International Journal of
Science Inventions Today
www.ijsit.com
ISSN 2319-5436
Review Article

THE INFLUENCE OF MONGOLIAN NEW MEDICINE-II ON CARDIAC FUNCTION IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION (AMI) AND CARDIOMYOPATHY-REVIEW

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ABSTRACT

Mongolian New Medicine-II is a traditional prescription medicine of Mongolian Medicine. It has an important heart strengthening effect on palpitation and chest pain caused by Qi deficiency. It has been used clinically in the management of coronary heart disease, ischemic cardiomyopathy for many years. It has been shown to have excellent outcomes on adverse ventricular remodeling. The primary mode of action of the drug is decrease in expressions of endoplasmic reticulum chaperone GRP78, GRP94, pro-apoptotic factor CHOP and caspase-3.

Keywords: Acute Myocardial Infarction, Mongolian new medicine-II, Percutaneous intervention, cardiac function, ischemic cardiomyopathy.

INTRODUCTION

Cardiovascular disease is the major cause of mortality and morbidity globally [1]. However, in China, coronary artery disease(CAD) sits in the second list of most important cause of mortality, after malignancy [2]. Although the mortality due to CAD is relatively low in China compared with western world but the rate is increasing day by day, because of change in lifestyle, diet and large number of ageing population.

Acute myocardial infarction(ami):

Acute myocardial infarction is a disorder characterized by acute onset of severe precordial chest pain due to total occlusion of coronary blood flow to the heart leading to necrosis of cardiac myocytes [3]. It usually results from rupture of an atherosclerotic plaque with thrombosis and complete blockade of coronary artery. Myocardial infarction can further be classified on the basis of size, location of occlusion, or commonly from electrocardiographic findings into ST-elevation myocardial infarction(STEMI) and Non-ST elevation myocardial infarction(NSTEMI) [4]. The patients whose cardiac enzymes are not raised are diagnosed as Unstable angina [5].

Pathophysiology of AMI:

Thrombus formation at the site of rupture of an atherosclerotic plaque blocks the coronary circulation resulting in myocardial necrosis distal to the block. The degree of necrosis depends on the site of the block and degree of block. Proximal coronary artery thrombosis causes more myocardial damage than distal branch thrombosis. Complete occlusion causes STEMI and partial occlusion causes NSTEMI or Unstable angina(UA). Cardiac enzymes are liberated from the necrosed myocardium.

Early diagnosis and appropriate treatment is the key of success in treatment of patients with acute myocardial infarction. Key clinical features includes:

- Chest pain-unprovoked, severe, prolonged and usually associated with tightness of chest. The pain is retrosternal and may radiate to arms, upper back, epigastrium. The pain is usually don't respond to nitroglycerine
- Breathlessness, exhaustion and fatigue
- Anxiety (fear of impending death)
- Sweating, nausea, vomiting
- Confusion, syncope or even sudden cardiac death (due to fatal arrhythmias).

Treatment of acute myocardial infarction:

Various treatment modalities are recommended for AMI based on initial findings of electrocardiography with the presence or absence of ST segment elevation [6]. The main goal of treatment is to alleviate pain, restore blood flow to to myocardium and prevent complications. There has been tremendous improvement in the treatment of acute myocardial infarction in recent years. Reperfusion can be done by pharmacologic(fibrinolysis) or catheter based(PCI). Reperfusion should be done as soon as practicable to salvage the myocardium.

Primary PCI remains the best ideal modality of treatment and should ideally be performed within 90 minutes of arrival at emergency room and consists of coronary angiography followed by balloon dilatation of occluded artery with stent insertion. Whenever primary PCI is not available and if no contraindications, thrombolysis should be carried out using pharmacological methods to dissolve clot and restore circulation in the coronary arteries. The aim of thrombolysis is to dissolve the clot and restore circulation in the coronary arteries as early as possible.

Current recommendations is to start thrombolysis within 30 minutes of diagnosis of AMI (door to needle time 30 minutes). Other adjunctive treatment modalities include antiplatelet therapy(Aspirin), nitroglycerin, morphine, beta-blockers, ACE-inhibitors.

Myocardial infarction(MI) is the major cause of heart failure, which has a significant morbidity and mortality [7,8]. During the development of cardiac failure caused by MI, cardiac fibroblasts(CFs) activate, proliferate and release proteins like collagens: collagens constitute the extracellular matrix(ECM), that replaces necrotic cardiomyocytes in order to maintain the myocardial structure [9]. However, hyperactivation of CFs results in excessive ECM protein accumulation and induces cardiac fibrosis [10], eventually leading to worsening of myocardial elasticity and cardiac failure l11]. Furthermore, uncontrolled accumulation of ECM amplify the possibility of cardiac arrhythmias [12]. Thus, finding for effective medicine to delay and/or reduce myocardial fibrosis is currently a crucial area of research.

Ischemic cadiomyopathy:

Coronary artery disease(CAD) and myocardial infarction are the leading causes of ischemic cardiomyopathy. Its primarily due to cardiac muscle necrosis caused by limitations of blood flow to the cardiomyocytes due to occlusion of coronary artery. Cardiomyopathies are a group of chronic diseases which involve myocardium primarily and are not the result of congenital, valvular or coronary heart disease or hypertension or pericardial diseases.

