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Original Research Article.

Comparison of Various Metabolite Ratios in Intracranial Lesions: A Hospital Based Survey

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ABSTRACT

Background: Despite numerous efforts no universally acceptable pathological classification of brain tumors has been proposed. Diagnosis of intracranial lesions substantially relies on the ability of the experienced professional to interpret a variety of rather indirect criteria. The aim of the present study is to compare various metabolite ratios in the intracranial lesions.

Materials and Methods: The present observational and prospective study was conducted in the Dept. of Radiology, Ananta Institute of Medical Science and Research Centre, Udaipur, Rajasthan. The study was conducted for a period of two years. MRA spectroscopy was performed amongst all the patients. The area under the curve of a metabolite was considered as relative concentration (integral values) and was measured in terms of ratios. For comparison of the three groups (grades) of astrocytomas, ANOVA test was applied. Probability value (P) <0.05 was regarded as significant.

Results: The study included a total of 65 subjects; out of this majority were males and rest females. The mean Cho/Cr ratio was found to be higher in the metastasis (3.48) than in the gliomas (3.27 in grade IV gliomas). However the Cho/NAA ratio in the high grade gliomas (7.96 in grade IV gliomas) was greater than in the metastasis. The mean Cho/Cr ratio in TB was 1.67 and in NCC was 1.12. The mean Cho/Cr ratio in abscess was 0.75. The mean Cho/NAA ratio in TB and Abscess was 1.08 and 0.89 respectively. The mean NAA/Cr ratio in NCC and abscess was 1.15 and 0.77 respectively.

Conclusion: It can be concluded that Proton MRS helps in better tissue characterization of different brain tumors. It has a complimentary role to MR imaging not only in providing a better diagnosis, but also in directing treatment and follow up of such brain tumors.

Keywords: Brain, Gliomas, Intracranial.

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INTRODUCTION

Brain tumors in adults comprise a diverse group of neoplasms that vary in their behaviour depending on such factors as cell of origin, site of occurrence, morphology and pattern of spread. Despite numerous efforts no universally acceptable pathological classification of brain tumors has been proposed. Intracranial space occupying lesions can produce various symptoms which are manifestations of the local neurological defects produced by the presence of the lesion itself, of the pressure effects produced in distal sites by the lesion and surrounding oedema or due to the raised intracranial pressure.

Any type of seizure occurring for the first time after the age of 15 years should suggest the possibility of intracranial space occupying lesions. It is due to disruption of cortical circuits by tumors that invade or compress cerebral cortex. Diagnosis of intracranial lesions substantially relies on the ability of the experienced professional to interpret a variety of rather indirect criteria. These include typical location, calcification, signs of raised intracranial pressure, cyst formation, on contrast enhancement, plain radiographs, angiograms, computed tomographic (CT) scans, and magnetic resonance (MR) images. However, a diagnosis based on morphologic and anatomic findings alone without histologic examination of the suspected tissue often remains dubious.

It was in 1946 that Purcell et al[1] and Bloch et al[2] first gave the principles of nuclear magnetic resonance. Magnetic resonance spectroscopy (MRS) of biological tissues was first reported in 1973 by Moon and Richards[3] using P-31 MRS for examination of intact red blood cells, and in 1974 by Hoult et al to check leg muscle from the rat. The major brain metabolites detected are choline, creatine, N-acetyl aspartate (NAA), lactate, myoinositol, glutamine and glutamate, lipids, and the amino acids leucine and alanine. The most prominent resonance in a proton spectrum is NAA.[3-6] The aim of the present study is to compare various metabolite ratios in the intracranial lesions.

MATERIALS AND METHODS

The present observational and prospective study was conducted in the Department of Radioogy, Ananta Institute of Medical Science and Research Centre, Udaipur, Rajasthan. The study was conducted for a period of two years.

