

Original Article

The effect of the combination of aspirin and clopidogrel on the adverse reactions and prognoses of elderly patients with acute coronary syndrome

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Abstract: Objective: To explore the clinical efficacy of aspirin combined with clopidogrel on elderly patients with acute coronary syndrome and the combination's effect on adverse reactions and prognosis. Methods: 98 elderly patients with acute coronary syndrome who were treated in our hospital were divided into an experimental group (EG, 55 cases, aspirin + clopidogrel) and a control group (CG, 43 cases, aspirin) according to the treatment methods they received. The effective rate, adverse reactions within 6 months, and the hs-CRP and MMP-9 levels before and after the treatment in the two groups of patients were compared. Results: (1) The EG had a higher effective rate compared with the CG ($P < 0.05$); (2) The hs-CRP and MMP-9 levels following the treatment in the EG were lower than they were in the CG ($P < 0.05$); (3) No differences in the incidences of adverse reactions such as nausea and vomiting, allergic reactions, abnormal liver and kidney function were found between the two groups ($P > 0.05$); (4) The overall incidence of arrhythmia, heart failure, angina pectoris, and myocardial infarction in the EG within 6 months of the treatment was lower than it was in the CG ($P < 0.05$). Conclusion: The combined administration of aspirin and clopidogrel in elderly patients with acute coronary syndrome improves clinical efficacy and can significantly reduce the risk of cardiovascular events.

Keywords: Aspirin, clopidogrel, acute coronary syndrome, clinical efficacy, adverse reactions, prognosis

Introduction

Acute coronary syndrome is caused by the partial rupture or erosion of atherosclerotic plaques [1, 2]. Clinical studies have found that the elderly population chiefly bears the burden of acute coronary syndrome. By the 2050s, it is expected that China's over 65-year-old population will reach more than 500 million, leading to a surge in the incidence of acute coronary syndrome [3, 4]. Studies indicate that individuals with a history of smoking, hypertension, hyperglycemia, hyperlipidemia, and a family history of coronary heart disease show elevated risks for acute coronary syndrome than do other populations, but the specific etiology of acute coronary syndrome is not clear [5-7]. Clinical practice shows that acute coronary syndrome can cause a variety of complications, such as arrhythmia, hypotension, shock, heart failure, ventricular tumors, etc., which affect the pati-

ent's quality of life or threaten patients' lives. Timely intervention can improve short- and long-term outcomes following acute coronary syndrome.

Medical therapies for acute coronary syndromes include drug therapy, surgical treatment, interventional therapy, etc. Drug treatment is the most prevalent due to its simplicity [8]. Aspirin is a derivative of salicylic acid. It is often used clinically to relieve mild or moderate pain. Studies in recent years have found that aspirin can also inhibit platelet aggregation and prevent thrombosis, and it is often used in the treatment of myocardial infarction and cerebral ischemia [9].

However, there are currently debates about the "correct" dosage of aspirin, and low-dose aspirin is less effective in preventing cardiovascular and cerebrovascular events [10], but high-dose

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aspirin is likely to cause adverse reactions such as gastrointestinal discomfort and bleeding, so a combination therapy had been explored to improve the prognosis of patients with acute coronary syndrome.

Clopidogrel is a type of platelet aggregation inhibitor, and it exhibits a good treatment effects in stroke, myocardial infarction, and peripheral artery disease patients [11-13]. At present, there are no clinical studies about aspirin combined with clopidogrel on elderly patients with acute coronary syndrome, which is the focus of this study.

Materials and methods

Baseline data

98 elderly patients with acute coronary syndrome who were treated in our hospital were enrolled, and they were divided into an experimental group (the EG, 55 cases) and a control group (the CG, 43 cases) according to the treatment method each received.

Inclusion criteria: (1) patients who met the diagnostic criteria for acute coronary syndrome in the *Acute Coronary Syndrome Diagnosis and Treatment Guidelines* issued by the Chinese Medical Association in 2016 [14], and who experienced typical manifestations such as retrosternal chest pain (>0.5 h); (2) patients with complete medical data; (3) patients with a clear awareness to cooperate with the research. The study was approved by ethics committee of our hospital. The patients or a member of their families signed the informed consent before participating in the study.

