
Abstract: Due to the incidence of type-2 diabetes and hypertension, chronic kidney disease (CKD) has emerged as a major public health problem worldwide. CKD results in premature death from accelerated cardiovascular disease and various other complications. Early detection, careful monitoring of renal function, and response to therapeutic intervention are critical for prevention of CKD progression and its complications. Unfortunately, traditional biomarkers of renal function are insufficiently sensitive or specific to detect early stages of disease when therapeutic intervention is most effective. Therefore, more sensitive biomarkers of kidney disease are needed for early diagnosis, monitoring, and effective treatment. CKD results in profound changes in lipid and lipoprotein metabolism that, in turn, contribute to progression of CKD and its cardiovascular complications. Lipids and lipid-derived metabolites play diverse and critically important roles in the structure and function of cells, tissues, and biolipids. Lipidomics is a branch of metabolomics, which encompasses the global study of lipids and their biologic function in health and disease including identification of biomarkers for diagnosis, prognosis, prevention, and therapeutic response for various diseases. This review summarizes recent developments in lipidomics and its application to various kidney diseases including chronic glomerulonephritis, IgA nephropathy, chronic renal failure, renal cell carcinoma, diabetic nephropathy, and acute renal failure in clinical and experimental research. Analytical technologies, data analysis, as well as currently known metabolic biomarkers of kidney diseases are addressed. Future perspectives and potential limitations of lipidomics are discussed.


Abstract: Atrial fibrillation (AF) is a common arrhythmia encountered after coronary artery bypass graft surgery (CABG) and is associated with poor outcomes. The purpose of this study was to examine whether initiation of statins before CABG reduces the risk of postoperative AF. We searched for clinical trials that randomized patients who underwent CABG to preoperative statin therapy versus placebo. We required that the trial reported the incidence of postoperative AF. Random-effects summary odds ratio (OR) was constructed. Sensitivity analysis for the trials that reported AF as a primary outcome along with subgroup analyses according to the different statins used was also conducted. Twelve trials with 2,980 patients met our inclusion criteria. Atorvastatin was tested in 8 trials, whereas rosuvastatin was studied in 2 studies. Statins were associated with a lower risk of postoperative AF (OR 0.42, 95% confidence interval [CI] 0.27 to 0.66, p <0.0001). There was benefit with atorvastatin (OR 0.35, 95% CI 0.25 to 0.50, p <0.0001) but not rosuvastatin (OR 0.69, 95% CI 0.28 to 1.71, p = 0.42). On sensitivity analysis limited to trials that reported AF as a primary outcome, the risk of postoperative AF was still reduced with statins (OR 0.40, 95% CI 0.25 to 0.90, p = 0.02). The mean duration of the hospital stay was significantly lower in the statin group: 8.5 +/- 1.8 days versus 9.1 +/- 2.2 days (p <0.0001). Statin therapy, particularly atorvastatin, before CABG was associated with a reduction in the risk of postoperative AF.


Abstract: Familial hypercholesterolemia (FH) is an autosomal dominant genetic disorder, associated with elevated level of serum low-density lipoprotein-cholesterol (LDL-C), which can lead to premature cardiovascular disease (CVD). Mutations in low density lipoprotein receptor (LDLR) and proprotein convertase subtilisin/kexin type 9 (PCSK9) have been identified to be the underlying cause of this disease. Genetic research of FH has already been extensively studied all over the world. However, reports of FH mutations in the Chinese population are still limited. In this paper, 20 unrelated FH families were enrolled to detect the candidate gene variants in Chinese FH population by DNA direct sequencing. We identified 12 LDLR variants in 13 FH probands. Importantly, we first reported two unique mutations (c.2000_2000delG/p.C667LfsX6 and c.605T>C/p.F202S) in LDLR gene. Our discoveries expand the spectrum of LDLR mutations and contribute to the genetic diagnosis and counseling for FH patients.


