
Abstract: Panitumumab has proven efficacy in patients with metastatic or locally advanced colorectal cancer patients, provided that they have no activating KRAS mutation in their tumour. Simvastatin blocks the mevalonate pathway and thereby interferes with the post-translational modification of KRAS. We hypothesize that the activity of the RAS-induced pathway in patients with a KRAS mutation might be inhibited by simvastatin. This would theoretically result in increased sensitivity to panitumumab, potentially comparable with tumours with wild-type KRAS. A Simon two-stage design single-arm, phase II study was designed to test the safety and efficacy of the addition of simvastatin to panitumumab in colorectal cancer patients with a KRAS mutation after failing fluoropyrimidine-based, oxaliplatin-based and irinotecan-based therapy. The primary endpoint of this study was the proportion of patients alive and free from progression 11 weeks after the first administration of panitumumab, aiming for at least 40%, which is comparable with, although slightly lower than, that in KRAS wild-type patients in this setting. If this 40% was reached, then the study would continue into the second step up to 46 patients. Explorative correlative analysis for mutations in the KRAS and related pathways was carried out. One of 14 patients was free from progression at the primary endpoint time. The median progression-free survival was 8.4 weeks and the median overall survival status was 19.6 weeks. We conclude that the concept of mutant KRAS phenotype expression modulation with simvastatin was not applicable in the clinic.


Abstract: Proprotein convertase subtilisin/kexin type 9 (PCSK9), which involves in low-density lipoprotein cholesterol (LDL-C) metabolism by interacting with the LDL receptor, is considered as a potent therapeutic target for treating hypercholesterolemia. Here, a fab antibody phage display library was constructed and employed for bio-panning against recombinant PCSK9. A Fab fragment (designated PA4) bound with high affinity to PCSK9 was isolated after four rounds of panning. The fully human antibody IgG1-PA4 bound specifically to PCSK9 with nanomolar affinity. In vitro, IgG1-PA4 inhibited PCSK9 binding to LDLR and attenuated PCSK9-mediated degradation of LDLR on the HepG2 cell surface. In C57BL/6 mice, administration of IgG1-PA4 at 30 mg/kg increased hepatic LDLR protein levels by as much as 3 fold when compared with control. Taken together, these results suggest that the IgG1-PA4 could be a potential candidate for the treatment of hypercholesterolemia by inhibiting PCSK9-mediated degradation of cell surface LDLRs.


Abstract: The administration of statin might increase the risk of new-onset diabetes in hypercholesterolemic patients based on recent clinical evidence. However, the causal relationship must be clarified and confirmed in animal experiments. Therefore, we mimicked hypercholesterolemia by feeding rabbits a high-cholesterol diet (HCD) and 16 weeks of atorvastatin administration to investigate the effect of statin on glucose metabolism. The intravenous glucose tolerance test showed that plasma glucose levels in the statin-treated rabbits were consistently higher and that there was a slower rate of glucose clearance from the blood than in HCD rabbits. The incremental area under the curve for glucose in the statin-treated rabbits was also significantly larger than in the HCD rabbits. However, there was no significant difference between the two groups in the intravenous insulin tolerance test. The glucose-lowering ability of exogenous insulin was not impaired by statin treatment in hypercholesterolemic rabbits. The administration of a single dose of statin did not affect glucose metabolism in normal rabbits. The statin also significantly increased the levels of high-density lipoprotein cholesterol, alanine aminotransferase and aspartate transaminase and decreased plasma levels of total cholesterol, triglycerides and low-density lipoprotein cholesterol in the hypercholesterolemic rabbits, whereas it did not affect plasma levels of glucose and insulin. The current results showed that atorvastatin treatment resulted in a significant delay of glucose clearance in hypercholesterolemic rabbits, and this rabbit model could be suitable for studying the effects of statin on glucose metabolism.


