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The following scientific abstracts were presented at the latest Annual Scientific Meeting of ISCP this year in Rome. They summarise the work of young investigators from different geographical regions worldwide. ISCP supports the scientific work of researchers round the Globe and offers a forum where the results of their investigations can be presented and discussed in the context of the annual meetings and other regional activities. This activity represents not only a possibility for young investigators to showcase their work but also an opportunity to have their results assessed and discussed by world experts in the field. ISCP sees this as a useful contribution to the development of young scientists working in the field of cardiovascular pharmacotherapy.

Serum Beta-2 Microglobulin Concentration Predicts Cardiovascular and All-Cause Mortality

Dr. CL. Cheung1, Dr. KSL. Lam2 and Dr. BMY. Cheung1

1Division of Clinical Pharmacology and Therapeutics, Department of Medicine, The University of Hong Kong, Hong Kong, China
2Division of Endocrinology, Department of Medicine, The University of Hong Kong, Hong Kong, China

Background: This study sought to assess the association between beta-2-microglobulin (B2M) and mortality. B2M is expressed in all nucleated cells and shed from cell surfaces. Serum B2M level predicts mortality in multiple myeloma and chronic kidney disease. We hypothesized that it would predict cardiovascular and all-cause mortality in the general population.

Methods: 6,554 adult participants of the Third National Health and Nutrition Examination Survey were included in the analysis. Serum B2M level was used in multivariable Cox regression analysis to predict all-cause and cardiovascular mortality. Reclassification of mortality was assessed using integrative discrimination index (IDI) and category-less net reclassification improvement (NRI).

Results: During a median follow-up of 13.5 years (79,528 person-years), 2,524 and 1,150 participants died from all causes and cardiovascular causes, respectively. Serum B2M level increased with cardiometabolic and inflammatory risk factors. In unadjusted analysis, quartile 4 of B2M was significantly associated with all-cause (hazard ratio (HR) = 20.83, 95% CI: 14.35-30.24) and cardiovascular mortality (HR = 29.83, 95% CI: 16.00-55.62). After multivariable adjustment, the HRs remained significant (2.3, 95% CI: 1.65-3.21, for all-cause mortality and 1.89, 95% CI: 1.03-3.44, for cardiovascular mortality). Similar results were obtained in the subgroup with normal estimated glomerular filtration rate level. The Harrell’s C-statistics of B2M was 0.759 and 0.786 for all-cause and cardiovascular mortality respectively. Serum B2M, when added to Framingham Risk Score, showed significant reclassification in terms of IDI and category-less NRI.

Conclusions: Serum B2M level is a powerful independent predictor of cardiovascular and all-cause mortality in the general population. Further studies are needed to see if it can be used to identify high risk individuals requiring intensive treatment.

Ivabradine and Heart Rate Variability

Dr. V. Ivan, Dr. M. Turcan, Dr. M. Tudoran and Dr. A. Apostol

Cardiology Department, Emergency Academic Hospital, Timisoara, Romania

Background and Method: Ivabradine is the only agent that provides pure heart rate reduction. Lowering heart rate reduces myocardial oxygen consumption which produces potent antiischemic effects. Heart rate variability is an independent risk factor for major cardiovascular events. In order
to assess to which extend heart rate variability is influenced by ivabradine treatment, we decided to perform a clinical pilot study in patients with CAD. The diagnosis of CAD was founded solely on clinical, ECG and echocardiographic criteria. We divided a group of 310 patients into 2 subgroups of which one was treated with ivabradine on top of the standard medication according to the guidelines and the other was used as control. Follow up was 9 months for the entire patient population. We performed clinical evaluation, echocardiography and heart rate variability in time domain analysis.

**Results:** From a clinical point of view, in terms of duration and frequency of angina episodes, a substantial improvement was seen in both groups. Heart rate reduction was, as expected important in both groups. However final heart rate was significantly lower in patients treated with ivabradine (58 bpm vs. 67 bpm) (sd 20bpm vs. 14 bpm). Echocardiographic parameters were largely unchanged at the end of the follow-up period, with the notable exception of diastolic left ventricular filling which was significantly better at the end of the study, but without differences between the ivabradine treated patients and the control group. The situation was different when RR time domain variability is concerned. Sd was improved both in the ivabradine population and in the control patients, but the improvement proved to be, after statistical analysis, significantly large for the ivabradine treated patients.

Moreover the significant difference (ivabradine better) was maintained even after allowing for heart rate difference between groups.

