Research Paper

Effect of Ticagrelor Combined with Acupuncture on Myocardial Infarction and its Effect on Levels of Serum Myocardial Enzymes, Cytokines and T Lymphocytes

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To investigate the effect of ticagrelor combined with acupuncture on myocardial infarction and its effect on levels of serum myocardial enzymes, cytokines and T lymphocytes. 90 patients with myocardial infarction were equally divided into observation and control groups. The observation group was treated with ticagrelor combined with acupuncture, while the control group was treated with ticagrelor only. Hemodynamic indexes, left ventricular parameters, serum myocardial enzyme levels, cytokine levels and T lymphocyte levels were analyzed. The incidence of cardiovascular events 1 mo and 3 mo after treatment was investigated. There were no significant differences in heart rate, left ventricular end systolic diameter, left ventricular end diastolic diameter, intermittent septum thickness and posterior wall of left ventricle between two groups (p>0.05), while systolic blood pressure, diastolic blood pressure, mean arterial pressure and left ventricular systolic pressure in the observation group decreased and left ventricular end-diastolic pressure increased (p<0.05). After treatment, the levels of serum myocardial enzymes, tumor necrosis factor alpha, interferon gamma, interleukin-6, interleukin-17, interleukin-21 and interleukin-23 of observation group were significantly lower than control group, while transforming growth factor beta and T lymphocyte levels were significantly higher (p<0.05). The incidences of cardiovascular events in observation group were 2.22 % and 4.44 %, 1 mo and 3 mo after treatment, while it was 4.44 % and 8.89 %, respectively, in control group (p<0.05).

Key words: Ticagrelor combined with acupuncture, myocardial infarction, serum myocardial enzymes, cytokines, T lymphocyte

In recent years, clinical statistics show that the majority of patients with myocardial infarction are the middle-aged and the elderly. The disease occurs rapidly and poses a serious threat to health and the prognosis of patients after treatment is relatively poor[1]. At present, Percutaneous Coronary Intervention (PCI) is one of the commonly used methods to treat patients with myocardial infarction. Although the clinical effect is ideal, patients need to take medicine for life after treatment and there may be occlusion again. According to traditional medicine, myocardial infarction belongs to the category of "chest stuffiness and heartache" and patients mainly show chest tightness and pain, even back pain, shortness of breath and insomnia, etc. In the clinical treatment process, acupuncture therapy has its unique advantages and characteristics in the treatment of myocardial infarction[2]. In addition, clopidogrel is often used to treat patients with myocardial infarction in clinic, but there are relatively few reports on ticagrelor treatment[3]. In this study, 90 patients with myocardial infarction were selected to explore the therapeutic effect of ticagrelor combined with acupuncture on myocardial infarction and its effects on levels of serum myocardial enzymes, cytokines and T lymphocytes.

MATERIALS AND METHODS

General data:

From April 2018 to October 2020, 90 patients with myocardial infarction in our hospital were selected as research objects, including 58 male patients and 32 female patients, with an average age of 60.43±5.56.

Inclusion criteria: Meeting the diagnostic criteria of myocardial infarction and the first incidence of myocardial infarction; cardiac Magnetic Resonance Imaging (MRI) indicating acute/subacute stage of myocardial infarction with obvious evidence of vascular stenosis and infarction. The clinical data of

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patients are complete and accurate, and there are no contraindications of chemotherapy and other physical diseases; all subjects have signed the informed consent form.

Exclusion criteria: Myocardial infarction patients are not diagnosed by pathological biopsy and cytological diagnosis; patients who have received chemotherapy; patients with severe organ failure such as heart, liver and kidney; patients who cannot cooperate to complete this experiment. There was no significant difference in general clinical data of all patients, such as age, weight and other diseases ($p>0.05$). The follow-up experiment could be carried out.

Methods:

90 patients with myocardial infarction were equally divided into observation group and control group, in which observation group was treated with ticagrelor combined with acupuncture, while control group was treated with ticagrelor only.