Exclusion criteria: (1) patients with mental illness; (2) patients who are allergic to the drugs used in this study; (3) patients with malignant tumors; (4) patients with severe liver or kidney dysfunction; (5) patients with coagulation dysfunction; (6) Patients who experienced gastrointestinal bleeding, cerebral hemorrhage, or severe bleeding within the 6 months before their enrollment; (7) patients with autoimmune diseases.

Methods

All the patients' medical histories were checked upon admission, and they underwent rou-

tine tests such as electrocardiograms and echocardiographies. The two groups of patients received the same nursing. The CG was treated with enteric-coated aspirin (manufacturer: Bayer Healthcare Co., Ltd., 100 mg/tablet, J20130078), the applied dose is 200 mg/d for 90 days; the patients in the EG were also treated with clopidogrel (Lepu Pharmaceutical Co., Ltd., 75 mg/tablet, H20123116), the applied dose is 75 mg/d for 90 days.

Outcome measurement

Effective rate: After 3 months of treatment, the effective rates of the two groups were evaluated, and the treatment effects were divided into three categories: markedly effective, effective, and ineffective. Markedly effective means that the clinical symptoms of the patients disappeared after the treatment, and indicators such as calcium protein concentrations returned to the normal level. Effective means that the clinical symptoms of the patient were significantly improved. Troponin and other indicators were also significantly improved compared to those before the treatment. Ineffective means that the clinical symptoms of the patient are not improved or even worsened, and there is no change in the levels of troponin and other indicators; Effective rate = (number of markedly effective + effective)/total number of cases $\times 100\%$ [15].

The Hs-CRP and MMP-9 levels before and after treatment: Venous blood in a fasting state was collected before and after the treatment in two groups, and the hs-CRP level before and after the treatment was measured using the immunoturbidimetric method. The kit was purchased from the American R&D System Company, and the operation was strictly implemented in accordance with the kit's instructions. Each measurement was performed 3 times and the average value was recorded.

Incidence of adverse reactions

The patients were followed up to record the incidences of adverse reactions such as nausea and vomiting, allergic reactions, and abnormal liver and kidney function during the treatment period, and a comparison of the adverse reactions was performed between the two groups.

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Table 1. Baseline data ($\bar{x} \pm s$)/[n (%)]

Clinical data	Control group (n=43)	Experimental group (n=55)	t/ χ^2	P
Male/Female	22/21	29/26	0.024	0.878
Average age (years)	63.59±1.51	63.44±1.36	0.516	0.607
Paroxysmal chest pain [n (%)]	26 (60.47)	33 (60.00)	0.002	0.963
Systolic pressure (mmHg)	126.53±3.25	127.55±2.61	1.723	0.088
Diastolic blood pressure (mmHg)	76.35±1.63	76.29±2.16	0.151	0.88
Heart rate (bpm)	70.26±1.66	69.82±1.77	1.255	0.212
Hypertension	16 (37.21)	20 (36.36)	0.007	0.931
Diabetes	19 (44.19)	26 (47.27)	1.626	0.202
Hyperlipidemia	17 (39.53)	23 (41.82)	0.052	0.819
BMI (kg/m ²)	21.69±1.66	22.04±1.09	1.256	0.212
Smoking history [n (%)]	21 (48.84)	29 (52.73)	0.146	0.702
Drinking history [n (%)]	20 (46.51)	25 (45.45)	0.011	0.917

Table 2. Comparison of the effective rates in the two groups [n (%)]

Grouping	Cases	Markedly effective	Effective	Ineffective	Effective rate
Experimental group	55	43 (78.18)	10 (18.18)	2 (3.64)	53 (96.36)
Control group	43	30 (69.77)	6 (13.95)	7 (16.28)	36 (83.72)
χ^2	-	-	-	-	4.625
P	-	-	-	-	0.032