**Conclusion:** Ivabradine determines pure heart rate reduction with proven antiischemic efficacy. It protects cardiac function and its efficacy is maintained over long term with no risk of rebound or tolerance. It does not interfere with cardiac, respiratory, sexual function or metabolic disorders, its efficacy is maintained in specific patients populations. There is a high potential for future indications. It remains to be seen to which extend ivabradine improves these parameters after a longer period, how long this benefit is maintained over the standard treated patients or after the discontinuation of ivabradine treatment.

### Effects of Pharmacological Therapy on Weight Gain After Smoking Cessation

**Dr. M.K. Komiyama**$^{1,2}$, **Dr. H.W. Wada**$^1$, **Dr. N.A. Asahara**$^1$, **Dr. H.K. Koyama**$^1$, **Dr. K.K. Kono**$^2$, **Dr. Y.T. Takahashi**$^3$ and **Dr. K.H. Hasegawa**$^1$

$^1$National Hospital Organization Kyoto Medical Center, Kyoto, Japan

$^2$Osaka Medical College, Osaka, Japan

$^3$Nara Women’s University Woman’s University, Nara, Japan

**Background & Aims:** Although smoking cessation is associated with decrease in cardiovascular events, weight gain often occurs after smoking abstinence, and such weight gain is thought to contribute to the worsening of glucose tolerance. However, factors associated with weight gain during pharmacological therapy for smoking cessation are undermined. Moreover, while nicotine replacement is useful to minimize post-cessation weight gain, the effect of varenicline, a partial nicotine antagonist, on post-smoking cessation weight gain is unknown.

**Methods:** We evaluated 186 patients (132 males and 54 females) who visited our outpatient clinic for smoking cessation, and successfully achieved smoking abstinence. We performed gender-adjusted regression analysis for the rate of BMI increase from the beginning of cessation to 3 months after the beginning. Furthermore, we performed multivariate analysis to investigate factors that determine BMI increase after smoking cessation. We also compared pre- and post-cessation changes between nicotine patch and varenicline treatment groups.

**Results:** The %BMI increase at 3 months after the initial consultation were 1.5%, and the increase were significantly correlated with triglyceride (p = 0.0006, [a = -0.260]), HDL-C (p = 0.0386, [a = -0.168]), daily cigarette consumption (p = 0.0385, [a = -0.154]) and the Fagerström Test for Nicotine Dependence (FTND) score (p = 0.0060, [a = -0.203]). Stepwise multivariate analysis demonstrated that the FTND score was the strongest factor that determines BMI increase after smoking cessation. Regarding comparison between nicotine patch and varenicline, in basic data, significant differences were recognized for age—the nicotine patch group was older (P < 0.05)—and, for the number of cigarettes smoked per day and FTND, respectively, the varenicline group was higher (P < 0.05, P < 0.01). Both groups showed the same level, 0.4 kg/m² of the BMI increase, and, thus, no significant difference was recognized between nicotine patch and varenicline. For categories other than the BMI, no significant inter-therapy group differences were recognized for pre- and post-smoking cessation changes.

**Conclusions:** The present study demonstrated that smoking patients with a high FTND score are more likely to gain weight after smoking cessation. The results also suggest that varenicline exerts suppressive effects on post-smoking cessation weight gain, and that such effects are not inferior to those by nicotine patch.
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Improvement of Blood Fluidity by Smoking Cessation

Dr. SS. Shimada1, Dr. KH. Hasegawa2, Dr. HW. Wada2, Dr. MK. Komiyama3, Dr. NA. Asahara4, Dr. AS. Shimatsu5 and Dr. YT. Takahashi
1National Hospital Organization Kyoto Medical Center, Kyoto, Japan
2Division of Translational Research, National Hospital Organization Kyoto Medical Center, Kyoto, Japan
3Department of Hygiene and Public Health, Osaka Medical College, Osaka, Japan
4Clinical Research Institute, National Hospital Organization Kyoto Medical Center, Kyoto, Japan
5Health Care Center, Nara Women’s University, Nara, Japan

Introduction: Blood rheology or fluidity, which is expressed as “viscous” or “non-viscous”, reflects the blood viscosity and the state of microthrombus formation. Reduced blood fluidity (BF) has been suggested to lead to cardiovascular thrombotic events such as myocardial and cerebral infarction. While cigarette smoking is an independent risk factor for cardiovascular events, to date, a useful and convenient method of predicting such events in smoking individuals has not been established.

Objectives: The present study investigated improvement of BF by smoking cessation (SC).

Methods: The Micro Channel Array Flow Analyzer (MC-FAN) is an instrument which measures the BF by employing the micro-channel method using a capillary model. We assessed BF in l) of smoking patients by measuring the blood passage time (BPT) in aliquot (100 blood samples using the MC-FAN.

