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Assessment of different brain lesions using Single-Voxel Proton Magnetic Resonance Spectroscopy

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Magnetic resonance spectroscopy (MRS) is an effective, safe imaging diagnostic tool which is useful to assess biochemical and metabolic changes in various brain lesions. The study aims to assess different brain lesions using Single Voxel Proton Magnetic Resonance Spectroscopy (MRS). This is a retrospective study conducted at Khartoum State in Sudan from the period of 2017-2019. The participants were examined using MRI and single-voxel proton MRS. The metabolite ratios were assessed and compared to different lesions using independent sample t-test and ANOVA tests. A total of 100 patients (54 males and 46 females; mean age was 43.75 years) were examined. The most prevalent brain lesions were glioblastoma multiforme (GBM) and glioma (24% and 22%). The Cho/Cr ratio was higher in GBM and lymphoma than other brain lesions (4.37 and 4.25 respectively). The NAA/Cr ratio is lower in lymphoma, tuberculoma, inflammation, and abscess (0.6, 1.2, 1.4, and 1.85). The Cho/Cr ratio was significantly higher in neoplastic brain lesions than nonneoplastic one (3.95 vs. 1.74, p-value < 0.001). The nonneoplastic brain lesions had significantly lower peaks of Cho/Cr than neoplastic lesions which have higher peak. GBM and lymphoma have the highest Cho/Cr ratio compared to other brain lesions.

Keywords: MRS; Single voxel; Brain lesions; NAA/Cr; Cho/Cr ratio.

INTRODUCTION

Proton magnetic resonance spectroscopy (MRS) provides additional functional and metabolic information about brain tumors by assessing biomarkers of nervous cell proliferation, neuronal integrity, energy metabolism, and pathological transformation of tissues, which complement the anatomical information available from conventional MRI (Nagar et al. 2007). Magnetic resonance imaging (MRI) with an enhanced-contrast medium is considered the gold standard for Neurosurgeons when performing biopsy tissue for the diagnosis of brain masses. However, differentiating the brain tumors from radiation-induced injuries is so difficult with MRI alone.

MRS assessed different metabolites of brain tumors, such as N-acetyl-aspartate (NAA), creatine(Cr) and Choline (Cho), at different MRS echo times (TEs), and showed a major advantage compared to x-rays exposure as an imaging tool for guiding and obtaining brain tumors biopsy procedures. Many studies stated that MRS could differentiate benign from malignant tumors and between high- and low-grade tumors (Wang et al., 2014). One of the previous studies found that Cho/NAA, Cho+Cr/NAA, and Cho/Cr are capable of determining the grade of the tumor, at intermediate TE, Cho/NAA, Cho+Cr/NAA, and Cho/Cr were significantly higher in high-grade tumors than low-grade ones (Naser et al. 2016)

The MRS characteristics of brain gliomas include elevated Cho signal with decreased NAA and Cr peaks, along with lactate/lipid peaks in some pathological conditions. The elevation of Cho in mitotic lesions was attributed to increased membrane cellularity and synthesis. Increased Cho/Cr ratio is generally associated with an increase in malignant tumors and considered as a safe index of tumors grading and characterization. The reduction of NAA peaks indicates loss of normality of neuronal elements since they are destroyed by active malignant cells (Kumar et al. 2003).

The metabolites included in this study are the ratios of Cho/Cr and NAA/Cr which produced from Choline (Cho), creatine (Cr), and N-Acetyl-L-aspartate (NAA).

The study aims to assess different types of brain lesions, and to differentiate between neoplastic and nonneoplastic brain lesions using single-voxel Proton MRS.

MATERIALS AND METHODS

This is an analytical retrospective study performed in Al-moalem Medical City Hospital, Khartoum Sudan. The study included 100 records of 54 males and 56 females with ages ranged 1-90 years. The mean age was 43.75 years. The patients diagnosed with brain lesions—the data collected from MRI PACS, which interpreted by two expert Radiologists. The MRI images were produced using Siemens-MRI machine with 1.5 Tesla. All the patients were investigated by MRI and MRS and results were reported by experienced radiologists. The MRS is done to confirm the presence of brain lesions. In MRS, the values of the Cho/Cr ratio and NAA/Cr ratio were assessed in every patient.

