In-vivo ^{1}H MRS Shows Increased Liver Choline Levels in Hepatitis C Viral Infection

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Introduction

Hepatitis C virus (HCV) is a RNA (ribonucleic acid) virus with diverse genotypes and a broad spectrum of clinical outcome. Due to the high prevalence of HCV infection and its progression to cirrhosis, liver failure and hepatocellular carcinoma, there is a need for new drugs to improve anti-viral treatment. Non-invasive methods for assessing disease severity and predicting and monitoring response to treatment would enable treatment stratification and facilitate drug development. Previous in-vivo and ex-vivo MRS studies involving HCV patients with a range from mild to severe liver disease have suggested that levels of lipid and choline containing compounds in the liver are related to disease severity and that choline/lipid ratios are predictive of response to treatment[1-3].

Aim

To investigate liver fat and total choline (tCho) levels in treatment-naïve hepatitis-C patients with early stage liver disease compared with healthy controls using in-vivo 1H MRS at multiple TE, allowing correction for T2 decay. This study forms a baseline for subsequent repeated measurements after anti-viral treatment with a lipid modifying drug.

Methods

Eligibility criteria for the study were: age 18-65 yrs, body mass index (BMI) < 38 and for the HCV cohort, treatment-naïve patients with HCV (genotype 1 and 3) without cirrhosis determined by biopsy or fibroscan, selected for anti-viral treatment, without excess alcohol consumption, diabetes or pregnancy. 11 patients with HCV (age 42.6 ± 12.3 yrs, male/female 7/4, genotype 1:3 = 9:2, BMI 24.2 ± 5.3) and 12 healthy controls (age 38.7 ± 14.5 yrs, all male, BMI 26.9 ± 4.3) were recruited to the study. Tests were also performed within 24 hours of the MRI scan to assess insulin sensitivity and resistance. MRS of the liver was performed on a Siemens Verio 3T MRI system using single-voxel PRESS-MRS, following orthogonal T1w VIBE (3D-GRE) breath-hold localisers of the thorax and abdomen. A (20×20×20) mm^3 MRS voxel was prescribed, localised in the central right lobe of the liver, avoiding major blood vessels and bile ducts. Image-based shimming was performed over a co-localised (40×40×40) mm^3 region, with manual adjustments where necessary to achieve water linewidth < 40Hz. To allow T2-corrected fat fraction measurements, MRS was acquired without water suppression during a single breath-hold (NSA=7, TR=3s, preps=0), with 4 repeated acquisitions at each of 4 selected TE's (TE=30,40,70,100 ms). MRS with water suppression was also acquired at the same TEs to further characterise the metabolite profile. All breath-hold scans were acquired at end-expiration with patient coaching. Spectra were fitted offline using Tarquin[4] with a customised basis set containing lipid and metabolite peaks. Strict quality control (QC) criteria were applied and visual inspection of fits was performed. Exponential fitting was performed to estimate water, lipid and metabolite T2s and lipid and metabolite levels were calculated relative to water at each TE with and without T2 correction.

Results

There was no significant difference in water T2 (~ 33 ms) or fat T2 (~ 57 ms) between the groups. No significant difference was found in CH_2 lipid levels between HCV (mean±s.e 0.9% ± 0.1% or 1.3% ± 0.3%) and controls (mean±s.e 0.8% ± 0.1% or 1.2% ± 0.2%), with or without T2 correction. One individual in each group had a much larger lipid fraction (> 5%) than the rest of the group, and they also had the highest BMIs (38 and 36). tCho was significantly higher in the HCV group compared with the controls at each TE both with and without T2 correction (fig. 1).

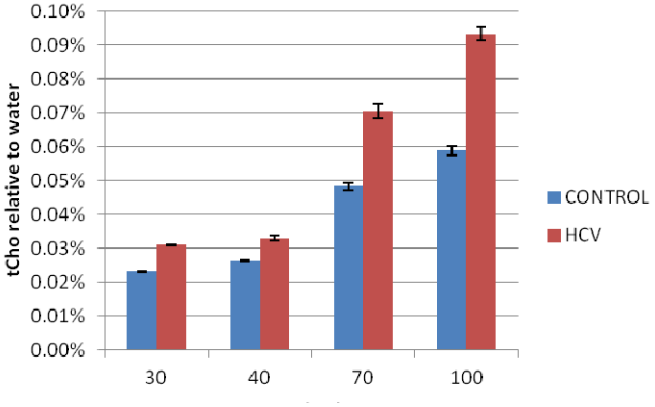

Figure 1. tCho levels relative to water at each TE for HCV and control cohorts (mean±s.e)

Discussion/Conclusion

HCV is known to hijack the host's lipid receptors to facilitate infection in vivo. The higher choline levels found here in the liver of HCV patients may suggest a link between choline found in cell membranes and the HCV life cycle. High choline levels have also been reported in the brain of patients with HCV[5]. Further investigation of potential changes in liver choline levels in response to a novel drug treatment in the HCV cohort will be performed.

References

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