Results: BPT was significantly related with smoking substances such as daily consumption of tobacco, Brinkman’s index, and Fagerstrom Test for Nicotine Dependence (FTND) score. Overall, SC in our outpatient clinic significantly (p = 0.015) decreased BPT (implying improvement of BF) from 57.7 sec to 52.3 sec (n = 126) at 3 months after the start of SC therapy. However, as BPT increased (implying deterioration of BF) even after SC in some patients, we divided the group exhibiting improvement of BF (I, n = 49), that showing deterioration (D, n = 27) and that showing no change (N, n = 50). West circumference and body mass index significantly increased after SC in N and D, but not in I. In contrast, serum HDL-cholesterol levels significantly increased in I, but not in N and D. Notably, serum triglyceride levels markedly increased after SC in D (p = 0.003, before:163.8, after:268.2 mg/dl), moderately increased in N (p = 0.012, before:127.0, after:151.3 mg/dl), but not in I (p = 0.366, before:176.0, after:191.3 mg/dl). We further evaluated BPT at one year after the start of therapy in D (n = 21). BPT significantly (p = 0.003) decreased from 3 months to one year after SC (before: 61.3 sec, 3 months: 74.0sec, one year: 52.1sec).

Conclusion: While decreased BF in smoking patients improves by 3 months of SC, obesity-associated hyperlipidemia after the cessation perturbs such improvement. As BF improves at one year in D, SC may finally lead to the decrease in cardiovascular risk even if obesity occurs after the cessation. However, management of hyperlipidemia associated with SC would further augment the improvement of BF, and reduce the risk of cardiovascular events.

Reduction of Oxidative Stress Measured by Salivary Oxidation-Reduction Potentials by Smoking Cessation

Mrs. NN. Nagaoka1, Dr. HW. Wada1, Dr. MK. Komiyama1, Dr. NA. Asahara1, Dr. AS. Shimatsu1, Dr. YT. Takahashi2 and Dr. KH. Hasegawa1
1National Hospital Organization Kyoto Medical Center, Kyoto, Japan
2Nara Women’s University, Nara, Japan

Background: Oxidative stress by cigarette smoking is associated with ruptures of atherosclerotic plaques and leads to the onset of cardiovascular events, such as myocardial infarction and cerebral infarction. As measurement of salivary oxidation-reduction potentials is very simple, it might be useful as a tool to evaluate the extent of oxidative stress.

Purpose: We measured the salivary oxidation-reduction potentials in smokers and evaluated time course changes in the oxidation-reduction potentials by smoking cessation.

Method: Ten smoking patients (male/female: 7/3, 53.3 years old of average age), who consulted our smoking cessation clinics and achieved smoking cessation were recruited. In these patients, we evaluated time course changes of the oxidation-reduction potential values during anti-smoking medical treatment. The salivary oxidation-reduction potential values were measured by using the oxidation-reduction measuring device called “ARA’ GENKI.”

We judged +40 mV or more of the potential values as an oxidative state, and less than +40 mV as a reductive state.

Result: At the time of the first consultation to our smoking cessation clinic, the potential value of these smokers exhibited the strong oxidization of +73.1 ± 29.4 mV. By smoking abstinence, the oxidation-reduction potential value demonstrated the significant trend of decreases (p = 0.003). Especially at the time of the 5th consultation (after 12 weeks of anti-smoking medical treatment starts), the potential value was +35.9 ± 24.8 mV, showing a relatively reductive state. The potential value at the time of the 5th consultation was significantly (p < 0.05) lower compared with the values at the first and 3rd consultations.

Conclusion: It was demonstrated, by measurement of the salivary oxidation-reduction potentials, that smokers are in a strong oxidative state and that such an oxidation is reduced by smoking cessation. Thus, measurement of salivary oxidation-reduction potentials might be simple and useful tool to evaluate the extent of oxidative stress by smoking.
Determinants of Circulating Oxidized LDL Level in Statin-Treated Diabetes Patients With Coronary Artery Diseases; Significance Of Serum Triglycerides and Underuse Of Metformin

Dr. M. Matsuda, Dr. R. Tamura, Dr. K. Kanno, Dr. T. Segawa, Dr. O. Nishimoto and Dr. H. Nishiyama

1Department of Internal Medicine, National Hospital Organization Kure Medical Center, Kure, Japan
2Institute of Clinical Research, National Hospital Organization Kyoto Medical Center, Kyoto, Japan
3Department of Cardiology, National Hospital Organization Kyoto Medical Center, Kyoto, Japan

Background and Aims: Lowering low-density lipoprotein (LDL) with statins has been an established strategy for cardiovascular prevention. Serum oxidized LDL level has long been recognized as a predictive marker for future events. However, it has been unclear what determines oxidized LDL level under standard prevention with statins. In this study, we aimed to clarify the clinical factors associated with oxidized LDL level in statin-treated diabetic patients with coronary artery diseases (CAD).

