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Research Article

# Preliminary study of albendazole liposome treatment of cerebral alveolar echinococcosis by $^{1}$H-MR spectroscopy

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**Abstract**

*Objective*: To investigate the $^{1}$H-MRS characteristics of cerebral alveolar echinococcosis (CAE) treated by albendazole liposome.
*Materials and methods*: Nine patients with 20 lesions proven histologically and clinically to be CAE positive were examined via conventional MRI and 2D multivoxel spectroscopy with a 3.0 T double gradient superconductivity magnetic resonance scanner. In patients who took medication regularly for at least one year, the levels of NAA, CR, Cho, MI, Lip, Lac, and other metabolites from the same lesion parenchyma were observed and then used to calculate NAA/Cr, NAA/Cho, NAA/(Cho+Cr), and (Lip+Lac)/Cr. Statistical analysis was performed using the Wilcoxon signed-rank test.
*Results*: Comparisons between cMRI scans taken before patients began taking medication and cMRI scans taken after patients completed one year of regular medication, the volume of legions increased slightly, and the signals of lesions increased on $T_2$WI. The medians and interquartile ranges of NAA/Cho, NAA/CR, NAA/(Cho+Cr), and (Lip+Lac)/Cr in the same lesions in CAE patients prior to treatment via albendazole liposomes were: 2.285 (1.388−3.655), 3.620 (2.173−5.165), 0.651 (0.552−0938), and 29 (15.219−41.609), respectively. The medians and interquartile ranges of NAA/Cho, NAA/CR, NAA/(Cho+Cr), and (Lip+Lac)/Cr in the same lesions in CAE patients after treatment via albendazole liposomes were: 5.120 (1.853−12.00), 6.120 (3.690−9.733), 0.900 (0.651−1.218), and 26.427 (16.536−49.904), respectively. Proton magnetic resonance spectroscopy images of patients with CAE before and after one year of treatment via albendazole liposomes were characterized by the increase of NAA with ratios of NAA/Cho, NAA/CR, and NAA/(Cho+Cr) increasing by different degrees. Compared with the same lesion before and after treatment twice, the differences were statistically significant ($P < 0.01$). In regard to the change in (Lip+Lac)/Cr ratios, the differences were not statistically significant ($P > 0.05$).
*Conclusion*: In patients with CAE, minimal change in CAE lesions imaged via conventional MRI, $^{1}$H-MRS was observed. Slight changes of cerebral alveolar echinococcosis lesions before and after treatment via albendazole liposome were observed, providing valuable imaging information for the treatment of CAE lesions.


*Keywords:* Alveolar echinococcosis; Albendazole liposome; Proton magnetic resonance spectroscopy; Cerebral

## 1. Brief overview

Cerebral alveolar echinococcosis (CAE), known colloquially as "insect cancer", is a zoonotic endemicity parasitic disease. The organs primarily affected by CAE are the liver, the lungs, and the brain with extrahepatic metastasis often occurring in the lungs and brain [1]. Infestation of the brain is usually considered the final stage of the disease [2]. In cases of CAE where surgical resection is not possible due to growth violations into vital areas, treatment via albendazole liposome is preferred [3]. Due to the serious, negative side effects and high costs of the drugs for the treatment of CAE, the main concern of clinicians has shifted towards developing a

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reasonable drug program. The specific antigens of echinococcus multilocularis serology and 18F-FDG PET can be used in the observation of albendazole liposomes; however, the specific antigens observed in echinococcus multilocularis serology examination cannot assess its vitality [4]. Given that PET/CT scanning is relatively expensive and involves exposure to radiation, conventional magnetic resonance imaging, as a non-radiative and non-invasive technique, has been widely used in recent years in the surveillance of CAE [5].

As a method for specifically analyzing atomic nuclei, magnetic resonance spectroscopy, which utilizes the magnetic resonance phenomena and chemical shift, is another noninvasive method for measuring changes in neurotrophic substances in the brain with the most widely used application being proton spectroscopy. Proton magnetic resonance spectroscopy ($^1$H-MRS) can thus be used to access the efficacy of CAE follow-up by observing the quantitative indicators of metabolic activity within lesions. Reliable, noninvasive imaging of CAE-related lesions is necessary and conducive to the clinic development of a reasonable drug program for the treatment of CAE. While MR proton spectroscopy of CAE has been reported [6], the utilization of $^1$H-MRS in examining the treatment of CAE via albendazole liposomes has not been reported.

