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Original Article

Effects of aspirin and clopidogrel on the clinical efficacy, adverse reactions and prognosis for elderly patients with acute coronary syndrome

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Abstract: Objective: To evaluate the effect of combinatorial aspirin and clopidogrel treatments on elderly patients with acute coronary syndrome (ACS). Methods: 178 ACS patients in our hospital were randomized into control and experimental groups (n = 89 for each). The control group was given aspirin on the basis of routine treatment, while the experimental group was given aspirin and clopidogrel on the basis of routine treatment. The levels of blood pressure, low density lipoprotein (LDL-C), high density lipoprotein (HDL-C), triglyceride (TG), and hypersensitive C reactive protein (hs-CRP) were compared before and after combinatorial treatments. Results: The systolic pressure (SBP) and diastolic pressure (DBP) after treatment in both groups were significantly lower than those before treatment ($P<0.05$). Meanwhile, the levels of SBP and DBP in the experimental group decreased more obviously than those of the control group ($P<0.05$). Compared with those before treatment, the levels of serum TG and LDL-C were decreased, while HDL-C was increased in both groups. The level of serum hs-CRP in the experimental group was significantly lower than that in the control group 0.5~7 days after admission ($P<0.05$). The treatment effect in the experimental group was obviously better than that in the control group ($P<0.05$). No significant difference was detected in the incidence of Major Adverse Cardiovascular Events (MACE) and bleeding between the two groups ($P>0.05$). Conclusion: The combined use of aspirin and clopidogrel has been proved to be safe and has significant clinical efficacy and expected clinical application value in elderly ACS patients.

Keywords: Acute coronary syndrome, aspirin, clopidogrel, clinical effect in elderly patients

Introduction

Acute coronary syndrome (ACS) is one of the most critical diseases in the emergency department. It is due to the instability or rupture of plaque in coronary atherosclerosis, which induces platelet aggregation and adhesion, and further leads to the formation of coronary artery embolism. The acute, subacute myocardial ischemia and necrosis of the myocardium caused by embolism result in the clinical syndromes [1]. In recent years, the incidence rate and mortality rate of ACS in the elderly persons over 70 are increasing rapidly. ACS sets urgently and changes quickly with high mortality rate and serious complications, which seriously threatens the safety and life quality of the patients, and brings a strong burden to both the family and society [2-5]. Percutaneous coronary intervention (PCI) has been regarded as one of the major treatments for ACS in recent years, but antiplatelet aggregation is still a timely and effective treatment for patients that are difficult to bear the risk of surgery or do not accept intervention due to financial pressure [6, 7]. Several studies have confirmed that eliminating platelet aggregation is the key for clinical ACS treatment. Timely and effective antiplatelet therapy can reduce the incidence of thrombotic events and improve the prognosis [8, 9]. Aspirin and clopidogrel are two commonly used antiplatelet drugs in clinic. They have some advantages including quick onset, safety and effectiveness. They are also the standard drugs recommended by authoritative guidelines worldwide [10, 11]. However, due to the age factor, there are usually many complications in elderly patients, such as diabetes, ch-

ronic renal insufficiency, and pulmonary diseases, which induce the significantly increased chance of bleeding. Therefore, there is no definite antiplatelet therapy for elderly patients with ACS [12, 13]. At present, aspirin or clopidogrel alone is mainly used as a clinical treatment plan, but for the combined use of aspirin and clopidogrel on the efficacy and prognosis of patients, the research report is relatively rare. In this study, the therapeutic effects and adverse reactions of aspirin combined with clopidogrel were discussed.

Materials and methods

General data

178 patients with ACS were collected between January 2017 and February 2018 in our hospital, including 74 cases with ST-segment elevation myocardial infarction (STEMI), 56 patients with non-ST-segment elevation myocardial infarction and 48 patients with unstable angina. All patients were over 70 years old (76.58± 3.62), including 103 males and 75 females. According to the number table method, patients were randomized into the control and experimental group. In the control group, the average age was 77.03±3.84 yrs, including 51 males and 38 females; in the experimental group, the average age was 76.35±3.68 yrs, including 52 males and 37 females. The study was approved by the hospital ethics committee.

Inclusion and exclusion criteria

Inclusion criteria: Compliance with the 2012 American Heart Association (ACC)/American Heart Association (AHA) Guidelines for the diagnosis and treatment of Acute Coronary Syndrome [14]; Age: more than 70 years.