Methods: We conducted a cross-sectional observational study on 186 patients with type 2 diabetes mellitus (T2DM). All subjects had documented CAD and were treated with statins for secondary prevention. Venous blood was drawn after an overnight fast. Serum concentrations of malondialdehyde-modified LDL (MDA-LDL) and various parameters of cardiovascular risk factors including LDL cholesterol (C), high density lipoprotein cholesterol (HDL-C), triglycerides (TG), hemoglobin (Hb) A1c, adiponectin and C-reactive protein (CRP) were determined. Extent of CAD was defined as number of segments with 50% stenosis or stent-implantation assessed by angiography or computed tomography.

Results: In univariate analysis, MDA-LDL level showed significant correlations with LDL-C (r = 0.516, p < 0.0001), TG (r = 0.370, p < 0.0001), adiponectin (r = -0.229, p = 0.002) and CRP (r = -0.173, p = 0.018), but not with HbA1c or the number of diseased segments in coronary arteries. Among these significant factors, multivariate analysis revealed that MDA-LDL level was independently associated with LDL-C (β = 0.489, p < 0.0001) and TG (β = 0.273, p < 0.0001), but not with adiponectin or CRP. Patients with metabolic syndrome (MS) had significantly higher MDA-LDL level than those without MS (p = 0.03, by ANOVA). The number of MS components was significantly associated with high level of MDA-LDL (p < 0.0001, by ANOVA). Among various medications combined with statins, the use of metformin was significantly associated with MDA-LDL level (adjusted odds ratio, 0.41; 95% confidence interval, 0.20–0.83), but the use of sulfonylurea or pioglitazone was not, in multivariate logistic analysis.

Conclusion: Circulating oxidized LDL level was significantly associated with serum TG level, which may be linked to MS, and the underuse of metformin, but not with glycemic control or the extent of CAD, in T2DM patients treated with statins. Control of hypertriglyceridemia and appropriate use of metformin may be important in patients with T2DM to further lower oxidized LDL level beyond statin treatment.

Vascular Endothelial Growth Factor-C, Dyslipidemia, and Atherosclerosis

Mr. S. Ura, Dr. H. Wada, Dr. N. Satoh-Asahara, Dr. T. Horie, Dr. K. Ono, Dr. A. Shimatsu and Dr. K. Hasegawa

1Division of Translational Research, National Hospital Organization Kyoto Medical Center, Kyoto, Japan
2Division of Diabetes Research, National Hospital Organization Kyoto Medical Center, Kyoto, Japan
3Department of Cardiovascular Medicine, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Background: The mechanisms that lead from obesity to atherosclerotic disease are not fully understood. Obesity involves angiogenesis in which vascular endothelial growth factor-A (VEGF-A) plays a key role. However, a population-based cross-sectional study revealed that circulating VEGF-A levels have only a minor impact on the development of atherosclerosis. Vascular endothelial growth factor-C (VEGF-C), a homologue of the VEGF family, plays a pivotal role in lymphangiogenesis. Circulating levels of both VEGF-A and VEGF-C are elevated in sera from obese subjects. However, relationships of VEGF-C with atherosclerotic risk factors and atherosclerosis are unknown.

Methods and Results: We determined circulating levels of VEGF-A and VEGF-C in 423 consecutive subjects not receiving any drugs at the Health Evaluation Center. After adjusting for age and gender, VEGF-A levels were significantly and more strongly correlated with the body mass index (BMI) and waist circumference than VEGF-C. Conversely, VEGF-C levels were significantly and more closely correlated with metabolic (e.g., fasting plasma glucose, hemoglobin A1c, immunoreactive insulin, and the homeostasis model assessment of insulin resistance) and lipid parameters (e.g., triglycerides, total cholesterol (TC), low-density-lipoprotein cholesterol (LDL-C), and non-high-density-lipoprotein cholesterol (non-HDL-C)) than VEGF-A. Stepwise regression analyses revealed that independent determinants of VEGF-A were the BMI and age, whereas strong independent determinants of VEGF-C were age, triglycerides, and non-HDL-C. In apolipoprotein E-deficient mice fed a high-fat-diet (HFD) or normal chow (NC) for 16 weeks,
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levels of VEGF-A were not significantly different between the two groups. However, levels of VEGF-C were significantly higher in HFD mice with advanced atherosclerosis and marked hypercholesterolemia than NC mice. Furthermore, immunohistochemistry revealed that the expression of VEGF-C in atheromatous plaque of the aortic sinus was significantly intensified by feeding HFD compared to NC, while that of VEGF-A was not. Within plaque areas, there were abundant cells expressing LYVE-1, a marker of lymphatic endothelium, while cells expressing CD31, a marker of vascular endothelium, were detected only in the surface of plaque.