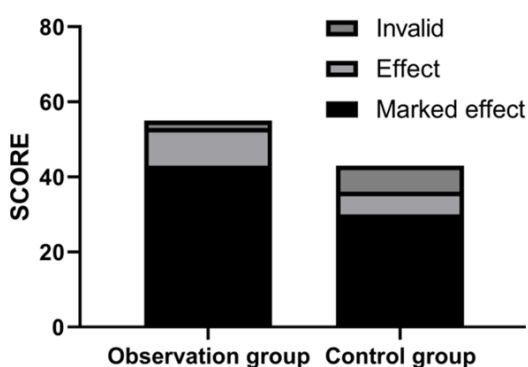


Figure 1. Comparison of the treatment efficacy in the Experimental group and the Control group. The experimental group's effective rate was 96.36%, which is higher than the control group (83.72%).

Comparison of the prognoses

The prognoses were evaluated within 6 months of the treatment. The incidences of cardiovascular events such as arrhythmia, heart failure, and angina pectoris during the treatment period were compared between the two groups.

Statistical methods

The statistical analysis was performed using SPSS 22.0. The measurement data were ex-

pressed as the mean \pm standard deviation. The intra-group and inter-group comparisons of the measurement data were performed using independent sample t tests. The count data were expressed as [n (%)]. The intra-group and inter-group comparisons of the count data were examined using χ^2 tests, and the intra-group comparisons of multiple points were analyzed using ANOVA. $P < 0.05$ was considered statistically significant.

Results

Baseline data

The clinical characteristics such as the gender, age, symptoms, systolic blood pressure, diastolic blood pressure, heart rate, medical history, and BMI of the two groups were not statistically significant ($P > 0.05$) (Table 1).

Comparison of the effective rates in the two groups

The effective rate of the EG was 96.36% (53/55), and the effective rate of the CG was 83.72% (36/43). The difference in the treatment efficiency between the two groups was statistically significant ($P < 0.05$) (Table 2; Figure 1).

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Table 3. Comparison of the hs-CRP and MMP-9 levels in the two groups ($\bar{x} \pm s$)

Grouping	Cases	hs-CRP (mg/L)		MMP-9 (ng/mL)	
		Before treatment	After treatment	Before treatment	After treatment
Experimental group	55	16.98±4.22*	4.16±2.15	168.88±50.14*	70.16±12.05
Control group	43	17.06±4.51*	6.62±3.22	170.51±46.35*	82.36±13.36
t	-	0.09	4.524	0.165	4.742
P	-	0.928	<0.001	0.869	<0.001

Note: *P<0.05 compared with those after treatment.

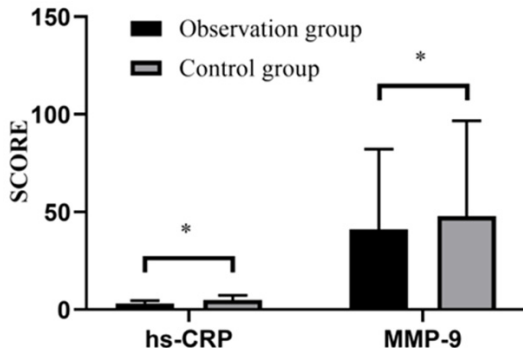


Figure 2. Comparison of the hs-CRP and MMP-9 levels after the treatment in the two groups. Compared with the MMP-9 levels after 3 months of treatment in control group, the experimental group showed significantly lower MMP-9 levels (P<0.05), *P<0.05.

Comparison of the hs-CRP and MMP-9 levels in the two groups

Significant reductions in the hs-CRP and MMP-9 levels were observed after the treatment in both groups (P<0.05), and the hs-CRP and MMP-9 levels in the EG were lower than they were in the CG (P<0.05) (Table 3; Figure 2).

Comparison of the adverse reactions in the two groups

The incidence of adverse reactions, such as nausea and vomiting, allergic reactions, abnormal liver and kidney function, in the EG was 9.09% (5/55), and the incidence of adverse reactions in the CG was 9.30% (4/43) (Table 4; Figure 3).

Comparison of the prognoses in the two groups

After the end of the six months' follow-up, no deaths occurred in the two groups. The incidence rates of arrhythmia, heart failure, angina pectoris, and myocardial infarction in the EG

and CG within 6 months of treatment were 7.27% (4/55), and 23.26% (10/43), respectively, and the difference between the two groups was statistically significant (P<0.05) (Table 5; Figure 4).

