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RESEARCH ARTICLE

ROLE OF MAGNETIC RESONANCE SPECTROSCOPY IN GRADING OF BRAIN GLIOMAS.

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Key words:-

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Abstract

Background: MR spectroscopic imaging (MRSI), or chemical shift imaging (CSI), is a newer noninvasive modality which provides biochemical information about different tissues that cannot be obtained by conventional MRI. It allows one to collect the spectral information from a volume consisting of many voxels where the ratios of peak areas or signal intensity of the metabolites are converted to an image and overlaid onto anatomic MR images, thus showing the quantitative or qualitative distribution of the metabolite within the brain area examined.

Objective: To assess the role of MR Spectroscopy using various metabolite ratios in grading of brain gliomas into high grade and low grade.

Methodology: 30 patients with gliomas evaluated on 1.5T conventional MR imaging followed by multivoxel proton MR spectroscopy, using Cho/Cr, Cho/NAA, NAA/Cr and lipid/lactate resonances.

Observations: The mean Cho/Cr and Cho/NAA ratio was significantly elevated in high grade gliomas as compared to low grade gliomas. Higher ratios indicate increasing grade of malignancy. The presence of lactate and lipid resonances indicates necrosis and appears to correlate with higher grades of malignancy.

Conclusion:

MR Spectroscopy evaluation of gliomas using Cho/Cr and Cho/NAA ratio when used in adjunct with conventional MRI findings can be near conclusive in grading of gliomas into high grade and low grade.

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Introduction:-

Gliomas are the most common primary brain tumour. Low-grade gliomas (LGGs) are WHO Grade II infiltrative brain tumours that typically appear solid and non-enhancing on magnetic resonance imaging (MRI) scans. People with LGG often have little or no neurologic deficit, so may opt for a watch-and-wait-approach over surgical resection, radiotherapy or both, as surgery can result in early neurologic disability. Occasionally, high-grade gliomas (HGGs, WHO Grade III and IV) may have the same MRI appearance as LGGs. Taking a watch-and-wait approach could be detrimental for the patient if the tumour progresses quickly. Advanced imaging techniques are increasingly

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used in clinical practice to predict the grade of the tumour and to aid clinical decision of when to intervene surgically.¹

One such advanced imaging technique is magnetic resonance spectroscopy (MRS) which analyses the metabolism of organs and cells, biochemical changes and quantitative analysis of compounds in humans. Various metabolites in brain tissue, such as N-acetyl aspartate (NAA), choline compounds (Cho), creatine and phosphocreatine (Cr), lactate and lipid, can be measured using proton MRS (1H-MRS).² The recent emphasis on the utilization of 1HMRS (coupled to routine MRI techniques) in the evaluation of tumors has arisen because it provides greater information concerning tumor activity and characterization of the tumor tissue than is possible with standard MRI techniques alone.³

Conventional MR imaging provides important information regarding contrast enhancement, peritumoral edema, distant tumor foci, hemorrhage, necrosis and mass effect which are helpful in characterizing tumor aggressiveness and hence tumor grade. However, often a high-grade glioma may be mistaken for a low-grade glioma when it demonstrates minimal edema, no contrast material enhancement, no necrosis, and no mass effect. Therefore, accurate preoperative grading of gliomas and planning of adequate treatment strategies are often difficult with conventional MR imaging alone. The addition of complementary biochemical information, as provided by 1HMRS imaging, could lead to further advances in the determination of the tumor grade of gliomas.

Methodology:-

Type of Study-

Observational/Retrospective.

Study Setting-

Tertiary Care Hospital

Study Period-

January 2015 to January 2017.

Sample Size-

30 patients. All patients were subjected to MR imaging followed by multivoxel MR Spectroscopy.

Study Instrument-

1.5 Tesla, Philips MR Achieva (Brain coil)

Participant Selection-

Inclusion criteria:

30 patients with gliomas evaluated on 1.5T Conventional MR imaging followed by multivoxel proton MR Spectroscopy

Exclusion criteria:

Patients with ferromagnetic implants, pacemakers and aneurysm clips.
Claustrophobic patients.

Interpretation of images:

There are two types of spectroscopic imaging, namely, single-voxel and multivoxel MR spectroscopy. Single-voxel imaging involves the sampling of only one region of tissue. PRESS (point-resolved spectroscopy) and STEAM (stimulated echo acquisition mode) are the two types of sequences used for single-voxel spectroscopy. Multiple volume MR spectroscopy is also referred to chemical shift imaging (CSI). It is a method for obtaining spectroscopic information from multiple adjacent volumes over a large volume of interest. It is essentially similar to single-voxel spectroscopy except that the defined volume is normally a large slab.

