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Original Research Article

Protective effect of combined use of standard drug therapy and spironolactone against arrhythmia and heart failure in patients with acute ST-segment elevated myocardial infarction after emergency percutaneous coronary intervention

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Abstract

Purpose: *To determine the mitigating impact of standardized drug therapy in combination with spironolactone on arrhythmia and heart failure in subjects with severe ST-segment elevation myocardial infarction (STEMI) following exigency percutaneous coronary intervention (PCI).*
Methods: *120 severe STEMI subjects who underwent exigency PCI were assigned to control and study groups, with 60 patients in each group. Control group received long-term aspirin therapy (85 mg/day, orally) after emergency PCI, while study group received long-term spironolactone therapy (50 mg/day, orally) plus control cohort drug regimen. Treatment effectiveness, heart function, quality of life, electrolyte levels (K^+ and Mg^{2+}), and incidence of cardiac adverse events were determined before and post-treatment.*
Results: *Treatment efficacy was markedly greater in study cohort. Post-treatment values of LVEF indicators in both groups were significantly greater than the pre-treatment levels, with markedly higher study cohort levels. In contrast, values of LVEDD and LVESD indicators were significantly reduced in both groups after treatment, but the levels in study group were significantly lower ($p < 0.05$). Scores on indices of physical function, psychological function, social function, and physical quality of life in both groups were significantly increased after treatment, with significantly higher scores in study cohort ($p < 0.05$). Post-therapy serum concentrations of K^+ and Mg^{2+} were markedly raised in both groups but with higher levels in study cohort. Incidents of unwanted heart situations were lower in study cohort.*
Conclusion: *Combined use of standard drugs and spironolactone for the treatment of severe STEM1 subjects following emergency PCI is effective. More studies are required to elaborate the mechanistic characteristics of this combination.*

Keywords: *Spironolactone, Percutaneous coronary intervention, Acute ST-segment elevation heart attack, Arrhythmia, Heart failure*

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INTRODUCTION

Acute ST-segment elevation myocardial infarction (STEMI) is a serious cardiovascular adverse event caused by continuous interruption of blood flow due to acute stenosis or occlusion of the coronary artery. This results in myocardial necrosis due to acute persistent ischemia and hypoxia. If not treated on time, it may lead to cardiogenic shock and death [1,2].

Percutaneous coronary intervention (PCI) is currently the main treatment strategy for coronary heart disease due to its advantages of minimal invasiveness, high success rate, and fast patient recovery. However, although PCI dredges the stenosis of coronary artery lumen and reduces the symptoms of myocardial ischemia in patients, it does not reverse the process of atherosclerosis. There is a high risk of re-stenosis of artery lumen in patients after surgery, which affects the recovery of cardiac function [4]. Therefore, it is crucial to provide scientific and effective cardiac rehabilitation care to patients with coronary heart disease after PCI so as to reduce cardiovascular risk factors and the incidence of coronary re-stenosis after PCI [5]. Previous studies have shown that over-stimulation of the neuroendocrine network promotes the reshaping of the ventricles following a heart attack [6]. Aldosterone is a crucial component of the renin-angiotensin-aldosterone system (RAAS).

The role of aldosterone in blood circulation coupled with “aldosterone escape mechanism” determines the vital role of its receptor antagonists (ARAs) in the treatment of cerebrovascular ailments [7]. Spironolactone is one of the aldosterone receptor antagonists that decrease ventricular remodeling and reduce the incidence of heart failure by blocking aldosterone receptors. It inhibits sodium retention and potassium excretion, thereby counteracting the pro-remodeling effects of aldosterone. This reduces myocardial fibrosis, hypertrophy, and oxidative stress, thereby preserving cardiac structure and function. Additionally, spironolactone mitigates neurohormonal activation by suppressing renin-angiotensin-aldosterone system and sympathetic nervous system overactivity [8].

This retrospective study aimed to determine the protective effect of combined use of standard drug therapy and spironolactone against arrhythmia and heart failure in patients with STEMI after emergency percutaneous coronary intervention (PCI).

METHODS

General information on patients

A total of 120 patients with acute STEMI who received emergency PCI treatment in Anqing Municipal Hospital from August 2021 to August 2023 were selected and randomly divided into a control group and a study group, with 60 patients in each group. This study was reviewed and approved by the Ethics Committee of Anqing Municipal Hospital (approval no. amh2023002), and all subjects signed informed consent, and complied with international guidelines for human studies.

Inclusion criteria

The included patients were those aged between 18 and 80 years; patients diagnosed with STEMI based on clinical symptoms, signs, and arteriographic examination [9]; patients with complete clinical medical records, and first-time PCI surgery patients who underwent successful operations.

