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Original Research Article

MR Spectroscopy and Post-Operative Histopathology in Diagnosis of Intra-Cranial Space Occupying Lesions – A Comparative Study

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Abstract

Aim: The aim of the present study was to assess the various MR Spectroscopy findings in Intra-cranial space occupying lesions that help to make a clinical diagnosis and effectiveness of MR Spectroscopy in diagnosing Intra-cranial space occupying lesions and its accuracy as confirmed by post-operative histopathological findings.

Methods: The present study was conducted in the Department of Neurosurgery, Government TD Medical College, Alappuzha, Kerala. 18 months after Institutional Ethics Committee approval. Data was collected for a period of 12 months and analysis was done at the end of 12 months. All patients admitted with intra-cranial space occupying lesion and undergoing surgery under Department of Neurosurgery, Government TD Medical College, Alappuzha, Kerala and who were willing to participate in the study.

Results: It was observed that out of the total 50 cases participated in the study, most of the cases i.e. 9 (18%) each , belong to the age group of 31-40 years and 51-60 years, followed by 8 (16%) each in age group of 41-50 years and 61-70 years. Out of total 50 cases participated in the study, 32 (64%) were males and 18 (36%) were females, with male to female ratio 1.8:1. Most common diagnosis among the participated cases was Glioma in 17 (34%) cases followed by meningioma in 11 (22%) cases, abscess in 3 (6%) cases and metastasis, pituitary tumour, lymphoma, pineal tumour each in 2 (4%) cases. After Histopathological examination, most common finding observed was Glioma in 17 (34%) cases followed by meningioma in 11 (22%) cases.

Conclusion: The present study has shown MRS can differentiate neoplastic from the non-neoplastic intracranial lesions, as well as diagnose various lesions based on metabolite ratios and spectrum, helps in better tissue characterization improving the accuracy and confidence level of neurosurgeons in their diagnosis.

Keywords: MR Spectroscopy; Intra-Cranial space occupying lesions; Data accuracy; metabolites; Specificity; Sensitivity

Introduction

The prognosis of patients with brain tumors improves if the tumor is discovered early. [1] Gliomas are one of the most common types of brain tumors, with a five-year survival rate of less than 5%. To plan, predict, and respond to treatment, it is important to accurately predict the grade. [2] Severe problems are associated with stereotactic brain biopsies needing definitive histology in determining the grade of malignancy, including seizures, temporary or permanent neurological damage, and intracranial bleeding. [3] A sample error, which can lead to a faulty diagnosis, is also a possibility. [1] Hence, neuroimaging, such as computed tomography (CT) and magnetic resonance imaging (MRI), can be used to detect and grade brain tumors. [4] Lesion aggressiveness is indicated by MRI findings such as postcontrast enhancement, necrosis inside the tumor, and substantial perilesional edema or mass impact. It is possible to use these characteristics to determine the grade of gliomas.

Biochemical indicators in the brain can be measured by magnetic resonance spectroscopy (MRS), which can be used in conjunction with standard MRI to predict the grade of the identified lesions. Resonance measurements of different metabolites in the brain can then be used to determine the amplitudes of these reactions. [5] MRS has high sensitivity and

specificity in distinguishing malignant and benign lesions. As the grade of malignancy increases, so does the concentration of choline (Cho)-containing substances and metabolites. [6] However, because the normal brain parenchyma is replaced by tumor cells, the normal metabolites of the brain tend to diminish. Normal brain tissue produces N-acetyl aspartate (NAA), which is considered to be a metabolite. [7]

Magnetic resonance imaging (MRI) is an excellent method for anatomical and structural diagnosis of the brain, but it does not provide functional or metabolic information. [8] Magnetic resonance spectroscopy (MRS) is used to detect the metabolic and biochemical profile of brain areas. Magnetic resonance spectroscopy (MRS) is a rapidly developing field of neuroimaging that allows non-invasive in vivo analysis of metabolites. It selectively excites a small volume of tissue (voxel) using gradients, then records the free induction decay (FID) and produces a spectrum from the FID originating from that voxel. [9] MRS is an analytical method used in chemistry that enables the identification and quantification of metabolites in samples. It differs from conventional MRI in that spectra provide physiological and chemical information instead of anatomy. [10]

The aim of the present study was to assess the various MR Spectroscopy findings in Intra-cranial space occupying lesions that help to make a clinical diagnosis and effectiveness of MR Spectroscopy in diagnosing Intra-cranial space occupying lesions and its accuracy as confirmed by post-operative histopathological findings.