CSI is better suited for evaluation of brain tumors because of their larger size and morphological and metabolic heterogeneity. It also allows for comparison and normalization of pathologic spectra to spectra in normal tissue.⁴ Spectral patterns or specific metabolite intensities can be overlaid onto gray-scale MR images either to compare changes in spectra from adjacent voxels or to obtain a distribution pattern of a particular metabolite within the tissue

examined. NAA is a marker for neuronal density and viability and therefore is decreased in all disease processes in which there is death of the neurons or replacement of neurons by other cells. The NAA peak is assigned at 2.0 ppm and is the largest peak. The second largest peak is creatine. The peak is assigned at 3.03 ppm and serves as a marker for energy-dependent systems in the brain cells. The Cho peak is assigned at 3.2 ppm and reflects the metabolism of cellular membrane turnover and therefore is increased in all processes leading to hypercellularity. An abnormal peak of lactate is normally not found in the brain. It is assigned at 1.32 ppm and when detected indicates the presence of anaerobic or nonoxidative metabolism, e.g. in necrosis.

Results:-

1. In present study of 30 patients, 14 were men (48%) and 16 were women (52%). Maximum 15 (50%) were in the age group of 31 to 40 years.
2. Out of 30 patients, 18 patients (60%) were diagnosed with high grade glioma and 12 patients (40%) with low grade glioma.
3. The mean Cho/Cr ratio and Cho/NAA ratio was higher in high grade gliomas (Figure.1), mean value was 4.28 and 4.98 respectively for high grade gliomas. (Table-1)
4. The mean Cho/Cr ratio was 1.44 and the mean Cho/NAA ratio was 2.08 for low grade gliomas. (Table-1)
5. Out of 18 patients with HGG, presence of lactate was seen in 14 patients (77%). (Table-2)
6. Out of 12 patients with LGG, only 1 patient (8.3%) showed presence of a small lactate peak. (Table-2)
7. Out of 18 patients with HGG, 12 patients (66%) showed presence of lipid peak. (Table-2)
8. Out of 12 patients with LGG, none of the patients showed presence of lipid peak. (Table-2)

LESIONS	CHOLINE TO CREATININE		CHOLINE TO N-ACETYL ASPARTATE		N-ACETYL ASPARTATE TO CREATININE	
	MEAN	SD	MEAN	SD	MEAN	SD
HGG	4.28	1.07	4.98	0.30	0.95	0.22
LGG	1.44	0.08	2.08	0.34	0.77	0.09
p value	<0.001		<0.001		0.350	

Table 1:-Mean Metabolite Ratio in HGG and LGG

LESIONS	TOTAL		LACTATE PEAK			LIPID PEAK	
			NO	%		NO	%
HGG		18	14	77		12	66
LGG		12	1	8.3		0	0.0

Table 2:-Lactate and Lipid in HGG and LGG

Discussion:-

1. HGG had higher Cho/Cr & Cho/NAA ratios as compared to LGG. The mean Cho/Cr ratio and Cho/NAA ratios was significantly high in high grade gliomas when compared to low grade gliomas ($p < 0.001$). Higher ratios indicate increasing grade of malignancy. (Figure.1)

Server A, Kulle B, Gadmar ØB, Josefsen R, Kumar T, Nakstad PH et al⁵ in their study demonstrated threshold values of 1.35 and 1.78 for Cho/Cr and Cho/NAA metabolite ratios respectively for determining high-grade gliomas.

2. NAA/Cr ratios were comparable and could not be used to distinguish between high and low grade gliomas. Hence the NAA/Cr ratio was of no significance.

Wang Q, Zhang H, Zhang J et al⁶ in their study concluded that MRS demonstrated moderate diagnostic performance in distinguishing HGGs from LGGs using tumoural metabolite ratios including Cho/Cr, Cho/NAA and NAA/Cr. Although there was no significant difference in AUC between Cho/Cr and Cho/NAA groups, Cho/NAA ratio showed higher sensitivity and specificity than Cho/Cr ratio and NAA/Cr ratio.

3. Lactate was elevated in 77% of patients with HGG. The presence of lactate appears to correlate with higher grade of malignancy. (Figure.2)

Martin Bulik, Radim Jancalek, Jiri Vanicek et al⁷ in their study on potential of MR spectroscopy for assessment of glioma grading stated that malignant transformation of the glial tumors is accompanied by the presence of lactate and lipids in MR spectra of grade III but mainly grade IV gliomas.