Exclusion criteria: Patients with bleeding tendency or history of bleeding; patients who had taken aspirin and other antiplatelet aggregation drugs within one week before admission; patients who were allergic to test drugs; patients complicated with severe liver dysfunction, recent gastrointestinal bleeding, congestive heart failure and malignant tumors.

Therapeutic methods

Patients in both groups received the same routine treatment, using angiotensin-converting enzyme (ACEI) inhibitors, nitrates, calcium antagonists, beta-blockers, statins and 5000 U low molecular weight heparin sodium subcutaneously (twice a day for 7 days). The control group received aspirin on the basis of the above conventional treatment (Production enterprises: JIU Ming Pharmaceutical Co., Ltd., Guangdong Province. Chinese medicine quasi character: H44021139. Specifications: 100 mg × 30). The first dose was 300 mg/d, then reduced to 150 mg/d, and the administration lasted for 30 days. Patients in the experimental group were administrated with clopidogrel based on the treatment of the control group (Manufacturing enterprise: Sanofi Winthrop Industrie. Chinese medicine quasi character: 3200J8310. Specifications: 75 mg × 7 tablets/box). The first dose was 150 mg/d, then changed to 75 mg/d, and was continued for 30 days.

Observation indexes

The height, weight, blood pressure and blood sugar were faithfully recorded. The fasting venous blood was collected, and the serum was separated after centrifugation. The levels of TG, HDL-C and LDL-C were all measured using Hitachi 7060 automatic biochemical analyzer. Serum levels of high-sensitivity C-reactive protein (hs-CRP) were monitored before admission and 12 h, 1 d, 2 d and 7 d after admission. ELISA was used for detection, and the protocol was in accordance with the instructions of the kit.

Effect evaluation

The evaluation was referred to the criteria of curative effect in NSTE-ACS guidelines for diagnosis and treatment. Markedly effective: the signs of patient's clinical symptoms disappeared, while the electrocardiogram (ECG) recovered or basically returned to normal. Effective: the clinical symptoms and signs improved, the degree of angina lessened, the times of attacks reduced, ST-segment in ECG increased more than 1 mm. Ineffectiveness: The symptoms and signs of the patients did not improve or became even worse, ECG abnormalities did not improve or was aggravated. Total effective rate = (effective + effective) number/total number × 100%.

Adverse reactions

Major adverse cardiac events contain cardiac death and new onset myocardial infarction dur-

Table 1. Comparison of general information between the two groups of patients

	Control group (n = 89)	Experimental group (n = 89)	t/χ^2	*P*
Age	77.03±3.84	76.35±3.68	1.206	0.115
Gender (male/female)	51/38	52/37	0.023	0.879
BMI (Kg/m^2)	23.82±4.93	24.07±5.41	0.322	0.374
Hypertension (n, %)	46	44	0.090	0.764
Diabetes (n, %)	21	24	0.268	0.605
Hyperlipidemia (n, %)	43	40	0.203	0.652
Smoking history (n, %)	37	40	0.206	0.650
platelet count ($\times 10^9$)	180.52±40.16	178.35±38.92	0.366	0.357
APTT	30.57±5.75	31.84±5.86	1.459	0.073

ing treatment. The occurrence of Major Adverse Cardiovascular Events (MACE) was compared between the two groups, and the hemorrhages such as massive hemorrhage and mild hemorrhage were evaluated according to Thrombolysis in Myocardial Infarction (TIMI) definition criteria.

Statistical analysis

SPSS 17 statistical software was used for data analysis and statistical comparison. Measurement data were presented as mean ± standard deviation, and the two independent samples *T* test was used for statistical analysis. Enumeration data were expressed by cases or percentages. The comparison of the rates was performed by the d^2 test. *P*<0.05 was considered as statistically significant.

Results

Comparison of general information between the two groups of patients

There was no significant difference in general information between the two groups, including age, sex, BMI, platelet count, APTT, hypertension, diabetes mellitus, hyperlipidemia and smoking history (*P*>0.05) (**Table 1**).

Blood pressure changes in patients before and after treatment in both groups

The levels of SBP and DBP in the two groups were significantly lower than those before treatment (*P<0.05*). There was no significant difference in SBP and DBP between the two groups before treatment (*P>0.05*), however, the levels SBP and DBP in the observation group were significantly lower than those in the control group after treatment (*P<0.05*) (**Table 2**).

Comparison of blood lipid indexes between the two groups before and after treatment

Before treatment, no significant difference could be detected in the levels of serum TG, HDL-C and LDL-C between control and experimental groups (*P*>0.05). After treatment, the level of serum LDL-C in the experimental group was lower than that in the control group (*P*<0.05). There was no difference in other indexes. Compared with those before treatment, the levels of serum TG and LDL-C were lower after treatment in the two groups, while the levels of HDL-C were higher (**Table 3**).