Ticagrelor treatment: Ticagrelor (AstraZeneca Pharmaceutical Co., Ltd., National Medicine Permission Number J20130020), oral dose of 180 mg, twice a day, medication time of 3 mo[4].

Ticagrelor combined with acupuncture treatment: On the basis of taking ticagrelor, acupuncture points were selected, including Baihui, Neiguan (bilateral), Zusanli (bilateral) and Sanyinjiao (bilateral). The acupuncture retention time was 20 min and the hand-manipulating of needle was performed once during the period. The acupuncture was performed once a day and 6 d a course, with 1 d between every 2 courses and a total of 4 courses[5].

Observation indicators and methods:

Comparative analysis of hemodynamic indexes in two groups: After treatment, 24 h dynamic electrocardiogram was performed in both groups[6] and Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), Left Ventricular Systolic Pressure (LVSP), Left Ventricular End-Diastolic Pressure (LVEDP), and Heart Rate (HR) were recorded simultaneously.

Comparative analysis of left ventricular parameters in two groups: After treatment, the patients in both groups were examined by color Doppler echocardiography[7] and the patients kept quiet and rested for 5 min between two examinations to maintain calm. The patient took the left lateral position. Left Ventricular End Systolic Diameter (LVESD), Left Ventricular End Diastolic Diameter (LVEDD), Intermittent Septum Thickness (IVS) and Posterior Wall of Left Ventricle (PWLV) were measured at the level of mitral chordae in the long axis section of parasternal left ventricle.

Comparative analysis of serum myocardial enzymes level in two groups: Before and after treatment, the elbow venous blood of patents of two groups was taken at 7:00 in the morning after overnight fasting. After centrifugation at 3500 r/min for 20 min, the supernatant was collected and stored in a refrigerator at -20° for later use. The levels of myocardial enzymes, including Aspartate Aminotransferase (AST), Lactate Dehydrogenase (LDH), Creatine Kinase (CK) and Creatine Kinase Myocardial Band (CKMB) were measured by automatic biochemical analyzer.

Comparative analysis of cytokines level in two groups: According to the method as shown in comparative analysis of serum myocardial enzymes level in two groups, the venous blood was centrifuged to collect serum and then the Tumor Necrosis Factor alpha (TNF-α), Interferon gamma (IFN-γ) and Transforming Growth Factor beta (TGF-β), Interleukin (IL)-6 (IL-6), IL-17, IL-21 and IL-23 were detected by enzyme-linked immunosorbent assay and were compared for analysis.

Comparative analysis of T lymphocytes level in two groups: According to the venous blood obtained by the method as shown in comparative analysis of serum myocardial enzymes level in two groups, the blood serum was collected by centrifugation. Then the values of Cluster of Differentiation (CD) 3 ($CD3^+$), $CD4^+$ and $CD8^+$ in the blood samples of the two groups were measured by flow cytometry and the ratio of $CD4^+/CD8^+$ was calculated.

Comparative analysis of cardiovascular events in two groups: Cardiovascular events include major cardiovascular events and minor cardiovascular events. The main cardiovascular events are cardiovascular-related deaths, non-fatal myocardial infarction and non-fatal stroke; minor cardiovascular events refer to recurrent angina pectoris and heart failure. Patients were followed up for 1 mo and 3 mo after treatment, and the incidence of cardiovascular events was statistically analyzed.

Statistical methods:

All the data in this study were processed by Statistical Package for the Social Sciences (SPSS) 20.0 statistical analysis software (IBM Company, USA). The measurement data was expressed by mean±standard deviation ($\bar{x}\pm s$). The comparison between groups was

made by one-way analysis of variance or repeated measurement variance analysis and the pairwise comparison between groups was made by Least Significant Difference (LSD) t test; the counting data was expressed by percentage (%) and the comparison between groups was analyzed by χ^2; $p<0.05$ indicated statistically significant difference.

RESULTS AND DISCUSSION

Hemodynamic indexes in the two groups were compared. There was no significant difference in HR between the two groups ($p>0.05$). Compared with control group, SBP, DBP, MAP and LVSP in observation group decreased, while LVEDP increased significantly, with statistical significance ($p<0.05$) (Table 1).