4. Lipids were elevated in 66% of patients with HGG. The presence of lipids appears to correlate with higher degrees of malignancy.(Figure.2)
5. Low grade gliomas showed low levels of choline with no significant lactate and absence of lipids.

Bulik M, Jancalek R, Vanicek J, Skoch A et al ⁸ in their study concluded that low-grade gliomas are generally characterized by low level of choline and absence of lactate and lipids.

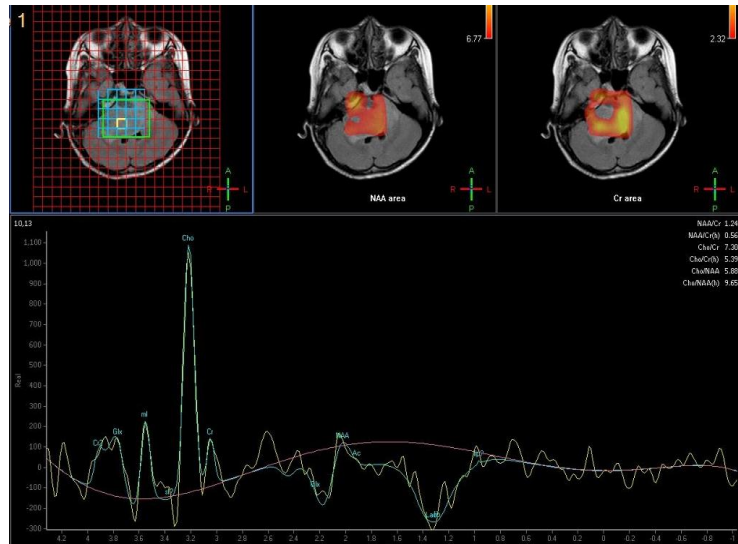


Figure 1:-Multivoxel MRS at long TE: Cho/Cr: 5.39. High Grade Intrinsic Pontine Glioma
Source: Department of Radiodiagnosis, GMC Nagpur, 1.5T MR.

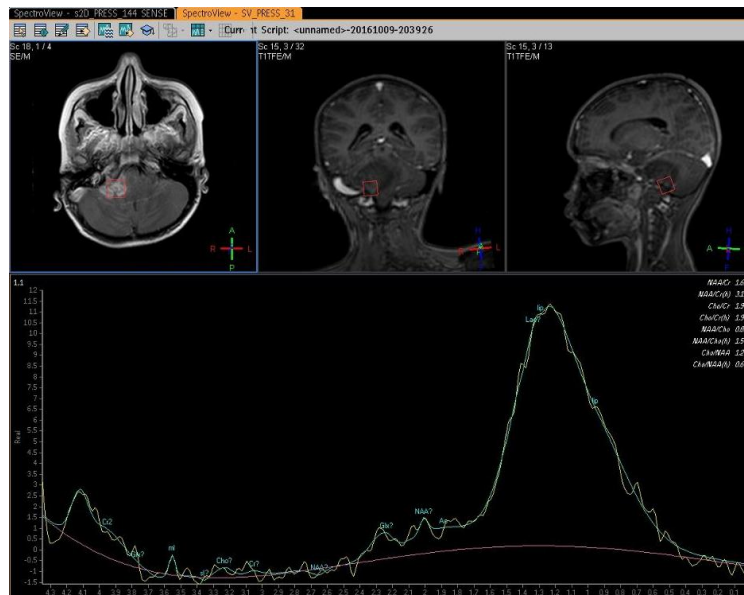


Figure 2:-Presence of lipid-lactate peak. High Grade Intrinsic Pontine Glioma
Source: Department of Radiodiagnosis, GMC Nagpur, 1.5T MR

Conclusion:-

The mean Cho/Cr and Cho/NAA ratio was significantly elevated in high grade gliomas as compared to low grade gliomas. Higher ratios indicate increasing grade of malignancy. So it can be concluded that Cho/Cr and Cho/NAA can be used in grading of malignancies. It was not possible to differentiate between high grade and low grade gliomas on basis of NAA/Cr ratios. The presence of lactate and lipids correlate with higher grades of malignancy. MR Spectroscopy is a newer noninvasive modality which provides biochemical information about different tissues that cannot be obtained by conventional MRI. It complements MRI and is particularly useful when MRI findings are

inconclusive. Thus it can be concluded that MRS helps in better characterization of gliomas and in differentiating high grade from low grade gliomas.

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