Resveratrol improves insulin sensitivity, reduces oxidative stress and activates the Akt pathway in type 2 diabetic patients

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Source

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Abstract

Although resveratrol has widely been studied for its potential health benefits, little is known about its metabolic effects in humans. Our aims were to determine whether the polyphenol resveratrol improves insulin sensitivity in type 2 diabetic patients and to gain some insight into the mechanism of its action. After an initial general examination (including blood chemistry), nineteen patients enrolled in the 4-week-long double-blind study were randomly assigned into two groups: a resveratrol group receiving oral 2 × 5 mg resveratrol and a control group receiving placebo. Before and after the second and fourth weeks of the trial, insulin resistance/sensitivity, creatinine-normalised ortho-tyrosine level in urine samples (as a measure of oxidative stress), incretin levels and phosphorylated protein kinase B (pAkt):protein kinase B (Akt) ratio in platelets were assessed and statistically analysed. After the fourth week, resveratrol significantly decreased insulin resistance (homeostasis model of assessment for insulin resistance) and urinary ortho-tyrosine excretion, while it increased the pAkt:Akt ratio in platelets. On the other hand, it had no effect on parameters that relate to β-cell function (i.e. homeostasis model of assessment of β-cell function). The present study shows for the first time that resveratrol improves insulin sensitivity in humans, which might be due to a resveratrol-induced decrease in oxidative stress that leads to a more efficient insulin signalling via the Akt pathway.

Cardioprotection by resveratrol: A human clinical trial in patients with stable coronary artery disease.

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Source

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Abstract

Several beneficial effects of resveratrol (RES), a natural antioxidant present in red wine have already been described. The aim of our study was to investigate if RES had a clinically measurable cardioprotective effect in patients after myocardial infarction. In this double-blind, placebo controlled trial 40 post-infarction Caucasian patients were randomized into two groups. One group received 10 mg RES capsule daily for 3 months. Systolic and diastolic left ventricular function, flow-mediated vasodilation (FMD), several laboratory and hemorheological parameters were measured before and after the treatment. Left ventricular ejection fraction showed an increasing tendency (ns) by RES treatment. However, left ventricular diastolic function was improved significantly ($p < 0.01$) by RES. A significant improvement in endothelial function measured by FMD was also observed ($p < 0.05$). Low-density lipoprotein (LDL) level significantly decreased ($p < 0.05$) in the RES treated group. Red blood cell deformability decreased and platelet aggregation increased significantly in the placebo group ($p < 0.05$), while resveratrol treatment has prevented these unfavourable changes. Concerning other measured parameters no significant changes were observed neither in placebo nor in RES group. Our results show that resveratrol improved left ventricle diastolic function, endothelial function, lowered LDL-cholesterol level and protected against unfavourable hemorheological changes measured in patients with coronary artery disease (CAD)

Effect of coenzyme q10 on myopathic symptoms in patients treated with statins

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Source

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Abstract

Treatment of hypercholesterolemia with statins (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors) is effective in the primary and secondary prevention of cardiovascular disease. However, statin use is often associated with a variety of muscle-related symptoms or myopathies. Myopathy may be related in part to statin inhibition of the endogenous synthesis of coenzyme Q10, an essential cofactor for mitochondrial energy production. The aim of this study is to determine whether coenzyme Q10 supplementation would reduce the degree of muscle pain associated with statin treatment. Patients with myopathic symptoms were randomly assigned in a double-blinded protocol to treatment with coenzyme Q10 (100 mg/day, n = 18) or vitamin E (400 IU/day, n = 14) for 30 days. Muscle pain and pain interference with daily activities were assessed before and after treatment. After a 30-day intervention, pain severity decreased by 40% ($p < 0.001$) and pain interference with daily activities decreased by 38% ($p < 0.02$) in the group treated with coenzyme Q10. In contrast, no changes in pain severity (+9%, p = NS) or pain interference with daily activities (-11%, p = NS) was observed in the group treated with vitamin E. In conclusion, results suggest that coenzyme Q10 supplementation may decrease muscle pain associated with statin treatment. Thus, coenzyme Q10 supplementation may offer an alternative to stopping treatment with these vital drugs.

Procyanidins from grape seeds protect endothelial cells from peroxynitrite damage and enhance endothelium-dependent relaxation in human artery: new evidences for cardio-protection.

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Source

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Abstract

The peroxynitrite scavenging ability of Procyanidins from Vitis vinifera L. seeds was studied in homogeneous solution and in human umbilical endothelial cells (EA.hy926 cell line) using 3-morpholinosydnonimine (SIN-1) as peroxynitrite generator. In homogeneous phase procyanidins dose-dependently inhibited 2',7'-dichloro-dihydrofluorescein (DCFH) oxidation induced by SIN-1 with an IC50 value of 0.28 microM. When endothelial cells (EC) were exposed to 5 mM SIN-1, marked morphological alterations indicating a necrotic cell