Left ventricular parameters in the two groups were compared. There was no significant difference in LVESD, LVEDD, IVS and PWLV between the two groups ($p>0.05$) (Table 2, fig. 1 and fig. 2).

Serum myocardial enzymes level in two groups was compared. There was no significant difference in serum myocardial enzymes level between the two groups before treatment ($p>0.05$).

After treatment, serum myocardial enzymes level of patients in both groups decreased. Compared with patients in control group, serum myocardial enzymes levels (AST, LDH, CK and CKMB) of patients in observation group decreased significantly ($p<0.05$), with statistically significant difference (Table 3).

Comparative analysis of cytokines level in two groups of patients was shown here. Before treatment, there was no significant difference between the two groups ($p>0.05$). After treatment, the levels of cytokines in both groups showed significant changes. Compared with control group, the levels of cytokines (TNF-α, IFN-γ, IL-6, IL-17, IL-21 and IL-23) in observation group decreased, while the level of TGF-β increased significantly, with statistically significant difference ($p<0.05$) (Table 4).

TABLE 1: COMPARATIVE ANALYSIS OF HEMODYNAMIC INDEXES IN TWO GROUPS ($\bar{x}\pm s$)

Group	SBP (mm Hg)	DBP (mm Hg)	MAP (mm Hg)	LVSP (mm Hg)	LVEDP (mm Hg)	HR (beats/min)
Control group	110.54±7.98	93.24±5.76	99.98±6.67	111.88±8.57	10.56±2.21	367±28
Observation group	94.45±6.80	80.09±5.64	86.65±7.65	96.45±4.54	9.11±1.98	356±21
t value	10.323	9.405	10.231	12.564	10.003	0.326
p value	0.002	0.001	0.001	0.001	0.001	0.543

TABLE 2: COMPARATIVE ANALYSIS OF LEFT VENTRICULAR PARAMETERS IN TWO GROUPS ($\bar{x}\pm s$, mm)

Group	LVESD	LVEDD	IVS	PWLV
Observation group	30.88±4.68	43.98±5.66	10.75±2.10	9.52±1.26
Control group	29.69±3.39	43.54±3.15	10.63±1.12	9.37±2.38
t value	0.447	0.315	0.324	0.312
p value	0.372	0.791	0.477	0.870

Fig. 1: Electrocardiogram of patients in observation group

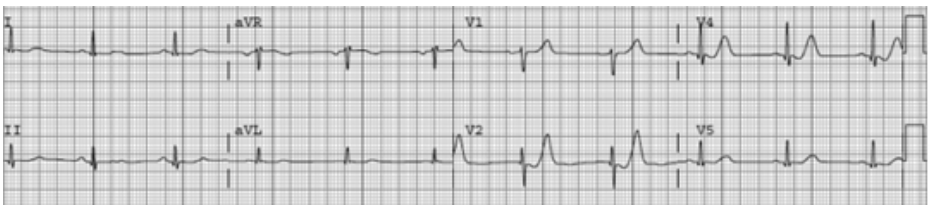

Fig. 2: Electrocardiogram of patients in control group

TABLE 3: COMPARATIVE ANALYSIS OF SERUM MYOCARDIAL ENZYMES LEVEL IN TWO GROUPS ($\bar{x}$±s, U/l)

Group	Index	Observation group	Control group	t value	p value
Before treatment	AST	135.43±43.32	137.83±36.75	0.831	0.554
	LDH	1023.43±109.21	1034.51±98.76	0.572	0.342
	CK	998.73±114.32	976.87±123.08	0.768	0.361
	CKMB	903.42±153.42	912.63±136.98	0.882	0.437
After treatment	AST	112.16±11.31	127.45±8.76	9.023	0.002
	LDH	812.07±61.15	974.23±48.46	8.651	0.001
	CK	704.06±30.55	820.49±34.43	9.992	0.001
	CKMB	754.43±35.89	822.12±76.54	6.547	0.002

