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Effect of atorvastatin combined with trimetazidine on oxidative stress, hemorheology, and NT−proBNP, hs−CRP in patients with coronary heart disease

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ABSTRACT

Objective: To explore the effect of Atorvastatin Combined with trimetazidine on oxidative stress, hemorheology and NT-proBNP and hs-CRP in patients with coronary heart disease. **Method:** A total of 84 patients with coronary heart disease were admitted in our hospital from February 2015 to February 2017 were randomly divided into the observation group and the control group, each group with 42 cases. The two groups received routine treatment of coronary heart disease, while the control group was treated with atorvastatin and the observation group was treated with Atorvastatin Combined with trimetazidine. Both groups were treated continuously for one month. The levels of oxidative stress indexes (SOD), malondialdehyde, (MDA), blood rheology indexes (ESR, whole blood hyposhear viscosity, whole blood hypershear viscosity, plasma viscosity, Fibrinogen (Fib) and serum N-terminal pro-brain natriuretic peptide (NT-proBNP), hypersensitive C reaction protein (hs-CRP) index in two groups were compared analytically. **Results:** Before treatment, there was no significant difference between the observation group and the control group in terms of oxidative stress, blood rheology and NT-proBNP and hs-CRP index. Compared with before treatment, the level of SOD in observation group and the control group was significantly increased and MDA significantly decreased. While the level of SOD in observation group was significantly higher than the control group, and MDA level was significantly lower than the control group after treatment. Compared with before treatment, the levels of hemorheology indexes included ESR, whole blood viscosity, plasma viscosity and Fib in observation group and control group were significantly decreased. After treatment, the levels of ESR, whole blood viscosity, plasma viscosity and Fib in the observation group were significantly lower than the control group. Compared with before treatment, the levels of NT-proBNP and hs-CRP in the observation group and control group were significantly decreased. After treatment, the levels of NT-proBNP and hs-CRP in the observation group were significantly lower than the control group,there was significantly statistical difference. **Conclusion:** Atorvastatin combined with trimetazidine can significantly reduce oxidative stress, restore normal blood rheology, and improve levels of NT-proBNP and hs-CRP in patients with coronary heart disease. This treatment is worthy of clinical promotion.

1. Introduction

Coronary heart disease was one of common cardiovascular diseases, which was ischemic cardiomyopathy resulted by coronary atherosclerosis, tracheal constriction, insufficient blood supply, prone to the elderly and trend to the young[1]. In the past mainly used vasodilator substance and inhalation, diuretic for treatment, but the efficacy was not good due to lack of pertinence[2]. Related research showed that oxidative stress, hemorheology and inflammation were closely related to genesis and development of coronary heart disease, in clinic reduced the genesis of bad cardiovascular disease through taking medicine for recovering the above change[3−5]. This

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research was aimed to observe effect of Atorvastatin Combined with trimetazidine on oxidative stress, hemorheology and NT-proBNP and hs-CRP in patients with coronary heart disease. Report as the following.

2. Material and method

2.1. General data

Selected 84 patients with coronary heart disease who were admitted in our hospital from February 2015 to February 2017, all of patients were conformed to clinical diagnostic criteria and signed informed consent. Excluded patients with cancer, autoimmune disease, chronic inflammatory disease combined with hepatorenal dysfunction, acute myocardial infarction; patients who took trimetazidine and statin drugs and allergic to these two drugs. Divided them into observation group and control group according to random data table, observation group: 42 cases, male 24 cases and female18 cases; aged from 42 to 74 years old. The control group, 42 cases, male 22 cases and female 20 cases; aged from 51 to 72 years old. The general data of gender, age in this two groups were no statistically significant difference ($P>0.05$).

