Efficacy of Danshen Chuanxiongqin Injection Combined with Standard Western Therapy in Acute Coronary Syndrome: A Prospective Cohort Study

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Abstract: This prospective cohort study evaluates the clinical efficacy of Danshen Chuanxiongqin (DSCXQ) injection, a Traditional Chinese Medicine (TCM) when used in conjunction with standard Western medical therapy in patients with Acute Coronary Syndrome (ACS). Conducted at Jinan Fuyuan Rehabilitation Hospital, China, the study involved 140 ACS patients randomized into two groups: treatment (n=70) receiving DSCXQ and standard therapy, and control (n=70) receiving only standard therapy. The primary outcomes measured were changes in serum levels of D-Dimer, BNP, Troponin, and cardiac ejection fraction (EF). The results revealed significant improvements in all primary biomarkers and EF in the treatment group compared to controls, with notable enhancements by day 5. However, elevated liver and kidney function markers in the treatment group suggest a need for careful monitoring. This study demonstrates the potential of integrating DSCXQ with conventional treatments to improve ACS management, although further research is necessary to establish long-term safety and efficacy.

1. Introduction

Acute coronary syndrome (ACS) is a series of acute coronary thrombosis, typically resulting from the rupture of atherosclerotic plaque, which may lead to myocardial ischemia or infarction. This encompasses unstable angina pectoris, non-ST elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI). ACS represents one of the most significant causes of cardiovascular disease-related mortality and morbidity globally. Although substantial progress has been made in the diagnosis and treatment of acute coronary syndromes, cardiovascular disease remains the leading cause of death globally, with nearly half of these deaths due to ischaemic heart disease.[1] In recent years, the incidence of ACS in our country has been high, with a rising trend year on year. The 2019 China Cardiovascular Health and Disease Report indicates that cardiovascular disease is the leading cause of death in both urban and rural China. In 2020, the mortality rate of coronary heart disease among urban and rural residents in China was 131.40 per 100,000. The mortality rate of acute myocardial infarction (AMI) was 69.47 per 100,000. Acute coronary syndrome (ACS) is characterized by a rapid onset, high incidence, high mortality and high recurrence rate, which has a significant impact on people's quality of life and standard of living. Although Western medicine provides effective acute intervention and drug therapy, there are still residual risks, including recurrent ischemic events and heart failure, due to lack of specificity, drug tolerance or adverse reactions in some patients, possible complications of interventional surgery, and poor patient compliance. Traditional Chinese Medicine (TCM) employs a tailored approach, selecting herbs with properties believed to support heart function, improve blood circulation, and reduce blood stasis. This is achieved through the holistic concept and the thinking concept of the Yin and Yang balance, addressing the root cause of heart imbalance. This is considered a beneficial supplement to standard treatment, addressing the aforementioned risks.[2]

One of the commonly used TCMs to treat patients with acute coronary syndrome is Danshen Chuanxiongqin (DSCXQ). DSCXQ injection is a TCM preparation composed of the extract of Salvia miltiorrhiza Bunge and Conioselinum anthriscoides ‘Chuanxiong’. It is listed as a recommended therapy for the treatment of cerebral infarction and coronary heart disease [3]. Studies have shown that DSCXQ could inhibit the production of malondialdehyde (MDA), effectively eliminating oxygen-free radicals in rats and increasing the resistance of vascular endothelium to thrombosis [4,5,6]. Phenolic acids are the main active components extracted from Danshen[7]. The effects of phenolic acid in Danshen are antioxidant, anticoagulant, anti-thrombotic and cell protection[8]. Danshen was also shown in a systematic review to be an adjuvant treatment of Western medicine for unstable angina where it was associated with significant improvement in the overall clinical outcome with significant reversal of T-wave inversion and improvement in blood lipid levels [9]. This study aims to assess the impact

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of DSCXQ injection on clinical outcomes in ACS patients when used alongside standard Western treatments.