Conclusions: These findings demonstrate that VEGF-C, rather than VEGF-A, is closely related to dyslipidemia and atherosclerosis.

α1-Antitrypsin-Low-Density-Lipoprotein and Smoking-Specific Oxidative Stress

Mr. S. Ura1, Dr. H. Wada1, Dr. N. Satoh-Asahara2, Dr. M. Akao3, Dr. M. Abe3, Dr. Y. Takahashi4 and Dr. K. Hasegawa1

1Division of Translational Research, National Hospital Organization Kyoto Medical Center, Kyoto, Japan
2Division of Diabetes Research, National Hospital Organization Kyoto Medical Center, Kyoto, Japan
3Department of Cardiology, National Hospital Organization Kyoto Medical Center, Kyoto, Japan
4Health Administration Center, Nara Women’s University, Nara, Japan

Background: Smoking is a major risk factor for cardiovascular diseases. Smoking cessation (SC) is associated with a reduction in cardiovascular events, and the benefit is seen relatively soon (one year) after cessation. Inflammatory biomarkers such as C-reactive protein (CRP) are reported to be associated with the smoking status. In contrast to the rapid reduction of the cardiovascular risk, the CRP level remains significantly raised several years after smoking cessation. Therefore, there may be better markers which reflect the smoking-related cardiovascular risk than inflammatory markers. Circulating levels of oxidatively modified low-density-lipoprotein (LDL) are associated with a high risk of cardiovascular diseases. Recently, two novel, oxidatively modified LDL markers, serum amyloid A-LDL (SAA-LDL) and α1-antitrypsin-LDL (AT-LDL), were identified. However, the significance of SAA-LDL and AT-LDL as cardiovascular risk markers is unknown.

Methods and Results: We carried out a cross-sectional study involving 243 patients, and determined serum levels of SAA-LDL and AT-LDL. Both serum levels of SAA-LDL and AT-LDL were significantly increased in current compared to non-current smokers. Stepwise regression analysis revealed that the current smoking status and duration of smoking were strong independent determinants of the AT-LDL level. In contrast, high-sensitivity CRP was the strongest determinant of the SAA-LDL level. In multiple logistic regression analysis, the current smoking status was most closely associated with the AT-LDL level. Successful SC employing a 12-week program significantly increased the body mass index and serum levels of obesity-related markers. Notably, successful SC significantly decreased levels of AT-LDL, but not those of SAA-LDL.

Conclusions: The present study provides the first evidence for the distinct characteristics of two novel, oxidatively modified LDL markers, SAA-LDL and AT-LDL. In contrast to SAA-LDL, an inflammatory marker, AT-LDL serves as a marker of smoking-specific oxidative stress. These findings warrant further investigations to clarify if AT-LDL provides a key link between smoking and cardiovascular diseases.

Safe Use of Cardiovascular Drugs in Drivers Suffering from Cardiovascular Diseases

Dr. JA. Isakova1,2 and Dr. V.V. Popov1,3

1Scientific Medical Center, Russian Railways, Moscow, Russia
2Central Clinical Hospital, Russian Railways, Moscow, Russia
3Sechenov 1st Moscow State Medical University, Moscow, Russia

Objective: Many drugs can potentially impair driving ability (mood, cognition, psychomotor functioning, etc.). There is little information about cardiovascular (CV) drugs use in drivers. The aim of the study was to analyse the data on safety of CV drugs use in drivers suffering from CV diseases. Pharmacological groups taken: 1) diuretics (D); 2) beta blocking agents (BBA); 3) calcium channels blockers (CCB); 4) agents acting on the renin-angiotensin system (RAS); 5) lipid modifying agents (LMA).

Methods: DRUID program materials and reports (www.druid-project.eu), world classification systems by safety for use in drivers, articles with original and epidemiological studies results, drug safety in drivers reviews (the source is MedScape/Pubmed), PILs, materials of Railway Medicine Department of MSUR (Moscow State University of Railways), safety data on drug use from WHO Pharmaceutical Newsletters, Warning Letters of the Federal Service of supervision in the field of healthcare and the Research Centre of remedies for medical use examinations in Russia found and analysed.