Abstract: INTRODUCTION: Low-density lipoprotein cholesterol (LDL-C) has been reported to increase platelet activation. Reducing the level of LDL-C with statins induces important pleiotropic effects such as platelet inhibition. This association between platelet activity and statin therapy may be clinically important in reducing the risk of ischemic stroke. We investigated the effect of simvastatin therapy on platelet activation markers (platelet CD62P, sP-selectin, and platelet-derived microparticles (PDMPs)) in hyperlipidemic patients after ischemic stroke. MATERIAL AND METHODS: The study group consisted of 21 hyperlipidemic patients after ischemic stroke confirmed by CT, and 20 healthy subjects served as controls. We assessed the CD62P expression on resting and thrombin-activated blood platelets. CD62P and PDMPs were analyzed by the use of monoclonal antibodies anti-CD61 and anti-CD62 on a flow cytometer. The level of sP-selectin in serum was measured by the ELISA (enzyme-linked immunosorbent assay) method. All markers were re-analyzed after 6 months of treatment with simvastatin (20 mg/day).

RESULTS: Hyperlipidemic patients presented a significantly higher percentage of CD62P+ platelets and higher reactivity to thrombin compared to control subjects. After simvastatin therapy hyperlipidemic patients showed a reduction of the percentage of resting CD62P(+) platelets (p < 0.005) and a reduction of expression and percentage of CD62P(+) platelets after activation by thrombin (median < p < 0.05; percentage: p = 0.001). A decrease of sP-selectin levels (p = 0.001) and percentage of PDMPs (p < 0.05) in this group was also observed. CONCLUSIONS: HMGC-CoA reductase inhibitor therapy in stroke patients with hyperlipidemia may be useful not only due to the lipid-lowering effect but also because of a significant role in reduction of platelet activation and reactivity.


Abstract: Numerous randomized, double-blind, placebo-controlled studies and observational studies have shown that statins reduce mortality and major cardiovascular events in older high-risk persons with hypercholesterolemia. The Heart Protection Study showed that statins reduced mortality and major cardiovascular events in high-risk persons regardless of the initial level of serum lipids, age, or gender. The updated National Cholesterol Education Program III guidelines state that in very high-risk persons, a serum low-density lipoprotein (LDL) cholesterol level of < 70 mg/dl (1.8 mmol/l) is a reasonable clinical strategy for moderately high-risk persons (2 or more risk factors and a 10-year risk for coronary artery disease of 10% to 20%), and the serum LDL cholesterol should be reduced to < 100 mg/dl (2.6 mmol/l). When LDL cholesterol-lowering drug therapy is used to treat high-risk persons or moderately high-risk persons, the serum LDL cholesterol should be reduced by at least 30% to 40%. The serum LDL cholesterol should be decreased to less than 160 mg/dl in persons at low risk for cardiovascular disease. Addition of other lipid-lowering drugs to statin therapy has not been demonstrated to further reduce cardiovascular events and mortality.


Abstract: BACKGROUND: The diagnosis of diabetes has important clinical implications for the prevention and management of cardiometabolic disorders. We aimed to investigate the awareness, treatment and control of hypertension and diabetes in newly-diagnosed and newly-diagnosed diabetes in Chinese adult population. METHODS: We conducted a cross-sectional survey in a nationally representative sample of 98658 Chinese adults aged 18 years or older in 2010, using a complex, multistage, probability sampling design. Glycemic status were defined according to the 2010 American Diabetes Association criteria. Hypertension was diagnosed by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Dyslipidemia was diagnosed by the 2004 National Cholesterol Education Program Adult Treatment Panel III. RESULTS: The weighted prevalence of hypertension and dyslipidemia gradually increased in adults with normal glucose regulation, prediabetes, newly-diagnosed diabetes and previously-diagnosed diabetes. Compared to newly-diagnosed diabetes patients, previously-diagnosed diabetes patients were more likely to be aware of hypertension (weighted percentage [95% confidence interval]: 55.2% [52.9%-57.5%] vs 37.6% [35.9%-39.3%]) and dyslipidemia (33.9% [31.8%-36.1%] vs 12.8% [11.7%-13.9%]), to receive blood pressure-lowering (43.7%
[41.5%-46.0%] vs 27.5% [26.0%-29.0%] and lipid-lowering (18.9% [17.2%-20.7%] vs 5.4% [4.6%-6.2%]) therapies, and to have controlled blood pressure (4.7% [3.5%-6.2%] vs 3.5% [2.6%-4.8%]) and lipid (15.9% [12.3%-20.3%] vs 9.5% [6.4%-13.8%]) levels. CONCLUSIONS: Detection and control of hypertension and dyslipidemia is far from optimal in Chinese adults, especially in newly-diagnosed diabetes. Improved screening for diabetes is required to promote a better prevention, treatment and control of hypertension and dyslipidemia in China.