2. Methods

2.1 Study Design and Population

This prospective cohort study aimed to observe and analyze the outcomes of two groups of patients over time. It was conducted at Fuyuan Rehabilitation Hospital of Jinan City between August 2022 and February 2023, with 140 patients diagnosed with acute coronary syndrome (ACS) participating. Patients were randomly assigned to either a treatment group (n=70) or a control group (n=70) using a simple randomization technique. This design ensures an unbiased comparison between the two groups. For instance, patient 1 is assigned to the treatment group, followed by patient 2 in the control group. The treatment group receives DSCXQ in addition to standard care, while the control group receives only standard care.

The sample size of 140 was determined through calculations that factored in an estimated population proportion of 10% out of a total of 72,000 potential patients. This calculation was based on the population size of Jinan City (7 million) and the number of patients diagnosed with ACS per annum in the city. The confidence interval was set at 95%, with a margin of error of 5%, and a standard deviation of 0.5. This sample size was validated against similar research in the field, notably the study conducted by Wu et al. (2009) on the effects of danshen ligustrazin in ACS patients which studied 98 patients[10].

2.2 Intervention

The treatment group received standard Western medicine treatment protocols for ACS, augmented with 5ml of intravenous DSCXQ diluted in 250ml of normal saline administered over 5 days. Conversely, the control group was treated with the standard Western medicine protocol alone, including dual antiplatelets, anticoagulants, statins, and blood pressure medication tailored to the patient's blood pressure and kidney function.

Key baseline markers such as serum D. Dimer, BNP, and Troponin levels were measured before the treatment commenced, and subsequently on day 2 and day 5. Routine Electrocardiograms (ECG) and Echocardiograms were performed at admission and on day 5 to assess cardiac function, specifically ejection fraction. Secondary data, including serum urea, creatinine (BUN), alanine transaminase (ALT), aspartate transaminase (AST), and vital signs (blood pressure, heart rate, and respiratory rate), were collected from case notes on day one and day five. All patients were required to sign a consent form following a thorough explanation and consenting process. Ethical approval from the hospital ethical committee was also obtained.

3. Outcome Measures

Primary outcomes were serum levels of D-Dimer, BNP, and Troponin, along with cardiac ejection fraction, measured at baseline, day 2, and day 5. Secondary outcomes included monitoring liver and kidney function markers (ALT, AST, and Creatinine).

D-dimer (D-dimer) is a specific degradation product of cross-linked proteins, and the fibrinolytic system is a very important anticoagulant system in the human body. D-dimer is an ideal indicator when reflecting the thrombin and fibrinolytic activity in the body. Elevated D-dimer indicates increased secondary fibrinolytic activity in the body, which is an important sign of intravascular hypercoagulability and thrombosis. The more acute the patient's condition, the higher the plasma D-dimer value, which can be used to measure the severity of ACS patients, and the D-dimer value is useful in the clinical classification of acute coronary syndromes.

B-type natriuretic peptide (BNP), also known as brain natriuretic peptide, N-terminal natriuretic peptide, and B-type natriuretic peptide, is a hormone secreted by the ventricles in response to overstretching of cardiac myocytes. Its function is to lower blood pressure and reduce cardiac workload by promoting vasodilation and increasing sodium and water excretion. In patients with ACS, hypervolemia, pulmonary hypertension, right ventricular hypertrophy, enlargement, and other factors promote the synthesis and secretion of BNP by ventricular myocytes. BNP concentrations increase within 24 hours of the onset of an acute coronary syndrome (ACS) and then plateau, whereas patients with massive infarctions may experience a second peak after approximately five days, reflecting the process of left ventricular (LV) remodelling . It is an important marker for predicting heart failure and mortality in patients with acute coronary syndrome.[11] Continuous monitoring of BNP levels from day one to day seven has been shown to be effective in identifying patients at increased risk of LV dysfunction, heart failure and mortality. The evidence from these studies supports the conclusion that assessment of BNP levels provides important and unique prognostic insights, making it an important tool in the diagnosis and management of patients with acute coronary syndromes.

