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Clinical study of Huxinkang tablet in treating unstable angina pectoris

Wang Guoqian¹, Yu Zhengke², Cheng Zhihong², Xie hongtu³

¹Graduate School, Hunan University of Chinese Medicine, No.300 Xueshi Road, Changsha, (CHINA)

²Affiliated Hospital, Hunan Academy of Chinese Medicine, No.58 Lushan Road, Changsha, (CHINA)

³College of Electronic Science and Engineering, National University of Defense Technology, No.109 Deya Road, Changsha, (CHINA)

ABSTRACT

To observe the clinical efficacy of Huxinkang Tablet on unstable angina pectoris (UAP). 65 patients of UAP were divided into the control group (32 cases) and treatment group (33 cases). All patients were treated with the western medicine. Then, patients in the control group and treatment group were administered Tongxinluo Capsule and Huxinkang Tablet, respectively. The changes of clinical efficacy, angina pectoris (AP), electrocardiograph (ECG), Chinese medicine syndrome (CMS), blood fat, homocysteine (Hcy) and high-sensitivity C-reactive protein (hs-CRP) of two groups were observed. Total effective rate of the treatment group was higher than the control group ($P < 0.05$). The treatment group had a better curative effect of AP, ECG and CMS than the control group ($P < 0.05$). Huxinkang Tablet had better effects to improve lipid metabolism and lower the levels of Hcy and hs-CRP than the control group ($P < 0.05$). It is effective that the clinical efficacy of Huxinkang Tablet in treating UAP.

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KEYWORDS

Huxinkang tablet;
Unstable angina pectoris;
Clinical efficacy.

INTRODUCTION

Coronary heart disease (CHD) that coronary atherosclerotic heart disease is a common clinical syndrome^[1]. Recently, patients of CHD have increased every year, which seriously harms the human's health and life. Unstable angina pectoris (UAP)^[2] is a clinical syndrome between the stable angina pectoris (SAP) and acute myocardial infarction (AMI), and is one of the most common acute coronary syndromes. UAP can be converted to SAP by aggressive treatment early, but may be deteriorated to AMI due to different reasons. Many clinical and experimental studies show that the syndrome of

Qi deficiency and phlegm and blood stasis (QDPBS) is one of the most common syndrome of UAP^[3-5].

The pathogenesis of UAP is unclear, which may be related to the endothelial injury, hypercoagulable state, inflammatory response, especially to blood-fat, homocysteine (Hcy) and high-sensitivity C-reactive protein (hs-CRP)^[6,7]. Huxinkang Tablet is a prescription summed by Professor Yu based on the clinical experience for years, which has the ability to supplement Qi and resolve phlegm and blood stasis. Researches show that Huxinkang Tablet have significant clinical efficacy in treating SAP^[8]. To compare the clinical efficacy of the Huxinkang Tablet and Tongxinluo Capsule in treat-

ing UAP with the syndrome of QDPBS, 65 patients were selected and observed, and results are reported below.

CLINICAL DATA

Diagnostic criteria

Diagnostic criterion of Western medicine

The diagnostic criterion is referred to the report "Naming and diagnostic criteria of the ischemic heart disease"^[1] and the paper "Diagnosis and treatment recommendations of UAP"^[2]. And, the grading criterion is according to the grading diagnostic criteria of angina pectoris (AP) of CHD^[9].

Dialectic criterion of Chinese medicine (CM)

According to the book "Chinese medicine clinical research guidelines"^[10], the syndrome of QDPBS is studied out. Main symptom: chest tingling and oppressed, palpitations and shortness of breath. Secondary symptoms: fatigue, body fat, phlegmatic and dark purple lips. Tongue: muddy, dark purple and fat. Pulse: weak. The syndrome can be diagnosed based on the main symptom and two terms of secondary symptom, combining with the tongue and pulse.

Grading criterion of CM syndrome (CMS)

Mild: CMS score is less than 13 point. Moderate: CMS syndrome score is between 14 and 26 point. Severe: CMS score is more than 26 point.

Selection criteria

Inclusion criteria

A. Comply with the diagnostic criteria of Western medicine, with the clinical risk stratification for low-intermediate risk patients and AP severity rating from class I to class b!; B. Syndrome of QDPBS; C. The resting 12-lead ECG has obvious myocardial ischemia; D. Between 40 and 70 years old; E. Not participate in other clinical trials within one month.

