ASSESSING THE EFFICACY OF DANSHENFORM COMPOUND IN PATIENTS WITH STABLE ANGINA PECTORIS

Mahmood ul Hassan[1], Saqib Qureshi[2], Chiragh Hussain[3], Adnan Mahmood Gul[4], Mohammad Hafizullah[5]

ABSTRACT

***Objective**: To assess the efficacy of danshenform compound in patient with angina pectoris already on optimal dose of anti anginal therapy assessed by exercise tolerance test.*

***Methodology**: Thirty eight patients with stable angina were included in the study. Patients were exercised on treadmill according to Bruce protocol at baseline and one week later. At second week, Danshenform compound 500 mg was prescribed bid for four weeks. At the end of 4 weeks, exercise tolerance test was performed. Duration and number of anginal episodes before and at the end of 4th week recorded. Total exercise time, onset of chest pain during exercise, onset of ST segments depression before and after treatment with Danshenform compound was recorded.*

***Results**: The number of anginal episodes after 4 weeks treatment with danshenform was reduced significantly from 4.2±2.4 to 1.4±1.6/week (p=0.001). Time of onset of chest pain improved from 4.63±2.4 to 5.4±3.7 minutes (p=0.35) on exercise tolerance test. Duration of exercise increased from 6.52±1.9 minutes to 8.32±2.3 (p=0.001).Time of onset of ST depression increased from 5.8±1.7 to 7.7+1.6 minutes (p=0.001) on stress test. Anginal class improved significantly after 4 weeks of treatment with danshenform compound (p=0.001) with no significant effect on resting heart rate (p=0.58) and systolic blood pressure (p=0.07) respectively.*

***Conclusion**: Danshenform compound is useful in reducing anginal episodes, increasing exercise duration, improving functional anginal class, delaying the onset of ST depression on exercise tolerance test in patient with ischemic heart disease.*

***Keywords**: Exercise Tolerance Test, Angina, Danshenform compound.*

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INTRODUCTION

Coronary Artery Disease (CAD) is one of the leading causes of morbidity and mortality in developing world[1]. The exact mechanism for atherogenesis is still not clear. Both traditional and novel risk factors have been found. It is believed that atherogenesis is caused by various reasons and the result of reciprocity of multiple factors and multiple cell components[2]. It is obvious that CAD involves complex, chronic and intractable pathological changes that involve many factors, various systems and different kinds of cells, which may act either independently or jointly. Ischemia exerts multiple insults in microcirculation frequently accompanied by endothelial cell injury, enhanced adhesion of leukocytes, macromolecules efflux, production of oxygen free radicals and mast cell degran-ulation[3].

Researcher and comprehensive clinical applications have demonstrated the beneficial action of pharmacological agent Danshen. Danshen is widely used in China as anti anginal medicine with excellent results. Danshen exerts its effects through improve metabolism of blood lipids, improve blood rheology, reduce viscosity, improve microcirculation, inhibit platelet aggregation and improve activity of fibrinolysis[4-6].

The objective of the present study was to assess the efficacy of danshenform compound in reducing anginal episodes in patients with stable angina pectoris already taking optimal anti anginal medications.

[1-5] Department of Cardiology, Lady Reading Hospital, Peshawar - Pakistan

Address for Correspondence:
Dr. Mahmood ul Hassan,
Department of Cardiology,
Lady Reading Hospital, Peshawar - Pakistan
E-mail: mahmoodlrh@yahoo.com

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METHODOLOGY

Forty patients who were known cases of coronary disease with the stable angina were included in the study and already taking optimum doses of anti anginal medication. Two patients were excluded from the study because they lost follow up. The exact data of 38 patients was available for analysis.

Angina was defined as pressure, burning retrosternally precipitated by exercise or emotion lasting 2-10 minutes[7]. Old myocardial infaction was defined documented from hospital discharge summary or the presence of Q waves on conventional ECG[8]. Diabetes mellitus was defined as already documented from patient record or already taking oral hypoglycemic agents.

Study was conducted in Cardiology department Lady Reading Hospital and Hayat Abad Medical complex Peshawar Pakistan. Danshen is freely available in Pakistan and is being used through out the country. Approval of the study was taken from the Institutional Review and Ethics Board, Postgraduate Medical Institute, Peshawar. Informed consent was taken, explaining purpose of the study. Patients were exercised on treadmill according to Bruce protocol as baseline and one week later. After second exercise test Danshenform compound 500 mg was given bid for four weeks. At the end of 4 weeks again exercise tolerance test was performed. ST depression of 80 m second after j point in three consecutive beat with stable baseline was considered to be a positive for ischemia on ETT[9]. Severity of angina was assessed by duration and number of anginal episodes before and at the end of 4th week were recorded. Severity of angina on ETT was assessed by time of onset of chest pain during exercise, time of onset of ST segments depression before and after treatment with Danshenform compound recorded. Baseline status of the subjects is given in Table 1.

Statistical Analysis

Mean and one SD for continuous variable calculated. To know the level of significance affected by the treatment Paired t- test was applied for continuous variables. P value of 0.05 considered significant. SPSS version 10 was used for statistical analysis.