Abstract: Restenosis following coronary intervention is a complex process the mechanisms of which remains mostly unknown. Tissue obtained by atherectomy is an important means to study restenosis. Previous studies on atherectomy-removed tissue have not identified histologic features that correlate with restenosis. We performed an histopathologic evaluation on atherosclerotic plaque tissue obtained by atherectomy from 58 patients, all of whom had a 6-month angiographic follow-up. We identified macrophages and lymphocytes and localized tumor necrosis factor-alpha expression in the tissue by immunohistochemistry. Histopathology was correlated with late angiographic outcomes. Of 10 histologic features evaluated in the plaque tissue, only the presence of foam cells, identified in paraffin sections, correlated positively with restenosis (p = 0.04). Immunohistochemistry showed that macrophages (p = 0.07), tumor necrosis factor-alpha (p = 0.07), and lymphocytes (p = 0.14) were more prominent, but not significantly so, in lesions from patients with foam cells and restenosis than in lesions from patients without foam cells or restenosis. Thus the presence of foam cells in primary lesions obtained by atherectomy as identified in paraffin-embedded tissue appears to be a marker for restenosis.


Abstract: This study’s aim was to test the low-density lipoprotein cholesterol- (LDL-c-) lowering efficacy of biscuits containing 2 g of plant stanols, which corresponded to 3.4 g of plant stanol esters. The biscuit is a new food format that can be consumed as a snack. In a double-blind, placebo-controlled parallel design study, 119 mildly to moderately hypercholesterolemic volunteers were randomized to plant stanol or control groups. Subjects were comparable in age, gender, lipid profiles, and body mass index. They consumed a control biscuit once a day for a two-week period, followed by a four-week intervention period that either had a plant stanol ester biscuit or a control. During the habitual diet, one biscuit per day was consumed at any time that subjects wished. Serum lipid profiles were measured at the first day of run-in, at baseline, and at the study’s end. Compared to the control, the total cholesterol (TC), LDL-c, and the LDL to high-density lipoprotein (LDL/HDL) ratio had serum reductions of 4.9%, 6.1%, and 4.3%, respectively, and were observed after 4 weeks of biscuit consumption added with plant stanols (P < 0.05). A significantly higher reduction in LDL-c (8.9%) and LDL/HDL ratio (11.4%) was measured in those taking a plant stanol biscuit with a meal compared to those who consumed a plant stanol biscuit without a biscuit. In conclusion, incorporating plant stanols into a biscuit is not an attractive, convenient, and acceptable way to modestly lower elevated cholesterol concentrations. For optimal efficacy, biscuits should be consumed with a meal as part of a healthy diet.


Abstract: BACKGROUND: Circulating PCSK9 levels are higher in women than men, in postmenopausal than premenopausal women, and in pregnant than non-pregnant women, suggesting that sex hormones may be related to PCSK9 levels. We have examined the relationship between serum estradiol (E2) and testosterone (T) and PCSK9, and the impact of E2 replacement therapy in women and T replacement and ablation therapy in men on circulating PCSK9. METHODS: We conducted a cross-sectional study to examine the correlation between serum T (in males) and E2 (in females) and serum PCSK9. We also conducted interventional studies to examine the effect of hormonal therapy on serum PCSK9 levels. RESULTS: In men, (1) serum T does not correlate with circulating PCSK9 or with LDLc in the basal state, (2) T replacement therapy does not have any effect on circulating PCSK9, and (3) T ablation therapy has mixed results. In women, (1) E2 correlates inversely with circulating PCSK9 and directly with serum LDLc, but (2) E2 replacement therapy does not have any effect on circulating PCSK9. CONCLUSIONS: We demonstrate differences between men and women in the relationship of their major sex hormones with circulating PCSK9. In men, circulating PCSK9 is not related to or affected by T except for a possible effect during T ablation therapy. In women, E2 is inversely related to circulating PCSK9 but the lack of effect of E2 therapy on circulating PCSK9 suggests that the E2-related differences in E2-related PCSK9 levels may be the result of differences in receptor-mediated PCSK9 clearance through E2-related pathways.