Exclusion criteria

Patients with other functional impairments or organ diseases; those who had severe complications after surgery; patients who had surgery or history of cerebrovascular accident within one month before study, and those who had severe dysfunctions in heart, liver, and kidney, were excluded.

Treatments

Patients in control group were given routine drug therapy after emergency PCI (the drug used was aspirin). Study group was treated with spironolactone (Sinopharm Rongsheng Pharmaceutical Co. Ltd., approval number: Guo Yao Zhen Zi H20093097; product specification: 20 mg x 30S), in addition to the conventional treatment. The dose of spironolactone was 20 mg once daily for 12 months after PCI [10].

Evaluation of parameters/indices

Clinical treatment efficacy

The clinical treatment effectiveness in each group was evaluated based on the clinical symptoms, signs, and cardiac function classification. It was divided into three levels: significantly effective (S), effective (E), and ineffective (I). Treatment was significantly effective if the symptoms of heart failure such as fatigue, difficulty in breathing, and edema were

significantly reduced, and cardiac function was improved by at least 2 levels. If the symptoms of heart failure such as fatigue, difficulty in breathing, and edema were reduced, and the cardiac function was improved by at least 1 level, the treatment outcome was deemed effective. Treatment effects not in keeping these outcomes were deemed ineffective. The overall treatment efficacy (T) was calculated using Eq 1 [11].

$$T (\%) = \{(S+E)/N\}100 \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

where N is the total number of patients in each group

Cardiac function

Color Doppler ultrasound was assigned values of LVEF, LVEDD, and LVESD in both groups of patients, before and after treatment [12].

Quality of life

The quality of life of each patient in the two groups was evaluated using the Generic Quality of Life Inventory-74 (GQOL-74), with each dimension scored from 0-100 [13]. The higher the score, the better the quality of life of the patient. It comprised 74 items covering physical function which involved evaluation of physical well-being, i.e., mobility, pain, and overall health; psychological function which assessed mental and emotional aspects such as anxiety, depression, and coping abilities; social function which evaluated social interactions, relationships, and support systems; and life status, which reflected overall life situation and material well-being.

Serum electrolyte levels

Early-morning peripheral blood (3 mL) was drawn from the vein of each subject in the fasted state. After a 10-min spinning at 3000 rpm, the resultant sera were kept in a -20°C refrigerator. The serum levels of potassium (K^+) and magnesium (Mg^{2+}) were determined using a 7060 automatic biochemical analyzer.

Adverse cardiac events

Incidents of adverse cardiac reactions (heart failure, arrhythmia, cardiogenic shock and angina) during the treatment period were recorded, and the incidence of adverse reactions (R) was calculated using Eq 2.

$$R (\%) = (n_a/N)100 \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots (2)$$

Where n_a is number of adverse reactions and N is total number of patients in each group.

Statistical analysis

Statistical analysis was performed using SPSS 20.0. Count data were compared using Chi-squared (χ^2) test. Rank-sum test was used for comparison of rank data. Measurement data are presented as mean ± standard deviation (SD). Comparisons were performed using Student's *t*-test. Values of $p < 0.05$ meant statistical significance of differences.

RESULTS

Clinical treatment efficacy

There were 35 men and 32 women of ages 40 - 80 years (average age = 62.47 ± 9.24 years), in the control cohort, with body mass index (BMI) ranging from 18 to 27 kg/m^2 (mean BMI = 23.75 ± 2.56 kg/m^2). Study group had 34 males and 26 females of ages 37 to 82 years (mean age = 61.46 ± 8.90 years), and BMI range of 19 to 27 kg/m^2 (mean BMI = 24.15 ± 2.84 kg/m^2). The two groups were comparable in basic general data. Total treatment effectiveness in study cohort was significantly higher than that in the control cohort ($p < 0.05$; Table 1).

Levels of cardiac function indices

Pre-treatment levels of cardiac function indicators were comparable in the 2 cohorts. However, the LVEF values in both cohorts were significantly raised by treatment, with significantly greater LVEF values in study cohort. In contrast, values of LVEDD and LVESD were significantly lowered after treatment, with significantly lower levels observed in study cohort (Table 2).

GQOL-74 scores

Pre-treatment GQOL-74 scores were comparable in the 2 cohorts. However, post-treatment scores on physical, psychological, social, and physical quality of life in the two groups were significantly higher than the corresponding pre-treatment values, with markedly greater scores in study cohort ($p < 0.05$). These results are shown in Table 3.

Serum electrolyte levels

Pre-treatment levels of K^+ and Mg^{2+} were comparable in the 2 cohorts. However, post-treatment levels of K^+ and Mg^{2+} were markedly raised, relative to pre-treatment, with significantly higher levels in study cohort (Table 4).