All the subjects showing radiological evidence of intracranial space occupying lesion were included in the study. Subjects with history of trauma, cerebrovascular accidents were not included in the study. Subjects with vascular malformations or aneurysms were also excluded. The contra lateral normal parts of brain were also studied as controls. MRA spectroscopy was performed amongst all the patients. The area under the curve of a metabolite was considered as relative concentration (integral values) and was measured in terms of ratios. Measuring metabolite peak area ratios has the advantage of cancelling out the effects of general reduction in measured metabolite concentrations due to variations in cellular density. As reference standards, values of Cho/Cr > 1.5, NAA/Cr < 1.6, Cho/NAA > 0.8, Lactate >1.34, Lipids >1.4, Glutamate >2.5, Glutamine >2.38, Alanine >1.48 were taken as abnormal. Imaging was performed using 1.5 tesla magnetic resonance imaging equipment from GE-HDXT and 3.0 tesla magnetic resonance imaging systems from PHILIPS. The MR spectroscopic data in our study was assumed to follow normal distribution. The level of significance was determined using the Student's t-test. For comparison of the three groups (grades) of astrocytomas, ANOVA test was applied. Probability value (P) <0.05 was regarded as significant.

Table 1: Comparison of the Spectroscopy findings in Gliomas and Metastasis

Tumor Type	Total cases	Cho/Cr (Mean)	Cho/NAA (Mean)	NAA/Cr (Mean)	Lactate (% of cases)	Lipid (% of cases)
Gr.II Glioma	6	1.48	2.08	0.77	33%	0
Gr.III Glioma	13	2.67	3.96	0.81	62%	62%
Gr.IV Glioma	12	3.27	7.96	0.47	67%	100%
Metastasis	6	3.48	3.90	1.12	66%	66%

(Normal Values: Cho/Cr < 1.5; Cho/NAA < 0.8; NAA/Cr > 1.6)

Table 2: Comparison of Metabolite ratios in various infectious lesions

Lesion	Cho/Cr (Mean)	Cho/NAA (Mean)	NAA/Cr (Mean)
T.B.	1.67	1.08	2.39
NCC	1.12	1.09	1.15
Abscess	0.75	0.89	0.77