2.2 Treatment method

This two groups were treated with conventional therapy, vasodilator substance, oxygen inhalation, diuretic and ca-antagonist and with scientific diet and suitable exercise under guidance of nurse. On this base control group was given orally atorvastatin (Henan Tianfang Pharmaceutical Co. Ltd. Approved by H20051984), 10 mg/L time, 1 time/d. In the meanwhile, observation group was given trimetazidine on the above base (Servier (Tianjin) Pharmaceutical Co. Ltd. Approved by H20055465), combined with atorvastatin (dosage was as same the control group) took orally trimetazidine 20 mg/time and 3 times/d, All patients the course of therapy in both groups was 30 d.

2.3 Detection index

The fasting peripheral venous blood was collected before and after treatment in this two groups, for the detection. (1) Oxidative stress indexes: detected MDA and SOD level of both groups by enzyme-linked immunosorbent assay (ELISA) (kits were purchased from Nanjing Jiancheng Technology Co. Ltd). (2) Hemorheology index: ESR, whole blood viscosity, plasma viscosity were detected by full automatic rheometer (adopted LBY-N6B full automatic rheometer, purchased from Beijing Precil instrument Co. Ltd), Fib was detected by full automatic coagulometer (Used BIVII full automatic biochemical analyzer, purchased by German Behring diagnostic product Co. Ltd). (3) NT-proBNP, hs-CRP detection: NT-proBNP was detected by chemiluminscene method (Kits were purchased by Shenzhen new industrial biomedical engineer Co. Ltd), enzyme-linked immunosorbent assay (ELISA) was used to hs-CRP detection (kits were purchased from Shanghai Bohu Biology Co. Ltd). Compared with index change before and after treatment.

2.4 Statistic method

The software SPSS 18.0 was used for all data analysis, measurement data was represented by Mean ± SD, t-test was use to that normal distribution, $P<0.05$ for the difference was statistical significant.

3. Result

3.1. Comparison of oxidative stress level of both groups

There was no difference in oxidative stress index MDA and SOD level in both groups ($P>0.05$). Compared with before treatment, MDA level was decreased obviously and SOD level was increased significantly after treatment in both groups, the difference was significant ($P<0.05$); After treatment, MDA level in observation group (4.65±1.60) μmol/mL was dramatically lower than control group (9.82±2.56) μmol/mL, SOD level in observation group (112.16 ± 24.41) U/mL was dramatically higher than control group (81.61±19.35) U/mL, difference was significant ($P<0.05$). As shown in Table 1.

3.2 Comparison of hemorheology level of both groups

Before treatment, ESR, whole blood viscosity, plasma viscosity and Fib index in both groups were no significant difference ($P>0.05$). Compared with before treatment, ESR, whole blood viscosity, plasma viscosity and Fib index were reduced obviously ($P<0.05$); After treatment, ESR level in observation group (19.02±2.07) mm/h was lower than control group (22.41±2.35) mm/h, whole blood viscosity hypershear level in observation group (3.71±0.79) mPa·s was obviously lower than control group (4.81±0.75) mPa·s, whole blood viscosity hyposhear level in observation group (12.68±2.15) mPa·s was obviously lower than control group (1.91±0.32 mPa s), Fib level in observation group (2.41±0.72) g/L was obviously lower than control group (3.54±0.84) g/L, difference was significant ($P<0.05$). As shown in Table 2.

3.3. Comparison of NT-proBNP, hs-CRP level of both groups

There was no difference in NT-proBNP, hs-CRP level in both groups ($P>0.05$). Compared with before treatment, NT-proBNP, hs-CRP level in both groups after treatment was decreased obviously, the difference was significant ($P<0.05$); after treatment, NT-proBNP

Table 1.
Comparison of oxidative stress level of both groups before and after treatment (n=42).

Group	Time	MDA (μmol/mL)	SOD (U/mL)
Control group	Before treatment	12.14±3.64	60.13±16.05
	After treatment	9.82±2.56*	81.61±19.35*
Observation group	Before treatment	12.38±4.72	61.21±12.63
	After treatment	4.65±1.60*#	112.16±24.41*#

Note: Compared with before treatment, *$P<0.05$; compared with after treatment control group, *#$P<0.05$.