Materials and Methods

The present study was conducted in the Department of Neurosurgery, Government TD Medical College, Alappuzha, Kerala. 18 months after Institutional Ethics Committee approval. Data was collected for a period of 12 months and analysis was done at the end of 12 months. All patients admitted with intra-cranial space occupying lesion and undergoing surgery under Department of Neurosurgery, Government TD Medical College, Alappuzha, Kerala and who were willing to participate in the study. Institute Ethics Committee clearance was obtained before start of study.

Inclusion Criteria:

1. All patients with Intra-cranial space occupying lesions undergoing pre- operative MR Spectroscopy followed by surgery with post-operative histopathology report were included.

2. All age groups and all genders.

Exclusion Criteria:

1. Traumatic cases

2. Conservatively managed cases

3.Unavailability of post-operative histopathological examination

4. Patients in whom Magnetic Resonance Imaging was contraindicated.

The study was time bound hospital based study done after taking written informed consent and including those fulfilling inclusion criteria. Since surgery done for intra- cranial space occupying lesions in Department of Neurosurgery, Government TD Medical College Hospital, Alappuzha is 3-4 per month and period of data collection was 12 months, hence sample size was calculated as 50.

Sampling Method: After obtaining written informed consent, participants underwent pre-operative MR Spectroscopy and were assessed for post-operative histopathology diagnosis.

Data Collection Procedure:

All patients admitted with Intra-Cranial space occupying lesion in Government TD medical college hospital, Alappuzha, Kerala, were subjected to detailed history and through clinical examination. Patients underwent routine investigations, Computerised Tomography scan/ Magnetic Resonance Imaging of head. All patients with Intra-cranial space occupying lesions detected on conventional Magnetic Resonance Imaging were subjected to MR Spectroscopy.

In cases of multiple repeat investigations, the latest final report was considered. Informed written consent was obtained. The final diagnosis was based on post- operative histopathological report, which is considered gold standard for tissue assessment in clinical decision making and in research. In all cases operative findings and post operative diagnosis was recorded. MR Spectroscopy diagnosis and post-operative histopathological diagnosis was noted in the proforma and was compared using Kappa statistics. The investigations performed in this study are otherwise necessary for the management of the underlying clinical condition. So the participants were not forced to undergo any extra investigations or procedures.

Statistical Analysis:

The data was entered in to excel worksheet and analysis performed using the Statistical Package for the Social Sciences- SPSS 20. Descriptive statistics were carried out. Results on continuous measurements are presented on mean±SD and results on categorical measurements are presented in number (%). Kappa statistics were used for comparison agreement. Sensitivity and Specificity was calculated. For a statistical significant change in proportions on a dichotomous trait at two time points

on the same population we used McNemar test for analysis. Significance was assessed at 5% level.

Ethical Considerations:

Written informed consent was obtained from all patients who were enrolled in the study. Undertaking was taken that no expense would be incurred by the subject and no risk was involved to the subject during the study. All information obtained will be kept confidential. Study was commenced only after getting approval from institutional ethics committee.

Expected outcome of the study:

MR Spectroscopy has potential application in pre-operative diagnosis of Intra- cranial space occupying lesions and is comparable to post-operative histopathology definitive diagnosis.

Results

Table 1: Demographic data

Age (Years)	No of cases	Percentage
11 – 20	5	10
21 – 30	4	8
31 – 40	9	18
41 – 50	8	16
51 – 60	9	18
61 – 70	8	16
71 & above	7	14
Gender		
Male	32	64
Female	18	36

It was observed that out of the total 50 cases participated in the study, most of the cases i.e. 9 (18%) each , belong to the age group of 31-40 years and 51-60 years, followed by 8 (16%) each in age group of 41-50 years and 61-70 years, 7 (14%) with age group 71 & above, 5 (10%) in 11-20 years and 4 (8%) in 21-30 years of age group. Out of total 50 cases participated in the study, 32 (64%) were males and 18 (36%) were females, with male to female ratio 1.8:1.