Exclusion criteria

A. AMI and other cardiac disease, hyperthyroidism, cervical disease, gallbladder disease, etc.; B. Combining with severe hypertension, diabetes, hyperlipidemia and arrhythmia; C. Pregnancy and lactating

women; D. Patients of mentally ill, multi-drug abusers and drug allergy; E. Obvious infection, fever and severe anemia; F. Patients cannot cooperate or are participating in other drug trials.

Patients data

In the study, 65 UAP patients were selected from the Affiliated Hospital of Hunan Institute of CM from May 2013 to August 2014. Treatment group (33 cases): 19 males, 14 females; age range (41-70 years); duration range (6 months-24 years); hyper-tension 13 case, hyperlipidemia 25 cases, diabetes 5 cases; low-risk 10 cases, intermediate-risk 23 cases; class I 8 cases, class II 17 cases, class III 8 cases; mild 1 case, moderate 31 cases, severe 1 case. The control group (32 cases): 19 males, 13 females; age range (42-69 years); duration range (4 months-23 years); hypertension 11 cases, hyperlipidemia 27 cases, diabetes 4 cases; low-risk 8 cases, intermediate-risk 24 cases; class I 6 cases, class II 17 cases, class III 9 cases; mild 0 case, moderate 30 cases, severe 2 cases. Statistically, the difference between two groups isn't statistically significant ($P>0.05$), so it is comparable.

METHODS

Treatment methods

Treatment group: Taking Hunxinkang Tablet based on Western medicine treatment (made by Affiliated Hospital of Hunan Institute of CM). 10 tablets every time, and 3 times every day. Control group: taking Tongxinluo Capsule based on Western medicine treatment (made by Yiling Pharmaceutical Company). 4 capsules every time, and 3 times every day. Two groups are treated and observed for 4 weeks of a course. If it is difficult to relieve AP it-self, the patients can take the nitroglycerin tablets as a temporary treatment.

Observation indication

Efficacy observation

A. Seizure frequency, duration and pain of AP and amount of nitroglycerin used are observed and recorded 2 times every week. B. ECG is recorded before and after treatment. C. Clinical symptoms are recorded before treatment and after treatment every week, and the score and integral of CMS are computed.

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Blood-fat, Hcy and hs-CRP detection

Changes of blood-fat (including triglyceride (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C) and lipoprotein a (Lp(a))), Hcy and hs-CRP are checked before and after treatment.

Efficacy criteria

Efficacy evaluation includes clinical efficacy, AP efficacy, ECG efficacy and CMS efficacy, which is evaluated according to the criteria "Evaluation criteria of AP of CHD and ECG efficacy"^[9] and the book "Chinese medicine clinical re-search guidelines"^[10].

Evaluation criteria of clinical efficacy

Marked: Main symptoms of AP disappear or achieve the marked standard, and ECG returns to the approximately normal ECG level. Effective: Main symptoms of AP basically disappear or achieve the effective standard, and ECG achieves the effective standard. Invalid: The main symptoms of AP have no improvement, and ECG is basically same as that before treatment. Deteriorative: Main symptoms of AP and ECG are worse than before treatment.

Evaluation criteria of AP efficacy

Marked: After treatment, AP symptoms disappear, its grade lowers 2, and the nitroglycerin isn't need. Effective: After treatment, the AP symptoms basically disappear, its grade lowers one, and the amount of nitroglycerin reduces half. Invalid: After treatment, the AP symptoms and amount of nitroglycerin have no change. Deteriorative: Seizure frequency, pain and duration of AP aggravates after treatment.

Evaluation criteria of ECG efficacy

Marked: ECG returns to the approximately normal ECG level after treatment. Effective: S-T segment level rebounds more than 0.05mV after treatment, but don't reach the normal level. Invalid: ECG is basically same as before treatment, or has a slight change but don't reach the ameliorative standard. Deteriorative: Compared with before treatment, S-T segment reduces more than 0.05mV after treatment.