Fig 1: Comparison of metabolite Ratios in benign and malignant lesions

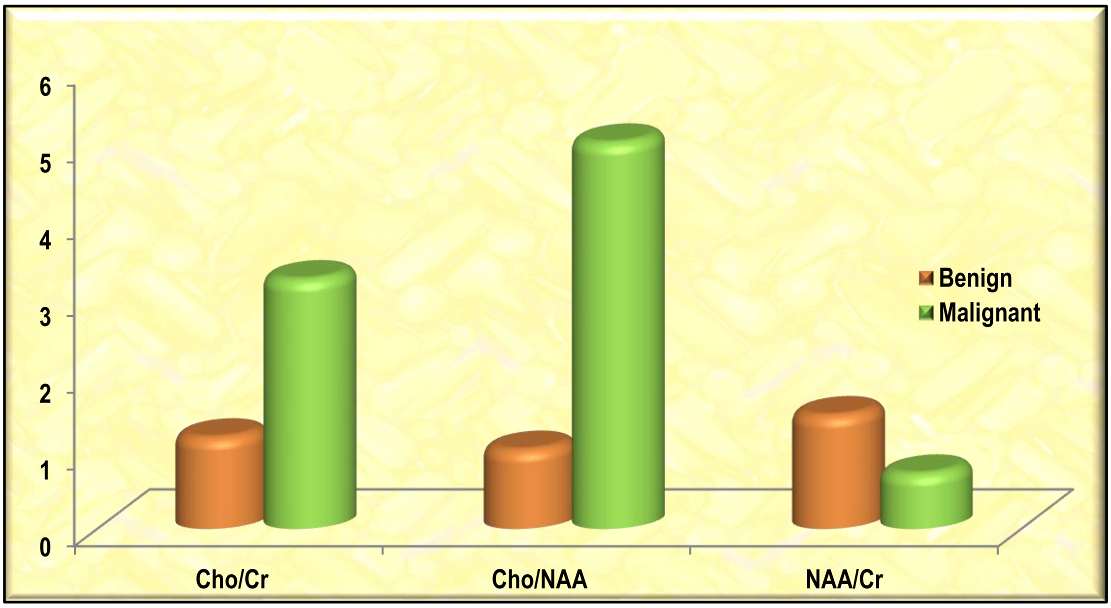

Table 3: Comparison of metabolite ratios in 3 grades of gliomas

Tumor Grade	Cho/Cr	Cho/NAA	NAA/Cr	ml/Cr
Grade II (n=6)	1.48 ±0.32	2.08 ±0.65	0.77 ±0.31	0.70 ±0.28
Grade III (n=13)	2.67 ±1.07	3.96 ±1.73	0.81 ±0.34	0.31 ±0.15
Grade IV (n=12)	3.27 ±1.91	7.96 ±4.23	0.47 ±0.24	0.23

RESULTS

The study included a total of 65 subjects, out of these majority were males and rest females. Table 1 shows the Comparison of the Spectroscopy findings in Gliomas and Metastasis. The mean Cho/Cr ratio was found to be higher in the metastasis (3.48) than in the gliomas (3.27 in grade IV gliomas). However the Cho/NAA ratio in the high grade gliomas (7.96 in grade IV gliomas) was greater than in the metastasis. NAA/Cr ratio was lowest in the grade IV gliomas. In general there was considerable overlap of metabolite ratios in the high grade gliomas and metastatic lesions. While Lactate peaks were seen in both gliomas and metastasis, there was higher incidence of prominent Lipid peaks in the grade IV gliomas (100%).

Table 2 shows the Comparison of Metabolite ratios in various infectious lesions. Mean choline, creatine and NAA levels were found to be lower in the abscesses than in the other infectious lesions. The mean Cho/Cr and NAA/Cr ratios were higher in the tuberculous lesions than in NCC and abscesses. The mean Cho/Cr ratio in TB was 1.67 and in NCC was 1.12. The mean Cho/Cr ratio in abscess was 0.75. The mean Cho/NAA ratio in TB and Abscess was 1.08 and 0.89 respectively. The mean NAA/Cr ratio in NCC and abscess was 1.15 and 0.77 respectively.

Figure 1 shows the Comparison of metabolite Ratios in benign and malignant lesions. The mean NAA/Cr ratio in Benign and malignant lesions were 1.48 and 0.72 respectively. The mean Cho/NAA ratio in Benign and malignant lesions were 1.03 and 05.03 respectively. The mean Cho/Cr ratio in Benign and malignant lesions were 1.19 and 3.25 respectively. On applying student t test the p value came out to be less than 0.05 indicating significant difference in the levels.

Table 3 shows the Comparison of metabolite ratios in 3 grades of gliomas. The Cho/Cr and Cho/NAA ratios show increase with increasing grade of malignancy, with maximum mean Cho/Cr ratio (3.27) and Cho/NAA ratio (7.96) seen in the grade IV gliomas. NAA/Cr ratio was lower in the higher grade gliomas than in the low grade gliomas, lowest in grade IV gliomas (0.47). mI/Cr ratio in the low grade gliomas was significantly higher (0.70) than in the high grade gliomas (0.32).

DISCUSSION

In 1989, a study by Bruhn H, Frahm J et al [7] on noninvasive differentiation of cerebral tumors with use of localized 1H MR Spectroscopy in vivo. All tumor spectra were remarkably different from spectra from normal brain tissue. Spectra obtained from different tumors exhibited reproducible differences, while histologically similar tumors yielded characteristic spectra with only minor differences. The spectral differences between the tumors are mainly due to the differing concentrations of lipids, lactic acid, and carbohydrates.