TABLE 4: COMPARATIVE ANALYSIS OF CYTOKINES LEVEL IN TWO GROUPS ($\bar{x}$±s, ng/ml)

Group	Index	Observation group	Control group	t value	p value
Before treatment	TNF-α	85.43±5.43	86.79±3.12	0.534	0.550
	IFN-γ	93.21±4.44	94.45±5.09	0.672	0.439
	TGF-β	276.87±34.29	289.09±42.12	0.983	0.567
	IL-6	156.32±27.86	162.31±33.41	0.447	0.531
	IL-17	80.31±9.83	82.23±7.06	0.546	0.365
	IL-21	178.93±54.42	181.34±48.98	0.482	0.672
	IL-23	124.54±38.97	137.76±45.02	0.558	0.347
After treatment	TNF-α	33.35±3.12	66.32±5.90	6.564	0.002
	IFN-γ	32.84±6.22	78.23±8.01	16.112	0.001
	TGF-β	650.32±67.03	476.52±34.42	14.820	0.001
	IL-6	77.45±6.12	103.44±12.54	17.217	0.001
	IL-17	19.34±5.65	40.33±15.32	12.264	0.002
	IL-21	81.88±5.32	120.34±16.53	9.632	0.001
	IL-23	63.76±4.44	96.77±28.23	10.539	0.001

T lymphocytes level in two groups was compared. Before treatment, there was no significant difference in T lymphocytes level between the two groups ($p>0.05$). After treatment, the level of T lymphocytes in both groups increased. Compared with control group, the levels of $CD3^+$, $CD4^+$, $CD8^+$ and $CD4^+/CD8^+$ in observation group significantly increased, with statistically significant difference ($p<0.05$) (Table 5).

Cardiovascular events in two groups were compared. The incidences of cardiovascular events in observation group were 2.22 % and 4.44 % 1 mo and 3 mo after treatment, while those in control group patients were 4.44 % and 8.89 %. Comparing the incidence of cardiovascular events between the two groups, the incidence of observation group was significantly less than that of control group, with statistically significant difference ($p<0.05$) (Table 6).

TABLE 5: COMPARATIVE ANALYSIS OF T LYMPHOCYTES LEVEL IN TWO GROUPS ($\bar{x}$±s, %)

Group	Index	Observation group	Control group	t value	p value
Before treatment	$CD3^+$	39.23±7.02	38.02±8.33	0.532	0.912
	$CD4^+$	13.21±4.39	12.29±3.41	0.447	0.374
	$CD8^+$	14.21±3.92	13.88±2.56	0.512	0.463
	$CD4^+/CD8^+$	0.48±0.14	0.46±0.29	0.983	0.527
After treatment	$CD3^+$	72.34±3.45	56.65±1.87	7.442	0.002
	$CD4^+$	42.35±4.12	26.12±3.65	7.512	0.001
	$CD8^+$	26.22±3.15	20.42±2.88	6.421	0.004
	$CD4^+/CD8^+$	2.13±0.14	1.49±0.53	6.976	0.005

TABLE 6: COMPARATIVE ANALYSIS OF CARDIOVASCULAR EVENTS IN TWO GROUPS

Group	1 mo after treatment		3 mo after treatment	
	Number of cases	Incidence (%)	Number of cases	Incidence (%)
Observation group (n=45)	1	2.22	2	4.44
Control group (n=45)	2	4.44	4	8.89
χ^2		8.932		12.293
p value		0.004		0.001