Abstract: Proprotein convertase subtilisin/kexin type 9 (PCSK9) regulates LDL cholesterol metabolism by targeting LDL receptors for degradation. Statins increase serum PCSK9 concentration limiting the potential of statins to reduce LDL cholesterol, whereas ezetimibe, inhibitor of cholesterol absorption, has ambiguous effects on circulating PCSK9 levels. Plant stanols also reduce cholesterol absorption, but their effect on serum PCSK9 concentration is not known. Therefore, we performed a controlled, randomized, double-blind study, in which 92 normo- to moderately hypercholesterolemic subjects (35 males and 57 females) consumed vegetable-oil spread 20 g/d enriched (plant stanol group, n=46) or not (control group, n=46) with plant stanol 3g/d as ester for 6 months. Fasting blood samples were drawn at baseline and at the end of the study. Serum PCSK9 concentration was analyzed by Quantikine Elisa Immunoassay, serum and lipoprotein lipids enzymatically, and serum non-cholesterol sterols with gas-liquid chromatography. At baseline, PCSK9 concentration varied from 91 to 716 ng/mL with a mean value of 278+/-11 (SEM) ng/mL with no gender difference. It correlated with serum and LDL cholesterol, serum triglycerides, age, BMI, and plasma glucose concentration, but not with variables of cholesterol metabolism when adjusted to serum cholesterol. Plant stanols reduced LDL cholesterol by 10% from controls (p<0.05), but PCSK9 levels were unchanged and did not differ between the groups. In conclusion, the present study demonstrated for the first time that inhibition of cholesterol absorption with plant stanol esters did not affect serum PCSK9 concentration. Thus, plant stanol esters provide an efficient dietary means to lower LDL cholesterol without interfering with the PCSK9 metabolism and in this regard the LDL receptor-mediated cellular cholesterol uptake and removal.


Abstract: BACKGROUND: Simvastatin is a statin used to lower low-density lipoprotein cholesterol, but has limitations in patients on complicated regimens due to concerns about drug-drug interactions. Pitavastatin is a newly developed statin with limited drug-drug interactions. We conducted a meta-analysis to compare the clinical efficacy of simvastatin and pitavastatin in the control of hypercholesterolemia. METHODS: Randomized clinical trials comparing the efficacy of pitavastatin and simvastatin were identified by searching PubMed (2000-2014) and EMBASE (2000-2014). The primary outcome subjected to meta-analysis was percent change in low-density lipoprotein cholesterol compared with baseline. RESULTS: Four clinical trials were selected for meta-analysis. A total of 908 patients treated with pitavastatin (2 or 4 mg/day) and 381 patients treated with simvastatin (20 or 40 mg/day) were included in the final statistical analysis. No statistically significant difference was identified between treatment with pitavastatin 4 mg/day and treatment with simvastatin 40 mg/day for 12 weeks (mean difference -0.66; 95% confidence interval -2.92, 1.61; P=0.57). Similarly, no statistically significant difference was observed between pitavastatin 2 mg/day and simvastatin 20 mg/day for 4 weeks (mean difference -2.19; 95% confidence interval -0.11, 4.49; P=0.06). Treatment with pitavastatin was noninferior to simvastatin in all of the secondary outcomes and the safety profile was similar between the two statins. CONCLUSION: Pitavastatin is noninferior to simvastatin in lowering low-density lipoprotein cholesterol.

Abstract: Metformin has been used for the treatment of diabetes, whereas atorvastatin reduces the incidence of atherosclerosis and ischemic heart disease. Therefore, combined treatment with metformin plus atorvastatin may be beneficial in diabetic patients associated with cardiac disease. The present study was designed to evaluate the combination therapy of metformin and atorvastatin on streptozotocin-induced diabetes mellitus in rats. Blood pressure, serum insulin, glucose, lipid profiles and antioxidant enzymes in pancreatic tissues were measured. Histopathological examination of pancreatic tissues was performed. Streptozotocin treated rats showed significant decrease in body weight and body mass index. Streptozotocin-treated rats showed a significant increase in the levels of blood pressure, serum glucose, triglycerides, total cholesterol and thiobarbituric acid reactive substance as well as a significant decrease in the levels of serum insulin, high density lipoprotein and reduced glutathione in pancreatic tissues. Administration of metformin plus atorvastatin for a period of 14 days significantly improved these biochemical parameters near to normal. The protective effect of metformin plus atorvastatin against streptozotocin-induced diabetes was further confirmed by histopathological examination. The results of present study suggest that metformin plus atorvastatin possess antioxidant activity and has a significant protective effect against streptozotocin-induced diabetes mellitus.