Table 2: MRS diagnosis wise distribution of cases in study group

MRS diagnosis	No of cases	Percentage
Glioma	17	34
Meningioma	11	22
Metastasis	2	4
Pituitary tumour	2	4
Lymphoma	2	4
Abscess	3	6
Tuberculoma	1	2
Pineal Tumour	2	4
Inconclusive	7	14
Cerebellar ICSOL	1	2
Infarct	1	2
Craniopharyngioma	1	2
Total	**50**	**100**

Most common diagnosis among the participated cases was Glioma in 17 (34%) cases followed by meningioma in 11 (22%) cases, abscess in 3 (6%) cases and metastasis, pituitary tumour, lymphoma, pineal tumour each in 2 (4%) cases. Tuberculoma, cerebellar ICSOL, infarct and craniopharyngioma was observed in 1(2%) case each and diagnosis was not conclusive in 7 (14%) cases.

Table 3: Histopathological finding wise distribution of cases in study group

HPE finding	No of cases	Percentage
Glioma	17	34
Meningioma	11	22
Metastasis	6	12
Pituitary tumour	2	4
Lymphoma	2	4
Abscess	4	8
Tuberculoma	2	4
Pineal Tumour	2	4
Inconclusive	4	8
Total	**50**	**100**

After Histopathological examination, most common finding observed was Glioma in 17 (34%) cases followed by meningioma in 11 (22%) cases, metastasis in 6 (12%) cases, abscess in 4 (8%) cases, pituitary, lymphoma, tuberculoma, pineal tumor in 2 (4%) cases and findings were not conclusive in 4 (8%) cases.

Table 4: Correlation between MRS diagnosis and HPE diagnosis in study group

MRS diagnosis	HPE diagnosis									Total
	Glioma	Meningioma	Metastasis	Pituitary	Lymphoma	Abscess	Tuberculoma	Pineal tumor	Inconclusive	
Glioma	16	0	0	0	0	0	1	0	0	17
Meningioma	0	11	0	0	0	0	0	0	0	11
Metastasis	0	0	2	0	0	0	0	0	0	2
Pituitary tumor	0	0	0	2	0	0	0	0	0	2
Lymphoma	0	0	0	0	2	0	0	0	0	2
Abscess	0	0	0	0	0	3	0	0	0	3
Tuberculoma	0	0	0	0	0	0	1	0	0	1
Pineal Tumour	0	0	0	0	0	0	0	2	0	2
Inconclusive	0	0	3	0	0	0	0	0	4	7
Cerebellar ICSOL	0	0	0	0	0	1	0	0	0	1
Infarct	0	0	1	0	0	0	0	0	0	1
Craniopharyngioma	1	0	0	0	0	0	0	0	0	1
Total	**17**	**11**	**6**	**2**	**2**	**4**	**2**	**2**	**4**	**50**

Out of 17 cases of Glioma, 16 were correctly identified by MRS, all the cases of Meningioma, Pituitary, lymphoma, Pineal tumor were identified correctly. Out of 6 cases of metastasis 2 and out of 4 cases of abscess 3 cases, were identified correctly. Overall diagnostic accuracy of MRS is 86%.

Table 5: Comparison of metabolite ratio in study group

Parameters	Cho/Cr	Cho/NAA	NAA/Cr
Low grade Glioma	1.54 ± 0.04	1.76 ± 0.05	1.30 ± 0.05
High grade Glioma	6.19 ± 0.10	5.24 ± 0.10	1.60 ± 0.09
t Value	121.42, P<0.0001	90.11, P<0.0001	8.32, P<0.0001
Metastasis	3.20 ± 0.03	4.56 ± 0.62	1.15 ± 0.04
Meningioma	6.18 ± 0.06	10.19 ± 0.08	1.80 ± 0.08
Normal Value	**<1.5**	**<0.8**	**>1.6**

