

POSTER PRESENTATIONS

Plasma 24-hydroxycholesterol is associated with narrower common carotid artery and greater flow velocities in relapsing multiple sclerosis

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Background

Multiple sclerosis (MS) studies suggest greater cardiovascular disease burden and disturbances in the cholesterol pathways^{1,2}. The potential impact of oxidized cholesterol molecules (oxysterols) on MS is emerging (Figure 1).³

Objective

To determine the relationship between multiple oxysterol molecules and atherosclerosis burden in MS patients.

Materials and methods

A total of 99 MS patients (61 relapsing-remitting MS (RRMS) and 38 progressive MS (PMS)) patients and 38 healthy controls (HCs) underwent magnetic resonance angiography (MRA) and the cross-sectional area (CSA) of the common carotid artery (CCA) was determined at three different levels before the bifurcation (C7, C6 and C5). Additionally, an echo-color Doppler ultrasound was performed and measures of blood flow velocities were derived. Blood samples acquired at the time of the imaging examinations were analyzed and 24-, 25-, 27-hydroxycholesterol (24HC, 25HC, 27HC) and 7-ketocholesterol (7KC) were quantified in ng/mL.

Results

In the MS patients, higher levels of 24HC were significantly associated with smaller CCA CSA measured at all three cervical levels ($r=-0.201$, $p=0.046$; $r=-0.228$, $p=0.023$, and $r=-0.215$, $p=0.032$, for C7, C6 and C5, respectively). These associations were driven by the RRMS group only ($r=-0.407$, $p=0.002$ for C7; $r=-0.414$, $p=0.002$, for C6; and $r=-0.368$, $p=0.006$ for C5). No associations were seen in the HCs. Despite adjusting for the significant age effect ($B=0.445$, $p=0.004$), higher 24HC levels were independently associated with smaller CCA CSA ($B=-0.20$, $p=0.045$). 24HC was

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additionally associated with greater time-averaged and peak diastolic CCA velocities. RRMS patients treated with potent anti-inflammatory therapies had lower oxysterol levels ($p=0.019$). RRMS patients in the lower 24HC quartiles had significantly higher expanded disability status scale (EDSS) scores when compared to RRMS patients in the higher two 24HC quartiles

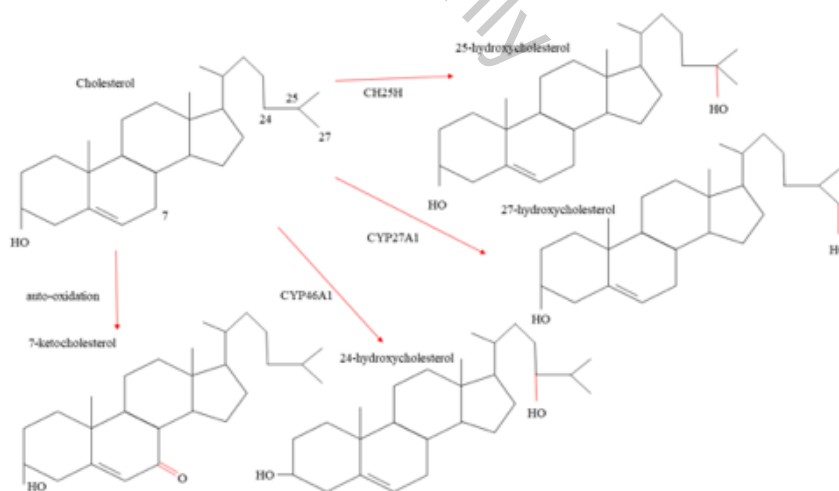


Figure 1. Graphical representation of cholesterol oxidation and formation of oxysterols. CYP: cytochrome P450; CH25H: cholesterol 25-hydroxylase; HO: hydroxide.

(2.5 (IQR 1.9-3.1) vs 2.0 (1.5-2.5), p=0.038).

Conclusions

Greater 24HC levels are associated with smaller CSA CCA and greater flow velocities in RRMS patients. The higher inflammatory activity in RRMS patients may contribute to the production of highly reactive oxysterols and worsen the atherosclerotic

burden in the MS population. Potent anti-inflammatory medications can significantly decrease oxysterol levels.

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