RESULTS

Total number of the patients was forty. Two patients lost follow up. The mean age of the patient studied was 46 $\pm$ 8.7 years. Male were 26(68.4 %). Female were 12(31.6 %). All patients were already on anti anginal therapy like aspirin, beta blockers, lipid lowering, nitrates, ACE inhibitors and clopidogrel. History of previous myocardial infarction was present in 6 (15.8%). Twelve patients were hypertensive and 2 were suffering from diabetes mellitus. The total duration of angina was 8.05 $\pm$ 7.7 months. The total duration of angina was 8.05 $\pm$ 7.7 months. The total duration of anti anginal medication was 7.95 $\pm$ 7.7 months (Table 1).

The number of anginal episodes after 4 weeks treatment with danshenform was reduced significantly from 4.2 $\pm$ 2.4 to 1.4 $\pm$ 1.6 / week.(p=0.001). Time of onset of chest pain improved from 4.63 $\pm$ 2.4 to 5.4 $\pm$ 3.7 minutes (p= 0.35) on exercise tolerance test. Duration of exercise increased from 6.52 $\pm$ 1.9 minutes to 8.32 $\pm$ 2.3 (p= 0.001).Time of onset of ST depression increased from 5.8 $\pm$ 1.7 to 7.7 + 1.6 minutes (p= 0.001) on stress test. Numbers of anginal episodes improved significantly after 4 weeks of treatment with danshenform compound (4.26$\pm$ 2.42 vs. 1.47$\pm$ 1.64, P= 0.001). No significant effect was noted on resting heart rate (p= 0.58) and systolic blood pressure (p= 0.07).Diastolic blood pressure dropped significantly after 4 weeks of treatment with danshenform compound (87.63 $\pm$ 8.55 vs. 83.68 + 7.60, P=0.002). In our study no side effect was recorded in any patient (Table 2).

Table 1: Baseline Characteristics of the Respondents

Total No	38
Male	26 (68.4%)
Female	12 (31.6%)
Age (years)	46.74 $\pm$ 8.73
Heart rate	77.37 $\pm$ 15.86
old Myocardial infarction	6 (15.8%)
Hypertension	12(31.6%)
Diabetes Mellitus	2(5.3%)

Table 2: Comparison of Variable Before and After 4 Weeks of Treatment

Variables	Before Treatment	After Treatment	p-Value
Anginal episodes	4.26± 2.42	1.47± 1.64	0.001
Onset of chest pain	4.63± 2.40	5.47 ± 3.70	0.352
Exercise duration	6.52 ± 1.93	8.32 ± 2.33	0.001
Onset of ST depression	5.85 ± 1.74	7.71± 1.68	0.001
Heart rate	76.11 ± 13.30	77.37 ± 15.86	058
Systolic BP	134.74 ± 12.86	122.79 ± 29.15	0.07
Diastolic BP	87.63 ± 8.55	83.68 + 7.60	0.002

DISCUSSION

Danshen, the dried root of Salvia miltiorrhiza is commonly used as traditional Chinese medicine for improving circulation and blood flow. In addition, it has been used for the treatment of cardiovascular disease such as coronary heart disease, hyperlipidemia, and cerebrovascular disease[10-12]. In the United States and European countries, danshen products can be obtained in herbal shops. The greatest use of Danshen is in the china, which has a market exceeding US$120 million in 2002[13].

In our study after four weeks of therapy with Danshenform compound along with already patient on anti anginal therapy has resulted in significant Improvement in reliving anginal symptoms and improving exercise time significantly. It has also resulted in reducing anginal episode per week. It has significantly resulted in delaying the onset of ST segment depression on ETT. It has also resulted in delaying the onset of chest pain on ETT but not statistically significant after weeks of Danshen therapy. No side effect was reported after 4 weeks of therapy with Danshenform compound 500 mg twice daily. We use anginal symptoms and ETT to asses the Danshenform compound in our trial which was used in different trials as efficacy marker. There are numerous clinical trials on Danshen products for the treatment of angina pectoris. The duration of the Danshen therapy lasting from 4 weeks to 2 months in some trials. All patients were with stable angina. These were randomized controlled trials. There end point was clinical and ECG efficacy. Results showed significant improvement in anginal symptoms and improvement in ECG changes[13-22]. Our study has similar design and similar result although all patients in our study were already on anti anginal medication and they also received Danshen compound which is real life medication scenario. In meta analysis of ECG test suggest that treatment with Danshen significant effect on improvement of ECG compared with nitrates (P<0.00001, RR=1.39,95% CI[1.28,1.50] [23]. The proposed mechanism of Danshen has been attributed to dilate coronary artery, inhibit platelet aggregation, improve microcirculation, and protect myocardium from reperfusion injury of the ischemic heart. The mechanism for some of its observed activity may be related to inhibition of Ca^{++} aggregation in cardiac muscle cells and prevention Ca^{++} overload. In addition Danshen has been found to be able to scavenge oxygen –free radicals. Inhibit myocardial cell apoptosis and protect the endothelial cells against homcysteinemia[4, 5, 24-28].

Limitation of the study:

The limitations of the study are the small number of patient and short follow up. There were no end points like mortality, quality of life, incidence of myocardial infarction. Large randomized, double blind, controlled trials are required.

CONCLUSION

Danshenform compound is effective agent in reducing anginal episodes, increasing exercise duration, improving functional anginal class, delaying the onset of ST depression on exercise tolerance test in patient with stable angina.

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None Declared

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CONTRIBUTORS

MUH, SQ, CH, AMG and HU contributed equally to the research and preparation of the manuscript. All authors listed contributed signi?cantly to the research that resulted in the submitted manuscript.