Evaluation criteria of CMS efficacy

Marked: Clinical symptoms and body sign are im-

proved markedly, and CMS score decreases e"70%. Effective: Clinical symptoms and body sign are improved effectively, and CMS score decreases e"30%. Invalid: Clinical symptoms and body sign have no significant improvement, and CMS score decreases <30%. Deteriorative: Clinical symptoms and body sign are worse, and CMS score decreases <0.

Statistics method

The data is processed and analyzed by the SPSS17.0 statistical software. Measurement data is presented as mean \pm standard deviation ($\bar{x} \pm s$), and analyzed using the t test. Count data is analyzed using the χ^2 test, and grade data is analyzed using the rank sum test. $P < 0.05$ presents statistically significant.

RESULTS AND ANALYSIS

Comparison of clinical efficacy

Total effective rates of clinical efficacy are 96.69% and 78.13% for the treatment and control groups, respectively. From the comparison between two groups, the difference is statistically significant ($P < 0.05$), which shows that the treatment group is excelled the control group in terms of improving clinical efficacy. Results are shown in TABLE 1.

Comparison of AP efficacy

Total effective rates of AP efficacy are 93.75% and 68.75% for the treatment and control groups, respectively. From the comparison between two groups, the difference is statistically significant ($P < 0.05$), which shows that the treatment group is excelled the control group in terms of improving AP efficacy. Results are shown in TABLE 2.

Comparison of ECG efficacy

Total effective rates of ECG efficacy are 84.85% and 62.50% for the treatment and control groups, respectively. From the comparison between two groups, the difference is statistically significant ($P < 0.05$), which shows that the treatment group is excelled the control group in terms of improving ECG efficacy. Results are shown in TABLE 3.

Comparison of CMS efficacy

Total effective rates of CMS efficacy are 93.75%

TABLE 1 : Comparison of clinical efficacy

| Groups | Total cases | Marked | Effective | Invalid | Deteriorative | Total effective rate (%) |
|-----------------|-------------|--------|-----------|---------|---------------|--------------------------|
| Treatment group | 33 | 23 | 9 | 1 | 0 | 96.69 |
| Control group | 32 | 15 | 10 | 6 | 1 | 78.13 |

Note: Rank sum test: $z=-2.137$, $P=0.0031$. Compared with the control group, $P<0.05$.

TABLE 2 : Comparison of AP efficacy

| Groups | Total cases | Marked | Effective | Invalid | Deteriorative | Total effective rate (%) |
|-----------------|-------------|--------|-----------|---------|---------------|--------------------------|
| Treatment group | 33 | 16 | 15 | 2 | 0 | 93.75 |
| Control group | 32 | 12 | 10 | 9 | 1 | 68.75 |

Note: Rank sum test: $z=-2.126$, $P=0.029$. Compared with the control group, $P<0.05$.

TABLE 3 : Comparison of ECG efficacy

| Groups | Total cases | Marked | Effective | Invalid | Deteriorative | Total effective rate (%) |
|-----------------|-------------|--------|-----------|---------|---------------|--------------------------|
| Treatment group | 33 | 13 | 15 | 5 | 0 | 84.85 |
| Control group | 32 | 8 | 12 | 11 | 1 | 62.50 |

Note: Rank sum test: $z=-2.312$, $P=0.042$. Compared with the control group, $P<0.05$.

TABLE 4 : Comparison of CMS efficacy

| Groups | Total cases | Marked | Effective | Invalid | Deteriorative | Total effective rate (%) |
|-----------------|-------------|--------|-----------|---------|---------------|--------------------------|
| Treatment group | 33 | 23 | 8 | 2 | 0 | 93.75 |
| Control group | 32 | 10 | 16 | 5 | 1 | 81.25 |

Note: Rank sum test: $z=-2.251$, $P=0.0274$. Compared with the control group, $P<0.05$.

and 81.25% for the treatment and control groups, respectively. From the comparison between two groups, the difference is statistically significant ($P<0.05$), which shows that the treatment group is excelled the control group in terms of improving CMS efficacy. Results are shown in TABLE 4.