Table 1**:** Clinical efficacy in the two groups (n=60)

Group	Significantly effective	Effective	Ineffective	Overall effectiveness
Study	42 (70.00)	15 (25.00)	3 (5.00)	57 (95.00)
Control	28 (46.67)	21 (35.00)	11 (18.33)	49 (81.67)
χ^2				5.175
P-value				0.023

Table 2: Cardiac function index levels in both cohorts (n=60)

Group	LVEF (%)		LVEDD (mm)		LVESD (mm)	
	Pre-	***Post-***	***Pre-***	***Post-***	***Pre-***	***Post-***
Study	38.46±5.72	56.23±4.85*	63.34±5.14	49.52±4.27*	49.40±5.38	37.23±3.56*
Control	39.21±6.33	46.28±5.57*#	62.75±4.82	55.24±6.02*#	50.22±4.94	42.67±4.30*#
T	-0.681	10.435	0.649	-6.003	-0.870	-7.548
P-value	0.497	0.000	0.518	0.000	0.386	0.000

Note: *$P < 0.05$, vs. pre-treatment. #$p < 0.05$, vs. post-treatment

Table 3: Comparison of GQOL-74 scores between the two groups (points; n=60)

Group	Physical function		Psychological function		Social function		Material life	
	Before	***After***	***Before***	***After***	***Before***	***After***	***Before***	***After***
Study	64.25±5.42	76.38±4.27*	62.38±6.37	78.25±6.54*	69.26±5.66	82.62±5.24*	65.38±5.46	77.56±5.44*
Control	65.23±6.21	70.33±5.26*#	63.37±6.28	72.39±5.21*#	70.12±6.40	75.62±4.74*#	66.18±4.82	71.34±4.70*#
T	0.921	6.917	-0.857	5.429	-0.780	7.674	-0.851	6.702
P-value	0.359	0.000	0.393	0.000	0.437	0.000	0.400	0.000

Note: *$P < 0.05$, vs. pre-treatment; #$p < 0.05$, vs. post-treatment

Table 4: Serum values of K^+ and Mg^{2+} in the 2 cohorts (n=60)

Group	K^+ (µmol/L)		Mg^{2+} (µmol/L)	
	Before	***After***	***Before***	***After***
Study	3.96±0.32	4.44±0.47*	0.84±0.16	0.99±0.17*
Control	3.95±0.36	4.02±0.35#	0.87±0.16	0.90±0.12#
T	0.161	5.552	-1.027	3.350
P-value	0.873	0.000	0.307	0.001

*$P < 0.05$, vs. pre-treatment; #$p < 0.05$, vs. post-treatment

Table 5: Incidence of adverse heart events in the 2 cohorts (n=60)

Group	Heart failure	Arrhythmia	Cardiogenic shock	Angina pectoris	Overall incidence
Study	2 (3.33)	3 (5.00)	1 (1.67)	2 (3.33)	8 (13.33)
Control	4 (6.67)	6 (10.00)	2 (3.33)	5 (8.33)	17 (28.33)
χ^2					4.093
P-value					0.043

Incidents of adverse heart events

There were significantly fewer incidence of adverse cardiac events in study group cohort than in the control cohort (Table 5).

DISCUSSION

The main event in the pathogenesis of coronary heart disease is coronary artery atherosclerosis. The early clinical symptoms of coronary atherosclerosis are not usually obvious in patients. However, with progression of the disease, the severity of coronary artery disease gradually increases, resulting in ischemic and hypoxic myocardial damage which leads to abnormal cardiac function and adverse cardiovascular events [14]. Acute STEMI is a common cardiovascular and cerebrovascular disease due to acute occlusive thrombosis which is exacerbated further by damage caused by coronary plaque.

A systematic review and meta-analysis found that the global prevalence of MI (including both STE-MI and non-ST-elevation MI) is as follows: 3.8 % in individuals below 60 years, and 9.5 % in individuals above 60 years [15]. It is characterized by acute onset, severity, and poor prognosis. If not treated on time, severe cases of STEMI may lead to death [16]. With continuous advancements in minimally invasive medical

techniques, PCI is becoming increasingly widely used as a safe and effective angioplasty technique in the treatment of patients with coronary heart disease [17]. Due to its early enhancement of ischemic myocardial reperfusion, reduction of infarct size, reduction of myocardial injury, protection of heart function, and improvement of clinical prognosis, PCI is often used in clinical practice in combination with other drugs for the treatment of patients with STEMI. This study determined the protective effect of combined use of standardized drug therapy and spironolactone against arrhythmia and heart failure in patients with STEMI after emergency PCI. The results obtained showed that this treatment method produced good clinical efficacy.

