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#### 4. CAROTID FLOW VELOCITY DIFFERENCE AS A SURROGATE FOR ISCHEMIC STROKE

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**Background:** Carotid flow peak velocity is increased in carotid artery stenosis. Carotid intima-media thickness (IMT) have been associated with an increased risk of ischemic stroke. We performed this study to evaluate the relationship between carotid flow velocity and carotid IMT in ischemic stroke without significant carotid stenosis.

**Methods:** A total of 559 patients with acute ischemic stroke were enrolled in this study. We evaluated the association of carotid IMT and carotid flow velocity difference from peak systolic to end diastolic velocity with age, sex, potential vascular risk factors, and cardiac function by echocardiography.

**Results:** Age and common carotid IMT was significantly associated with carotid flow velocity difference ( $r = -0.106$ ,  $p = 0.014$ ). We did not found a significant relationship between carotid flow velocity difference and gender or traditional cardiovascular risk factors such as hypertension, diabetes, smoking and dyslipidemia. Left ventricle end diastolic dimension and diastolic parameter  $e/e'$  from echocardiography was also related with carotid blood flow velocity ( $r = 0.107$ ,  $p = 0.015$ ,  $r = 0.108$ ,  $p = 0.016$ ). Linear regression analysis demonstrate that carotid flow velocity difference was independently associated with carotid IMT ( $\beta = -0.094$ ,  $p = 0.040$ ) and  $e/e'$  ( $\beta = 0.116$ ,  $p = 0.011$ ).

**Conclusion:** The present results indicated that carotid flow velocity difference was independently associated with carotid IMT and left ventricle diastolic function. We further suggest that carotid flow velocity difference is another surrogate for ischemic stroke in the spite of absence of significant carotid stenosis.

#### 5. THE EFFECT OF CILOSTAZOL TO ARTERIAL STIFFNESS IN THE HYPERTENSIVE PATIENT

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**Background:** Cilostazol is a potent antiplatelet agent that selectively inhibits phosphodiesterase III, and also it has beneficial effect to peripheral arterial disease, like intermittent claudication, by direct vasodilative action. But the effect of cilostazol on arterial stiffness is unclear. We investigated the effect of cilostazol on arterial stiffness by using Pulse Wave Velocity (PWV) which is most common and non-invasive measure technique.

**Methods:** From May, 2006, Total 708 hypertension patients were examined PWV study. 86 patients were taking cilostazol at least 3 month ago before PWV study. The rest 622 patients did not take cilostazol. All value of each aortic PWV, arm PWV, leg PWV of all patients were measured by using pp-1000 and analysed.

**Results:** In cilostazol group, mean period of taking medicine is 823 days (130-1390days). In baseline characteristics, cilostazol group is older than control group (63.3 vs 56.9  $p < 0.001$ ), have higher proportion of DM (41.9% vs 32.5%  $p < 0.001$ ), and more frequently taking aspirin and lipid-lowering agent (50.0% vs 33.4%  $p = 0.004$ , 52.3% vs 32.5%  $p < 0.001$  respectively). There is no difference between two groups in aortic PWV and arm PWV (7.73 vs 7.61 m/sec  $p = 0.475$ , 8.06 vs 8.32 m/sec  $p = 0.092$  respectively). But, there is statistically significant difference in leg PWV (9.73 vs 10.12 m/sec,  $p = 0.029$ ). Also, cilostazol use is the independent variable of leg PWV by multiple regression analysis ( $\beta = -0.075$   $p = 0.047$ ).

**Conclusion:** In hypertensive patients, the use of cilostazol did not affect aortic PWV and arm PWV. But, leg PWV value was improved significantly. We conclude that cilostazol is more effective on lower extremity arterial stiffness than central arterial stiffness. Further study will need whether effect of cilostazol on peripheral artery disease have related to these improvement of arterial stiffness of lower extremity.

#### 6. BERBERINE -INDUCED UPREGULATION OF CIRCULATING ENDOTHELIAL PROGENITOR CELLS IMPROVES ENDOTHELIAL FUNCTION AND ARTERIAL ELASTICITY IN HEALTHY SUBJECTS

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**Background:** It has been proved that Berberine(BR) can improve endothelial function recently. However, the underlying mechanisms about the effect of

berberine on endothelial function are not completely clear. The number and function of circulating endothelial progenitor cells(EPC) are involved in the endothelia function alteration. We hypothesize that BR-related improvement of endothelial function is associated with the BR-induced upregulation of the number and function of circulating EPCs.