Comparison of blood-fat change

Before treatment, the difference of blood-fat level between two groups isn't statistically ($P>0.05$). After treatment, for both two groups, the TG, TC, LDL-C and Lp(a) levels decrease, while the HDL-C level increases. Compared with before treatment, the differences are statistically significant ($P<0.01$ or $P<0.05$), which shows that both two groups can improve blood-fat level in patients after treatment. However, after treatment, the differences of TG, TC and LDL-C levels between two groups are statistically significant ($P<0.01$ or $P<0.05$), but the differences of HDL-C and Lp(a) levels between two groups aren't statistically ($P>0.05$). It can be concluded that the treatment group is excelled the control group in terms of improving blood-fat level in patients. Results are shown in TABLE 5.

Comparison of Hcy and hs-CRP

Before treatment, the difference of Hcy and hs-CRP levels between the two groups is not statistically ($P>0.05$). After treatment, for both two groups, Hcy and hs-CRP levels decrease. Compared with before treatment, the differences are statistically significant ($P<0.05$), which shows that both two groups can improve the Hcy and hs-CRP levels in patients after treatment. However, after treatment, the differences of Hcy and hs-CRP levels between two groups are statistically significant ($P<0.05$). It can be concluded that the treatment group is excelled the control group in terms of improving Hcy and hs-CRP levels in patients. Results are shown in TABLE 6.

Security surveillance

The blood, urine, stool and liver and kidney function are checked before and after treatment, results show that they aren't basically changed. During the treatment, all patients have no adverse reactions and the drug is well tolerated. Therefore, Huxingkang Tablet is safe to treat the UPA with the syndrome of QDPBS.

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TABLE 5 : Comparison of blood-fat change

| Group | Time | Total cases | TG (mmol/L) | TC (mmol/L) | LDL-C (mmol/L) | HDL-C (mmol/L) | Lp(a) (mg/dL) |
|-----------------|------------------|-------------|-------------|---------------|----------------|----------------|---------------|
| Treatment group | Before treatment | 33 | 3.69±0.72 | 7.36±0.56 | 5.43±0.81 | 1.23±0.62 | 33.51±26.76 |
| Treatment group | After treatment | 33 | 1.73±0.34Δ* | 5.07±0.41ΔΔ** | 3.23±0.45Δ* | 1.59±0.49Δ | 19.21±15.97Δ |
| Control group | Before treatment | 32 | 3.77±0.86 | 7.47±0.68 | 5.39±0.817 | 1.25±0.33 | 33.90±20.15 |
| Control group | After treatment | 32 | 2.35±0.75Δ | 6.83±0.56Δ | 4.88±0.785Δ | 1.57±0.27Δ | 20.96±13.20Δ |

Note: Compared with itself before treatment, ΔP<0.05, ΔΔP<0.01; Compared with the control group after treatment, *P<0.05, **P<0.01.

TABLE 6 : Comparison of Hcy and hs-CRP

| Group | Time | Total cases | Hcy(μmol/L) | hs-CRP(mg/L) |
|-----------------|------------------|-------------|--------------|--------------|
| Treatment group | Before treatment | 33 | 26.28±4.68 | 13.45±6.29 |
| Treatment group | After treatment | 33 | 12.53±2.32Δ* | 5.45±2.35Δ* |
| Control group | Before treatment | 32 | 27.26±5.31 | 13.42±6.21 |
| Control group | After treatment | 32 | 19.63±3.12Δ | 9.88±4.42Δ |

Note: Compared with itself before treatment, ΔP<0.05; Compared with the control group after treatment, *P<0.05.

DISCUSS

Based on the clinical practice in treating UAP for many years, my instructor finds that the Qi deficiency, phlegm and blood stasis is the major causative factor of such diseases, which play an important role in UAP occurrence and development^[11]. So, he proposes the treatment idea based on Qi deficiency, phlegm and blood stasis, i.e. they should be all considered in treating UAP patients.

This clinical study shows that Huxingkang Tablet can effectively reduce seizure frequency, pain content and duration of AP, and improve the patient's ECG and CMS. Significantly, the clinical efficacy, AP efficacy, ECG efficacy and CMS efficacy of the treatment group are excelled control group. Besides, it can significantly improve the lipid metabolism in patients, i.e. lower TG, TC, LDL-C and Lp(a) levels and increase HDL-C level. Finally, compared with control group, it can significantly reduce Hcy and hs-CRP levels in patients. Summarily, Huxingkang Tablet can effectively treat UAP with the syndrome of QDPBS, and its application becomes wide.

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