Table 2.
Comparison of hemorheology level of both groups before and after treatment (n=42).

Group	Time	ESR (mm/h)	Whole blood viscosity (mPa·s) hypershear	Whole blood viscosity (mPa·s) hyposhear	Plasma viscosity (mPa·s)	Fib (g/L)
Control group	Before treatment	26.88±2.72	5.68±1.37	15.74±1.87	2.31±0.38	4.67±1.05
	After treatment	22.41±2.35*	4.81±0.75*	14.37±2.36*	1.91±0.32*	3.54±0.84*
Observation group	Before treatment	26.94±2.41	5.72±0.41	15.65±1.84	2.28±0.62	4.73±0.92
	After treatment	19.02±2.07*#	3.71±0.79*#	12.68±2.15*#	1.45±0.37*#	2.41±0.72*#

Note: Compared with before treatment, *P<0.05; compared with after treatment control group, *#P<0.05.

Table 3.
Comparison of NT-proBNP, hs-CRP level of both groups before and after treatment (n=42).

Group	Time	NT-proBNP (pg/mL)	hs-CRP (mg/L)
Control group	Before treatment	3 824.57±341.23	57.43±6.15
	After treatment	3 352.02±311.58*	20.02±2.10*
Observation group	Before treatment	3 865.93±357.23	56.82±6.74
	After treatment	1 902.04±189.67*#	8.34±1.37*#

Note: Compared with before treatment, *P<0.05; compared with after treatment control group, *#P<0.05.

level in observation group (1 902.04±189.67) pg/mL was obviously lower than control group (3 352.02±311.58) pg/mL, hs-CRP level in observation group was lower than control group (20.02±2.10) mg/L, the difference was significant difference (P<0.05). As shown in Table 3.

4. Discussion

Coronary heart disease was one of common cardiovascular disease, its pathogenesis was tracheal constriction caused myocardial ischemia and formed coronary atherosclerosis[6]. Atherosis could cause blood viscosity increase, accelerate microcirculation vascular endothelial injury, thereby aggravate tissue cell ischemia and anoxia which resulted in red blood cell collected abnormally, blood viscosity increased and formed thrombosis[3]. In clinic, usually given conventional drug therapy such as vasiodilator substance, diuretic, on the base of changing life style and dietary structure of patients with coronary heart disease[2]. Clinical drug for patients with coronary heart disease was atorvastatin belonged to statin, which was able to regulate blood lipid level through inhibiting low density protein cholesterol synthesis, reducing fibrinogen content in plasma, with decreasing lipid level and anti-inflammation effect, protecting blood vessel through inhibiting atherosclerotic plaque, preventing atherosclerosis[7]. Trimetazidine was piperazine drug that prevented free fatty acid metabolism and free radical formation, improved coronary blood circulation and promoted myocardial metabolism through reducing blood viscosity and inhibiting platelet aggregation; in the meanwhile, trimetazidine also could promote glucose oxidase and enhance high-energy phosphate bond and contribute to recover myocardial oxygen supply balance[8]. This research was aimed to explore effect of combined therapy on oxidative stress, hemorheology and NT-proBNP, hs-CRP in patients with coronary heart disease.

