

# Therapeutic Effect of Nitroglycerin in Conjunction with Low Molecular Weight Heparin Sodium in Managing Angina Pectoris in Coronary Heart Disease

PENGYAN ZHAO, QIONG ZHANG\*, JING YANG AND WEI SHU

Department of Cardiovascular Medicine, Chengdu Third People's Hospital Pujiang County (Sichuan) Hospital, Chengdu, Pujiang 611630, China

## Zhao *et al.*: Nitroglycerin and Heparin Sodium in Managing Angina Pectoris

To observe the therapeutic effect of nitroglycerin in conjunction with low molecular weight heparin sodium in managing angina pectoris in individuals with coronary heart disease. Between June 2022 and June 2023, our hospital received 414 patients with angina due to coronary heart disease who were enrolled in the study. They were randomly assigned to either a control group (210 cases) or an observation group (204 cases). Aspirin and calcium channel blockers were prescribed based on individual patient evaluations to ensure optimal therapeutic outcomes. Alongside the standard treatment, the control group was subjected to nitroglycerin intravenous infusion, while the observation group received a combination therapy involving both nitroglycerin intravenous infusion and low molecular weight heparin sodium treatment subsequent to the initial treatment. The assessment of therapeutic efficacy was conducted following a 2 w course of treatment. The effectiveness of treatment in the observation group was notably higher, with a total effective rate of 90.20 %, as compared to the control groups' rate of 78.10 %, thus highlighting a statistically significant difference ( $p < 0.05$ ). In the observation group, there was a notable reduction in the duration and frequency of angina attacks, surpassing the control group with statistically significant differences ( $p < 0.05$ ). After the administration of treatment, both stroke volume and the 6 min walking distance exhibited significant increases. Of particular significance, these improvements were significantly more apparent in the observation group in comparison to the control group ( $p < 0.05$ ). The utilization of nitroglycerin in conjunction with low molecular weight heparin sodium yields significant, short-term therapeutic benefits for individuals suffering from angina pectoris associated with coronary heart disease. This combined treatment approach leads to a notable reduction in the frequency and duration of angina attacks while enhancing cardiac function.

**Key words:** Nitroglycerin, heparin sodium, coronary heart disease, angina pectoris, therapeutic effect

Coronary heart disease-related angina pectoris is defined as a clinical syndrome characterized by temporary myocardial ischemia and hypoxia triggered by either coronary artery atherosclerosis or spasms, culminating in the constriction of coronary lumen and impeded coronary blood flow<sup>[1,2]</sup>. Paroxysmal angina or sensations of chest discomfort in the sternum and precordial region represent the predominant clinical presentation<sup>[3,4]</sup>. This condition is prevalent among middle-aged and elderly populations and, if not appropriately managed, can result in acute myocardial infarction or sudden death. Currently, there has been no major breakthrough in its treatment methods, and it is associated with a high

disability and recurrence rate<sup>[5]</sup>. Nitroglycerin, which serves as a representative nitrate ester drug, has solidified its status as a classic pharmaceutical intervention in the management of angina pectoris within the realm of coronary heart disease. It proffers noteworthy benefits, such as mitigating myocardial ischemia and enhancing left ventricular function. Nonetheless, continuous administration of nitroglycerin may result in the development of tolerance, and higher doses can elicit excessive reduction in blood pressure<sup>[6,7]</sup>. Conversely, low molecular weight heparin sodium, functioning as an anticoagulant, facilitates improved coronary artery blood flow and suppresses platelet aggregation<sup>[8,9]</sup>.