Troponins Cardiac troponin I and cardiac troponin T are the primary and preferred biomarkers for the diagnosis of acute coronary syndrome (ACS). Their high specificity and sensitivity in detecting myocardial injury, make them indispensable tests for emergency patients presenting with symptoms of acute coronary syndrome. Troponin is a key protein complex integral to the contractility of the heart and is unique to heart tissue. In patients with acute coronary syndrome (ACS), even elevated low levels of cardiac troponin T or I were associated with a higher risk of death and recurrent ischemic events compared to patients with troponin levels below the appropriate decision limit.[12] Detection of troponin in the blood signals myocardial damage, making it an indispensable biomarker for the diagnosis of cardiac events, including acute coronary syndromes.

Ejection fraction (EF) is usually expressed as a percentage, reflecting the amount of blood expelled from

the left ventricle during each heartbeat. The percentage of left ventricular output is an important predictor of severity and survival in patients diagnosed with acute coronary syndrome (ACS) and thus may be the most critical indicator The role of ejection fraction in monitoring ACS provides insight into the efficiency of the heart and its trajectory of recovery after an ACS event. Ejection fraction, the percentage of blood pumped by the left ventricle per heartbeat, is the focal point for clinicians to measure the immediate and long-term effects of ACS on cardiac function.

4. Statistical Analysis

The statistical analysis for the study was conducted using the SPSS version 26.0. The Mann-Whitney U test was used to compare baseline characteristics and key outcome variables between the treatment and control groups. Additionally, the chi-square test was utilized to assess categorical data, such as the distribution of gender and other nominal variables across the two groups. Repeated measures ANOVA was employed to analyse changes in serum biomarkers (D.Dimer, BNP, and Troponin) and cardiac ejection fraction over multiple time points (baseline, day 2, and day 5). The Wilcoxon signed-rank test was also used to compare the changes in these parameters within each group separately across different times. A p-value of less than 0.05 was considered statistically significant.

5. Results

A comparison of age, gender, blood pressure, and urea nitrogen between the two groups of patients revealed no statistically significant differences ($p > 0.05$). However, a comparison of creatinine (CREAT), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) levels between the two groups revealed that patients in the treatment group exhibited higher levels than those in the control group, with the differences being statistically significant ($p < 0.05$). Regarding ejection fraction (EF), the Mann-Whitney U test was employed to assess the ejection fraction (EF) of the two groups of patients. The results demonstrated that on the first day of treatment, the ejection fraction (EF) of the treatment group was significantly greater than that of the control group, with a statistically significant difference ($p < 0.05$). However, on day 5 of treatment, there was no significant difference in EF measurements between the two groups ($p>0.05$). Furthermore, the Wilcoxon signed rank test performed within each group indicated that there was no significant difference in EF measurements between the treatment and control groups on the first day of treatment ($p>0.05$). However, on day 5 of treatment, the ejection fraction (EF) of the control group decreased significantly ($p < 0.05$) compared to day 1. On the first day of the intervention, our study observed a statistically significant ($p < 0.05$) increase in the ejection fraction (EF) values in the treatment group compared to the conventional (control) group, which suggests that the treatment had a direct positive effect on cardiac function. However, by day 5 of the treatment, the difference in EF values between the two groups decreased to non-statistically significant levels ($p>0.05$), indicating a convergence of cardiac performance indicators. The lack of sustained improvement in ejection fraction in both groups throughout the study period implies that while treatment may initially enhance cardiac function, the effect is not sustained or canceled out over time.Refer to Table 1 for more detailed information.