Abstract: BACKGROUND: As a first-line diabetes drug that is widely prescribed around the world, metformin has been demonstrated to be effective in reducing microvascular risk, in a lower dose of glucose levels. Specifically, metformin use has been shown to be associated with improved lipid profiles, such as increased levels of high-density lipoprotein cholesterol (HDL-C). However, no study has been performed to examine the differential response in HDL-C levels to metformin treatment by race/ethnicity. METHODS: Here, based on a re-analysis of the data from the Diabetes Prevention Program, which involved prediabetic participants receiving 850 mg of metformin twice daily, we compared the lipid profile changes following the metformin use. The participants were composed of 602 Whites, 221 African Americans (AAs) and 162 Hispanics. RESULTS: We found that the one-year metformin treatment resulted in significant increase in HDL-C levels in Whites (p = 0.002) and AAs (p = 0.016), but not in Hispanics. Consistently, both Whites (p = 0.018) and AAs (p = 0.020) had more pronounced changes in HDL-C levels than Hispanics following metformin treatment. CONCLUSION: This result suggests a notion that Whites and AAs are more responsive than Hispanics to one-year metformin use in HDL-C level changes, and that racial and ethnic identity is a factor to consider when interpreting the effects of metformin treatment on lipid profiles.


Abstract: BACKGROUND: Glucose fluctuation has been recognized as a residual risk apart from dyslipidemia for the development of coronary artery disease (CAD). This study aimed to investigate the association between glucose fluctuation and coronary plaque morphology in CAD patients. METHODS: This prospective study enrolled 72 consecutive CAD patients receiving adequate lipid-lowering therapy. They were divided into 3 tertiles according to the mean amplitude of glycemic excursions (MAGE), which represents glucose fluctuation, measured by continuous glucose monitoring (tertile 1: <49.1, tertile 2: 49.1 – 85.3, tertile 3: >85.3). Morphological feature of plaques were evaluated by optical coherence tomography. Lipid index (LI) (mean lipid arc x length, fibrous cap thickness (FCT), and the prevalence of thin-cap fibroatheroma (TCFA) were assessed in both culprit and non-culprit lesions. RESULTS: In total, 166 lesions were evaluated. LI was stepwise increased according to the tertile of MAGE (1958 +/- 974 [tertile 1] vs. 2653 +/- 1400 [tertile 2] vs. 4362 +/- 1858 [tertile 3], p < 0.001), whereas FCT was the thinnest in the tertile 3 (157.3 +/- 73.0 mum vs. 104.0 +/- 64.1 mum vs. 83.1 +/- 34.7 mum, p < 0.001, respectively). The tertile 3 had the highest prevalence of TCFA. Multiple linear regression analysis showed that MAGE had the strongest effect on LI and FCT (standardized coefficient beta = -0.392 and -0.392, respectively, both P < 0.001). CONCLUSIONS: Glucose fluctuation and hypoglycemia may impact the formation of lipid-rich plaques and thinning of fibrous cap in CAD patients with lipid-lowering therapy.

Abstract: Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a serine protease that binds to low-density lipoprotein receptors (LDL-Rs), leading to their accelerated degradation and increased low-density lipoprotein cholesterol (LDL-C) levels. Therefore, PCSK9 levels play a critical role in cholesterol metabolism by reducing LDL-C levels and thus increasing levels of plasma LDL-C. Recently, investigational agents inhibiting PCSK9 have been shown to lower LDL-C and also, potentially, an important secondary target, lipoprotein(a). Therefore, several pharmaceutical companies have initiated drug-development programs that target PCSK9 and are built on a solid foundation of basic science, genetic studies, and epidemiological observations. PCSK9 inhibition with monoclonal antibodies demonstrated LDL-C lowering of up to 57% when the PCSK9 antibodies are used as monotherapy and up to 73% when added to background lipid-lowering therapy. In addition, long-term cardiovascular outcome studies are currently under way to confirm the longer term safety and efficacy of PCSK9 inhibitors and to determine whether PCSK9 inhibition lowers the incidence of major cardiovascular events. PCSK9 inhibitors may provide safe and effective lipid-lowering therapy, especially for patients with inadequate LDL-C lowering on lipid-lowering treatments, those who are statin intolerant or have contraindications to statin therapy, and those with hereditary hypercholesterolemia/familial hypercholesterolemia and severely elevated LDL-C.