The remodeling of ventricles following STEMI encompasses alterations in ventricular features and anatomy, as well as myocardial damage-induced physiological changes in cardiac tissue. Following STEMI, there are several alterations in the structure and histopathology of the myocardium of the left ventricle which result in a gradual decrease in its function. These changes after STEM1 lead to weakening of myocardial contractile function and reduction in the amount of blood pumped by the left ventricle. Myocardial cells are the main cells associated with remodeling, although collagen, interstitial tissue, fibroblasts and heart vessels are also crucial in myocardial remodeling, albeit to lesser extents. Aldosterone is produced in adrenal region and in heart muscle RAAS system itself, e.g., infarcted heart muscle. In addition, angiotensin II enhances myocardial aldosterone production [19]. Previous research has shown that during the acute phase of myocardial infarction, the uptake of aldosterone by myocardial cells induces ventricular remodeling [20]. Therefore, cardiac muscle remodeling may be averted by cutting off any link in the RAAS route. The intake of angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists results in an acute decline in aldosterone levels, but aldosterone levels rise once more ("aldosterone escape") [21].

It has been shown that the combined use of receptor antagonists for aldosterone and angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists may prevent myocardial hypertrophy caused by aldosterone escape. This is of great significance in treating cardiac muscle remodeling and congestive cardiac failure. In this study, both groups of patients were routinely given ACEIs or antagonists of angiotensin II receptor, but additionally, study group received spironolactone. Hence, ventricular remodeling was markedly inhibited in study cohort.

The pathogenesis of chronic heart failure has not yet been fully elucidated. However, recent studies have demonstrated that myocardial injury induces activation of protective compensatory mechanisms which excessively excite the RAAS and sympathetic nervous system (SNS). This enhances the secretion of neuroendocrine factors such as norepinephrine, angiotensin II (Ang II), and aldosterone (ALD), leading to ventricular remodeling [22]. This study revealed markedly greater total treatment effectiveness and markedly fewer incidents of cardiac events in study cohort. Moreover, post-treatment serum levels of K^+ and Mg^{2+} were greater in study cohort, and also higher than pre-treatment levels. Treatment led to raised LVEF levels in the two groups of patients, but with greater LVEF levels in study cohort than in control cohort. However, treatment markedly lowered LVEDD and LVESD levels in both groups, with lesser values of LVEDD and LVESD in study cohort. Therefore, the use of standard drugs in combination with spironolactone in emergency PCI for the treatment of patients with acute STEMI produced good clinical effectiveness which may be beneficial in preventing postoperative arrhythmia and heart failure in patients. The treatment of heart failure is mainly based on suppression of the activation of the RAAS system. Excessive activation of mineralocorticoid receptors may trigger inflammatory responses, leading to cardiac fibrosis, vascular fibrosis, and remodeling, as well as renal tubulointerstitial fibrosis. Clinical trials have shown that the mineralocorticoid receptor antagonist spironolactone effectively reduces the incidence of chronic heart failure and acute myocardial infarction with left ventricular systolic dysfunction and acute heart failure, as well as the associated mortality [23].

In addition, the anti-arrhythmic effect of aldosterone blockade has been widely supported by findings that link aldosterone stimulation and overexpression of cardiac mineralocorticoid receptors to various electrophysiological changes at the cellular levels. These include regulation of potassium and calcium currents, abnormal calcium release, and prolongation of duration of ventricular re-polarization. In addition, ischemia-induced production of free fatty acids and oxygen free radicals, acidosis, uneven conduction, and refractoriness have the potential to induce re-entrant arrhythmias and increased catecholamine production [24]. The association between ischemia-induced arrhythmic status, high aldosterone levels soon after STEMI onset,

and the arrhythmic effects of aldosterone, may constitute a factor that triggers life-threatening arrhythmias. This association may be prevented by early mineralocorticoid receptor blockade. Therefore, spironolactone is beneficial in reducing the incidence of arrhythmia in patients with STEMI [25].

Limitations of this study

The sample size is small and only one study center was used. This may affect the validity of results obtained in this study.

CONCLUSION

The combined use of standard drugs and spironolactone for treatment of patients with acute STEMI after emergency PCI produced good clinical efficacy. Therefore, combination therapy has the potential to prevent postoperative arrhythmia and heart failure in patients. More studies in larger populations are required to elaborate the mechanistic implications of these combinations.

DECLARATIONS

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Ethical approval

This study was approved by the Ethics Committee of Anqing Municipal Hospital (approval no. amh2023002).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was performed by the authors named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Rongrong Wang designed study, supervised the data collection, and analyzed the data. Rongrong Wang interpreted the data and prepared the manuscript for publication. Yuanxi Zheng and Liangchuan Chen supervised the data collection, analyzed the data and reviewed the draft of the manuscript.

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