Ratios of major metabolites were calculated after the analysis of spectra from the values relative to the integral. In low grade and high grade Glioma Cho/Cr ratio observed was 1.54 ± 0.04 and 6.19 ± 0.10 respectively. Cho/NAA ratio observed in low and high grade Glioma was 1.76 ± 0.05 and 5.24 ± 0.10 respectively. NAA/Cr ratio observed in low and high grade Glioma was 1.30 ± 0.05 and 1.60 ± 0.09 respectively. All the ratios were more in high grade compared to low grade Gliomas and difference observed was statistically significant. In Metastasis Cho/Cr, Cho/NAA and NAA/Cr observed was 3.20 ± 0.03, 4.56 ± 0.62 and 1.15 ± 0.04 respectively. In Meningioma Cho/Cr, Cho/NAA and NAA/Cr observed was 6.18 ± 0.06, 10.19 ± 0.08 and 1.80 ± 0.08 respectively.

Table 6: Presentation and symptoms of ICSOL wise distribution of cases in the study group

Presentation & symptoms	No. of cases	Percentage (n=50)
Headache	40	80
Vomiting	32	64
Loss Of Consciousness	23	46
Fever	13	26
Seizures	24	48
Giddiness	25	50
Altered sensorium	25	50
Hemiparesis	4	8
Vision disturbances	2	4

Most common presentation & symptoms observed among the study participants was headache in 40 (80%) cases followed by vomiting in 32 (64%) cases, giddiness & altered sensorium in 25 (50%) cases each, s, seizures in 24 (48%) cases, Loss of Consciousness in 23 (46%) cases, fever in 13 (26%) cases, hemiparesis in 4 (8%) cases and 2 (4%) cases with vision disturbances.

Table 7: Mr spectroscopy diagnosis

MR SPECTROSCOPY DIAGNOSIS	
Sensitivity	93%
Specificity	50%
Positive Predictive Value	91%
Negative Predictive Value	57%
Accuracy	86%

MRS diagnosis was correct in 39 cases and not correct in 4 cases with sensitivity and specificity of 93% and 50% respectively. Positive predictive value (PPV), Negative Predictive value (NPV) and accuracy of test was 91%, 57% and 86% respectively and accuracy of MRS diagnosis was 86%. Difference observed was statistically significant.

Discussion

Magnetic Resonance Spectroscopy is a new and emerging imaging modality which offers a level of tissue characterization that can match histological and biochemical diagnosis. In the clinical setting, diagnosis of intracranial mass lesions can be complicated by ambiguous neuroradiological findings, uncharacteristic clinical symptoms or symptom onset. When discussing spectroscopic data of brain lesions, the significance of calculation of signal ratios and the use of these ratios for determining the degree of tumour malignancy or for characterizing histologic tumour types or subtypes is often stressed. MRS renders five principal metabolite peaks such as choline comprising compounds peaks representing membrane turnover, creatinine peak replicating energy synthesis, NAA peaks serving as a marker of neuronal cells, lactate representing anaerobic metabolism, and lipid reflects dead necrotic cells. [11]

Age wise distribution of cases revealed that most of the cases i.e. 9 (18%) each belongs to age group of 31-40 years and 51-60 years, followed by, 8 (16%) each in age group of 41-50 years and 61-70 years, 7 (14%) with age group 71 & above, 5 (10%) in 11-20 years and 4 (8%) in 21-30 years of age group. Study conducted by Mehtab Ahmad et al [12] observed that majority of patients in the study belonged to the 30-45 year age group, constituting 28.33% of the cases. In the present study 32 (64%) males and 18 (36%) females, with male to female ratio 1.8:1 were involved. Study conducted by Mehtab Ahmad et al [12] observed that majority of the patients in the study were males forming 58.3%. Vikas Singh et al [13] revealed majority of the patents were Males i.e. 65.5% followed by 35.5% Females.

