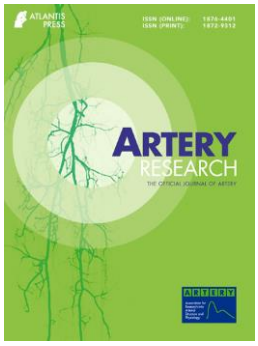

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P1.08: EFFECTS OF ANTIOXIDANTS ON SERUM URIC ACID AS A MARKER OF VASCULAR FUNCTION

H.W. Huisman, A.E. Schutte, J.M. van Rooyen, R. Schutte, N.T. Malan, L. Malan, C.M.T. Fourie

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P1.07
ROSUVASTATIN INCREASES EXTRACELLULAR ADENOSINE IN HUMANS IN VIVO: A NEW PERSPECTIVE ON CARDIOVASCULAR PROTECTION

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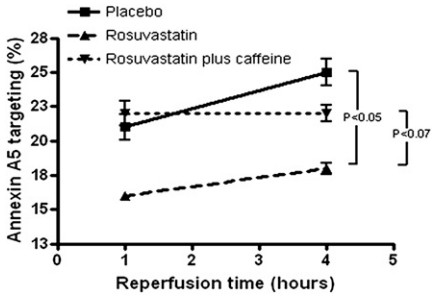
Background: Increased extracellular adenosine formation provides a cholesterol-independent explanation for the therapeutic benefit of statins. This theory was tested in humans in-vivo using dipyridamole-induced vasodilation as a read out for local adenosine formation. Its relevance was explored using a foream model of ischemia-reperfusion injury.
Methods: Twenty-one healthy volunteers were randomly allocated to receive either rosuvastatin (20 mg/day for eight days) or placebo in a double-blind parallel design. The vasodilator response to the nucleoside transport inhibitor dipyridamole was determined in the absence and presence of the adenosine antagonist caffeine. In two additional studies, healthy volunteers were randomly divided in four groups to receive either placebo (n=10), rosuvastatin (20 mg/day for 7 days; n=22), or rosuvastatin combined with intravenous caffeine (4 mg/kg, single dose; n=12). Subsequently, volunteers performed ischemic exercise of the non-dominant forearm. At reperfusion, Tc-99m-labeled annexin A5 was infused intravenously and scintigraphic images were acquired using a gamma camera, providing an early marker of injury.
Results: Rosuvastatin treatment significantly increased the vasodilator response to dipyridamole. This effect was completely abolished by caffeine. Rosuvastatin increased tolerance to ischemia-reperfusion injury, an effect which was attenuated by adenosine receptor blockade.
Conclusion: Rosuvastatin increases extracellular adenosine formation and protects against ischemia-reperfusion injury in humans in-vivo. Our observations prove the concept that statins and dipyridamole interact synergistically whereas caffeine consumption hinders the therapeutic action of statins.



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P1.08
EFFECTS OF ANTIOXIDANTS ON SERUM URIC ACID AS A MARKER OF VASCULAR FUNCTION

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Introduction: Serum uric acid is linked to vascular nitric oxide activity and therefore can blunt endothelium-dependent vasodilation. Antioxidants may increase nitric oxide activity and endothelial function and this might result in decreased uric acid levels.
Aim: The objective was to investigate if supplementation with antioxidants has a beneficial effect on uric acid.
Method: 74 borderline hypertensive Caucasian men participated (aged 45-65 years) in a randomized double-blind, cross-over intervention trial receiving either an antioxidant cocktail (vitamin C, E and folic acid) or placebo. Cardiovascular parameters were recorded with the Finometer. The Complior SP was used to measure the carotid-radialis PWV.
Results: Folic acid (as an indicator of compliance to antioxidant intake) increased significantly with 30% (P=0.005) with no changes in the placebo group. Uric acid was lower after the antioxidant intervention (changed from 0.53 mmol/L to 0.49 mmol/L (p=0.007), with no change in the placebo group. No significant differences were found between the pre and post intervention values for blood pressure, total peripheral resistance and PWV for both interventions . Significant correlations were found between uric acid and total cholesterol (placebo r=0.54: P< 0.001; antioxidant r=0.25: P=0.04).
Conclusion: With antioxidant intervention the lowered uric acid level point to a improvement in vascular function and oxidative stress. The weaker correlation between uric acid and cholesterol also points to improved vascular function since uric acid is strongly linked to cholesterol in vascular disease.

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P1.09
THE EFFECTS OF RIMONABANT-INDUCED WEIGHT LOSS ON ARTERIAL FUNCTION AND GLYCAEMIA IN OBESE ADULTS WITH TYPE 2 DIABETES

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Premature large artery stiffening is a major contributor to the development of cardiovascular disease in type 2 diabetes. Intentional weight loss through lifestyle intervention is associated with a reduction in arterial stiffness. Rimonabant is a cannabinoid-1 receptor blocker that reduces body weight and improves the cardiovascular risk profile in obese subjects. The purpose of this study was to examine the effects of rimonabant therapy on arterial function in obese subjects with type 2 diabetes.
Twenty-nine obese subjects (age range 30-72yrs) (13 male, 16 females) with type 2 diabetes (13 insulin-treated) were studied. Twenty subjects were studied before, during and after 6 months therapy with rimonabant in conjunction with dietary and lifestyle advice. Nine subjects received dietary and lifestyle advice only without rimonabant. Arterial function was assessed by measuring aortic and brachial pulse wave velocity (PWV) and augmentation index (Sphygmocor).
After 6 months, Rimonabant therapy led to significant weight loss (mean weight loss 5±4Kg, p<0.0001), improved glycaemia (HbA1c reduction 0.6±1.1%, p<0.05) and lipid profile (HDL cholesterol increase of 0.1±0.1mmol/L, p<0.01). Aortic systolic pressure was lowered by 5±9mmHg (p<0.05) but there were no changes to peripheral blood pressure, augmentation index or aortic PWV.
In conclusion, rimonabant therapy in association with dietary and lifestyle change leads to significant weight loss and improved glycaemic control in obese adults with type 2 diabetes. However, these clinical benefits do not appear to be accompanied by a reduction in arterial stiffness or wave reflection.

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P1.10
CIMT MEASUREMENT IS MORE RELIABLE THAN WEIGHT REDUCTION IN OVERWEIGHT YOUNG ADULTS TO ASSESS LIFESTYLE IMPACT

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The Insulin Resistance Syndrome is characterized by decreased tissue sensitivity to the action of insulin, obesity and a thick Carotid Intima Media Thickness (CIMT). Homeostasis Model Assessment (HOMA) remains an excellent to assess the level of insulin resistance. We studied the impact of a healthy lifestyle modification in young overweight BMI >27 and non-overweight adults BMI <22 m/kg2. The intervention consisted of a 16 weeks dietary consultation, exercise and a personalized vascular image.
Results:

overweight	BMI>27	(n=18)	normal weight	BMI <22 (n=10)
age	8-12 years		8-12 years	
HOMA glucose x Insulin/22.5	4.6	2.4	1.9	1.8
glucose mg/dl	92	88	78	77
insulin µU/ml	21	17	9.7	9.5
CIMT µ	539	530	522	520
Cholesterol mg/dl	160	162	148	143
HDL-C mg/dl	38	41	57	59
BP mmHg	130/76	126/72	110/68	108/70

Discussion: Both groups lost some weight and showed an improvement in different parameters. The relative change in CIMT was significantly more in the obese group A positive correlation between HOMA and CIMT was observed, (r= 0.717, p< 0.02). in the overweight cases increasing significantly (r=0.832, p<0.01) (delta change p<0.05).