## 2. Materials and methods

### 2.1. General information

The Medical Ethics Committee of the First Affiliated Hospital of Xinjiang Medical University approved this study. The subject-pool for this study consisted of 17 patients selected from The First Affiliated Hospital of Xinjiang Medical University and diagnosed with cerebral alveolar echinococcosis from April of 2011 to February of 2016. The final subject-pool consisted of nine patients, of which four had a pathological diagnosis and five had a clinical diagnosis, comprising a total of 20 effective lesions.

All patients were informed and consented to examination by way of MR imaging. The clinical diagnostic criteria are as follows: (1) patients resided in pastoral areas and had a history of contact with dogs and sheep; (2) the clinical presentation of patients was either asymptomatic or with corresponding, localized symptoms of the nervous system; (3) CT and MRI scans of patients showed visible lesions; (4) patients tested positive in hydatid immunological tests, though a negative test did not necessarily exclude a patient; (5) other intracranial lesions not associated with CAE were excluded.

The inclusion criteria are as follows: (1) patients received a diagnosis post-operation; patients with a CAE diagnosis under MR examination and had undergone previous surgical intervention for CAE lesions in the liver, lungs, or other parts of the body with no intracranial tumor(s) or history of tuberculosis; (2) patients regularly took albendazole liposome for at least one year; (3) the Region of Interest (ROI) viewed under $^1$H-MRS for one lesion in one patient includes the normal affected area of CAE and the normal parenchyma region of the contralateral section of the lesion; (4) a lesion diameter of more than 5 mm.

The exclusion criteria are as follows: (1) patients who were forbidden from undergoing MR examination, (2) patients who were not medication compliant, (3) patients whose MR examination did not have qualified images under $^1$H-MRS post-processing.

### 2.2. MR examination and image acquisition

A total of 9 patients underwent conventional MRI and 2D multi-voxel MR proton spectroscopy using a Signa Hdx 3.0T double-gradient superimposed MR scanner and 8-channel head coil.

The brain axis $T_2$WI and the liquid attenuation inversion recovery (FLAIR) sequence $T_2$WI were selected as the positioning image of the spectrum. The ROI was then selected based on the localization image. The selected ROI needed to include the parenchyma region of lesion and the corresponding parenchymal region in opposite, using 2D point resolved selective spectroscopy (PRESS). Imaging parameters are as follows: (1) Scanning: TR 3200 ms, TE 144 ms; (2) Thickness:10 mm, FOV 18 cm × 18 cm; (3) Matrix: 256 × 192; and (4) Imaging Time:5 min 28s; (5) scanning peripheral saturation band to avoid interference from other tissues; (6) scanning after the shimming; (7) water suppression. To ensure a stable baseline, shimming requirements of the water resonance peak of the half-line width remained within 10 Hz. The automatic shading water suppression effect was set to more than 95%.

### 2.3. Image processing

According to MR scan with feature enhancement to determine the lesion ROI: MR images with proton magnetic resonance spectroscopy of the lesion parenchyma (including the small necrotic lesions less than 1 mm that can not be distinguished by naked eye), contralateral normal brain parenchyma, the size of ROI is 31.6 mm$^2$, image post-processing under the GE ADW4.4 post-processing workstation.

In order to avoid the effect of microcirculation perfusion on the measured value, set up of the ROI should avoid the area of local sulcus, bleeding, necrosis, calcification, the skull, and other areas. The line conforms to a relatively stable and straight baseline, and the peak of the metabolite peak has a distinct boundary at the specific frequency. The peaks of N-Acetyl-Aspartate,(NAA) (2.02 ppm), Creatine (Cr) (3.02 ppm), Choline (Cho), Myoinositol(mI), Lipids(Lip) (0.8−1.5 ppm), Lactate(Lac) (0.33−1.35 ppm) and other metabolites from the same lesion parenchyma were observed in patients who regularly took one-year medication. The figures for NAA/Cr, NAA/Cho, NAA/(Cho+Cr), and (Lip+Lac)/Cr were then calculated. As the Lip and Lac frequency overlapped, Lip and Lac could not be completed separated into two measurements; therefore, LL (Lip + Lac) was used to represent both.