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THE ANTI-INFLAMMATORY EFFECTS OF ATORVASTATINS IN PATIENTS SUFFERING METABOLIC SYNDROME

ANTIINFLAMATORNI EFEKTI ATORVASTATINA KOD PACIJENATA SA METABOLIČKIM SINDROMOM

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atorvastatin, circulate immune complexes, C4 component of complements, metabolic syndrome

Ključne reči
atorvastatin, CIC, C4, metabolički sindrom

Abstract

Introduction: Inflammation plays a key role in all stages of atherosclerosis. Both humoral and cellular mechanisms have been proposed to participate in the onset and/or progression of atherosclerotic lesions, and postulates for the involvement of auto antibodies against oxidative modified LDL, phospholipids and circulating immune complexes have met with considerable experimental support.
Aim of study was to point on anti-inflammatory effect of atorvastatins in metabolic syndrome patients.
Materials and methods: Study included 46 patients who fulfilled criteria for MetS and they have atorvastatin therapy in dose of 10 mg/day. Serum samples were taken for measurement concentrations of: glucose, triglycerides (tg), total cholesterols (ch), high-density lipoprotein (HDL-C) cholesterol, low-density lipoprotein (LDL-C) cholesterol, factor for coronary diseases (CHD), index of atherosclerosis (IA), circulate immune complexes (CIC), C-reactive proteins (CRP) and C4 component of complements (C4) before and after four weeks of atorvastatin therapy.
Results: Four weeks atorvastatin therapy in dose of 10 mg per a day have significantly decreased concentration of total cholesterol ($p<0.008$), LDL-C ($p<0.005$) and index of atherosclerosis ($p<0.018$). Additionally concentration of acute markers of inflammation CRP ($p<0.008$) and C4 ($p<0.034$) were significantly decreased.
Conclusion: Atorvastatins have very potent anti-inflammatory effects on atherosclerotic plaques in metabolic syndromes.

INTRODUCTION

Inflammation is thought to play a key role in all stages of atherosclerosis and in the genesis of acute coronary syndromes[(1)]. A key step in the formation and maturation of atherosclerotic plaques is endothelial cell activation[(2)]. Elevated plasma levels of several markers of the inflammatory cascade have been shown to predict a future risk of cardiovascular events, including the acute-phase reactants, C-reactive protein (CRP) and fibrinogen[(3)]. Cardiovascular disease (CVD) is the major cause of morbidity and mortality in developed countries [(4)]. Searching for the underlying risk factors has revealed that a cluster of contributors is often present simultaneously. This risk factor clustering, most notably the core trio insulin resistance, dyslipidemia and hypertension, has been called by a number of different names including metabolic syndrome (MetS), insulin resistance syndrome, the deadly quartet and Syndrome X [(4-10)]. Although somewhat controversial, the usefulness of clustering this syndrome remains clear. The mechanistic connections among syndrome the trio are not completely under-

stood. In the past decade, there has been an upsurge of interest in the role of immune mechanisms in the development and regulation of atherosclerosis and its complications [11]. Both humoral and cellular mechanisms have been proposed to participate in the onset and/or progression of atherosclerotic lesions, and postulates for the involvement of auto antibodies against oxidative modified LDL, phospholipids and circulating immune complexes have met with considerable experimental support [12-15].

The aim of study was to point on anti-inflammatory effect of atorvastatins in metabolic syndrome patients.

MATERIAL AND METHODS

Study included 46 patients who fulfilled criteria's for MetS and they received atorvastatin 10mg/day. Serum samples were taken for measurement concentrations of: glucose, triglycerides (tg), total cholesterols (ch), high-density lipoprotein (HDL-C) cholesterol, low-density lipoprotein (LDL-C) cholesterol, factor for coronary diseases (CHD), index of atherosclerosis (IA), circulate immune complexes (CIC), C-reactive proteins (CRP) and C4 component of complements (C4) at the start of study. All measurements were repeated after 4 weeks of therapy.

All analyses were performed using the Statistical Package for the Social Science (SPSS), statistical software for Windows, Version 12.0 (SPSS Inc., IL, USA). The difference were assesed by Student's t-test and Perason's correlation test. Probabiliy (p) less than 0.05 and 0.01 was considered significantly different and less than 0.001 highly significantly different.