Magnetic resonance spectroscopic Technique

The participants were examined using an MRI examination, with the patient lies supine on the examination table. The head was positioned within the head coil and adjusted so that the inter papillary line is parallel to the table, and the head is straight. The patient is positioned in the mid-line of the cough with the longitudinal alignment light adjusted in the midline, and the horizontal alignment light passes across the nation. Straps and foam pads were used from immobilization and then inter to the gantry of MR and then applied the MR protocols (T1, T2, diffusion, and flair). The T1-weighted image was obtained after intravenous gadolinium administration at least two planes. After conventional MRI, all MRS images were performed through a single-voxel technique (SVS). Initially, localization methods were used to localize the voxel from MR image in a clinical proton MRS including point – resolved surface coil spectroscopy (PRESS) to give voxel size ranging between 2cc to 8cc. Then the voxel was placed on the volume of interest and suppression of water signal done by using chemical shift selective expiation (CHESS). At the same time, the suppression of fat applied by excluding the area of the tumor contains fat. Analysis of differences in the metabolite resonance frequency was performed in the presence of a uniformly homogenous magnetic field. A heterogeneous magnetic field was avoided since it leads to the dispersion of resonance frequency. The magnetic field is maintained homogenized in the region of interest before MRS acquisition. MRS studies were obtained using a localized single volume (PRESS). However, using the chemical –shift imaging is possible to obtain one or two-dimensional data sets that display metabolites from adjacent compartments; and encompassing a large tissue volume to give imaging as mapping explaining the concentration of metabolites in MRS image. TEs of 136 milliseconds are long enough to identify the signal from metabolites in the brain, which has long TE.

Statistical analysis

The data were analyzed using SPSS version 19. Frequency and percentage are estimated for categorical variables using descriptive statistics. The independent student t-test and one -way Anova tests were performed to compare the neoplastic and nonneoplastic masses and assess the mean ratios among different brain lesions.

RESULTS

A total of 100 patients have been selected by using a convenient sampling method. The incidence of brain lesions was higher in males than females (54% vs. 46%), male: female ratio is 1: 0.85), as shown in figure 1. the mean age 43.75 years. The most affected age group was 48-57 years and 58-67 years followed by 18-27 years than 68-77 years (19%, 17%,18%, and 11% respectively), as shown in (table 1).

The study found that the Cho/Cr ratio was 3.76±1.89, while the mean NAA/Cr ratio was 1.81± 1.30, while. The minimum Cho/Cr was 0.65 and a maximum of 10.98, while the minimum NAA∣Cr was 0.08, the maximum was 7.78, (table 2).

It was found that the most prevalent brain lesion diagnosed by MRS was GBM 24%, followed by glioma 22%, then neoplastic process 18% then Mets, meningioma, lymphoma, and tuberculoma were less frequent as shown in figure 2.

The mean Cho/Cr ratio were higher in GBM (glioblastoma multiforme) followed by lymphoma, neoplastic process, glioma, meningioma then DENS, Mets and astrocytoma respectively (4.37 ± 1.66, 4.25 ±1.68, 4.16 ± 2.09 ,3.88 ± 2.22 ,3.87 ± 2.11, 3.62 ± 0.00, 3.55 ±1.23, 3.36 ± 2.35), while Cho/Cr ratios were lower in radiation necrosis and inflammatory process (1.03 ±0.00 and 1.00 ± 0.00 respectively). NAA/Cr ratio yielded lower values in lymphoma (0.61±0.39), followed by tuberculoma, inflammation and GBM respectively (1.20± 0.48, 1.40±0.00 and 1.45±0.6), as shown in Table3.

Abscess had lower Cho/Cr (1.71± 0.73) than NAA/Cr (1.85 ±1.28), Radiation necrosis had higher NAA/Cr (2.04 ± 0.00) and very lower Cho/Cr (1.03 ± 0.00) compared to GBM, as shown in Table 3

Neoplastic brain lesions caused high Cho/Cr ratio and low NAA/Cr, while non-neoplastic such as abscess and inflammation have less Cho/Cr ratios compare to neoplastic one. A significant difference was found between neoplastic and non-neoplastic brain lesions concerning the Cho/Cr ratio (p <001), while in NAA/Cr ratio no significant difference found between them (p > 0.05). In contrast in neoplastic lesions the Cho/Cr ratio is extremely high compared to nonneoplastic one, while NAA/Cr had not significant different compared to nonneoplastic lesions as shown in Table 4.