Results: Driver-impairing side effects are incident to the medicines used to treat CV diseases. The use of ACE inhibitors, CCB and D in drivers is considered to be the most dangerous. Many differences in drug categories within various classifications for CV drugs were detected. All the classes observed have the status of “safe for drivers” according to the results of DRUID program. Whereas, D are detected as “unsafe for drivers” according
Changes in The Level of Plasma Adipokine Visfatin Hypertensive Patients in Combination with Obesity on the Background of Antihypertensive Therapy

Mrs. Anastasia Andrieieva1, Dr. Vira Shkolnik1, Prof. Alexander Belovol1 and Prof. Oleg Babak1
1Kharkiv National Medical University, Kharkiv, Ukraine

The visfatin is the adipokine which produced adipose tissue, and requires special attention. This is due to open properties involved in angiogenesis, cell proliferation, inflammation, and endothelial dysfunction (Dahl et al. 2007). Consequently, it is able to increase the cardiovascular risk and mortality in hypertensive patients by obesity and requires medical correction. The purpose of the study to evaluate the effectiveness of antihypertensive therapy in patients with hypertension combined with obesity based on the measurement of blood pressure and plasma levels of visfatin. Methods. There were hypertensive patients combined with obesity (n = 185) in the presence of increasing body mass index (BMI) over 30 kg/m2, and the other group consisted of patients with hypertension (n = 150) and control group (n = 32). The course of treatment were 12 months, controls were 3 month and 12 month. Both groups treated with an ACE inhibitor perindopril at a dose of 8 mg and diuretic indapamide 1.5 mg in furthering 3 months, then if you do not reach target blood pressure (BP) numbers, patients receiving angiotensin receptor blocker olmesartan 20 mg 1 time per day and the calcium antagonist amlodipine 10 mg 1 time per day. The average age of which was (60.2 ± 1.9) years. The ELISA test was determined the level of visfatin in the blood plasma (RayBiotech, USA). Statistical analysis was performed with the help of «Statistika 6.0» (StatSoft Inc, USA). Results. In the systolic BP (SBP) and diastolic BP (DBP) found in the first group (166.2 ± 4.9) mm Hg and (98.2 ± 3.6) mm Hg, while in the second group (161.2 ± 5.1) mm Hg and (96.6 ± 3.4) mm Hg. Level of visfatin in plasma was the first group (53.4 ± 4.42) ng/ml and was significantly higher compared with the control group ((183.3 ± 6.51) ng/ml, p < 0.05). In the second group visfatin concentration was not significantly different from control values ((22.2 ± 9.8) ng/ml, respectively, p>0.05). After three months of treatment only in patients with hypertension was achieved target BP, namely for SBP (138.5 ± 4.9) mm Hg and for DBP (82.7 ± 3.2) mm Hg, (p < 0.05). Due to the fact that in the first group was not achieved target BP changed the combination of antihypertensive drugs. After 12 months of antihypertensive treatment in both groups were achieved target BP, (p < 0.05). The level of visfatin significantly decreased in the first group and was on 18% (p < 0.05), in the second also decrease on 15% (p>0.05). Conclusion. The drug of choice in obese patients should be olmesartan and amlodipine, which have cardio protective properties.

Controversies on Patient Persistence in Antihypertensive Drug Treatment: A Systematic Review

Dr. B. Wettermark1,2, Mrs. M. Qvarnström2, Dr. J. Hasselström1,3 and Prof. T. Kahle4,5
1Department of Healthcare Development, Public Healthcare Services Committee, Stockholm County Council Stockholm, Sweden
2Karolinska Institutet, Centre for Pharmacoepidemiology, Clinical Epidemiology Unit, Department of Medicine, Karolinska University Hospital Solna, Stockholm, Sweden
3Karolinska Institutet, Center for Family and Community Medicine, Department of Neurobiology, Care Sciences and Society, Stockholm, Sweden
4Karolinska Institutet, Department of Clinical Sciences, Danderyd Hospital, Division of Cardiovascular Medicine, Stockholm, Sweden
5Department of Cardiology, Danderyd University Hospital Corp, Stockholm, Sweden

Background and Aims: Hypertension is the most important risk factor for morbidity and premature mortality, affecting more than a quarter of the population in the world, and its global burden is increasing. The benefits of antihypertensive therapy and blood pressure control are very well established. Discontinuation of antihypertensive treatment is associated with poor blood pressure control. Our objective was to review studies of
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Patient persistence with antihypertensive drug treatment. Specific aims were to compare methods used, patient or prescriber characteristics for which association to persistence has been studied, and results reported.

Methods: English language papers published between January 2006 and December 2011 investigating patient persistence with antihypertensive drugs were identified through systematic searches of the MEDLINE and EMBASE databases. Methods, definitions and variables, as well as reported results were compared between the studies.