Monitoring of the level of serum hs-CRP in the two groups of patients

No significant difference could be observed in serum hs-CRP between the two groups before treatment (*P>0.05*). The level of hs-CRP of the two groups reached a peak at 24 hours after admission, and then gradually decreased. At 0.5-7 days after admission, the level of hs-CRP in the experimental group was significantly lower than that in the control group (*P*<0.05) (**Table 4** and **Figure 1**).

Analysis of the clinical efficacy of the two groups

The total effective rate of the experimental group (92.13%) was significantly higher than that of the control group (80.90%) (*P*<0.05) (**Table 5**).

Adverse reactions in the two groups

In the control group, 1 patient died of cardiogenic death, 2 patients suffered from new myocardial infarction, 1 patient suffered from mild intracranial hemorrhage, and 5 patients suffered from gastrointestinal bleeding, gingival bleeding and other minor bleeding. The occurrence of adverse reactions was 10.11%. In the experimental group, 1 patient died of cardiac arrest, 2 patients suffered from new myocardial infarction, 2 patients suffered from mild

Table 2. Comparison of blood lipid indexes between the two groups before and after treatment

	SBP		DBP	
	Before treatment	After treatment	Before treatment	After treatment
Control group	156.84±9.52	131.43±10.26*	97.14±10.23	85.25±9.32*
Experimental group	158.07±9.68	123.75±9.79*	96.85±9.64	79.38±9.84*
t	0.855	5.109	0.195	4.086
P	0.394	<0.001	0.846	<0.001

Note: *$P<0.05$ vs. before treatment.

Table 3. Comparison of blood lipid indexes between the two groups before and after treatment

	TG		HDL-C		LDL-C	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	2.28±0.57	1.71±0.36*	1.10±0.31	1.21±0.29*	3.27±0.41	2.43±0.22*
Experimental group	2.25±0.61	1.63±0.32*	1.13±0.32	1.25±0.25*	3.23±0.44	2.07±0.35*
t	0.339	1.567	0.635	0.986	0.628	8.21
P	0.735	0.119	0.526	0.326	0.531	<0.001

Note: *$P<0.05$ vs. before treatment.

Table 4. Comparison of serum hs-CRP levels between the two groups of patients

	At admission	0.5 d	1 d	2 d	7 d
Control group	14.52±5.18	21.35±7.08*	30.66±6.54*	26.38±5.52*	21.24±6.76*
Experimental group	15.37±4.42	17.16±6.14*	23.79±7.83*	17.52±5.75*	12.26±5.83*
t	1.178	4.220	6.353	10.487	9.490
P	0.241	<0.001	<0.001	<0.001	<0.001

Note: *$P<0.05$ vs. at admission.

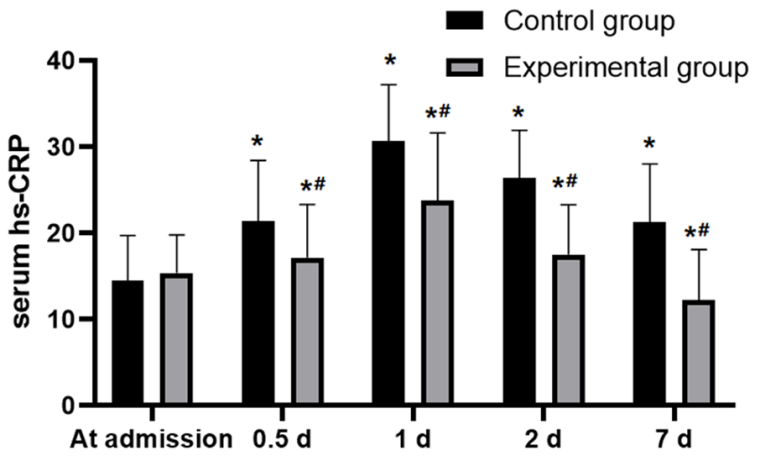

Figure 1. Comparison of serum hs-CRP levels between the two groups of patients. *$P<0.05$ vs. at admission. #$P<0.05$ vs. control group.

intracranial hemorrhage, and 7 patients suffered from gastrointestinal hemorrhage, gingival hemorrhage and other minor bleeding. The incidence of adverse reactions was 13.48%. No significant difference was detected in the MACE and bleeding rate between the two groups ($P>0.05$).