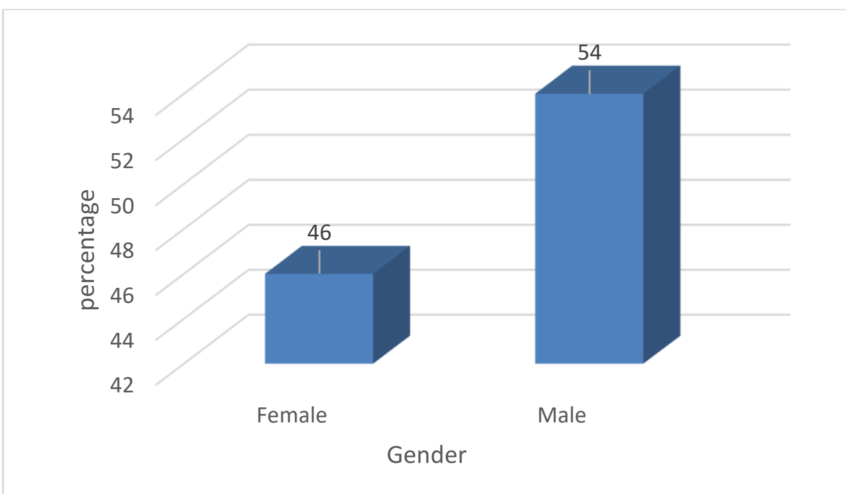

Figure 1: Gender distribution of the participants

Table 1: Distribution of age groups of the patients

Age/years	Frequency	Percent
1-17	10	10.0
18-27	18	18.0
28-37	10	10.0
38-47	12	12.0
48-57	19	19.0
58-67	17	17.0
68-77	11	11.0
78-90	3	3.0
Total	100	100.0

Table 2: Descriptive statistic for age, Cho/Cr and NAA/Cr ratios

Variables	Minimum	Maximum	Mean±SD
Age	1	90	43.75 ±20.08
Cho/Cr	.65	10.98	3.76 ±1.91
NAA/Cr	.08	7.87	1.81 ± 1.30

Table 3: Comparison of Cho/Cr and NAA/Cr ratios in different brain lesions

Final MRS diagnosis	Cho/Cr	NAA/Cr	P-value
	Mean± SD		
GBM	4.37±1.66	1.45±0.67	>0.05
Glioma	3.88±2.22	2.28±1.66	
Mets	3.55±1.23	1.92± 0.65	
Astrocytoma	3.36±2.35	1.80 ±0.73	
Neoplastic process	4.16±2.09	1.67 ±1.21	
Lymphoma	4.25±1.68	0.61± 0.39	
Abscess	1.71± 0.73	1.85± 1.28	
Meningiomas	3.87±2.11	2.53 ±2.59	
Inflammation	1.00±0.00	1.40±0.00	
Tuberculoma	2.51±1.16	1.20± 0.48	
Granuloma	2.22±.183	1.83± 0.07	
DENS	3.62±0.00	2.55±0.00	
Radiation necrosis	1.03±0.00	2.04±0.00	