---

\*Address for correspondence  
E-mail: zpy05804723@163.com

Considering that angina in coronary heart disease primarily stems from inadequate coronary blood supply<sup>[10]</sup>, the synergistic utilization of nitroglycerin and low molecular weight heparin sodium may yield enhanced therapeutic effects. Limited investigation has been conducted on the therapeutic effectiveness of nitroglycerin in conjunction with low molecular weight heparin sodium in the treatment of angina pectoris in individuals with coronary heart disease. The absence of extensive large-sample, multicenter, randomized controlled studies has created a knowledge gap concerning the therapeutic effect of combining nitroglycerin with low molecular weight heparin sodium in the management of angina pectoris among individuals with coronary heart disease. In light of this, the objective of the present study is to observe and assess the therapeutic efficacy of this combination therapy in a specific cohort of patients with coronary heart disease. The study results aim to contribute more precise and reliable evidence to inform clinical treatment approaches for individuals with coronary heart disease. Between June 2022 and June 2023, our hospital received 414 patients with angina due to coronary heart disease who were enrolled in the study. They were randomly assigned to either a control group (210 cases) or an observation group (204 cases). The control group comprised 132 male and 78 female participants, ranging in age from 53 y to 75 y, with an average age of (66.53±3.67) y. The duration of the medical condition varied from 1 y to 12 y, with an average duration of (5.93±2.28) y. Within the observation group, there were 127 male participants and 77 female participants, aged between 54 y and 75 y, with an average age of (65.68±3.53) y. The duration of the disease ranged from 1 y to 11 y, with an average duration of (6.07±2.45) y. The general characteristics exhibited no remarkable distinctions between the two groups ( $p>0.05$ ), affirming their comparability. Approval for this study was granted by the medical ethics committee of our hospital, and informed consent was obtained from the patients and their families. In this study, the inclusion criteria encompassed; confirmation of angina pectoris in coronary heart disease based on electrocardiographic examination, discerning S-T segment depression during angina attacks and presentation of symptoms, including varying degrees of throat constriction, squeezing pain, dull pain, or chest tightness. The exclusion criteria consisted of patients with coagulation disorders or inadequately managed blood pressure; patients exhibiting allergies

to the drugs employed in this study; patients diagnosed with glaucoma; patients experiencing severe hypotension and patients presenting with acute circulatory failure. Assure optimization, smoking cessation counseling, and alcohol abstinence advice, were implemented for both groups to ensure adequate physical well-being. Additionally, treatment plans encompassed the use of aspirin and calcium channel blockers, tailored to individual patient needs. Alongside standard therapies, patients in the control group were administered nitroglycerin (Beijing Yimin Pharmaceutical Co., Ltd., National Drug Approval Number H11020289). The dosage varied between 5 and 15 mg and was infused intravenously with a mixture of 250 ml of normal saline and 5 % glucose solution, at a rate of 10 to 25 drops per minute, once daily. In the observation group, the treatment plan encompassed the administration of low molecular weight heparin sodium (National Drug Approval Number H20056845, Shenzhen Tiandao Pharmaceuticals Co., Ltd) at a dose of approximately 600 U. Prior to administration, the baseline value of Activated Clotting Time (ACT) was assessed, with subsequent measurements taken every 12 h to adapt the infusion rate according to requirements, typically ranging from 1.5 to 2.0 times the standard rate<sup>[3]</sup>. Evaluation of treatment response was performed after a 2 w period of continuous therapy. A comparison was made between the two groups regarding their clinical efficacy and various indicators, such as the frequency and duration of angina attacks, ST segment depression, and cardiac function parameters (including Stroke Volume (SV) and 6 min walking distance). SV was assessed using Doppler ultrasound, while the 6 min walking distance was measured during the follow-up period<sup>[11]</sup>. The evaluation criteria for therapeutic efficacy were as follows; in significant improvement, the patient showed no clinical symptoms of angina, and the results of resting Electrocardiography (ECG) were within normal range. In effective, the number of angina attacks decreased by >50 %, and the ST segment gradually approached 0.05 mV during the resting ECG, but the criteria for significant improvement were not met. In ineffective, there were no noticeable changes in the patient's clinical symptoms, and the frequency of angina attacks and resting ECG did not show significant changes. The overall effective rate was calculated as (significant improvement+effective cases) divided by the total number of cases, multiplied by 100 %. Statistical

Package for the Social Sciences (SPSS) 25.0 will be employed to perform the statistical analysis in this research. Continuous variables will be presented as mean and standard deviations, and their analysis will be conducted using t-tests. Categorical variables, on the other hand, will be expressed as frequencies and percentages n (%) and assessed using Chi-square ( $\chi^2$ ) tests. To establish statistical significance, a threshold of  $p < 0.05$  will be utilized. Following the completion of the treatment, the experimental group demonstrated a noteworthy overall effective rate of 90.20 %, surpassing the control groups' rate of 78.10 % with statistical significance ( $p < 0.05$ ) as shown in Table 1. Following the administration of treatment, the observation group exhibited noteworthy reductions in the duration and frequency of angina attacks when compared to the control group, with both disparities reaching statistical significance ( $p < 0.05$ ) as shown in Table 2. Post-treatment, notable enhancements were observed in both SV and the 6 min walking distance, surpassing the baseline measurements. Furthermore, these improvements were substantially greater in the observation group than in the control group, reaching

