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The Effect of Atorvastatin on Serum Inflammatory Factors in Patients with Diabetic Macro-angiopathy

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Abstract: Objective to observe the effect of atorvastatin on serum high-sensitivity-reactive protein (Hs-CRP) and interleukin-8 (IL-8) in patients with diabetic macro-angiopathy .Methods 110 patients with type 2 diabetes incorporated large vascular complications were randomly divided into experimental group and control group. The control group given general treatment, the experimental group on the basis of this combined with atorvastatin 40 mg/d, were observed 12 weeks. All the subjects were determined the serum Hs-CRP, IL-8 and fasting blood glucose and blood lipids before treatment and after it for 4 weeks, 8 weeks and 12 weeks.There was no statistically significant difference in serum Hs-CRP and IL-8 level between the two groups before treatment (P>0.05).There was no statistically significant difference in serum Hs-CRP and IL-8 level between the two groups before treatment (P>0.05). it was significantly reduced with the prolonged treatment time that the levels of plasma Hs-CRP and IL-8 in the treatment group (P<0.05),experimental group was significantly lower than the control group After treatment (P<0.05). It was positively correlated between Plasma Hs-CRP and IL-8 (P<0.01).Inflammatory factors Hs-CRP and IL-8 were involved in the development of diabetic macro-angiopathy complications. It is possible for atorvastatin to suppression that progression of diabetic macro-angiopathy lesion by inhibiting inflammatory response.

Keywords: Diabetes; Atorvastatin; Inflammation; Hs-CRP; IL - 8

1. Introduction

Diabetic macro-angiopathy (DMA) is one of the most common and serious chronic complications of diabetes. Researches in recent years show that inflammatory response is a key factor in the continuous progress of DMA. Atorvastatin is an inhibitor of HMG-CoA reductase, which has effects on cell signal transduction, cell proliferation and inhibition of inflammatory response except for its own liposuction . In this study, the effect of atorvastatin may inhibit inflammation and suppress the progress of diabetic vascular lesions by observing serum Hs-CRP and IL - 8 in patients with DMA After the application of atorvastatin.

1.1. Clinical data

There are 110 cases of DMA patients in the department of endocrinology, neurology, and internal medicine in October of 2009 to December of 2012, men(60)and women (50), Age 40-74(50.3 + 9.8), years of illness (5-25). It was in accordance with WHO diabetes diagnostic standard of 1999 and has one of the following conditions: (1) coronary angiography diagnosis of coronary heart disease;(2)Head CT or MRI diagnosis of cerebral infarction; (3) The color doppler ultrasonography was used to examine the intimate- middle thickness of the neck or bilateral lower extremity;(4)Gangrene. Exclusion criteria: acute and chronic infection within 2 weeks; Trauma, tumor, immune system disease; Acute myocardial infarction; Severe cardiac renal insufficiency. The 110 patients were randomly divided into observation group, males (32) and females(23) and in the control group, males (30)and females(25). There was no statistically significant difference between the two groups in age, gender and fasting blood glucose (P<0.05)

1.2. Methods

Both groups were treated with DMA routinized treatment, and the treatment group was treated with atorvastatin 40mg/d on the basis of routinized treatment for 12 weeks. It were measured that blood glucose, serum Hs-CRP, IL-8 and triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c) and LDL cholesterol (IDL-c) before and after treatment. The serum Hs-CRP was determined by micro-particle enhanced transmission immunoassay, and the determination of blood glucose, blood lipids and Hs-CRP were all performed by the Japanese olympusAU5400 automatic biochemical analyzer. The interleukin-8 kit is provided by Beijing qisong biological co, LTD, strictly according to the instructions.

1.3. Statistical methods

All data using SPSS 13.0 statistical software for processing, measurement data with standard deviation of mean $\overline{X}$ ±s, matching data using T test, more than two sets of data comparison using single factor analysis of variance. The difference is statistically significant of P≤0.05.