Symptoms of cardiomyopathy includes dyspnea (orthopnea, paroxysmal nocturnal dyspnea), fatigability, pulmonary edema, features of right heart failure, and cardiac enlargement. Ischemic cardiomyopathy(CM) is the loss or weakening of cardiac myocytes secondary to ischemia. It is due to ischaemia of left ventricle (secondary to CAD or heart attacks) leading to enlargement, dilatation and weakening of left ventricle compromising heart's capacity to pump blood. If effective treatment is not provided timely, the disease will be progressively aggravated, leading to a sharp decline in myocardial contractility and cardiac failure that can even result in death of patients. At present, we do not have any specific treatment for dilated cardiomyopathy with cardiac failure, and the clinical mortality rate is relatively high. Therefore, it is still an important task to actively carry out research on the etiology and management of heart failure caused by dilated cardiomyopathy at present and from now on.

Mongolian new medicine-ii:

Mongolian new medicine-II is being traditionally used in Mongolian medicine for prevention and treatment of cardiomyopathy induced by cardiac ischaemia. At Inner Mongolia University for the Nationalities

affiliated hospital, Tongliao city, a study was conducted in 2016 to note the effects of new Mongolian medicine-II on cardiac functions, endoplasmic reticulum stress and apoptosis in congestive cardiac failure in rats with dilated cardiomyopathy. The primary action of the drug is reduction in expressions of endoplasmic reticulum chaperone GRP78, GRP94, pro-apoptotic factor CHOP and caspase-3.

During the study, thirty SD rats were randomly divided into 3 groups(n=30): control group, dilated cardiomyopathy group and Mongolian new medicine-II group. During the study, intraperitoneal injection of Adriamycin 2mg/kg body weight, once a week for 4 weeks was given to induce dilated cardiomyopathy. Similarly, in Mongolian new medicine-II group, Mongolian new medicine-II (30mg/kg/day was given orally along with similar doses of Adriamycin). 8 weeks later, cardiac functions of rats were measured using high frequency echocardiography, and then they were killed. The morphological changes of myocardial tissues were studied using HE staining, VG staining and electron microscope. The myocardial apoptosis was identified using TUNEL method and the expressions of ER chaperone GRP78, GRP94, pro-apoptotic factor CHOP and caspace-3 were observed by Western blot [13].

Flavonoids of propolis is an important ingredient of Mongolian new medicine-II. Propolis is believed to have various beneficial impacts in human beings including antiatherosclerosis [14], antioxidative stress and antihypertensive [15]. A study showed that flavonoids of propolis can inhibit Adriamycin-induced cardiomyocyte apoptosis in rats suffering from chronic heart failure, and significantly improve heart functions in rats having heart failure. Experiments and clinical trials have shown that apoptosis intervention is an effective new way to prevent and treat heart failure. The mechanism of apoptosis is complex. It is reported that endoplasmic reticulum stress-mediated apoptosis is a new signal transduction pathway of apoptosis. When the homeostasis of endoplasmic reticulum is unbalanced, the function of the correctly folded proteins in the endoplasmic reticulum is abnormal, which can lead to the abnormal accumulation of the misfolded proteins in the endoplasmic reticulum. At the same time, the secretion of the stress proteins in the endoplasmic reticulum is increased, and the misfolded proteins are recognized and degraded by proteasomes. These processes are endoplasmic reticulum stress (ERS). After ERS, ER alleviates ERS by up-regulating the expression of chaperone protein GRP78 and GRP94, inhibiting protein synthesis, accelerating misfolding and unfolding protein degradation. However, persistent or severe ERS triggers apoptotic signals and induces the expression and activation of apoptotic factors such as CHOP and caspase- 3.

The results were very convincing which are presented below.

Compared with the cardiomyopathy group, the cardiac functions (both systolic and diastolic) were significantly improved in new Mongolian medicine-II group evidenced by decrease in left ventricular contraction diameter(LVIDs), and left ventricular end-diastolic diameter(LVIDd), and rise in left ventricular shortening fraction(FS) and ejection fraction(EF). The hemodynamic parameters of rats were also improved significantly in Mongolian new medicine-II group. Compared with dilated cardiomyopathy group, the apoptosis myocardial cells were decreased. Furthermore, the expressions of endoplasmic reticulum chaperone GRP78, GRP94, pro-apoptotic factor CHOP and caspase-3 were decreased in Mongolian new medicine-II group [13].

The pathophysiology of ventricular remodeling was well-established by the Pfeffer and Pfeffer during experimental study with rats where it was concluded that mortality in rats was highly co-related to the extent of cardiac dilatation and reduced EF [16,17]. In the study, they also found that rats treated with angiotensin converting enzyme(ACE) inhibitors prevents reverse cardiac remodeling and also slows down remodeling with better prognosis. Later, Pfeffer also conducted the SAVE study in which it was concluded that remodeling remodeling also occurs in human heart and treatment with ACE inhibitors has beneficial role on adverse remodeling. Patients diagnosed with MI and EF less than 40% treated with captopril showed about 40% decrease in cardiovascular adverse effects [18]. Thus, it we can conclude that Mongolian new medicine-II would be a highly effective modality of treatment to prevent and treat adverse cardiac remodeling with even better outcomes. Limited research in humans is the only major limitations for its widespread use in modern medicine.

CONCLUSION

Researches and study of Mongolian new medicine-II in human is very limited, however it is widely used with great success in Mongolian medicine. In this review article, we tried to show the positive effects of Mongolian new medicine-II in post- PCI patients with AMI on cardiac functions. The Mongolian new-II drug can prove to be very valuable medicine in the prevention and treatment of dilated cardiomyopathy caused by ischaemia in patients with myocardial infarction. Thus, it will serve to reduce the morbidity and mortality in patients following per-cutaneous intervention with AMI by preventing adverse cardiac remodeling and improving hemodynamic parameters.

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