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Coenzyme Q10 supplementation does not improve simvastatin tolerance in patients with previous statin-myalgia

Joanna M. Young¹, Christopher M. Florkowski^{1,2}, Sarah M. Molyneux², Roberta G. McEwan¹, Christopher M. Frampton³, Peter M. George², Russell S. Scott¹

- 1. Lipid and Diabetes Research Group, Christchurch Hospital**
- 2. Clinical Biochemistry Unit, Canterbury Health Laboratories**
- 3. Department of Medicine, Christchurch School of Medicine & Health Sciences**

Myalgia is one of the most frequently reported adverse effects associated with statin therapy, often necessitating reduction in statin dose and compromising cardiovascular risk management. Statins inhibit synthesis of mevalonate, a precursor of coenzyme Q10 (CoQ) that is an essential component of the mitochondrial electron transport chain, resulting in a decrease in plasma CoQ. The mechanism for statin-induced myalgia remains unclear, but may be linked to CoQ depletion.

The impact of CoQ supplementation on statin myalgia has not been assessed in a placebo-controlled trial. We therefore studied whether CoQ improves statin tolerance and myalgia during simvastatin therapy in a double-blind placebo-controlled trial. Forty-four patients with prior statin-induced myalgia were randomised to 12-weeks treatment with upward dose titration of simvastatin (10mg/day–40mg/day) in combination with CoQ (Q-Gel®) 200mg/day or matching lactose-filled placebo, after a 2-week wash-out of lipid lowering therapies. The primary outcome was the change in myalgia scores.

The study was powered (80%) to detect a 9mm difference in myalgia scores between treatment groups. Patients experiencing significant myalgia reduced their statin dose or discontinued treatment. Myalgia was assessed using a visual analogue scale for scoring severity of symptoms. CoQ levels increased with combined treatment (131%; 95 CI 75–186%; $p < 0.001$), and decreased with statin alone (-34%; 95 CI -40–28%; $p < 0.001$). ITT analysis showed the change in myalgia scores did not differ between treatments ((6.0 (2.1- 8.8) v 2.3 (0 – 12.8); $p = 0.63$). Further, there was no difference in the number of patients who tolerated simvastatin at the 40mg/d dose (CoQ 16/22 (73%) v placebo 13/22 (59%); $p = 0.34$), or the number remaining on any simvastatin dose 16/22 (73%) v 18/22 (82%); $p = 0.47$).

Despite achieving significant increases in CoQ levels with combined treatment, CoQ supplementation was not associated with improved statin tolerability. Our findings do not support the concomitant use of CoQ in statin-treated patients who experience myalgic symptoms, however larger studies are warranted.

The risk of recurrent stroke after intracerebral haemorrhage

H Carl Hanger¹, Timothy J Wilkinson^{1,2}, Nancy Fayed-Iskander², Richard Sainsbury^{1,2}.

- 1. Older Persons Health, The Princess Margaret Hospital**
- 2. Department of Health Care of the Elderly, Christchurch School of Medicine & Health Sciences**

The risks of recurrent intracerebral haemorrhage (ICH) vary widely (0 to 24%). Patients with ICH also have risk factors for ischaemic stroke (IS) and a proportion of ICH survivors re-present with an IS. This has implications for secondary prevention. This study aims to determine the risk of recurrent stroke events (both ICH and IS) following an index bleed and whether ICH recurrence risk varies according to location of index bleed.

All patients diagnosed with an acute ICH presenting over an 8.5 year period were identified. Each ICH was confirmed by reviewing all radiology results, and where necessary the clinical case notes or post mortem data. Recurrent stroke events (ICH and IS) were identified by re-appearance of these patients on our stroke database. Coronal post-mortem results for the same period were also reviewed. Each recurrent event was reviewed to confirm the diagnosis and location of stroke.

Of the 7686 stroke events recorded, 768 (10%) were ICH. Four hundred and sixty-four ICH patients survived beyond the index hospital stay. There were 19 recurrent ICH and 17 new IS in these 464 patients. The recurrence rate for ICH was 2.1% in the first year following ICH, but 1.2/100/year for the full follow-up period. This compares with 1.3/100/year overall for IS. Most ICH recurrences were “lobar-lobar” type.