death (cell viability reduced to 16 +/- 2.5%) were observed. Cell damage was suppressed by procyanidins, with a minimal effective concentration of 1 microM (cell morphology and integrity completely recovered at 20 microM). Cellular localization of procyanidins in EC was confirmed using a new staining procedure and site-specific peroxyl radical inducers: AAPH and cumene hydroperoxide (CuOOH). Endothelial cells (EC) pre-incubated with procyanidins (20 microM) and exposed to FeCl3/K3Fe(CN)6 showed a characteristic blue staining, index of a site-specific binding of procyanidins to EC. Procyanidins dose-dependently inhibit the AAPH induced lipid oxidation and reverse the consequent loss of cell viability, but were ineffective when oxidation was driven at intracellular level (CuOOH). This demonstrates that the protective effect is due to their specific binding to the outer surface of EC thus to quench exogenous harmful radicals. Procyanidins dose-dependently relaxed human internal mammary aortic (IMA) rings (with intact endothelium) pre-contracted with norepinephrine (NE), showing a maximal vasorelaxant effect (85 +/- 9%) at 50 microM (catechin: 18 +/- 2% relaxation at 50 microM). This effect was completely abolished when IMA-rings were de-endothelized and when IMA-rings with intact endothelium were pretreated with L-NMMA or with the soluble guanylate cyclase inhibitor, ODQ. Pre-incubation with indomethacin reduces (by almost 50%) the vasodilating effect of procyanidins, indicating the involvement also of a COX-dependent mechanism. This was confirmed in another set of experiments, where procyanidins dose-dependently stimulate the prostacyclin (PGI2) release, reaching a plateau between 25 and 50 microM. Finally, pre-incubation of IMA-rings with procyanidins (from 6.25 to 25 microM) resulted in a dose-dependent prevention of the endothelin-1 (ET-1) vasoconstriction. The ability of procyanidins to prevent peroxynitrite attack to vascular cells, by layering on the surface of coronary EC, and to enhance endothelial NO-synthase-mediated relaxation in IMA rings provide further insight into the molecular mechanisms through which they exert cardioprotective activity in ischemia/reperfusion injury in vivo

Synergistic anti-cancer effects of grape seed extract and conventional cytotoxic agent doxorubicin against human breast carcinoma cells.

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Source

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Abstract

With an approach to enhance the efficacy of chemotherapy agents against breast cancer treatment, here, we investigated the anti-cancer effects of grape seed extract (GSE) and doxorubicin (Dox), either alone or in combination, in estrogen receptor-positive MCF-7 and receptor-negative MDA-MB468 human breast carcinoma cells. GSE (25-200 micro g/ml) treatment of cells resulted in 16-72% growth inhibition and 9-33% cell death, in a dose- and a time-dependent manner. In other studies, Dox (10-100 nM) treatment showed 23-96% growth inhibition and 10-55% cell death. Based on these results, several combinations of GSE (25-100 micro g/ml) with Dox (10-75 nM) were next assessed for their synergistic, additive and/or antagonistic efficacy towards cell growth inhibition and death. In both MCF-7 and MDA-MB468 cells, a combination of 100 micro g/ml GSE with 25-75 nM Dox treatment for 48 h showed a strong synergistic effect [combination index (CI) < 0.5] in cell growth inhibition, but mostly an additive effect (CI approximately 1) in cell death. In cell-cycle progression studies, GSE plus Dox combination resulted in a moderate increase in G1 arrest in MCF-7 cells compared to each agent alone. GSE plus Dox combination showed a very strong and significant G1 arrest in MDA-MB468 cells when compared with Dox alone, however, it was less than that observed with GSE alone. In quantitative apoptosis studies, GSE and Dox alone and in combination showed comparable apoptotic death of MCF-7 cells, however, a combination of the two was inhibitory to Dox induced apoptosis in MDA-MB468 cells. This was further confirmed in another estrogen receptor-negative MDA-MB231 cell line, in which GSE and Dox combination strongly inhibited cell growth but did not show any increase in apoptotic cell death caused by Dox. Together, these results suggest a strong possibility of synergistic efficacy of GSE and Dox combination for breast cancer treatment, independent of estrogen receptor status of the cancer cell.

Vitamin D and prognosis in acute myocardial infarction.

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Source

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Abstract

BACKGROUND:

Vitamin D status (VDS) has been linked to mortality and incident acute myocardial infarction (AMI) in healthy cohorts. Associations with recurrent adverse cardiovascular events in those with cardiovascular disease are less clear. Our objective was to assess the prevalence and prognostic impact of VDS on patients presenting with AMI.

METHODS:

We measured plasma 25-(OH)D(3) and 25-(OH)D(2) using isotope dilution tandem mass spectrometry, in 1259 AMI patients (908 men, mean age 65.7±12.8years). The primary endpoint was major adverse events (MACE), a composite of death (n=141), heart failure hospitalisation (n=111) and recurrent AMI (n=147) over median follow-up of 550days (range 131-1095). Secondary endpoints were fatal and non-fatal MACE.

RESULTS:

Almost 74% of the patients were vitamin D deficient (<20ng/ml 25-(OH)D). Plasma 25-(OH)D existed mainly as 25-(OH)D(3) which varied with month of recruitment. Multivariable survival Cox regression models stratified by recruitment month (adjusted for age, gender, past history of AMI/angina, hypertension, diabetes, hypercholesterolaemia, ECG ST change, Killip class, eGFR, smoking, plasma NTproBNP), showed 25-(OH)D(3) quartile as an independent predictor of MACE(P<0.001) and non-fatal MACE(P<0.01), but not death. Using the lowest 25-(OH)D(3) quartile(<7.3ng/ml) as reference for MACE prediction, the 2nd, 3rd and 4th quartiles showed significantly lower hazard ratios (HR 0.59(P<0.002), 0.58(P<0.001), and 0.59(P<0.003) respectively). For non-fatal MACE prediction, the 2nd, 3rd and 4th 25-(OH)D(3) quartiles were all significantly different from the lowest reference quartile (HR 0.69(P<0.05), 0.54(P<0.003) and 0.59(P<0.014) respectively).

CONCLUSIONS:

VDS is prognostic for MACE (predominantly non-fatal MACE) post-AMI, with approximate 40% risk reduction for 25-(OH)D(3) levels above 7.3ng/ml.