Abstract: AIM: Ezetimibe reduces plasma levels of low-density lipoprotein (LDL) cholesterol by inhibiting Niemann-Pick C1-Like protein 1 (NPC1L1), the transporter responsible for cholesterol uptake from the intestine into enterocytes and from the bile into hepatocytes. We tested the hypothesis that genetic variation in NPC1L1, mimicking the effect of ezetimibe, was associated with reduced risk of ischaemic vascular disease (IVD) and with increased risk of symptomatic gallstone disease. METHODS AND RESULTS: We included 67 385 individuals from the general population. Of these, 5255 and 3886 individuals developed IVD or symptomatic gallstone disease, respectively, during follow-up from 1977 to 2013. We genotyped four common NPC1L1 variants, previously associated with reduced LDL cholesterol levels, thus mimicking the effect of ezetimibe, and calculated a weighted genotype score. With increasing genotype score, LDL cholesterol decreased stepwise up to 3.5% (0.12 mmol/L) and total cholesterol up to 1.9% (0.11 mmol/L) (P-trend: 2 x 10^{-12} and 2 x 10^{-9}). The cumulative incidence by age of IVD decreased, while that of symptomatic gallstone disease increased as a function of increasing genotype score (P-trend: 0.005 and 0.01). Hazard ratios for genotype scores >5.0 vs. <2.0 were 0.82 (95% confidence interval: 0.70-0.95) for IVD and 1.22 (0.99-1.49) for gallstone disease (P-trend across genotype scores: 0.004 and 0.01). CONCLUSION: Genetic variation in NPC1L1 is associated with a reduction in risk of IVD, with a corresponding reduction in LDL cholesterol, but with a concomitant increased risk of gallstone disease. These data support the hypothesis that treatment with ezetimibe protects against IVD but raise the question whether long-term treatment increases the risk of gallstone disease.


Abstract: BACKGROUND: Adiponectin has cardioprotective properties, suggesting that lower levels seen in obesity and diabetes could heighten risk of atrial fibrillation (AF). Among older adults, however, higher adiponectin has been linked to greater incidence of adverse outcomes associated with AF, although recent reports have shown this association to be U-shaped. We postulated that higher adiponectin would be linked to increased risk for AF in older adults in a U-shaped manner.

METHODS: We examined the associations of total and high-molecular-weight (HMW) adiponectin with incident AF among individuals free of prevalent cardiovascular disease (CVD) participating in a population-based cohort study of older adults (n=3190; age=74+/-5 years). RESULTS: During median follow-up of 11.4 years, there were 886 incident AF events. Adjusted cubic splines showed a positive and linear association between adiponectin and incident AF. After adjusting for potential confounders, including amino-terminal pro-B-type natriuretic peptide 1-76, the HR (95% CI) for AF per SD increase in total adiponectin was 1.14 (1.05 to 1.24), while that for HMW adiponectin was 1.17 (1.08 to 1.27). Additional adjustment for putative mediators, including subclinical CVD, diabetes, lipids and inflammation, did not significantly affect these estimates. CONCLUSIONS: The present findings demonstrate that higher, not lower, levels of adiponectin are independently associated with increased risk of AF in older adults despite its documented cardiometabolic benefits. Additional work is necessary to determine if adiponectin is a marker of failed counter-regulatory pathways or whether this hormone is directly harmful in the setting of or as a result of advanced age.


Abstract: Genetic factors can determine the high variability observed in response to lipid-lowering therapy with statins. Nonetheless, the frequency of single nucleotide polymorphisms (SNPs) and their impact can vary due to ethnicity. Because the Chilean population carries a strong Amerindian background, the objective of this study was to evaluate the influence of apoipoprotein E (APOE) variants (rs429358, rs7412) and the 1959C>T SNP (rs5925) in the low-density lipoprotein receptor (LDLR) in response to atorvastatin treatment in hypercholesterolemic individuals. A hundred and thirty nine subjects undergoing statin therapy were included. Identification of Amerindian mtDNA haplogroups was determined by polymerase chain reaction (PCR) and PCR followed by restriction fragment length polymorphism (RFLP), respectively. SNPs were determined by PCR-RFLP. Out of the 139 individuals studied, 84.4% had an Amerindian background, according to mtDNA analysis. In relation to APOE variants, carriers of the E3/4 genotype presented lower cholesterol reduction compared to genotype E3/3 (LDL-C: -18% vs. -29%, p < 0.001). On the other hand, the LDLR rs5925 SNP was not related to atorvastatin response (p = 0.5760). Our results suggest that APOE SNPs are potential predictors to atorvastatin therapy in Amerindian Chilean subjects.