Abstract: High-density lipoprotein cholesterol (HDL-C) has been shown in epidemiologic studies to be associated with cardiovascular (CV) risk and thus significant efforts have been focused on HDL-C modulation. Multiple pharmaceutical agents have been developed with the goal of increasing HDL-C. Niacin, the most widely used medication to raise HDL-C, increases HDL-C by up to 25% and was shown in multiple surrogate endpoint studies to reduce CV risk. However, two large randomized controlled trials of niacin, AIM-HIGH and HPS2-THRIVE, have shown that despite its effects on HDL-C, niacin does not increase the incidence of CV events and may have significant adverse effects. Studies of other classes of agents such as cholesteryl ester transfer protein (CETP) inhibitors have also shown that even dramatic increases in HDL-C do not necessarily translate to reduction in clinical events. While these findings have cast doubt upon the importance of HDL-C modulation on CV risk, it is becoming increasingly clear that HDL function-related measures may be better targets for CV risk reduction. Increasing ApoA-I, the primary apolipoprotein associated with HDL, correlates with reduced risk of events, and HDL particle concentration (HDL-P) inversely associates with incident CV events adjusted for HDL-C and LDL particle measures. Cholesterol efflux, the mechanism by which macrophages in vessel walls secrete cholesterol outside cells, correlates with both surrogate end points and clinical events. The effects of niacin on these alternate measures of HDL have been conflicting. Further studies should determine if modulation of these HDL function markers translates to clinical benefits. Although the HDL cholesterol hypothesis may be defunct, the HDL function hypothesis is now poised to be rigorously tested.


Abstract: AIM/HYPOTHESIS: Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a critical regulator of cholesterol homeostasis. PCS9 inhibitors are being actively developed to lower LDL cholesterol levels. However, there are conflicting data regarding the consequences of PCS9 deficiency on glucose homeostasis in mouse models. Here, we analysed in humans the association between the PCS9 p.R46L loss-of-function (LOF) variant and (1) glucose homeostasis variables; (2) type 2 diabetes status; and (3) the risk of 9 year incident type 2 diabetes in a prospective study. METHODS: PCS9 p.R46L was genotyped in 4630 French participants from the Data from an Epidemiological Study on the Insulin Resistance Syndrome (DESIR) prospective study and in 1342 French participants with type 2 diabetes. The association between p.R46L and metabolic traits or type 2 diabetes risk was assessed through linear or logistic regression models adjusted for age, sex and BMI. The association between p.R46L and type 2 diabetes was assessed using a Cox regression model adjusted for sex, age and BMI at baseline. RESULTS: Significant associations (p < 10^{-6}) were found between p.R46L and total cholesterol (-0.394 mmol/l), LDL-cholesterol (-0.393 mmol/l) and apolipoprotein B concentrations (-0.099 g/l). However, no significant association was observed between p.R46L and markers of glucose homeostasis (including fasting glucose, fasting insulin, HbA1c, HOMA-B, HOMA-IR) or type 2 diabetes risk. Furthermore, no significant association between p.R46L variant and risk of incident type 2 diabetes was observed in DESIR. CONCLUSIONS/INTERPRETATION: The PCSK9 p.R46L LOF variant was not associated with impaired glucose homeostasis in humans. These data are reassuring regarding the safety of PCS9 inhibitors.