Most common diagnosis on MRS among the participated cases was Glioma in 17 (34%) cases followed by meningioma in 11 (22%) cases, abscess in 3 (6%) cases and metastasis, pituitary tumour, lymphoma, pineal tumour each in 2 (4%) cases. Tuberculoma, cerebellar ICSOL, infarct and craniopharyngioma was observed in 1(2%) case each and diagnosis was not conclusive in 7 (14%) cases. Raj Kumar et al [14] revealed metastasis was the most common diagnosis among the malignant intracranial lesion and Meningioma was the most common benign ICSOL. After histopathological examination, most common finding observed was Glioma in 17 (34%) cases followed by meningioma in 11 (22%) cases, metastasis in 6 (12%) cases, abscess in 4 (8%) cases, pituitary tumour, lymphoma, tuberculoma, pineal tumor in 2 each (4%) cases and findings were not conclusive in 4 (8%) cases. Out of 17 cases of Glioma, 16 were correctly identified by MRS. All the cases of Meningioma, Pituitary tumour, lymphoma, Pineal tumor, Abscess were identified correctly. Out of 6 cases of metastasis , 2 were identified correctly. Overall diagnostic accuracy of MRS is 86%. Out of total 17 cases of Glioma, 16 were correctly diagnosed by MRS with sensitivity of 94%. Out of 33 non Glioma cases, 32 were correctly identified as non-Glioma with specificity of 97%. Positive predictive value (PPV) and Negative predictive value (NPV) of MRS diagnosis was 94% and 97% respectively. Difference observed was statistically significant. Raj Kumar et al [14] revealed Correct MRS diagnoses in 52 of the 55 malignant cases. Sensitivity of 94.5%, specificity of 75%, positive predictive value of 96.29%, and negative predictive value of 66.66%. Ratios of major metabolites were calculated after the analysis of spectra from the values relative to the integral. In low grade and high grade Glioma, Cho/Cr ratio observed was 1.54 ± 0.04 and 6.19 ± 0.10 respectively. Cho/NAA ratio observed in low and high grade Glioma was 1.76 ± 0.05 and 5.24 ± 0.10 respectively. NAA/Cr ratio observed in low and high grade Glioma was 1.30 ± 0.05 and 1.60 ± 0.09 respectively.

All the ratios were more in high grade compared to low grade Gliomas and difference observed was

statistically significant. In Metastasis, Cho/Cr, Cho/NAA and NAA/Cr observed was 3.20 ± 0.03, 4.56 ±0.62 and 1.15 ± 0.04 respectively. In Meningioma, Cho/Cr, Cho/NAA and NAA/Cr observed was 6.18 ± 0.06, 10.19± 0.08 and 1.80 ± 0.08 respectively. Mehtab Ahmad et al[12] observed that the significant difference seen in the Cho/ Cr and Cho/NAA ratios of low and high grades of gliomas ($p< 0.05$). Mean Cho/NAA ratio was high in all the lesions, with highest values seen in the meningiomas (10.20) and Gliomas (5.81). Mean NAA/Cr ratio was variable, and found to be inconclusive in most of the lesions, lowest values were seen in the metastasis (1.22) and meningioma (1.89).

Rajendra V Mali et al [15] observed that in neoplastic lesions, high grade gliomas clearly had higher Cho/Cr and Cho/NAA ratios when compared to low-grade gliomas, infectious lesions, as well as nonneoplastic lesions. However, NAA/Cr metabolite ratio was found to be non significant. Sutton et al [16] observed that NAA/Cr levels in both low- and high-grade gliomas were found to be nonsignificant. Muhammad Shahbaz Alam et al [17] concluded that MR Spectroscopy has a sensitivity of 93.02%, specificity of 70%, positive predictive value of 93.02%, negative predictive value of 70% and diagnostic accuracy of 88.67 % in differentiating neoplastic and non-neoplastic brain lesions. Naveen Meena et al [18] observed that the Sensitivity and Specificity of MRS in detecting and characterization of intracranial tumoral lesions are 95.83% and 92.31% respectively. The Positive predictive value and Negative predictive value 92% and 96% respectively. The Diagnostic accuracy of MRS combined with conventional MRI is 94% keeping Histopathology as Gold standard.

Conclusion

The present study has shown MRS can differentiate neoplastic from the non neoplastic intracranial lesions, as well as diagnose various lesions based on metabolite ratios and spectrum, helps in better tissue characterization improving the accuracy and confidence level of neurosurgeons in their diagnosis. When diagnostic dilemmas present themselves, MR spectroscopy considered in perspective with MR imaging and clinicopath-ological features has complimentary role in providing a better diagnosis and directing treatment.

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