Several studies have assessed the potential of targeting the renin angiotensin system (RAS) with therapeutics for ischaemic stroke. The counter regulatory RAS peptide, angiotensin-(1–9) has been shown to act via the angiotensin II type 2 receptor (AT2R) to oppose detrimental effects of RAS dysregulation. We hypothesise that Ang-(1–9) may have a beneficial effect on stroke outcome in the spontaneously hypertensive stroke prone rat (SHRSP). Initial qPCR experiments have assessed temporal changes in RAS gene expression (angiotensin converting enzyme 2; ACE2, AT2R; AGTR2, Mas receptor; Mas) following 35 min transient middle cerebral artery occlusion (tMCAO) followed by varying reperfusion times: no reperfusion (n=4), 2 hour (n=4) and 24 hour (n=4), compared to sham surgery (n=7).

In infarcted tissue, there was a significant 10- and 11-fold reduction in ACE2 and Mas expression respectively, 24 hour post tMCAO vs sham (RQ+RQmax: ACE2: sham 1.0±0.2; 24 hour post tMCAO 0.1±0.01, p<0.01, Mas: sham 1.0±0.2; 24 hour post tMCAO 0.09±0.03 p<0.01). However, in the same tissue, AGTR2 showed a 4-fold increase in expression after 35 min occlusion vs sham (RQ+RQmax: sham 1.0±0.3; 35 min MCAO 4.2±0.2, p<0.05). Additionally, in the subcortical remainder tissue, ACE2 and AGTR2 expression decreased by 2.5- and 5-fold respectively 24 hour post tMCAO (RQ+RQmax: ACE2: sham 1.0±0.1; 24 hour post tMCAO 0.4±0.1, p<0.05, AGTR2: sham 1.0±0.4 ; 24 hour post tMCAO 0.2±0.1 p<0.05).

These results demonstrate altered counter regulatory RAS gene expression in the ipsilateral hemisphere in the 24 hours following tMCAO in SHRSP. Additional experiments have demonstrated successful transduction of a control reporter gene-expressing, adeno-associated virus serotype 9 (AAV9) expressing enhanced green fluorescent protein (eGFP) (AAV9-eGFP) in the SHRSP brain via stereotactic delivery after both 4 and 7 days. Future studies will assess the therapeutic potential of Ang-(1–9) in tMCAO induced experimental stroke in SHRSP by delivering Ang-(1–9) via stereotactic delivery of an AAV9 vector.
Abstracts

Introduction Electronic cigarettes (EC) are currently the preferred nicotine replacement product to support tobacco smoking quit attempts. Despite the potential harm reduction associated with EC, their use remains controversial. The aim of this study was to evaluate doctors’ knowledge and perceptions of NRT and EC.

Methods An online and paper survey was distributed to healthcare professionals working within NHS Greater Glasgow and Clyde from 3rd to 19th October 2017.

Results 2291 healthcare professionals completed the survey of which 338 were completed by doctors and were included in this analysis. Out of these, 83.2% (n=281) regularly see patients who smoke tobacco cigarettes. When asked the question ‘Do you think EC are a good thing?’, 30.2% (n=102) disagreed; 31.3% (n=106) agreed and 38.5% (n=130) remained neutral. The majority of doctors perceived that nicotine replacement patches (NRP) and EC were less harmful in comparison to tobacco smoking (NRP 97.3%, n=329; EC 83.4%, n=282). 53.3% (n=180) of doctors said they would recommend EC as a method to stop smoking, while 46.7% (n=158) would not. 65.5% (n=222) of doctors agreed that they did not feel confident about advising patients regarding EC use and 76.1% (n=257) felt that they required more information and guidance.

Conclusions Whilst the majority of doctors perceived EC as a safer alternative to tobacco smoking there is a discrepancy between their perceptions and what they would clinically recommend to patients. Our data highlight that in the context of smoking cessation and the unknown long-term health effects from EC exposure, doctors may benefit from having access to medical evidence and latest recommendations regarding EC.


3 RED YEAST RICE EXTRACT REDUCES IL-1β SECRETION FROM PBMCs WHEN TREATED WITH CHOLESTEROL CRYSTALS

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Abstracts

Introduction Considerable evidence implicates a role for interleukin-1 beta (IL-1β) in the pathogenesis of atherosclerosis revealing its potential as a novel therapeutic target. Statins are known to have anti-inflammatory effects, however the specific mechanisms remain to be established. To test the anti-inflammatory effects of simvastatin, PBMCs were isolated from healthy donors and treated in vitro with simvastatin (100 µM) or from hyperlipidaemic patients at baseline and following 8 weeks simvastatin (10–20 mg) daily treatment. PBMCs were then stimulated with LPS (100 ng/ml) for 3 hour followed by cholesterol crystal (CC) (1 mg/ml) stimulation overnight to activate the NLRP3 inflammasome complex involved in processing IL-1β to its mature secreted form. IL-1β levels in the supernatants form PBMCs was measured by ELISA. All experiments carried out were approved by the Medical Research Ethics Committees at St James Hospital/AMNCH, Dublin 8, Ireland and comply fully with the Declaration of Helsinki. Patients (n=9) taking simvastatin (10–20 mg daily) over 8 weeks exhibited reduced LDL cholesterol, (4.87±0.76 mmol/L) pre vs 3.78±0.67 mmol/L post statin treatment. Simvastatin treatment also reduced levels of IL-1β secretion by PBMCs, when stimulated with LPS and CC, (5.27±0.6 ng/ml) pre vs (4.27±0.5 ng/ml) post statin treatment. Similarly, in vitro treatment of PBMCs with simvastatin (100 µM) reduced IL-1β secretion upon activation with LPS and CC, (2.37±0.17 ng/ml) control vs (0.64±0.06 ng/ml) simvastatin treatment. Values presented are mean ±SEM. We have demonstrated that CC induced IL-1β release by PBMCs from hyperlipidaemic patients, is reduced after treatment with simvastatin. These data identify a previously unappreciated beneficial role for statin therapy in atherosclerotic patients.

References