Table 1. General data comparison between the two groups of patients

Parameters		Treatment group(n=70)	Control group(n=70)	p-value
Age, mean, (Q25, Q75)		53.51 (44.51,60.25)	54.00(47.75,61.25)	0.286
Gender, mean (%)	Male	44 (62.86%)	26(37.14%)	1.000
	Female	44 (62.86%)	26(37.14%)	
BP,mean,(Q25,Q75)	Sytolic	140.00 (131.50,150.00)	137.00(132.00,146.50)	0.334
	Diastolic	90.00 (83.75,95.50)	87.00(80.75,95.00)	0.057
BUN mean,(Q25,Q75)		4.97 (4.54,5.28)	4.97(4.46,5.28)	0.696
CREAT mean,(Q25,Q75)		44.00 (39.00,61.00)	40.00(37.25,60.25)	0.049
ALT mean,(Q25,Q75)		21.50 (16.75,35.00)	15.00(10.00,39.00)	0.026
AST mean,(Q25,Q75)		22.00 (15.00,28.00)	14.50(12.00,22.50)	0.001

The measurements of Brain Natriuretic Peptide (BNP) in the two groups showed no statistically significant difference on days 1 and 2 of treatment ($p>0.05$). However, on the 5th day of treatment, the BNP values of the treatment group were significantly lower than those of the control group, with all differences being statistically significant ($p<0.05$). The Wilcoxon signed-rank test comparing BNP within each group demonstrated a decreasing trend on days 1, 2, and 5 of treatment, with statistically significant differences ($p<0.001$). This decline in BNP levels may indicate enhanced cardiac function or reduced cardiac stress in the treatment group. Over time, both groups exhibited a decreasing trend in BNP values, suggesting a potential overall improvement in cardiac function. This positive trend could be attributed to the quality of care provided, rather than solely the specific treatment under investigation. For additional details, see Table 2.

Regarding troponin (T) levels, the results revealed lower troponin levels in the treatment group compared to the control group on days 1, 2, and 5 of treatment, with all differences being statistically significant ($p<0.05$). The comparison of troponin values within each group using the Wilcoxon signed-rank test showed no statistically significant difference between days 1 and 2 of treatment ($p>0.05$). However, troponin levels were significantly lower on days 1 and 2 compared to day 5 ($p<0.001$). Troponin levels tended to decrease in the control group on

days 1, 2, and 5 of treatment, with all differences being statistically significant ($p<0.05$). The consistently lower troponin levels in the treatment group suggest a potential protective effect against cardiac injury. Although troponin levels decreased in the control group over time, the more pronounced decrease in the treatment group emphasizes the potential added benefit of the treatment. For additional details, see Table 2.

In terms of D-dimer (D) values, the results indicated that patients in the treatment group had lower D-dimer values than the control group on days 1 and 2 of treatment, with a statistically significant difference ($p<0.05$). This suggests a potentially beneficial effect of the treatment on reducing coagulant activity or thrombosis in the early stages of treatment. However, on day 5, the D-dimer values in the treatment group were not statistically significant compared to the control group ($p>0.05$). The comparison of D-dimer values within the treatment group showed no significant difference between days 1 and 2, as well as between days 2 and 5 ($p>0.05$). D-dimer values were higher on day 1 compared to day 5 in the treatment group, with all differences being statistically significant ($p<0.001$). Similarly, the control group exhibited a decreasing trend in D-dimer values on days 1, 2, and 5 of treatment, with all differences being statistically significant ($p<0.01$).For additional details, see Table 2.

The analysis of variance using repeated measures demonstrated significantly lower levels of BNP, troponin (T), and D-dimer (D) in the treatment group compared to the control group on days 1, 2, and 5 of treatment ($p<0.05$). As treatment progressed, BNP and D-dimer levels tended to decrease in both treatment and control groups, while troponin (T) levels showed a pattern of initially increasing and then decreasing. This trend was statistically significant for time, subgroup assignment, and the interaction between these factors ($p<0.05$). A combined repeated-measures ANOVA provided longitudinal analysis, highlighting significant differences between the two groups in BNP, troponin, and D-dimer levels over time. This analysis confirmed a consistent pattern of improvement in these key metrics in the treatment groups, reinforcing the potential clinical benefit of the treatment in ACS management. For additional details, see Table 2.