statistical significance ( $p < 0.05$ ), as shown in Table 3. The pathophysiology underlying angina pectoris in coronary heart disease is attributed to the interplay of factors such as atherosclerotic plaque development, heightened platelet reactivity, and coronary artery constriction. Nitroglycerin, as a representative drug of nitrate esters, has become a classic medication for treating angina pectoris in coronary heart disease and improving myocardial ischemia and left ventricular function<sup>[12]</sup>. Through intravenous infusion, it can relax coronary vessels, relieve vasospasm, improve myocardial blood supply, and when combined with antithrombotic drugs, it can effectively alleviate and prevent angina, and minimize the occurrence of myocardial infarction<sup>[13]</sup>. Low molecular weight heparin sodium is a degradation product of conventional heparin with a lower molecular weight. It has antithrombotic and anticoagulant effects<sup>[14,15]</sup>. Compared to conventional heparin, low molecular weight heparin sodium has a lower relative molecular weight and exhibits activation of the fibrinolytic system, effectively inhibiting the clotting of thrombin with platelets<sup>[16]</sup>.

**TABLE 1: CURATIVE EFFECT**

Group (n)	Marked improvement	Improvement	Ineffectiveness	Overall effective rate
Observation (204)	153 (75.00)	31 (10.29)	20 (9.80)	184 (90.20)
Control (210)	126 (60.00)	38 (18.10)	46 (21.90)	164 (78.10)
$\chi^2$				11.307
p				0.001

**TABLE 2: INDICATORS OF ANGINA PECTORIS**

Group (n)	Duration of angina attacks		Number of episodes (times/day)	
	Before	After	Before	After
Observation (204)	9.04±1.72	2.07±0.86*	4.69±0.56	2.04±0.41*
Control (210)	8.57±2.28	2.64±0.99*	4.78±0.58	2.62±0.57*
t	-0.664	7.366	0.647	12.386
p	0.507	0.000	0.743	0.000

Note: (\*): Indicates significant difference after treatment compared with before treatment

**TABLE 3: CARDIAC FUNCTION**

Group (n)	SV (ml)		6 min walking distance (m)	
	Before	After	Before	After
Observation (204)	47.22±4.74	54.51±5.10*	267.19±37.32	435.41±52.55*
Control (210)	47.49±5.01	50.85±5.13*	265.60±41.84	365.01±52.72*
t	0.255	-7.460	-0.456	-13.685
p	0.798	0.000	0.649	0.000

Note: (\*): Indicates significant difference after treatment compared with before treatment

This study aimed to evaluate the therapeutic impact of the combined treatment approach, which includes nitroglycerin in conjunction with low molecular weight heparin sodium, for patients with angina pectoris in coronary heart disease. Supplementary to the routine treatment, the observation group was administered a combination therapy consisting of nitroglycerin and low molecular weight heparin sodium, whereas the control group received nitroglycerin alone. Following a 2 w treatment period, the observation group achieved a notable overall effective rate of 90.20 %, surpassing the control group's rate of 78.10 % with statistical significance. The observation group also exhibited shorter durations and lower frequencies of angina attacks compared to the control group, both of which demonstrated statistical significance ( $p < 0.05$ ). Furthermore, significant enhancements were witnessed in cardiac function indicators, including SV and the distance achieved during the 6 min walking test, within the observation group. Notably, these improvements exceeded those observed in the control group ( $p < 0.05$ ). The results support the notion that the combined treatment approach involving nitroglycerin and low molecular weight heparin sodium surpasses the efficacy of nitroglycerin alone. Nitroglycerin acts by alleviating vasospasm, dilating coronary blood vessels, and improving left ventricular function and myocardial ischemia, thus preventing myocardial infarction and relieving angina<sup>[17]</sup>. On the other hand, low molecular weight heparin sodium, as an anticoagulant, catalyzes the reaction of antithrombin, inhibits platelet adhesion and aggregation, and reduces blood viscosity. It protects ischemic myocardial cells, reducing ischemic injury and promoting coronary endocardial blood supply, thereby preventing thrombosis formation and development. The combination of these two drugs can synergistically enhance therapeutic efficacy and improve the frequency and duration of angina attacks. It should be noted that, although this study shows a significant advantage of combining nitroglycerin with low molecular weight heparin sodium in the treatment of angina pectoris in coronary heart disease, there are still some limitations. First, this study utilized a retrospective observational design, which may introduce some bias. Second, the sample size was relatively small, and further large-scale, multicenter, randomized controlled studies are needed to validate the reliability and generalizability of the results. Lastly, long-term follow-up is necessary to assess