Abstract: BACKGROUND: In patients with very high cardiovascular risk, low-density lipoprotein cholesterol (LDL-C) less than 70 mg/dL or at least 50% reduction of LDL-C are recommended targets. High-dose atorvastatin has been shown to reduce death and ischemic events among patients with acute coronary syndrome.

OBJECTIVE: To evaluate the proportion of STEMI patients that achieve LDL-C goal after hospital discharge from a real-world setting in Thailand. To determine if the formulation of statin prescribed affected the LDL-C goal achievement. MATERIAL AND METHOD: The authors analyzed data from a cohort of patients with STEMI enrolled from June 1, 2008 through May 31, 2011. Patients who survived, were prescribed atorvastatin on discharge and had LDL-C data at follow-up were analyzed. The formulation of statin was categorized as simvastatin or other statins (atorvastatin or rosuvastatin) group. RESULTS: Ninety-seven percent (n = 265 of 272) of patients were prescribed a statin at discharge. Of these, 216 patients had LDL-C data during a 3-month follow-up period, 75% were men, the mean age was 60.5 +/- 12.2 years, and the mean baseline LDL-C was 118.1 +/- 41.2 mg/dL. 73% (n = 157) of patients received simvastatin and 27% (n = 59) received other statins. At discharge, the median daily dose of simvastatin, atorvastatin and rosuvastatin were 20, 20 and 10 mg respectively. At follow-up, target LDL-C < 70 mg/dL or LDL-C reduction >= 50% was achieved in 30.1% (n = 65) of patients, 27.4% (n = 43) on simvastatin and 37.3% (n = 22) on other statins, (p = 0.158, simvastatin versus other statins). When stratified by the dose intensity of statin, a significantly greater proportion of patients on moderate to high intensity statin attained LDL-C goals than those on low intensity statin: (36.3% versus 24.3%, p = 0.038). CONCLUSION: Most patients with STEMI are prescribed statin therapy at discharge. Despite this, the target LDL-C is attained in a minority of the patients due to suboptimal statin dosing. The formulation of statin did not affect LDL-C goal attainment. High-dose statin therapy is underused in real-world clinical practice. These findings emphasize the opportunities to improve outcomes of STEMI patients with evidence-based therapies.
Abstract: To evaluate the lipid-altering efficacy and safety of ezetimibe monotherapy in young children with heterozygous familial hypercholesterolemia (HeFH) or nonfamilial hypercholesterolemia (nonFH). STUDY DESIGN: One hundred thirty-eight children 6-10 years of age with diagnosed HeFH or clinically important nonFH (low-density lipoprotein cholesterol [LDL-C] >/= 160 mg/dL [4.1 mmol/L]) were enrolled into a multicenter, 12-week, randomized, double-blind, placebo-controlled study. Following screening/diagnostic workup and a 5-week single-blind placebo-run-in with diet stabilization, subjects were randomized 2:1 to daily ezetimibe 10 mg (n = 93) or placebo (n = 45) for 12 weeks. Lipid-altering efficacy and safety were assessed in all treated patients. RESULTS: Overall, mean age was 8.3 years, 57% were girls, 80% were white, mean baseline LDL-C was 228 mg/dL (5.9 mmol/L), and 91% had HeFH. After 12 weeks, ezetimibe significantly reduced LDL-C by 27% after adjustment for placebo (P < .001) and produced significant reductions in total cholesterol (21%), non-high-density lipoprotein cholesterol (26%), and apolipoprotein B (20%) (P < .001 for all). LDL-C lowering response in sex, race, baseline lipids, and HeFH/nonFH subgroups was generally consistent with overall study results. Ezetimibe was well tolerated, with a safety profile similar to studies in older children, adolescents, and adults. CONCLUSIONS: Ezetimibe monotherapy produced clinically relevant reductions in LDL-C and other key lipid variables in young children with primary HeFH or clinically important nonFH, with a favorable safety/tolerability profile. TRIAL REGISTRATION: ClinicalTrials.gov: NCT00867165