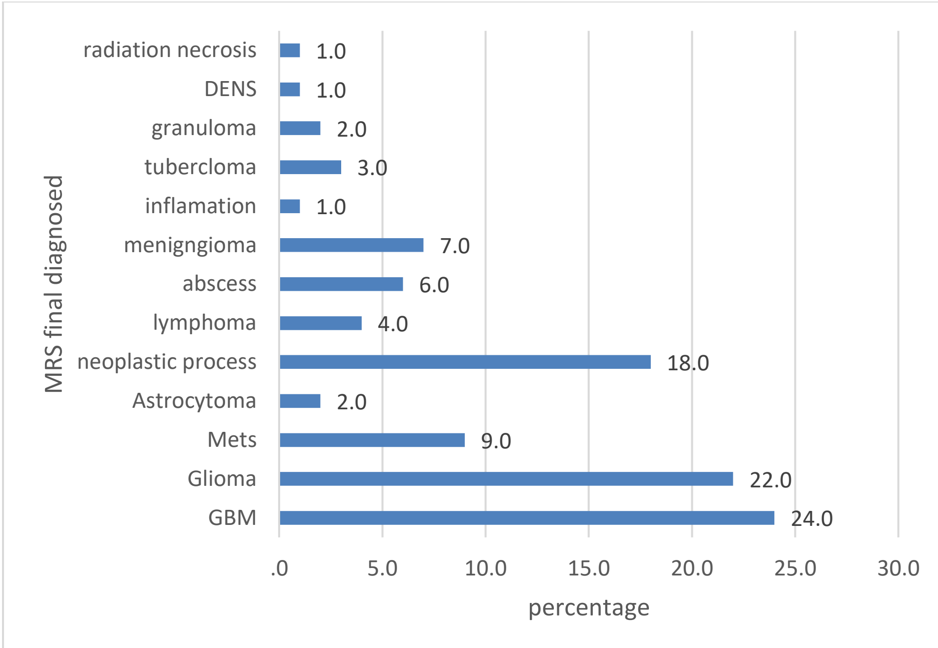

Figure 2: Distribution of MRS final diagnosed

Table 4: Comparison between neoplastic and nonneoplastic brain lesions in Cho/Cr and NAA/Cr ratios (independent sample t-test)

Metabolites ratios	Neoplastic	Nonneoplastic	P value
Cho/Cr (Mean ±SD)	3.95±1.87	1.74±.67	<0.001**
NAA/Cr (Mean ±SD)	1.80±1.32	1.79 ±1.18	>0.5

DISCUSSION

MR spectroscopy was proven to be a useful imaging tool to discriminate between various brain lesions (Aydın et al. 2019). In our study, MRS improved the accuracy of assessing the neoplastic and nonneoplastic brain lesions. This study was achieved by the evaluation of two metabolite ratios– Cho/Cr and NAA/Cr.

The present study revealed that GBM was the most common brain lesion, followed by glioma and the neoplastic process, then Mets meningioma, abscess, and lymphoma. It was found that patients with GBM have the highest value of the Cho/Cr ratio compared to other brain lesions. In previous studies, it was reported that all brain masses have reduced NAA signals, and have increased Cho, leading to elevated Cho/NAA ratios. The reduction in NAA peak is mainly attributed to the loss, dysfunction, and displacement of the healthy neuronal tissue since NAA metabolite is considered a primary origin of neurons and axons (Barker, 2001; Chae et al. 2019; Mcintyre et al. 2012). Tsougos et al. (2012) reported that Cho/Cr and Cho/NAA have significantly differentiated GBM from other intracranial metastases.

The present study found that the NAA/Cr ratio was mostly lower in lymphoma, tuberculoma, then GBM, neoplastic process, astrocytoma, Mets, and glioma. It was observed that in high-grade tumors such as GBM and lymphoma, the Cho/Cr ratio was high, and NAA/Cr was low compared to low-grade tumors (glioma). These findings were consistent with Warren, who reported that brain tumors showed elevated Cho/Cr and decreased NAA/Cr ratios indicating loss of integrity of neurons and increased myelin turnover (Warren, 2004) Additionally, several studies determined that the MRS findings of the brain tumors included a marked reduction in NAA, a slight decrease of Cr, and a marked increase of Cho. Similarly, our findings agreed with those results which reported increased in Cho/Cr ratio and decreased NAA/Cr in brain masses (Wilken et al., 2000; Vuori et al., 2004; Negendank et al., 1996; Butzen et al., 2000;

Usenius et al. 1994; Ott et al.1993).

In this study, it was observed that the nonneoplastic brain lesions such as abscess, inflammatory process yielded lower values of the Cho/Cr ratio compared to neoplastic lesions. Alberto Surur et al. 2010 found that in most cases of inflammatory lesions, a slight elevation in the Cho peak was noted while the NAA peak remained slightly reduced (Alberto Surur et al 2010). Attia et al. (2020) reported metabolite ratios to have high sensitivity and specificity to differentiate neoplastic from nonneoplastic brain lesions. Another study reported that MRS is accurate in characterizing neoplastic and nonneoplastic brain tumors without histopathological analysis (Mania et al. 2018).

CONCLUSION

MRS provides accurate information about brain lesions. It can characterize various brain lesions. The Cho/Cr and NAA/Cr had significant values to distinguish neoplastic from nonneoplastic brain masses.

RECOMMENDATIONS

Further studies were recommended to compare the MRS metabolites ratios to biopsy analysis for better accuracy. MRS should be joined with the routine MRI examinations in all suspected brain masses for further assessment.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

All the authors have made considerable contributions to the study, design
Acquisition of data, analysis and interpretation of data; and revising the manuscript; and all authors have reviewed and approved the final layout of the manuscript.

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