Discussion

ACS is one of the acute critical illnesses with high morbidity and mortality in clinic. The main causes of ACS are platelet aggregation and thrombosis induced by rupture of coronary atherosclerotic plaque, resulting in embolism of vascular lumen which leads to severe myocardial ischemia and necrosis [16]. Medical experts all over the world agree that eliminating platelet aggregation is the key to clinical treatment of ACS [17, 18]. Aspirin and clopidogrel are commonly used antiplatelet drugs in clinic. Aspirin is one of the widely used drugs in

Table 5. Comparison of clinical efficacy between the two groups of patients (n, %)

	Markedly effective	Effective	Ineffective	Total effective rate
Control group	37 (41.57)	35 (39.33)	17 (19.10)	72 (80.90)
Experimental group	61 (68.54)	21 (23.60)	7 (7.86)	82 (92.13)
χ^2		4.816		
P		0.028		

the prevention and treatment of cardiovascular and cerebrovascular diseases. It can not only inhibit the release of endogenous adenosine diphosphate (ADP) and 5-hydroxytryptamine (5-HT), but also significantly inhibit the release of platelets and improve the clinical symptoms and signs of cerebral thrombosis, angina pectoris and ischemic heart disease [19]. As an ADP receptor antagonist, clopidogrel is a new type of antiplatelet thiophene pyridine drugs, which can quickly inhibit platelet aggregation for a long time and alleviate coronary thrombosis [20, 21]. In this study, for elderly patients with ACS over 70 years old, the clinical efficacy of combined treatment with two drugs was significantly better than that of aspirin alone, and no statistical significance could be found in the incidence of adverse events such as MACE and bleeding between the two regimens, which was similar to previous studies [13, 22], suggesting that the combination of aspirin and clopidogrel has better application value and safety for elderly patients over 70 years old with ACS.

Many studies have confirmed that hypertension and hyperlipidemia are risk factors for ACS [23]. Hypertension promotes coronary atherosclerosis, narrows lumens, and leads to ventricular hypertrophy, which reduces myocardial blood supply. In addition, hypertension is prone to cause spastic contraction of the coronary artery or rupture of atherosclerotic plaque, leading to coronary artery occlusion, inducing ACS. Therefore, the blood pressure level is one of the main indicators to evaluate the therapeutic efficacy of ACS. The blood pressure level of ACS patients can be decreased significantly after the symptoms of vasospasm or embolism are relieved. In this study, the levels of SBP and DBP in both groups decreased significantly after 30 days, and the reduction in the experimental group was substantially greater. During the progression of ACS, unstable atherosclerotic plaque may lead to dyslipidemia [25]. In this study, after treatment, the levels of serum TG and LDL-C in both groups decreased, while the levels of HDL-C increased. In addition, the levels of serum LDL-C in the experimental group were lower than those in the control group. The mechanism may be that macrophages infiltrate in subendothelial LDL and oxidize it to form oxidized low-density lipoprotein (ox-LDL) which is engulfed by scavenger receptor (SR) on the surface of macrophages, resulting in a large amount of cholesterol accumulated in cells to form foam cells and promote the formation of atherosclerotic plaques. After treatment, the process was relieved, and the level of LDL-C decreased [26, 27].

Hs-CRP is a systemic inflammatory response molecule synthesized by the liver. It has been found that hs-CRP can stimulate the release of a large number of inflammatory factors by macrophages through mediating and regulating the uptake of LDL, aggravate inflammation in atherosclerotic plaques, increase plaque fragility, exacerbate plaque rupture and erosion, and further promote the occurrence and development of ACS [28]. The level of serum hs-CRP in patients with ACS increases rapidly after onset, and it can increase by ten times in severe cases. The level of serum hs-CRP can be reduced to the reference range in a short time after remission. Therefore, hs-CRP is the preferred marker for evaluating the degree of inflammation in patients with coronary heart disease [29]. The results showed that the levels of hs-CRP in the two groups reached a peak 24 hours after admission, and then gradually decreased. The levels of serum hs-CRP at 0.5, 1, 2 and 7 days after admission in the experimental group were significantly lower. These results suggest that aspirin combined with clopidogrel can significantly inhibit the increase of hs-CRP in elderly patients with ACS and effectively inhibit the inflammatory activity of atherosclerosis.

As the sample size of this study is small and the observation time is short, the research results may be biased, so further research needs to expand the sample size and extend the obser-

vation time to obtain more reliable conclusions.

In conclusion, the combination of aspirin and clopidogrel has a significant clinical efficacy on elderly ACS patients and has greater clinical value.

Disclosure of conflict of interest

None.

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