RESULTS

Table 1 summarizes serum concentrations of glucose, cholesterol (ch), triglycerides, HDL-C, LDL-C, factor for coronary diseases (CHD), index of atherosclerosis (IA) before and after 4 weeks of atorvastatins therapy.

levels	Baseline	4 week therapy	P
Glucose	5.87 ± 1.64	6.09 ± 1.28	ns
Cholesterol	7.14 ± 1.94	6.09 ± 2.10	p<0.008
Triglycerides	2.20 ± 1.65	2.12 ± 1.51	ns
HDL-C	1.36 ± 0.45	1.31 ± 0.50	ns
LDL-C	4.82 ± 1.99	3.74 ± 2.0	p<0.005
CHD	5.67 ± 2.09	4.97 ± 1.79	ns
IA	3.80 ± 1.81	2.99 ± 1.40	ns

***Table 1**. Serum concentration of glucose, cholesterols and its fraction HDL and LDL, triglycerides and risk factors before and after 4 weeks atorvastatins therapy*

Levels	Baseline	4 weeks therapy	P
CIC	1.02 ± 0.74	1.12 ± 1.04	
CRP	1.57 ± 0.81	1.11 ± 0.64	p<0.008
C4	0.41 ± 0.10	0.38 ± 0.11	p<0.034

***Table 2**. Concentration of CRP, CIC and C4 component of complement*

Parameters of inflammation, circulate immune complexes (CIC), C-reactive protein (CRP) and C4 component of complements, are presented in table 2.

Four weeks therapy by 10 mg atorvastatins significantly decreased concentration of total cholesterol (p<0.008), LDL-C (p<0.005) and index of atherosclerosis (p<0.018). Concentration of acute markers of inflammation also were significantly decreased, CRP (p<0.008) and C4 (p<0.034).

DISCUSSION

Recent studies indicate that statins have salutary physiologic effects within weeks. In conjunction with lowering total and low-density lipoprotein (LDL) cholesterol, statins may improve endothelial functions (16), decrease platelet aggregability and thrombus deposition (17) and reduce vascular inflammation (18). The observation that statins reduce the risk of cardiovascular events even in the absence of a significant decrease of blood cholesterol levels, supports the relevance of the potential "pleiotropic" function of this drug class (19). The REVERSAL trial suggests several potential mechanisms for the greater benefit observed with an intensive treatment regimen. Most atherogenic lipoproteins were reduced to a greater extent in the intensive treatment by atorvastatin, including levels of LDL-C, total cholesterol, and triglycerides. However, factors other than greater LDL-C-reducing efficacy may also have influenced the results, including the differential effect on inflammation. Approximately, all in vitro and in vivo studies uniformly support anti-inflammatory roles of statins which highlight the relationship between the extent of reduction in CRP or other inflammatory markers and the effect on the progression of atherosclerosis.

CONCLUSION

Atorvastatins have very potent anti-inflammatory effects on atherosclerotic plaques in metabolic syndromes.

Sažetak

Uvod: Inflamacija igra značajnu ulogu u svim stadijumima ateroskleroze. Značajna je uloga i humoralnog i celularnog imunskog odgovora u početku i/ili progresiji aterosklerotskih lezija kroz auto-antitijela na oksidisani LDL frakcije, fosfolipide i cirkulišuće imune komplekse.
Cilj rada: je bio da se ukaže na antiinflamatirni efekat atorvastatina u pacijenata sa metaboličkim sindromom.
Materijali i metode: Studija je obuhvatila 46 pacijenata koji su ispunjavali kriterijume za metabolički sindrom i koji su započeli terapiju atorvastatinom u dozi od 10 mg/dnevno. Uzorci seruma za određivanje koncentracija: glikemije, triglicerida (tg), ukupnog holesterola (chol), holesterolska frakcija visoke gustine (HDL-C), holesterolska frakcija male gustine (LDL-C), faktora za koronarna oboljenja (CHD), indeks ateroskleroze (IA), C-reaktovnog proteina (CRP), cirkulišućih imunskih kompleksa (CIC) i C4 komponente komplementa (C4) uzeti su bazalno i nakon četiri nedjelje terapije atorvastatinom.
Rezultati: Četiri nedjelje terapije atirvastatinom u dozi od 10 mg/dnevno dovelo je do značajnog smanjenja koncentracije chol ($p<0.008$), LDL-C ($p<0.005$) i IA ($p<0.018$). Značajno su bile smanjene i koncentracije reaktanata akutne faze CRP ($p<0.008$) i C4 ($p<0.034$).
Zaključak: Atorvastatin ima snažno antiinflamatorno djelovanje na aterosklerotske lezije u metaboličkom sindromu.