2. Results

Table 1. The plasma CRP results were compared in two groups of patients($\overline{X}$ ±s)

Group	Cases	Prior treatment	4 weeks	8 weeks	12 weeks	F	P
Control group	40	6.54±1.44	6.67±0.32	6.43±0.31	6.51±0.33	0.95	>0.05
Treatment group	40	6.52±1.33	5.74±1.24	4.54±1.37	2.54±1.16	74.61	0.01
t		1.31	1.665	2.028	2.843		
p		>0.05	＜0.05	＜0.025	＜0.01		

Table 2. Comparison of plasma IL-8 results in two groups of patients($\overline{X}$ ±s)

Group	Cases	Prior treatment	4 weeks	8 weeks	12 weeks	F	P
Control group	40	84.27	83.15	82.37	81.10	5.68	0.02
Treatment group	40	84.31	79.56	63.76	54.62	7.62	0.01
t		0.043	1.62	1.874	2.46		
p		0.68	0.07	0.035	0.007		

Table 3. The blood glucose and blood lipids of the two groups were compared in 4 weeks（ $\overline{X}$ ±s mmol/L）

Group	n	FPG	TC	TG	HDL	LDL
Control group	40	8.57±1.14	5.32±1.16	2.77±1.25	1.34±0.29	3.31±0.91
Treatment group	40	8.60±1.21	5.29±1.21	2.75±1.26	1.33±0.27	3.33±0.89

3. Discussion

It is arterial atherosclerosis that pathology of diabetic angiopathy. Investigation of prospective diabetes in UK shows, blood sugar control did not significantly reduce the incidence of diabetes vascular lesions, other factors play an important role in addition to the high blood sugar in the occurrence and development of diabetic vascular lesions. It is believed that atherosclerosis is caused by an abnormal arterial wall inflammatory disease in the endothelial system.

Atherosclerosis is a chronic inflammatory disease characterized by progressive lipid deposition of arterial wall, inflammatory cells ,smooth muscle cells infiltration and extra-cellular matrix reconstruction. there are a large number of inflammatory transmitters such as cytokines, growth factors, inflammatory lipids in atherosclerotic plaques.

Hypersensitive c-reactive protein is a very sensitive acute phase protein, which is a highly sensitive indicator of inflammation.The Hs-CRP in the plasma significantly increased when the body had febrile disease, various inflammation and trauma in normal conditions. Many existing studies support atherosclerosis as a chronic inflammatory disease [2]. A large number of literature's reported that Hs-CRP level was directly related to the occurrence, development and prognosis of atherosclerosis. It is significantly higher in diabetic patients due to coronary heart disease, ischemic cerebrovascular disease, renal arteriosclerosis and arteriosclerosis. It needs to be further studied that relationship between Hs-CRP and atherosclerosis.

IL-8 has all the characteristics of neutrophil chemo-tactic agent, which can induce cell morphological change and chemo-taxis, Promote white blood cell adhesion secretion of mac-1 (CDm/CD) expression, activate leukocyte adhesion and which Can cause cytoplasmic free ca concentration and short rise rapidly, degranulation reaction, adhesion protein increases, formation and respiratory burst, bio-active lipid super-oxide release and lysosomal enzyme and promotes the inflammatory response. The experiment confirmed that there were a large number of inflammatory cells in the cap and shoulder of atherosclerotic plaques. Simonini [3] confirmed that the expression of IL-8 mRNA was significantly increased in the direct resection specimen of human coronary atherosclerotic plaque. IL-8 is a form of vascular production factor that's a strong tendency for inflammatory cytokinesis .Various factors can regulate the synthesis and secretion of IL-8, which can induce atherosclerosis.

Statin drugs are reductase inhibitor of hydroxymethylpentacyl-coa (HMG-CoA), which is widely used for regulating lipid in clinical . Studies have found that statins can prevent and treat AS, improve vascular endothelial function, anti-inflammatory and regulation immunity, anti-oxidation, inhibit smooth muscle cell proliferation and migration, inhibit thrombosis, and stabilize AS plaques [4].

In this study, the content of IL-8 in two group was similar, and it was significantly reduced after atorvastatin intervention on the treatment group. It is illustrate that atorvastatin could reduce the inflammatory response to the vascular wall and inhibit the expression of inflammatory mediators, which may be related to the prevent from growth of lymphocytes and other monocyte cells through multiple channels unrelated to lipid metabolism.

In conclusion,it can effectively inhibit the chronic inflammatory response of DMA patients and prevent the formation and development of atherosclerosis with early application of statin drugs on the basis of controlling blood glucose, which is independent of its lipid lowering effect.

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