**Methods:** To address this assumption, 20 healthy volunteers were recruited and received BR 0.4g three times per day for 30 days. The number of circulating CD34/KDR double-positive cells as well as the number of the cells demonstrating Dil-acLDL and FITC-lectin double-positive fluorescence cultured from peripheral blood was measured by flow cytometry and fluorescence microscopy before and after BR therapy, respectively. We also assessed the proliferative, adhesive and migratory activities of circulating EPCs, Flow-mediated vasodilation(FMD), C1 large and C2 small artery elasticity indices before and after treatment.

**Results:** The number of CD34/KDR double positive EPCs increased significantly after BR treatment( $0.032 \pm 0.019\%$  vs  $0.018 \pm 0.011\%$ ,  $P < 0.05$ ). The number of Dil-acLDL/FITC-lectin double positive cells from cell cultured also increased significantly( $61.76 \pm 17.58$  EPCs/field vs  $31.60 \pm 6.41$  EPCs/field,  $P < 0.05$ ). The function of EPCs including proliferation, adhesion and migration was increased. After 30-days BR therapy, FMD promoted but NMD did not change. C2 increased significantly ( $6.21 \pm 2.80$  ml per mm Hg/100 vs  $4.06 \pm 2.67$  ml per mm Hg/100,  $P < 0.01$ ) and C1 remained unchanged ( $10.79 \pm 3.27$  ml per mm Hg/10 vs  $10.06 \pm 2.08$  ml per mm Hg/10,  $P > 0.05$ ). The increment of CD34/KDR double-positive EPCs was positively correlated with both the increment of FMD ( $r = 0.52$ ,  $P < 0.05$ ) and the increment of C2 ( $r = 0.68$ ,  $P < 0.01$ ). Multiple regression analysis indicated that only the  $\Delta$ EPC was identified as the independent value for determining  $\Delta$ FMD ( $R^2 = 0.27$ ,  $P < 0.01$ ) and  $\Delta$ C2 ( $R^2 = 0.46$ ,  $P < 0.01$ ).

**Conclusion:** BR-induced upregulation of the number and function of circulating EPCs contributes to improvement of endothelial function and small artery elasticity in healthy subjects.

#### 7. KOREAN PANAX RED GINSENG IMPROVES ENDOTHELIAL DYSFUNCTION AND ARTERIAL STIFFNESS IN PATIENTS WITH CORONARY ARTERY DISEASE PROBABLY BY DECREASING RHO-ASSOCIATED KINASE ACTIVITY OF PERIPHERAL BLOOD MONONUCLEAR CELLS

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**Background:** Korean Panax Red Ginseng (KPRG) is known to enhance endothelium-dependent vasorelaxation by activating eNOS. Activation of Rho-associated kinase (ROCK) is implicated in endothelial dysfunction in part through destabilization of eNOS mRNA. This study, a randomized, double-blind, placebo-controlled, crossover trial, is aimed to analyze the effect of KPRG on endothelial function, arterial stiffness, and ROCK activity of peripheral blood mononuclear cells (PBMC) in patients with coronary artery disease (CAD).

**Methods:** Patients ( $n = 20$ , 12 males, 62.5 yrs) with stable angina (multi-vessel disease:  $n = 10$ ) were treated alternatively with either KPRG (3g/d) or placebo (starch, 3g/d) for 10 weeks (washout period for 4 wks). Measurements of flow mediated dilation (FMD) and nitroglycerine mediated dilation (NMD) from the brachial artery and collection of peripheral venous blood for the biochemical study were performed at day 0 (baseline) and after completion (endpoint) of each treatment. Activity of ROCK of PBMC was assessed by analyzing phospho-Thr853 in the myosin binding subunit (MBS) of myosine light chain phosphatase with use of Western blot, and was expressed as the % ratio of phospho-Thr853-MBS/total MBS at endpoint versus baseline. Patients were classified into low ( $< 5\%$ ) FMD group ( $n = 11$ ) and high ( $> 5\%$ ) FMD group ( $n = 9$ ).

**Results:** Treatment with KPRG significantly increased FMD in low FMD group ( $3.49 \pm 0.35\%$  vs  $5.50 \pm 0.72\%$ ,  $p = 0.013$ ), but not in high FMD group. Brachial ankle pulse wave velocity (ba-PWV), measured by VP2000, tends to be decreased by KPRG ( $1770 \pm 185$  vs.  $1499 \pm 95$ ,  $p = 0.05$ ). There was no significant changes in nitroglycerine mediated dilation after each drug treatment in both patient groups. Treatment with KPRG significantly decreased ROCK activity in PBMC of CAD patients ( $n = 6$ ) by  $23.9 \pm 3.01$  as compared with the baseline ( $p < 0.05$ ). Placebo treatment did not change any of these indices significantly.

**Conclusion:** In conclusions, KPRG improves endothelial dysfunction and peripheral arterial stiffness in patients with CAD probably by decreasing ROCK activity of PBMC.