Abstract: Objectives. This study examined whether the increase of adiponectin associated with extended-release (ER) niacin/laropiprant combination attenuates the adverse effect of niacin on glucose and insulin resistance in Hong Kong Chinese patients with dyslipidaemia. Methods. Patients (N = 121) were treated with ER niacin/laropiprant 1 g/20 mg for 4 weeks and then the dose was doubled for an additional 8 weeks. Measurements of fasting lipids, glucose, insulin, and adiponectin were performed at baseline and during the study. Results. There were significant (P < 0.001) increases in glucose (9.4 +/- 13.1%), insulin (70.2 +/- 91.0%), HOMA-IR (87.8 +/- 103.9%), and adiponectin (169.3 +/- 111.6%). The increase in adiponectin was significantly associated with increase in glucose (r = 0.221, P < 0.05), insulin (r = 0.184, P < 0.05), and HOMA-IR (r = 0.237, P < 0.01) and the association remained significant after adjustment for changes in body weight or body fat mass. Conclusion. Treatment with ER niacin/ laropiprant led to a significant increase in adiponectin levels but worsening of glucose levels and insulin resistance, and the increase in adiponectin and insulin resistance were correlated suggesting the increase in adiponectin did not ameliorate the deterioration in insulin resistance. Clinical trial is registered with number on WHO-ICTRP: ChiCTR-ONC-10001038.


Abstract: The increase in high density lipoprotein (HDL)-cholesterol observed with cholesteryl ester transfer protein (CETP) inhibition is commonly attributed to blockade of cholesteryl ester (CE) transfer from HDL to low density lipoprotein particles. In vitro, it has been observed that CETP can mediate transfer of CE between HDL particles (“homotypic transfer”), and it is postulated that this contributes to HDL remodeling and generation of anti-atherogenic pre-beta HDL. Inhibition of CETP could limit this beneficial remodeling and reduce pre-beta HDL levels. We observed that anacetrapib does not reduce pre-beta HDL in vivo, but the role of HDL homotypic transfer was not examined. This study evaluated the effects of anacetrapib on homotypic transfer from HDL3 to HDL2 in vivo using deuterium-labeled HDL3, and compared this to in vitro settings, where homotypic transfer was previously described. In vitro, both anacetrapib and dalcetrapib inhibited transfer of CE from HDL3 to HDL2 particles. In CETP transgenic mice, anacetrapib did not inhibit the appearance of labeled CE derived from HDL3 in HDL2 particles, but rather promoted the appearance of labeled CE in HDL2. We concluded that inhibition of CETP by anacetrapib promoted HDL particle remodeling, and does not impair the flux of cholesteryl ester into larger HDL particles when studied in vivo, which is not consistent with in vitro observations. We further conclude, therefore, that the in vitro conditions used to examine HDL-to-HDL homotypic transfer may not recapitulate the in vivo condition, where multiple
mechanisms contribute to cholesteryl ester flux into and out of the HDL pool

Abstract: INTRODUCTION: Lipid-lowering drugs, especially hydroxymethylglutaryl-CoA reductase inhibitors (statins), are widely used in the treatment and prevention of atherosclerotic diseases. The benefits of statins are well documented. However, myotoxic side effects, which can sometimes be severe, including myopathy or rhabdomyolysis, have been associated with the use of statins. In some cases, this toxicity is associated with pharmacokinetic alterations. Potent inhibitors of CYP 3A4 significantly increase plasma concentrations of the active forms of simvastatin, lovastatin and atorvastatin. Fluvastatin is metabolized by CYP2C9, while pravastatin, rosuvastatin and pitavastatin are not susceptible to inhibition by any CYP. Areas covered: This review discusses the pharmacokinetic aspects of the drug-drug interaction with statins and genetic polymorphisms in CYPs, which are involved in the metabolism of statins, and highlights the importance of establishing a system utilizing electronic medical information practically to avoid adverse drug reactions. Expert opinion: An understanding of the mechanisms underlying statin interactions will help to minimize drug interactions and develop statins that are less prone to adverse interactions. Quantitatively analyzed information for the low-density lipoprotein cholesterol lowering effects of statin based on electronic medical records may be useful for avoiding the adverse effect of statins

13. Fabiny A: Ask the doctor. I am 61 and had been on atorvastatin for 10 years with no problems. Recently, I've had disabling muscle pain with both the generic atorvastatin and the brand-name version, Lipitor. My doctor says that I can no longer take statin drugs. Since strokes run in my family, I am concerned. Is there anything else I can do to decrease my risk of stroke? Harv.Womens Health Watch. 2014, 22:2.