Table 2. Repeated measures ANOVA comparison of BNP, T, and D values between the two groups of patients (mean ± standard deviation)

Parameters	Group	Day 1	Day 2	Day 5	Time effect	
					F-value	p-value
BNP	Treatment	499.68±150.12	467.8±137.34	207.49±74.34	48.700	<0.001
	Control	507.45±163.11	501.4±162.37	488.6±344.83		
T	Treatment	0.07±0.02	0.16±0.19	0.01±0.01	16.657	<0.001
	Control	0.32±0.36	0.34±0.40	0.29±0.39		
D	Treatment	0.65±0.22	0.64±0.22	0.64±0.22	22.840	<0.001
	Control	0.85±0.42	0.80±0.36	0.67±0.22		

6. Discussion

The results of the study indicated several positive outcomes in the treatment group. Notably, there were significant improvements in serum levels of D-Dimer, B-type natriuretic peptide (BNP), and Troponin when compared to the control group, especially pronounced by day 5.[13] These biomarkers are crucial in the diagnosis and monitoring of ACS, suggesting that DSCXQ may enhance the biochemical profile of ACS patients. Furthermore, cardiac ejection fraction (EF), a critical measure of cardiac function, was initially higher in the treatment group, indicating an improvement in cardiac output[14,15]. However, this effect did not persist, as the EF levels in the treatment group aligned with those of the control group by day 5.

Despite these promising results, the study also identified several limitations. Firstly, the treatment group showed elevated levels of liver enzymes (ALT and AST) and creatinine, indicating potential liver and kidney stress, which calls for cautious monitoring of these organs in patients receiving DSCXQ. These findings suggest that while DSCXQ may improve certain biochemical markers of ACS, it could also pose risks to liver and kidney function. The unexpected findings concerning liver and kidney function markers in our study necessitate a cautious approach to TCM integration. These findings echo the concerns raised by Wang et al. who reported on the hepatotoxicity risks associated with certain herbal medicines, emphasizing the need for rigorous clinical monitoring and patient selection criteria. [16]

Additionally, the study itself had several design limitations. The sample size of 70 patients per group may not provide a broad enough basis to generalize the findings universally. Moreover, the study's duration was limited to a short-term follow-up of just five days, which does not allow for the assessment of the long-term effects and safety of DSCXQ treatment. The absence of a double-blind design could also introduce bias in outcome assessment. Furthermore, the study did not account comprehensively for potential confounding factors that might affect the results, such as concurrent medications or other treatments, nor did it evaluate the impact of the intervention on clinical symptoms, quality of life, or functional status of the patients.

These limitations underscore the need for further research with larger sample sizes, longer follow-up periods, and more rigorous study designs to fully elucidate the efficacy and safety of DSCXQ as an adjunct treatment for ACS. Such studies should aim to confirm these preliminary findings and clarify the clinical significance of DSCXQ in the broader context of ACS management.

7. Conclusion

The results of the study indicated that the treatment group, which received both standard ACS treatment and DSCXQ injections, showed significant improvements in serum levels of D-Dimer, BNP (Brain Natriuretic Peptide), and Troponin compared to the control group, which received only the standard ACS treatment. These biomarkers are critical in diagnosing and evaluating the severity of ACS, suggesting that DSCXQ could enhance the therapeutic effects of conventional treatments. Furthermore, an initial improvement in cardiac ejection fraction was observed in the treatment group, although this effect equalized with the control group by the end of the study period.

Despite these positive outcomes, the study also highlighted potential safety concerns as elevated liver and kidney function markers were observed in the treatment group, suggesting that DSCXQ may exert some strain on these organs. This finding underscores the necessity for cautious monitoring when integrating DSCXQ into standard ACS therapy.[17]

Overall, this study supports the potential benefits of integrating TCM with Western medical practices in treating ACS, indicating that DSCXQ can improve crucial clinical outcomes. However, it also calls for further research to thoroughly investigate the long-term safety and efficacy of such integrative approaches. The findings encourage a balanced view in which TCM can be seen not just as an alternative but as a complementary therapy that might offer additional benefits to conventional treatment modalities.[18] Future studies should aim to expand on these findings with larger sample sizes and longer follow-up periods to build a robust evidence base that can guide clinical practice in the integration of TCM in the treatment of ACS.

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