Abstract: BACKGROUND: Little is known about the effect of low-density lipoprotein (LDL) cholesterol, triglyceride (TG), and high-density lipoprotein (HDL) cholesterol levels on renal function decline in patients receiving specialized pre-dialysis care. METHODS: In the prospective PREPARE-2 study, incident patients starting pre-dialysis care were included if they were referred to one of the 25 participating Dutch specialized pre-dialysis outpatient clinics (2004-2011). Clinical and laboratory data were collected every 6 months. A linear mixed model was used to compare renal function decline between patients with LDL cholesterol, TG, or HDL cholesterol levels above and below the target goals (LDL cholesterol: <2.50 mmol/L, TG: <2.25 mmol/L, and HDL cholesterol: }>1.00 mmol/L). Additionally the HDL/LDL cholesterol ratio was investigated (>/>0.4). RESULTS: In our study population (n = 306), the median age was 69 years and 70% were male. Patients with LDL cholesterol levels above the target of 2.50 mmol/L experienced an accelerated renal function decline compared to patients with levels below the target (crude additional decline: 0.10 ml/min/1.73 m2/month, 95% CI 0.00-0.20; p < 0.05). A similar trend was found for TG levels above the target of 2.25 mmol/L (0.05 ml/min/1.73 m2/month, 95% CI -0.06 to 0.16) and for a HDL/LDL cholesterol ratio below 0.4 (0.16 ml/min/1.73 m2/month, 95% CI -0.05 to 0.18). Adjustment for potential confounders resulted in similar results, and the exclusion of patients who were prescribed lipid-lowering medication (statin, fibrate, or cholesterol absorption inhibitor) resulted in a slightly larger estimated effect. CONCLUSION: High levels of LDL cholesterol were associated with an accelerated renal function decline, independent of the prescription of lipid-lowering medication.


Abstract: Dyslipidemia is a well-established traditional risk factor for cardiovascular events in the general population, particularly those with preexisting cardiovascular disease (CVD). In this population, reductions in total and low density lipoprotein cholesterol (LDL-C) levels are effective in reducing coronary artery events and mortality. Dyslipidemia is more common in patients with chronic kidney disease (CKD) and is believed to contribute to the high prevalence of CVD in these patients. To date, the treatment of dyslipidemia in patients with CKD followed the guidelines recommended by the US National Cholesterol Education Program Adult Treatment Panel III (ATP III) for the treatment of lipid abnormalities. These guidelines recommend that initiation of lipid-lowering therapy be based on LDL-C level and the projected 10-year risk for coronary artery disease (CAD). However, we now recognize that the relationship between serum cholesterol and CVD is more complex in patients with CKD, particularly those receiving maintenance hemodialysis. This has been demonstrated by the failure of three large randomized clinical trials to show a beneficial effect of lipid-lowering therapy in reducing mortality in dialysis patients despite significant reduction in LDL-C levels. These results have caused uncertainty among nephrologists about how best to manage dyslipidemia in their patients. In this review, the role of dyslipidemia as a risk factor for atherosclerosis in ESRD patients and the results of the 3 clinical trials and other studies, including their limitations will be discussed, and a schema for treating dyslipidemia in dialysis patients will be proposed.


Abstract: The discovery of proprotein convertase subtilisin kexin 9 (PCSK9) has considerably changed the therapeutic options in the field of lipid management. PCSK9 reduces LDL receptor recycling, leading to a decrease of low-density lipoprotein cholesterol (LDL-C) receptors on the surface of hepatocytes and a subsequent increase of circulating LDL-C levels. In observational studies, the loss-of-function mutations of PCSK9 have been associated with a reduction of LDL-C levels and cardiovascular disease (CVD) events. In contrast, humans with high levels of PCSK9 have higher level of plasma LDL-C and significantly enhanced CVD risk during their lifetime, gain-of-function mutations on PCSK9 are, for instance, causatively associated with familial hypercholesterolaemia (FH). Inhibition of PCSK9 is therefore a promising therapeutic option for the lowering of LDL-C levels. The clinical development of human monoclonal antibodies against PCSK9 has progressed, with promising results reported from phase 2 clinical studies in patients with FH or intolerant to statin with LDL-C levels not on target levels. Phase I studies demonstrated safety and efficacy. In phase II, a 60%-70% reduction in LDL-C was observed, especially when subcutaneous injections were performed regularly every two weeks. No significant side effects were observed, with the exception of injection site reactions. Three large phase III programmes with the new anti PCSK9 antibodies are currently underway in patients with acute coronary syndrome (ACS) and LDL-C inadequately controlled by standard treatments. The main objective of these studies is to evaluate the effect of PCSK9 inhibition on the occurrence of CVD events in patients with ACS.