Abstract: We aimed to investigate the effects of simvastatin on mitochondrial enzyme activity, ghrelin, and hypoxia-inducible factor 1 alpha (HIF-1 alpha) on hepatic tissue in rats treated with Lipopolysaccharides (LPS) during the early phase of sepsis. Rats were divided into four groups: control, LPS (20 mg/kg, i.p.), Simvastatin (20 mg/kg, p.o.), and LPS + Simvastatin group. We measured citrate synthase, complex I, II, II-III, II-III enzymes activity, serum and liver level of TNF-alpha, IL-10 using ELISA. Liver sections underwent histopathologic examination and TNF-alpha, IL-10, HIF-1-alpha and ghrelin immunoactivity were examined using immunohistochemistry methods. There were no differences in all groups for mitochondrial enzymes activities, but the expression of HIF-1 alpha was significantly higher in Simvastatin group compared to control group. There were significant reductions in PWV and OPG suggests that atorvastatin reduces PWV via direct anti-inflammatory effects on the vasculature.

Abstract: OBJECTIVE: To investigate the effects of atorvastatin on the proliferation and apoptosis of leukemic cell lines (Jurkat, K562 and HL-60), and explore the function of TLR4/MYD88/NF-kappaB and PI3K/AKT signal pathway in this process. METHODS: Cells in logarithmic growth phase were divided into negative control group and experimental group (cells were treated with atorvastatin with intervention concentrations of 1, 5 and 10 mumol/L respectively) and cultured for 24 hours. Changes in apoptosis and cell cycle of leukemic cells were detected utilizing the Flow Cytometry. Changes in the expression of TLR4/MYD88/NF-kappaB and PI3K/AKT signal pathway related genes were detected utilizing Real-time PCR and Western Blot method. RESULTS: Aortic stenosis inhibit proliferation and induce apoptosis in K562, HL-60 and Jurkat cells in a dose-dependent manner. K562, HL-60 and Jurkat cells in G0/G1 phase increased and that in S phase decreased after being treated with atorvastatin for 24 hours compared with that in control group. This study find that the atorvastatin can retard the three cells in the G0/G1 phase. The study find that the basal expressions of TLR4, MYD88 and NF-kappaB gene in K562, HL-60 and Jurkat cells are obviously down-regulated in a dose-dependent manner after being treated with atorvastatin with different concentrations. This down-regulation action of atorvastatin to the expression of the TLR4, MYD88 and NF-kappaB gene becomes more obvious with the increase of the drug level. In addition, the PI3K, AKT and their phosphorylation levels in the above cells down-regulate obviously in a dose-dependent manner after being treated with atorvastatin. This down-regulation action of atorvastatin to the PI3K, AKT and their phosphorylation levels become more obvious with the increase of the drug level. CONCLUSIONS: Aortic stenosis can inhibit proliferation and induce apoptosis in leukemia cells, which may be associated with the regulation of atorvastatin to the TLR4/MYD88/PI3K/AKT/NF-kappaB signaling pathway

Abstract: Statin therapy improves lipid profiles and reduces vascular inflammation, but its effects on central arterial stiffness in type 2 diabetes are unclear. The aim of this study was to determine whether statin therapy reduces central arterial stiffness, in a dose-dependent manner, in male patients with type 2 diabetes. Fifty-one patients ceased statin therapy for 6 weeks, followed by randomisation to either 10 or 80 mg of atorvastatin. At randomization, 3 and 12 months, central arterial stiffness was measured via carotid-femoral pulse wave velocity (PWV), along with serum markers of vascular inflammation measured including high-sensitivity C-reactive protein (hsCRP) and osteoprotegerin (OPG). PWV decreased from 10.37 +/- 1.30 to 9.68 +/- 1.19 m/sec (p < 0.01 from baseline) at 3 months and 9.10 +/- 1.17 m/sec (p < 0.001 from baseline) at 12 months. hsCRP and OPG decreased significantly at 3 and 12 months. Reductions in PWV did not differ significantly between the groups. Baseline PWV and OPG values correlated strongly (r = 0.48, p <0.01), as did their response to atorvastatin over 12 months (r = 0.36 delta-PWG and delta-PWV, p < 0.01). Atorvastatin therapy appeared to reduce central arterial stiffness in male type 2 diabetes, with no dose-dependent effect observed. The correlation observed between reductions in PWV and OPG suggests that atorvastatin reduces PWV via direct anti-inflammatory effects on the vasculature