Discussion

With the aging of China's population, the incidence of cardiovascular and cerebrovascular diseases has also increased. Data show that there were approximately 57 million deaths worldwide in 2008, of which about 48% were caused by cardiovascular and cerebrovascular events. A survey indicates that there are approximately 290 million patients with cardiovascular and cerebrovascular diseases in China, of which 2.5 million are patients with myocardial infarction, and for every 5 deaths, there were 2 deaths that resulted from cardiovascular disease [3, 16]. Acute coronary syndrome is characterized by paroxysmal pain, oppression, radiating pain, dyspnea, syncope, and angina pectoris, posing a serious threat to patient health. Studies have found that the one-year mortality rate of patients with acute coronary syndrome is about 15% and the 5-year mortality rate is as high as 20% [17, 18]. Therefore, early intervention can improve the patients' prognoses.

Patients with acute coronary syndrome can be divided into two groups: those with unstable angina pectoris and those with acute myocardial infarction. The etiology of this disease can be summarized as the rupture of atherosclerotic plaque leading to the exposure of sub-endothelial collagen tissue, and platelet aggregation forms hemostatic plugs which block the coronary arteries and induces a series of clinical symptoms in patients [19]. The current treatment for acute coronary syndrome mainly includes drug therapy and interventional tre-

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Table 4. Comparison of the incidence of adverse reactions in the two groups [n (%)]

Grouping	Cases	Nausea and vomiting	Allergic reactions	kidney dysfunction	Incidence
Experimental group	55	3 (5.45)	1 (1.82)	1 (1.82)	5 (9.09)
Control group	43	2 (4.65)	1 (2.33)	1 (2.33)	4 (9.30)
χ^2	-	-	-	-	0.001
<i>P</i>	-	-	-	-	0.971

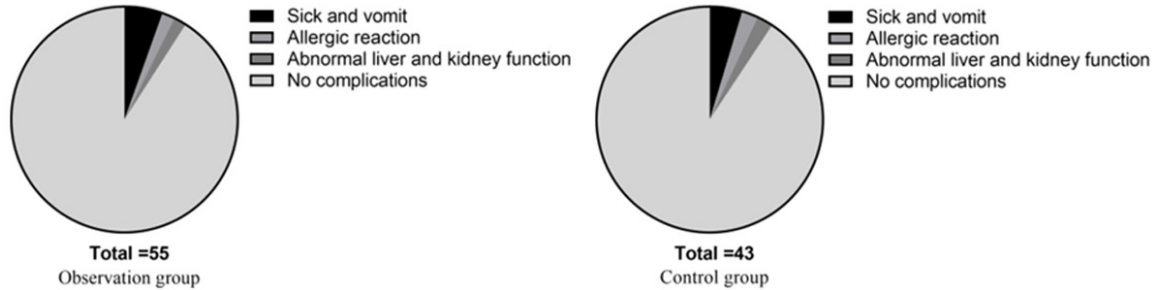


Figure 3. Comparison of the adverse reactions in the two groups of patients. The difference in the incidences of adverse reactions in the two groups was not statistically significant ($P > 0.05$).

Table 5. Comparison of the prognoses in the two groups [n (%)]

Grouping	Arrhythmia	Heart failure	Angina pectoris	Myocardial infarction	Incidence
Experimental group	2 (3.64)	0 (0.00)	2 (3.64)	0 (0.00)	4 (7.27)
Control group	5 (11.63)	1 (2.33)	3 (6.98)	1 (2.33)	10 (23.26)
χ^2	-	-	-	-	5.035
<i>P</i>	-	-	-	-	0.025