In 1991, Arnold DL et al [4] used phosphorus magnetic resonance spectroscopy to monitor pH changes in malignant gliomas following treatment with intravenous and intra-arterial 1,3-bis-(2-chloroethyl)-1-nitrosourea (BCNU). Initial intravenous BCNU treatment was followed by a transient decrease of tumor intracellular pH by 0.15 +/- 0.03 pH units (mean +/- SD). These changes occurred prior to any changes on x-ray, computed tomography (CT), or magnetic resonance imaging (MRI). They concluded that in addition to enhancing understanding of the metabolic effects of BCNU, such changes may correlate with drug efficacy or toxicity and may be useful in guiding therapy in the future. In 1991, a study by Arnold DL, Emrich JF et al [4] used phosphorous MRS to assess tumor grade and type. They obtained localized phosphorus MR spectra from 10 normal brains, four low-grade astrocytomas, six glioblastomas, four meningiomas, and three pituitary adenomas and found differences in the spectra of each tumor type. Compared to normal brain, the spectra from low-grade astrocytomas showed a significant reduction of the phosphodiester (PDE) peak. Glioblastomas were characterized by a significant reduction of the PDE peak, elevation of the phosphomonoester (PME) peak, and a relatively alkaline intracellular pH.

In 1992, a study done by Fulham et al[8] using 64 ^{1}H-MRS scans on 50 adults with brain tumors and reported that NAA levels were lower in all tumors and in areas of radiation necrosis and that Cho levels were higher in most solid brain tumors. In the present study, Mean choline, creatine and NAA levels were found to be lower in the abscesses than in the other infectious lesions. The mean Cho/Cr and NAA/Cr ratios were higher in the tuberculous lesions than in NCC and abscesses. The mean Cho/Cr ratio in TB was 1.67 and in NCC was 1.12. The mean Cho/Cr ratio in abscess was 0.75. The mean Cho/NAA ratio in TB and Abscess was 1.08 and 0.89 respectively. The mean NAA/Cr ratio in NCC and abscess was 1.15 and 0.77 respectively.

In 1992, a study by Sutton et al[9], Tzikka et al[10] demonstrated that, like adult brain tumors, malignant paediatric brain tumors are characterized by an increase in the Cho:NAA ratio and a decrease in the NAA: Cr ratio, a general decrease in the NAA and Cr peaks, and an increase in Cho. In the present study, The mean NAA/Cr ratio in Benign and malignant lesions were 1.48 and 0.72 respectively. The mean Cho/NAA ratio in Benign and malignant lesions were 1.03 and 05.03 respectively. The mean Cho/Cr ratio in Benign and malignant lesions were 1.19 and 3.25 respectively. On applying student t test the p value came out to be less than 0.05 indicating significant difference in the levels. In 1993, a study by Castillo M et al [11] showed that Proton MRS NAA and Cr levels are virtually zero in meningiomas and schwannomas as they are nonneuronal neoplasms. Presence of NAA and Cr usually indicates contamination by adjacent parenchyma. Presence of Alanine and Glutamine are highly suggestive of meningioma. The spectra from a meningioma may show only lipids.

In 1996, Hiroaki Shimizu, Toshihiro Kumabe et al [12] studied the usefulness of 1H-MRS as a noninvasive method of evaluation of brain tumors and, using water-suppressed single-voxel point resolved spectroscopy in the frontal white matter of 17 healthy volunteers and 25 patients with brain tumors, obtained spectra with peaks of *N*-acetyl aspartate (NAA), choline-containing compounds (Cho), creatine/ phosphocreatine (Cr), and lactate. They concluded that higher grades of brain tumors were associated with higher Cho/ reference and lower NAA/reference values and suggested that clinical proton MR spectroscopy may help predict tumor malignancy.