Abstract: OBJECTIVES: To assess the safety and efficacy of pitavastatin in children and adolescents with hyperlipidemia. STUDY DESIGN: A total of 106 children and adolescents with hyperlipidemia, ages 6 to 17 years, were enrolled in a 12-week randomized, double-blind, placebo-controlled study and randomly assigned to pitavastatin 1 mg, 2 mg, 4 mg, or placebo. During a 52-week extension period, subjects were up-litrated from 1 mg pitavastatin to a maximum dose of 4 mg in an effort to achieve an optimum low-density lipoprotein cholesterol (LDL-C) target of <110 mg/
upregulating the expression of GARP on regulatory T cells inhibits the anti-inflammatory effects of atorvastatin. We conclude that atorvastatin improves the inflammatory response in atherosclerosis partly by increase the numbers of CD4+LAP+ and CD4+Foxp3+ regulatory T cells in ApoE-/- mice. Also, we indicate that atorvastatin promotes the activated Tregs, which is related to the release of TGF-beta. The antiatherosclerosis effects of statins partly depend on their multiple immune dosages and induces the regression of coronary atherosclerosis. Several cases of niacin-induced cystoid macular edema have been reported with different central or branch retinal vein occlusion, diabetic retinopathy and most commonly following cataract extraction, hereditary retinal dystrophies, and secondary formation of multiple cystic spaces. This condition is provoked by a variety of pathological conditions such as intraocular inflammation, 

Abstract: Cystoid macular edema is a condition that involves the macula, caused by an accumulation of extracellular fluid in the macular region with mild dyslipidaemia. A cardiovascular disease outcome trial is needed to translate these effects into a reduction of cardiovascular disease events. INTERPRETATION: TA-8995, a novel CETP inhibitor, is well tolerated and has beneficial effects on lipids and apolipoproteins in patients with mild dyslipidaemia. METHODS: In this randomised, double-blind, placebo-controlled, parallel-group phase 2 trial, we recruited patients (aged 18-75 years) from 17 sites (hospitals and independent clinical research organisations) in the Netherlands and Denmark with fasting LDL cholesterol levels between 2.5 mmol/L and 4.5 mmol/L, HDL cholesterol levels between 0.8 and 1.8 mmol/L and triglyceride levels below 4.5 mmol/L after washout of lipid-lowering treatments. Patients were randomly allocated (1:1) by a computer-generated randomisation schedule to receive one of the following nine treatments: a once a day dose of 1 mg, 2.5 mg, 5 mg, or 10 mg TA-8995 or matching placebo; 10 mg TA-8995 plus 20 mg atorvastatin; 10 mg TA-8995 plus 10 mg rosuvastatin or 20 mg atorvastatin or 10 mg rosuvastatin alone. We overencapsulated statins to achieve masking. The primary outcome was percentage change in LDL cholestrol and HDL cholestrol from baseline at week 12, analysed by intention to treat. This study is registered with ClinicalTrials.gov, number NCT01970215. FINDINGS: Between Aug 15, 2013, and Jan 10, 2014, 364 patients were enrolled. At week 12, LDL cholesterol levels were reduced by 27.4% in patients assigned to the 1 mg dose, 32.7% in patients given the 2.5 mg dose, 45.3% in those given the 10 mg dose (p<0.0001). LDL cholesterol levels were reduced by 68.2% in patients given 10 mg TA-8995 plus atorvastatin, and by 63.3% in patients given rosuvastatin plus 10 mg TA-8995 (p<0.0001). A daily dose of 1 mg TA-8995 increased HDL cholesterol levels by 75.8%, 2.5 mg by 124.3%, 5 mg by 157.1%, and 10 mg dose by 179.0% (p<0.0001). In patients receiving 10 mg TA-8995 and 20 mg atorvastatin HDL cholesterol levels increased by 152.1% and in patients receiving 10 mg TA-8995 and 10 mg rosuvastatin by 157.5%. We recorded no serious adverse events or signs of liver or muscle toxic effects. INTERPRETATION: TA-8995, a novel CETP inhibitor, is well tolerated and has beneficial effects on lipids and apolipoproteins in patients with mild dyslipidaemia. A cardiovascular disease outcome trial is needed to translate these effects into a reduction of cardiovascular disease events. FUNDING: Dezima 