Researched showed that lipid peroxidation reaction caused by oxidative stress was closely related to genesis and development process of coronary heart disease[9]. SOD was antioxidase, its activity reflected anti-oxygen free radical and eliminated oxygen free radical, evaluated lipid peroxidation reaction degree, therefore detected SOD level of patients could indirectly reflect injury condition of free radical to body; myocardial tissue SOD activity decreased after massive oxygen free radical produced by myocardial ischemia combined with side chain of unsaturated fatty acid on membrane, thereby caused myocardial cell membrane structure change and resulted in myocardial injury of patients with coronary heart disease[10]. MDA was one of important lipid peroxidative metabolism which reflected indirectly lipid peroxidative rate and lipid peroxidative injury degree, indicated cellular oxygen free radical level; MDA level was higher when tissue injury was more serious[11]. This research showed that compared with before treatment, MDA level decreased and SOD level increased in both groups after treatment, the difference was significant (P<0.05); After treatment, MDA level in observation group was dramatically lower than control group, SOD level in observation group was obviously higher than control group difference was significant (P<0.05). This result indicated that both therapies could improve oxidative stress level of patient effectively and the efficacy of observation group was better than control group. The reason might be therapy enhance anti-oxidation ability and could prevent chain reaction of lipid peroxidation, promote myocardial cell maintain oxidative and anti-oxidative balance, thereby increased SOD level and reduced MDA level obviously. Combination of trimetazidine and atorvastatin could more effectively improve oxidative stress level than singly used atorvastatin, might play jointly anti-oxidative effect which enhanced therapeutic effect.

Many researches demonstrated that[12-14] abnormal hemorheology level was closely related to genesis and development process of coronary heart disease, hemorheology played important role in many factors that caused coronary heart disease such as diabetes, hypertension, hyperhomocysteinemia and injury mechanism at molecular level. Research showed that[15] pathogenesis of coronary heart disease was related to blood viscosity increased and myocardial ischemia severe degree. Plasma viscosity, fibrinogen and red blood cell aggregation increased could cause blood viscosity excessively high, which extremely resulted in myocrdial ischemia thereby affected coronary blood supply level. In this research, compared with before treatment, ESR, whole blood viscosity hypershear level, whole blood viscosity hyposhear level, plasma viscosity and Fib index were reduced obviously (P<0.05); After treatment, ESR, whole blood viscosity hypershear level, whole blood viscosity hyposhear level, plasma viscosity and Fib index in observation group were obviously lower than control group (P<0.05). These indexes decreased obviously after treatment was were due to atorvastatin effectively inhibit total cholesterol synthesis, thereby

promoted myocardial energy produce and myocardial metabolism, further improved hemorheologic level and reduced blood viscosity of patients, eventually improved ESR, whole blood viscosity hypershear level, whole blood viscosity hyposhear level, plasma viscosity and Fib index level. The efficacy of observation group was obviously better than control group, this indicated that combination of both drugs contributed to decrease heart failure degree and reduce artery thrombosis occurrence rate, thereby improved heart function.

Brain natriuretic peptide mainly secreted by ventricular cell that reflected cardiac function damage level, massively synthesis and release resulted in its level enhanced when myocardial was ischemia and anoxia, ventricular capacity pressure was changed[16]. NT-proBNP was inactive terminal of BNP fission, reflected heart failure condition of patients and also used as index evaluated cardiac function damage degree in clinic[17]. Inflammatory factor hs-CRP was critical factor that affected genesis and development of coronary heart disease, played role in local inflammation, and process of atherosclerotic plaque formation which activated complement of inner membrane of atherosclerotic plaque, released lipid formed plaque, promoted plaque formation and destroyed endothelial function; it was an important index of nonspecific inflammatory reaction and reflected cardiovascular disease severe degree at some extent[18-20]. This research result indicated that compared with before treatment, NT-proBNP, hs-CRP level in both groups after treatment was decreased obviously (P<0.05); after treatment, NT-proBNP and hs-CRP level in observation group was obviously lower than control group, the difference was significant difference (P<0.05). Both therapies significantly decreased NT-proBNP, hs-CRP level, which was due to the reduce lipid and anti-inflammation effect of atorvastatin that inhibited atherosclerotic plaque formation, moreover trimetazidine enhanced glucose metabolism, promoted myocardial metabolism, thereby improved NT-proBNP, hs-CRP level of patients.

In conclusion, Atorvastatin combined with trimetazidine can significantly reduce oxidative stress, decrease blood rheology indexes, reduced blood viscosity and improve cardiac function damage degree and inflammatory reaction in patients with coronary heart disease. Moreover compared with singly used atorvastatin for treatment, its efficacy was better. It is worthy for clinical application.

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