Results: A total of 43 published studies were identified. The most common data source was pharmacy-based electronic databases of dispensed prescriptions. The time of follow up varied between 3 months and 9 years. The lowest recorded therapy persistence was 7.2% after nine years, while the highest reported persistence in another study was 97% after 180 days of follow up. Associations were studied for a total of 30 different factors related to patient characteristics, healthcare organization, or the choice of treatment. Men, younger age, and use of diuretics were in most studies associated with lower with antihypertensive drug treatment.

Conclusions: Reported studies confirm that non-compliance with antihypertensive drug treatment is a significant problem with potential important clinical implications. Men, younger age, and use of diuretics were associated with lower persistence. However, variations in study design make it difficult to compare data on persistence between studies. This calls for more methodological rigor, and the development of scientific guidelines for studies on persistence. An improved persistence with antihypertensive drug treatment is likely to have important clinical implications.

Microrna-33 Deficiency Reduces Atherosclerosis Formation In Vivo

Dr. T.H. Horie1,2, Dr. O.B. Baba1, Dr. M.N. Nishiga1, Prof. K.H. Hasegawa3, Prof. M.Y. Yokod4, Dr. T. Kawamoto5, Prof. T.K. Kimura1 and Prof. K.O. Ono1

1Department of Cardiovascular Medicine, Kyoto University, Kyoto, Japan
2Department of Clinical Innovative Medicine, Institute for Advancement of Clinical and Translational Science, Kyoto University, Kyoto, Japan
3Division of Translational Research, Kyoto Medical Center, Kyoto, Japan
4Department of Cardiology, National Hospital Organization Kure Medical Center, Kure, Japan

Backgrounds: Atherosclerosis is the major cause of cardiovascular disease. Recently, we reported that microRNA-33 reduced serum HDL-C by targeting ABCA1. We generated microRNA-33 deficient mice and found that these mice showed significant increase of ABCA1 levels and serum HDL-C. Because HDL-C is inversely correlated with cardiovascular disease, we hypothesized that microRNA-33 might affect atherosclerosis formation.

Methods and results: To assess the impact of microRNA-33 on atherosclerosis formation, microRNA-33 and apoE double knockout mice were obtained by mating microRNA-33 deficient mice with apoE deficient mice. The expression levels of ABCA1 and ABCG1, which were targets of microRNA-33, were significantly increased in peritoneal macrophages from these double knockout mice compared with macrophages from apoE deficient mice. In accordance with these expressions, cholesterol efflux to both apoA-I and HDL-C were also significantly elevated in macrophages from double knockout mice. Free cholesterol loading-induced apoptosis by treating with acLDL and ACAT inhibitor was significantly reduced in macrophages from double knockout mice. These mice were fed a western diet containing 0.15% cholesterol for 16 weeks from 6 weeks old and analyzed. Plaque areas, lipid accumulation areas and CD68-positive areas at the atherosclerotic plaque were significantly reduced in microRNA-33 and apoE double knockout mice compared with apoE deficient mice. Moreover, the number of apoptotic cells at the plaque was also significantly reduced in double knockout mice. Double knockout mice showed a significant increase of ABCA1 expression in the liver and serum HDL-C compared with apoE deficient mice. ApoB-depleted serum from double knockout mice significantly promoted cholesterol efflux in J774 mouse macrophages.

Conclusions: MicroRNA-33 deficiency reduced atherosclerosis in apoE deficient mice, probably by increasing macrophage cholesterol efflux, increasing functional serum HDL-C, reducing macrophage infiltration and inhibiting apoptosis at the plaque. Inhibition of microRNA-33 can be a novel therapeutical approach for atherosclerosis.

Effect of Extended-Release Niacin/Laropiprant Combination on Pcsk9 Levels in Chinese Patients with Dyslipidaemia

Prof. B. Tomlinson1, Dr. YL. Yang1 and Dr. M. Hu1

1Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, The People’s Republic of China

Background and Aims: Proprotein convertase subtilisin kexin type 9 (PCSK9) is a key regulator of serum low-density lipoprotein cholesterol (LDL-C) levels. Previous studies showed that serum PCSK9 was increased with statin treatment and fibrates had variable effects, but there are no reports about the effect of niacin on PCSK9 levels. This study examined the effect of extended-release (ER) niacin/laropiprant on PCSK9 levels in Hong Kong Chinese patients with dyslipidaemia.
Methods: Patients with dyslipidaemia were treated with ER niacin 1-g/laropiprant 20-mg for 4 weeks then ER niacin 2-g/laropiprant 40-mg for an additional 8 weeks. Measurements of fasting lipids and PCSK9 were performed at baseline and after 12 weeks treatment with ER niacin/laropiprant.