the impact of combination therapy on cardiovascular events in patients with coronary heart disease. To conclude, the combination of nitroglycerin and low molecular weight heparin sodium has exhibited noteworthy therapeutic effectiveness for the short-term management of angina pectoris in individuals with coronary heart disease. This combined treatment approach significantly alleviates the frequency and duration of angina attacks and yields improvements in cardiac function. Nevertheless, additional clinical research is warranted to validate the long-term efficacy and safety profile of this treatment regimen, ultimately offering more efficacious and dependable options for the management of angina pectoris in coronary heart disease.

#### Conflict of interests:

The authors declared no conflict of interests.

#### REFERENCES

1. Wang Z, Fan J. Modern research progress in traditional Chinese medicine for coronary heart disease and angina pectoris. *J Integr Tradit Chin Western Med Cardiovasc Dis* 2020;18(24):4.
2. Luo Y, Zhu C. Observations on the therapeutic effect of Shuxuetong combined with Tigrel in treating angina pectoris after myocardial infarction. *J Integr Tradit Chin Western Med Cardiovasc Dis* 2018;5:16-8.
3. Li J. Clinical treatment analysis of angina pectoris caused by coronary atherosclerotic heart disease. *Mod Pract Med* 2013;25(2):186-7.
4. Yin C, Wei J, Hao H. Clinical characteristics, diagnostic evaluation, management status, and prognosis analysis of variant angina pectoris. *Chin J Circ* 2011;26(5):359-62.
5. Zhang L, Su X. Research progress in drug treatment of angina pectoris. *Chin Pharm J* 2008;19(23):3.
6. Wang Y. Clinical observation of nitroglycerin combined with low molecular weight heparin sodium in the treatment of coronary heart disease and angina pectoris. *Youjiang Med J* 2012;40(5):2-5.
7. Hu S, Xu T. Clinical efficacy analysis of low molecular weight heparin combined with nitroglycerin in the treatment of unstable angina pectoris. *J Math Med* 2011;24(6):3-7.
8. Tong Y. Clinical efficacy analysis of nitroglycerin+valsartan+low-molecular-weight heparin sodium in the treatment of coronary heart disease and heart failure. *Chin J Mod Drug Appl* 2022;16(11):3.
9. Qi M. Observation on the efficacy of simvastatin combined with low molecular weight heparin sodium in the treatment of coronary heart disease and angina pectoris. *Chin Commun Phys* 2020;36(20):2.
10. Li D, Wang T, Zhang H. Systematic evaluation of the efficacy and safety of Dazhu hongjingtian injection in the treatment of coronary heart disease and angina pectoris. *Chin J Gen Med* 2021;24(26):10.
11. Tan J, Zhong S, Zhang Q. Exploring the mechanism of action of Xuefu Zhuyu Tang in treating coronary heart disease with blood stasis syndrome based on mitochondrial energy metabolism. *Shi Zhen Guoyi Guoyao* 2023;34(2):4-8.

12. Chen Y. The pharmaceutical application value of nitrates in the treatment of cardiovascular diseases. *Chin J Sci Technol Database Med Health* 2020;5:2-4.
13. Sun X. Analysis of the efficacy of nitroglycerin combined with atorvastatin in the treatment of coronary heart disease and angina pectoris. *Chin J Mod Drug Appl* 2021;15(20):98-100.
14. Xiong C. Analysis of the efficacy and adverse reaction rate of nitroglycerin and low molecular weight heparin sodium in the treatment of coronary heart disease and angina pectoris. *Health Care Guidelines* 2019;12:4-7.
15. Xiang Q. Clinical efficacy and nursing experience of using low molecular weight heparin sodium in unstable angina. *Health Care Guidelines* 2020;33:141-46.
16. Teng W, Tan Xi. Comparison of clinical applications of low molecular weight heparin and heparin sodium. *Med J* 2007;26(1):4-9.
17. Lin L. Effect analysis of low molecular weight heparin combined with isosorbide mononitrate in the treatment of acute exacerbation of pulmonary heart disease. *Chin Med Guidelines* 2018;16(7):2.

---

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms

**This article was originally published in a special issue,  
"Recent Progression in Pharmacological and Health Sciences"  
Indian J Pharm Sci 2024;86(2) Spl Issue "264-268"**