REFERENCES

1. Libby P., Ridker PM., Maseri A. Inflammation and atherosclerosis. Circulation 2002;105(9):1135-43
2. Kinlay S., Libby P., Ganz P. Endothelial function and coronary artery disease. Curr Opin Lipidol 2001;12(4):383-9
3. Blake GJ., Ridkler PM. Novel clinical markers of vascular wall inflammation. Circ Res 2001;89(9):763-71
4. Kahn R., Buse J., Ferrannini E., Stern M. The metabolic syndrome: time for a critical appraisal: joint statement from American diabetes association and European association for the study of diabetes. Diabetes Care 2005;28(9):2289-304
5. Kaplan NM. The deadly quartet, upper-body obesity, glucose intolerance, hypertrigliceridemia and hypertension. Archives Internal Medicine 1989;149(7):1514-20
6. DeFronzo RA, Ferrannini E. Insulin resistance: a multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia and atherosclerotic cardiovascular disease. Diabetes Care 1991;14(3):173-94
7. Zimmet P., Magliano D., Matsuzawa Y. The metabolic syndrome: a global public health problem and a new definition. J Atheroscler Thromb 2005;12(6):295-300
8. Eckel RH., Grundy SM., Zimmet P. The metabolic syndrome. Lancet 2005;365(9468):1415-28
9. Shaw DI., Hall WL., Williams CM. Metabolic syndrome: what is it and what are the implications. Proc Nutr Soc. 2005;64(3):349-57
10. Shulman AI., Mangelsdorf D.J. Retinod X receptor heterodimers in the metabolic syndrome. NEngl J Med 2005;353(6):604-15
11. Libby P., Hansson G.K. Biology of disease: involvement of the immune system in human atherosclerosis: current knowledge and unanswered questions. Lab Invest. 1991;64(1):5-15
12. Hamsten A., Bjorkholm M., Norberg R. Antibodies to cardiolipin in young survivors of myocardial infection: an association with recurrent cardiovascular events. Lancet 1986;1(8473):113-116
13. Bergmark C., Wu R., deFaire U. Patients with early-onset peripheral vascular disease has increased levels of autoantibodies against oxidized LDL. Arteriscl. Thromb Vasc Biol. 1995;15(4):441-5
14. Vaarala O., Manttari M., Manninen V. Anti-cardiolipin antibodies and risc of myocardial infarction in a prospective cohort of middle-aged men. Circulation 1995;91(1):23-7
15. Salonen JT., Yia-Herttula S., Yamamoto R. Autoantibody against oxidized LDL and progression of carotid atherosclerosis. Lancet 1992;339(8798):883-7
16. Dupuis J., Tardif J.C., Cemacek P., Theroux P. Cholesterol reduction rapidly improves endothelial function after acute coronary syndromes: the RECIFE trial. Circulation 1999;99(25):3227-33
17. Lacoste L., Lam JYT., Hung J., Letchacovski G., Solymoss CB., Waters D. Hyperlipidemia and coronary disease: correction of the increased thrombogenic potential with cholesterol reduction. Circulation 1995;92(11):3172-7
18. Ridker PM., Rifai N., Pfeffer MA., Sacks F., Braunwald E. Long term effects of pravastatin on plasma concentration of C-reactive protein. The cholesterol and recurrent events (CARE) investigators. Circulation 1999;100(3):230-5
19. Downs JR., Clarfield M., Weis S., Whitney E., Shapiro DR. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels. JAMA 1998;279(20):1615-22

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