The cumulative risk of recurrent ICH in this population is similar to that of IS after the first year. The findings would suggest that, after the first year, a previous ICH should not be an absolute contraindication for thromboembolic prophylaxis.

Optimization of selected ion flow tube – mass spectrometry for the measurement of acetone in breath

Jack Dummer¹, Maureen Swanney², Katherine Ledingham³, Senti Senthilmohan³, Jenny Scotter³, Randall Allardyce³, Christopher Frampton¹, Michael Epton¹

- 1. Department of Medicine, Christchurch School of Medicine & Health Sciences**
- 2. Respiratory Physiology Laboratory, Christchurch Hospital**
- 3. Syft Technologies, Christchurch**

Selected Ion Flow Tube – Mass Spectrometry (SIFT-MS) is an analytical technique that can measure volatile organic compounds in breath on-line and in real time. Optimization of analysis conditions, determination of dynamic response times, and comparison of different breathing manoeuvres are important to gain meaningful repeatable data from breath. We hypothesized that a slow exhalation of vital capacity

was an appropriate breathing manoeuvre for measuring acetone in breath by SIFT-MS and that there would be no difference between sampling via mouth or nose.

We measured dynamic response time and inter-measurement variability data using known concentrations of acetone in vitro. Six volunteers then performed three slow exhalations to residual volume via both mouth and nose while SIFT-MS measurements were taken.

The dynamic response time of the instrument for acetone was 506 ± 32 ms (mean \pm SE). Exhalations resulted in plateaux giving reproducible measurements of acetone concentration (intra-subject coefficients of variation of 1.8% for exhalations via mouth and 4.8% via nose). Mean acetone concentrations for exhalations via mouth and nose were 471 ± 56 and 479 ± 56 ppb (mean \pm SE), (mean difference 8.0 ppb; SE difference 5.2 ppb). The difference was not significant ($p = 0.17$).

Slow vital capacity breathing manoeuvres were appropriate given the dynamic response time of the instrument and resulted in reproducible measurements of acetone concentration. No significant difference in acetone concentration between breaths via mouth and nose was found. This experiment may serve as a template for optimizing measurement of any compound in breath using SIFT-MS.

Using MRI to identify microstructural changes in the brain

Michael Chappell^{1,2}, Timothy Anderson^{2,3}, Jennifer Brown^{2,4}, John Dalrymple-Alford^{2,5}, Marcus Heitger², Saskia van Stockum⁵, Richard Watts^{1,2}

- 1. Department of Physics and Astronomy, University of Canterbury**
- 2. Van der Veer Institute for Parkinson's and Brain Research, Christchurch**
- 3. Department of Medicine, Christchurch School of Medicine & Health Sciences**
- 4. Department of Mathematics and Statistics, University of Canterbury**
- 5. Department of Psychology, University of Canterbury**

Magnetic resonance imaging (MRI) can be made sensitive to the movement of water through the brain. This movement, or diffusion, is known to depend on the microstructure of the local environment. Thus diffusion weighted MRI can be used to identify microstructural changes in the brain that are not apparent on standard anatomical MR images.

We used this to investigate the correlation of microstructural changes with neuropsychological variables in Parkinsonian patients, and to localise structural abnormalities in the brains of non-symptomatic professional boxers. In both cases, scanning was done using a single shot 2D spin echo Echo Planar Imaging (EPI) sequence. All brain images were spatially normalized to allow for statistical comparisons with $\alpha = 0.05$, and correction for multiple comparisons done using false discovery rate methodology.

Twelve Parkinsonian patients with varying degrees of cognitive impairment were studied. Clusters of voxels showing statistically significant correlation between diffusion measures and neuropsychological variables marking cognitive decline were most apparent for periventricular regions, the medial temporal lobe and the thalamus.

59 male professional boxers and 12 normal male controls in the same age range were studied. Regions showing microstructural changes in the boxers who had received mild, repetitive, non-symptomatic head trauma were identified in subcortical white matter in the brainstem/midbrain, cerebral peduncle, corticospinal tract, the posterior limb of the internal capsule, corona radiata and the frontal lobes. We have developed new tests that enable the use of more than one diffusion measure at a time. These are shown to be more sensitive with the boxer data than conventional univariate techniques.