Results: In the 123 patients (38.2% females, 38.2% not on other lipid-lowering treatment) who completed the study with PCSK9 data available, baseline PCSK9 level was higher in females compared with males (381.7 ± 133.1 vs. 324.7 ± 108.6 ng/ml, P < 0.05). At baseline, patients treated with statins only (n = 54) or on other single or multiple lipid-lowering drugs (n = 22) had higher PCSK9 levels compared with those patients (n = 47) who were not on any lipid-lowering treatment (395.7 ± 122.0 ng/ml vs. 266.9 ± 65.1 ng/ml, P < 0.001). Baseline PCSK9 levels were correlated with baseline LDL-C levels after adjustment for gender and baseline use of lipid-lowering treatment (r = 0.265, P = 0.003). After 12 weeks treatment with ER niacin/ laropiprant, the median (interquartile range) PCSK9 levels decreased significantly by -8.1% (-25.5, 8.6%). Multivariate linear regression analysis showed that being on lipid-lowering treatment at baseline (r = 0.319, P < 0.001) and baseline PCSK9 levels (r = -0.463, P < 0.001) were independent factors that influence the PCSK9 changes during the study. Patients not on any lipid-lowering treatment at baseline had a mean -14.9% (95% confidence interval: -25.8, -3.9%) greater reduction in PCSK9 levels than those on statins (P < 0.01). There was no association between the changes of LDL-C or triglycerides and PCSK9 with ER niacin/laropiprant treatment.

Conclusion: This study showed that the baseline PCSK9 level was higher in females and in those patients on statins or other lipid-lowering drugs and was correlated with the LDL-C level. Treatment with ER niacin/laropiprant led to a significant decrease in PCSK9 levels, which was greater among those with higher baseline PCSK9 levels and in patients not on lipid-lowering treatments at baseline.

Platelet Aggregation in Children with Cardiomyopathy Associated with Rare Genetic Diseases

N.D. Vashakmadze¹, L.S. Namazova-Baranova¹, O.B. Gordeeva¹, A.K. Gevorkyan¹, E.G. Chernavina¹ and M.A. Babaykina¹

¹Federal State Budgetary Institution “Scientific Centre of Children Health” under the Russian Academy of Medical Sciences, Moscow, Russia

Mucopolysaccharidosis (MPS), GHARGE syndrome and SOTOS syndrome are rare genetic diseases leading to heart failure. Abnormal platelet function is often associated with different forms of cardiovascular disease and can contribute to impaired prognosis in these conditions.

Aim: To compare platelet function in children with MPS versus those with GHARGE or SOTOS syndrome.

Materials and methods: 16 patients, 2 to 16 years of age, with cardiomyopathy and MPS, GHARGE and SOTOS syndromes were assessed. The patients were subdivided in 2 groups: Group 1 comprised 10 patients with MPS and Group 2, 6 patients with GHARGE and SOTOS syndromes. 16 healthy children matched by age and gender were used as a control group. Nine patients in Group 1 were treated with the angiotensin converting enzyme (ACE) inhibitor (captopril) and pentoxifylline and the remaining patient was treated with a β-blocker. In Group 2, 6 patients were treated with the angiotensin II receptor blocker I Losartan or ACE inhibitors and β-blockers. Platelet aggregation was assessed in whole blood using the Multiplate (VD, Germany) device with thrombin, ADP and arachidonic acid (AA) in all children.

Results: In Group 1, thrombin testing showed that platelet aggregation was reduced in 5 cases (Median (Me) – 67U; 95% CI – 22-111 U) and hyperaggregability was detected in 1 patient. Four patients had normal values. With ADP, 8 patients showed reduced aggregability (Me- 27 U; 95% CI: 13-42 U) and 2 patients had normal values. Hypoaggregability was found in 9 patients with AA (Me-28 U; 95%CI 2-47 U). The control group showed normal platelet aggregation values which were significantly different compared with patients in Group 1 (p < 0.05). In Group 2 no significant differences in platelet aggregation were detected.

Conclusion: Abnormalities in platelet function are more common in patients with MPS receiving treatment with ACE inhibitors compared with GHARGE and SOTOS’s patients receiving treatment predominantly with β-blockers and angiotensin II receptor blockers. Whether abnormal platelet function is related to the treatment selected or associated with the baseline genetic condition needs to be investigated further as it may determine drug treatment choice. The variable response of platelets in the MPS group to the different tests employed in the study also deserves further investigation.