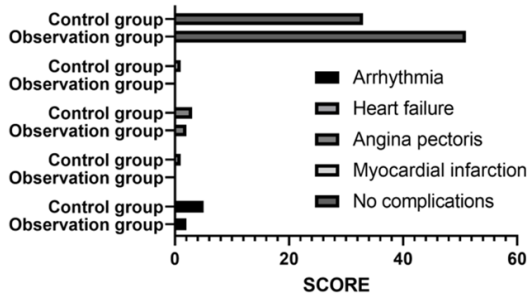


Figure 4. Comparison of the prognosis in the two groups. There were 2 cases of arrhythmia, 0 cases of heart failure, 2 cases of angina pectoris, and 0 cases of myocardial infarction in the experimental group for a total incidence rate of 7.27% (4/55). There were 5 cases of arrhythmia, 1 case of heart failure, 3 cases of angina pectoris, and 1 case of myocardial infarction in the control group for a total incidence rate of 23.26% (10/43), and the difference between the two groups was significant ($P < 0.05$).

atment. The interventional treatment yields fast results and noticeable symptom improvements. Symptoms such as myocardial ische-

mia and hypoxia will be improved immediately after surgery. Thus interventional treatment is favored by many medical workers and patients [20]. In particular, the invention of the drug-eluting stents significantly reduces the risk of restenosis after interventional treatment, which leads to the wide use of this treatment in clinical practice.

However, some studies have pointed out that interventional treatment brings new problems, such as the damage to the vascular endothelium during the stent implantation, resulting in delayed intimal healing, the excessive activation of platelets, thus increasing the risk of vascular events. Therefore, drug therapy is irreplaceable [21]. Many studies have found that platelet aggregation and activation are involved in the occurrence and development of acute coronary syndromes and subsequent thrombotic-induced acute ischemic events after plaque rupture. Therefore, the goal of the clinical treatment is to reduce platelet activation and platelet aggregation [22].

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The results of this study show that compared with the CG treated with aspirin alone, the patients in the EG showed a higher effective rate, which is similar to the results of an earlier study [23] which showed that the platelet aggregation rate in patients with acute coronary syndrome after the administration of aspirin and clopidogrel was significantly lower than it was in those treated with aspirin alone. That study also showed that the mortality rate of patients in the combined treatment group was 8.0%, which was much lower than the CG's 28.0%, suggesting that the combined treatment can significantly reduce the mortality of patients with acute and subacute stent thrombosis.

This study also showed that the hs-CRP and MMP-9 levels in the EG were significantly lower than the corresponding levels in the CG after the treatment. hs-CRP is an acute-phase protein and a marker of tissue damage. Many studies have shown that hs-CRP is not only a marker of acute inflammation, but it is also an independent risk factor for cardiovascular disease, including myocardial infarction and coronary artery disease [24, 25]. MMP-9 is a type of matrix metalloproteinase, and its main sources include neutrophils, macrophages, monocytes, and endothelial cells. Clinical studies indicate that MMP-9 can degrade collagen and elastin in atherosclerotic plaques and aggravate plaque instability, so it is often used as a prognostic indicator [26, 27].

The results of this study showed that the levels of hs-CRP and MMP-9 in the EG were significantly lower than they were before the treatment, and the levels of the above indicators were lower in the EG than they were in the CG. Studies [28] have pointed out that hs-CRP and MMP-9 can reflect the inflammatory state of patients with acute coronary syndrome, and the hs-CRP and MMP-9 levels can be reduced by alleviating the inflammatory state. Our study suggested that the combination of aspirin and clopidogrel can reduce the release and expression of inflammatory mediators in the body and then exert anti-atherosclerotic effects.

The results of this study showed that the incidence of adverse reactions in the EG was not significantly different from the CG, suggesting that the combination therapy was safe. The 6-month follow-up results showed that the inci-

dence of cardiovascular events such as arrhythmia, heart failure, angina pectoris, and myocardial infarction in the EG were lower than they were in the CG. The reason may be that the administration of clopidogrel can significantly reduce the occurrence of aspirin resistance, thus reducing the occurrence of ischemic events, and showing a positive significance for improving the clinical symptoms and patient prognosis.

In summary, the combined use of aspirin and clopidogrel in elderly patients with acute coronary syndrome showed satisfactory treatment effects, significantly alleviated the inflammatory state of the patients and reduced the incidence of cardiovascular events.

Disclosure of conflict of interest

None.

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