signal reduction, it appears to be a good indicator in epileptic focus and could therefore be useful diagnostic marker.[14] Meta-analysis of 1H MR spectroscopy literature comprising 22 studies (19 performed with 1.5-T units) indicates that ipsilateral MR spectroscopy abnormality is associated with good outcome following surgery. Decreased tNAA/tCr and/or tNAA/(tCr + tCho) ratios were the most common MR spectroscopy indexes for epileptogenic zone.[15] H-MRS can give sensitive and reliable results, may aid in the lateralization of epileptic foci and the diagnosis of MTLE. Lateralization is a procedure that is used to determine the hemisphere which is responsible for the genesis of seizures. MR imaging demonstrates atrophy or changes in hippocampal T2-weighted signal intensity in 30% to 90% of patients. [1]H-MRS reveals abnormal low resonance intensities of NAA/Cr with in one or both temporal lobes of patients of temporal lobe epilepsy, with greater reduction in intensities seen on the side from which the seizure originates.[16] Patients with mesial temporal lobe epilepsy typically demonstrate extensive reduction in NAA in the temporal lobe and insular cortex, whereas symmetrical generalised reduction of NAA can occur in both cerebral hemispheres as demonstrated on multi-voxel MR spectroscopy, and probably reflects metabolic impairment due to repeated seizures. Therefore NAA asymmetry in the temporal lobe and insular cortex robustly lateralises the seizure focus.[17] Neurotransmitter MRS studies have potential therapeutic impact in seizure patients. Glutamate and γ amino-butyric-acid(GABA) can be measured using MRS editing techniques. Intracellular glutamate concentrations remain elevated in the epileptogenic hippocampus and neocortex, and contribute to the epileptic state by increasing cellular excitability.[18] Multivoxel MR spectroscopy can achieve higher sensitivity and better spectral quality, improving lateralization of the seizure focus.[19] Intracranial EEG recordings are often used to further localize the epileptic focus when seizure focus localization is ambiguous and to assist with mapping the lateral cortical areas in TLE patients with normal MRI scans.[20,21]

CONCLUSION

MR spectroscopy differs from conventional magnetic resonance imaging (MRI) since it provides physiological and chemical information instead of only anatomy. MR spectroscopy has demonstrated consistent metabolic abnormalities in temporal lobe epilepsy by detecting abnormal spectra of various brain metabolites. The side of maximum reduced NAA/Cho + Cr ratio often coincides with the side of EEG abnormality.

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