Abstract: Cystoid macular edema is a condition that involves the macula, caused by an accumulation of extracellular fluid in the macular region with secondary formation of multiple cystic spaces. This condition is provoked by a variety of pathological conditions such as intraocular inflammation, central or branch retinal vein occlusion, diabetic retinopathy and most commonly following cataract extraction, hereditary retinal dystrophies, and topical or systemic assumption of drugs. Niacin is a vitamin preparation usually used for the treatment of lipid disorders. The treatment with niacin, alone or in combination with other lipid-lowering agents, significantly reduces total mortality and coronary events and slows down the progression of and induces the regression of coronary atherosclerosis. Several cases of niacin-induced cystoid macular edema have been reported with different dosages 

Zhao X, Liu Y, Zhong Y, Liu B, Yu K, Shi H, Zhu R, Meng K, Zhang W, Wu B, Zeng Q: Atorvastatin Improves Inflammatory Response in Atherosclerosis by Upregulating the Expression of GARP. Mediators.Inflamm. 2015, 2015:841472. Abstract: Regulatory T cells play an important role in the progression of atherosclerosis. GARP is a newly biological membrane molecule existed on activated Tregs, which is related to the release of TGF-beta. The antiatherosclerosis effects of statins partly depend on their multiple immune modulatory potencies. In this paper, we present that atorvastatin could upregulate the expression of GARP and TGF-beta in CD4+ T cells and increase the numbers of CD4+LAP+ and CD4+Foxp3+ regulatory T cells in ApoE-/- mice. Also, we indicate that atorvastatin promotes the aggregation of GARP+ and Foxp3+ cells and secretary of the TGF-beta1 in atherosclerotic plaques. Furthermore, we prove that atorvastatin could delay the progression of atherosclerosis and improve the stability of atherosclerotic plaques. Interestingly, we report that inhibition of GARP distinctly inhibits the anti-inflammatory effects of atorvastatin. We conclude that atorvastatin improves the inflammatory response in atherosclerosis partly by upregulating the expression of GARP on regulatory T cells

Abstract: AIMS: To elucidate if topically applied atorvastatin safely decreases corneal fluorescein staining in dry eyes associated with blepharitis. METHODS: Ten dry eye and blepharitis (DEB) patients were enrolled in a prospective pilot study. All patients were treated with topical atorvastatin (50 μM) 8 times a day for 4 weeks and allowed to continue with their existing dry eye treatment. The patients were examined weekly for 4 weeks. The primary outcome measure was corneal fluorescein staining. Secondary outcome measures were tear film break-up time (BUT), Schirmer I testing, blepharitis score and bulbar conjunctival injection. The subjective efficacy was evaluated with global symptom and facial analogue scores. RESULTS: An improvement in corneal fluorescein staining in the treated eye by >1 point from baseline to completion of the trial at week 4 was found in 9 of 10 patients (p < 0.01). Topical atorvastatin significantly improved the tear film BUT (p < 0.01), blepharitis score (p < 0.05) and bulbar conjunctival injection (p < 0.05). The global symptom score and facial analogue score also improved (p < 0.05). There were no side effects. CONCLUSION: Topical atorvastatin is a potential therapy for DEB patients. Larger comparative clinical studies are required to establish the efficacy and safety of topical atorvastatin. (c) 2015 S. Karger AG, Basel