Myocardial infarction is a critical disease in cardiology and misdiagnosis often occurs due to the high risk of this disease. In addition, it also causes a series of complications, especially arrhythmia or heart failure[8]. Generally, coronary intervention is commonly used 6 h after the attack, so that ischemic myocardium can be reconstructed and dying myocardial cells can be saved to avoid further increasing the area of myocardial infarction[9]. Before coronary intervention, patients receive antiplatelet therapy to relieve blood viscosity and inhibit thrombosis. As an antithrombotic drug, ticagrelor has a remarkable antiplatelet effect. The clinical mechanism of this drug is similar to clopidogrel, but the difference is that there is an interaction effect between ticagrelor and platelet Purinergic Receptor ($P2Y_{12}$) adenosine diphosphate receptor. In addition, it has certain reversibility and there is no conformation, and the signal transmission path has not changed. When the drug is stopped, the platelet function in the blood is obviously restored and the therapeutic effect is stable[10,11]. Acupuncture based on syndrome differentiation can warm yang, dispel cold, promote qi and remove blood stasis, and acupoints massaging can regulate the functions of yin and yang and viscera, so as to stimulate the heart-yang, regulate qi and relieve pain[12]. Clinical studies have found that massage at points such as Zusanli, Shenmen and Gongsun can relax vascular smooth muscle and relieve coronary spasm, thus improving the myocardial ischemia and hypoxia of patients[13].

The results of this study showed that SBP, DBP, MAP and LVSP of observation group patients decreased after treatment, while LVEDP increased significantly ($p<0.05$). In addition, levels of serum myogenic enzymes (TNF-α, IFN-γ, IL-6, IL-17, IL-21 and IL-23) were significantly lower than those in control group, while TGF-β and T lymphocytes levels were significantly higher than those in control group ($p<0.05$). Clinical detection of serum myocardial enzymes is mainly used to judge whether patients have myocardial ischemia symptoms, including AST, LDH, CK and CKMB[14]. Among them, CK is the most important energy regulating enzyme in myocardium and CKMB is the isoenzyme of CK. At the same time, detection of the levels of CK and CKMB is helpful to accurately diagnose myocardial ischemia. Some scholars treated rats with electroacupuncture at Neiguan and Hegu points for 20 min, then stopped for 40 min and then resumed reperfusion after acupuncture at the same point for 20 min. Venous blood was collected and separated to obtain serum. It was found that the myocardial enzyme activity of rats in acupuncture treatment group decreased significantly, indicating that acupuncture at Neiguan and Hegu points could significantly inhibit myocardial enzyme activity[15]. Similarly, acupuncture was done at Neiguan and Shanzhong points of rats and the content of CK in rat serum was detected after eyeball blood collection. The results showed that acupuncture at Neiguan and Shanzhong points could obviously reduce the content of CK in rat blood[16]. New Zealand white rabbits were used for myocardial infarction modeling. Before the model was made, electroacupuncture or moxibustion at Neiguan point was adopted and then serum CK content was detected by enzyme-linked immunosorbent assay. The results showed that electroacupuncture and moxibustion pretreatment had preventive and protective effects on myocardial cells. They reduced serum CK content and both had delayed protective effects[17].

In addition, clinically, the changes of T lymphocytes level are generally reflected by detecting the changes of $CD3^+$, $CD4^+$, $CD8^+$ and $CD4^+/CD8^+$ ratio, so as to judge the abnormal immune characteristics of myocardial infarction. T lymphocytes subsets mainly play an immunomodulatory role in $CD4^+$ cells and $CD8^+$ cells[18]. Usually, $CD4^+$ and $CD8^+$ interact to restrict and promote the immune function of the body in a balanced state. If the number and function of a certain T lymphocytes subgroup are abnormal, the body will suffer the disorder of immune system, which will lead to a series of pathological changes. Therefore, the change of $CD4^+/CD8^+$ ratio is particularly important for clinical diagnosis of pathological infection[19,20]. The results of this study also showed that the incidences of cardiovascular events 1 mo and 3 mo after treatment were 2.22 % and 4.44 % in observation group and

were 4.44 % and 8.89 % in control group ($p<0.05$). Therefore, the clinical safety of ticagrelor combined with acupuncture was better than that of ticagrelor alone.

To sum up, ticagrelor combined with acupuncture was effective and safe in treating myocardial infarction, which may be related to reducing serum myocardial enzymes level, inhibiting inflammatory cytokines expression and increasing T lymphocytes level. The combination of the two methods could improve patient's myocardial infarction and promote the recovery of cardiac function. It is worthy of clinical application.

Conflict of interests:

The authors declared no conflict of interest.

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