In 1996, Bhujwalla ZM and Glickson JD [13] conducted studies to investigate the effects of radiation on levels of metabolites such as lactate and choline compounds detected by 1H magnetic resonance spectroscopy (MRS). Changes in lactate observed in this study are consistent with an increased blood flow observed in previous studies (15) in the same tumor model following 20 Gy X-irradiation and thus pointed to the feasibility of detecting response to clinical doses of fractionated radiation therapy by 1H MRS. According to a study by SH Kim, KH Chang et al [14], the patterns from in vivo H-1 MR spectroscopy may permit differentiation of brain abscess from necrotic or cystic tumor.

CONCLUSION

Grading of gliomas could be done reliably on the basis of Cho/Cr and Cho/NAA ratios. However, in certain cases, these ratios were not sufficient to predict grade, and presence of lipids was a differentiating feature for the tumor grade in these lesions. The mI/Cr ratio was seen to be higher in the low grade gliomas than high grade tumors, infections or normal control values. This suggests a potential role for myoinositol levels in diagnosis of low grade gliomas. It can be concluded that Proton MRS helps in better tissue characterization of different brain tumors. It has a complimentary role to MR imaging not only in providing a better diagnosis, but also in directing treatment and follow up of such brain tumors.

REFERENCES

1. Purcell EM, Torrey HC, Pound RV. Resonance absorption by nuclear magnetic moments in a solid. Physiol Rev 1946; 69:37-38.
2. Bloch R, Hansen WW, Packard ME. Nuclear induction. Physiol Rev 1946; 69: 127.
3. Najem ES, et al. Thoracic Spine. In : Stark DD, Bradley WG, editors. Magnetic Resonance Imaging. 3rd ed. St. Louis: C.V. Mosby; 1999: 903.
4. Arnold DL, Emrich JF, Shoubridge EA, Villemure JG, Feindel W, et al. Characterization of astrocytomas, meningiomas and pituitary adenomas by phosphorus magnetic resonance spectroscopy. J Neurosurg 1991; 74(3): 447-453.
5. Atlas SW. Magnetic Resonance Imaging of the Brain and Spine. 3rd ed. Philadelphia: Williams and Wilkins; 2002: 2028-29.
6. Cadoux-Hudson TA, Blackledge MJ, Rajagopalan B, et al. Human primary brain tumor metabolism in vivo: a phosphorus magnetic resonance spectroscopy study. Br J Cancer. 1989; 60(3): 430-436.
7. Bruhn H, Frahm J, Gyngell ML, Merbold KD, et al. Noninvasive differentiation of tumors with use of localized H-1 MR spectroscopy in vivo: initial experience in patients with cerebral tumors. Radiology 1989; 172(2): 541-548.
8. Fulham MJ, Bizzi A, Dietz MJ et al. Mapping of brain tumor metabolites with proton MR spectroscopic imaging: clinical relevance. Radiology 1992; 185(3): 675–686.
9. Sutton LN, Wang Z, Gusnard D, et al. Proton magnetic resonance spectroscopy of pediatric brain tumors. Neurosurgery 1992; 31: 195–202.
10. Tzika AA, Vajapeyam S, Barnes PD. Multivoxel proton MR spectroscopy and hemodynamic MR imaging of childhood brain tumors: preliminary observations. AJNR Am J Neuroradiol 1997; 18: 203–218.
11. Castillo M, Kwock L, Scatliff J, Gudeman S, Greenwood R. Proton MR spectroscopic characteristics of a presumed giant subcortical heterotopia. AJNR Am J Neuroradiol 1993; 14:426-29.
12. Hiroaki Shimizu, Toshihiro Kumabe, Teiji Tominaga, et al. Noninvasive evaluation of malignancy of brain tumors with proton MR spectroscopy. AJNR Am J Neuroradiol 1996; 17(4): 737–747.
13. Bhujwalla ZM, Glickson JD. Detection of tumor response to radiation therapy by in vivo proton MR spectroscopy. Int J Radiat Oncol Biol Phys 1996; 36(3): 635-639.
14. SH Kim, KH Chang, IC Song, et al. Brain abscess and brain tumor: discrimination with in vivo H-1 MR spectroscopy. Radiology 1997; 204(1): 239-245.

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