Abstract: Despite the clinical benefits of lowering levels of low-density lipoprotein cholesterol, many patients continue to experience cardiovascular events. This residual risk suggests that additional risk factors require aggressive modification to result in more effective prevention of cardiovascular disease. Hypertriglyceridermia has presented a considerable challenge with regard to understanding its role in the promotion of cardiovascular risk. Increasing evidence has established a clear causal role for elevated triglyceride levels in vascular risk. As a result, there is increasing interest in the development of specific therapeutic strategies that directly target hypertriglyceridermia. This has seen a resurgence in the use of omega-3 fatty acids for the therapeutic lowering of triglyceride levels. The role of these agents and other emerging strategies to reduce triglyceride levels in order to decrease vascular risk are reviewed.


Abstract: Nonalcoholic fatty liver disease (NAFLD)/nonalcoholic steatohepatitis (NASH) is considered to be a hepatic manifestation of metabolic syndrome, and its incidence is rapidly increasing worldwide. It is currently the most common chronic liver disease. NASH can progress to liver cirrhosis and hepatocellular carcinoma, and may result in liver-related death. Currently, the principal treatment for NAFLD/NASH is lifestyle modification by diet and exercise. However, pharmacological therapy is indispensable because obese patients with NAFLD often have difficulty maintaining improved lifestyles. The pathogenesis of NAFLD/NASH has not been completely elucidated. However, insulin resistance, inflammatory cytokines, and oxidative stress are thought to be important in the development and/or progression of the disease. Currently, insulin sensitizers (thiazolidinediones) and antioxidants (vitamin E) seem to be the most promising therapeutic agents for NAFLD/NASH, and lipid-lowering drugs, pentoxifylline, angiotensin receptor blockers, and n-3 polyunsaturated fatty acids also have promise. However, there is a lack
of consensus regarding the most effective and appropriate pharmacotherapy for NAFLD/NASH. Animal experiments suggest that herbal medicines and natural products may be promising therapeutic agents for NAFLD/NASH, but their efficacy and safety are yet to be investigated in human studies. In this paper, we review the existing and potential pharmacological therapies for NAFLD/NASH.


Abstract: PURPOSE: To evaluate the effects of simvastatin and atorvastatin in elderly male patients with benign prostatic hyperplasia (BPH) accompanied by metabolic syndrome (MetS). METHODS: Eligible patients aged >60 year with BPH accompanied by MetS were randomly assigned to receive 40 mg of simvastatin daily, 20 mg of atorvastatin daily or placebo (control group) treatment for 12 months. Serum lipids, interleukin 6 (IL-6), high-sensitivity C-reactive protein (hs-CRP), prostate-specific antigen, prostate volume (PV) and the International Prostate Symptom Score (IPSS) were tested before and after treatment. RESULTS: The levels of serum total cholesterol (TC), triglycerides, low-density lipoprotein cholesterol, hs-CRP, IL-6 and IPSS was decreased, serum high-density lipoprotein cholesterol (HDL-C) was increased, and PV was reduced in the patients following treatments with statins. The PV of the patients who received simvastatin were reduced more than those of the patients who received atorvastatin. The decrease in PV was more significant in the obesity patients than in the normal weight patients and in the hyperlipidemia patients than in the normal-lipid patients following the statin interventions. The reduction in PV was positively related to the decreases in the levels of TC and IL-6 and to the increase in the level of HDL-C. CONCLUSIONS: Simvastatin and atorvastatin significantly reduced PV, improved lower urinary tract symptoms, and slowed the clinical progression of BPH possibly by lowering cholesterol and anti-inflammatory factors.