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Clinical Efficacy of Flupentixol and Melitracen Tablets in the Treatment of Coronary Heart Disease with Depression

Yu-Hong Yang[1], Qiu-Ming Ji[1]*, Yu Chen[1], Juan Qiao[1], Ji-Hua Zeng[1]*, Hai-Ying Chen[1]*, Xiao-Jun Wang[1], Hua-Xin Lu[1], Wen-Jie Wei[1], Chun-Xi Wu[1], Hong-Yuan Chen[1] and Ming-Chao Li[2]

[1]*Department of Psychiatry, Wuhan Wudong Hospital, Wuhan 43G Hospital, Wuhan 430084, China*
[2]*Department of Psychiatry, Wuhan Mental Health Center, Wuhan 430022, China*

Yu-Hong Yang, Yu Chen and Juan Qiao contributed equally to this study.

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Depression, Anxiety, Flupentixol and melitracen tablets, Self-rating depression scale, Self-rating anxiety scale

ABSTRACT

The occurrence of patients with coronary heart disease (CHD) complicated with depression is quite significant. The purpose of this study was to explore the clinical efficacy of flupentixol and melitracen tablets in the treatment of CHD with depression. A total of 125 patients were evaluated psychologically, and 60 patients with depression and anxiety were identified. These 60 patients were then randomly divided into a study group and a control group, each consisting of 30 patients. Based on the conventional treatment of CHD, the study group was treated with Flupentixol and Melitracen tablets for the course of treatment (four weeks). The changes in the self-rating depression scale (SDS), self-rating anxiety scale (SAS), myocardial ischemia range (NST) and myocardial ischemia degree (EST) were compared before and after treatment. The incidence of depression and anxiety in patients with CHD in this study was 48.0%. After four weeks of treatment, the SDS and SAS scores of patients with CHD in the study group were significantly lower than those in the control group, and there was a significant difference between the two groups (SAS: $t = 6.609$, $P = 0.001$; SDS: $t = 7.424$, $P = 0.003$). After four weeks of treatment, the NST and EST scores of patients with CHD in the study group were significantly lower than those of the control group, and there was a significant difference between the two groups (NST: $t = 4.652$, $P < 0.05$; EST: $t = 3.384$, $P < 0.05$). After four weeks of treatment, the effective rate of the study group (96.7%) was significantly higher than that of the control group (83.3%). Flupentixol and melitracen tablets can significantly reduce anxiety, improve symptoms of depression, and improve the clinical efficacy of treating CHD patients with anxiety and depression.

INTRODUCTION

Coronary heart disease (CHD) is also called ischemic heart disease (Chen *et al*., 2020). CHD is known as 'the number one killer of mankind' because of its high morbidity and high mortality rate (Nowbar *et al*., 2019). At present, CHD is still the leading cause of death worldwide. Although the global age-adjusted mortality rate of CHD has declined, the absolute number of deaths is increasing, partly due to population growth and aging, as well as important lifestyle and food system changes that may undermine prevention outcomes (Barquera *et al*., 2015). The course of the disease is long. Even if the symptoms are relieved, it does not mean that the disease is cured, which brings heavy economic burdens and mental stress to patients and their families (Moran *et al*., 2014). According to literature reports, 40% to 70% of patients with CHD have symptoms of anxiety and depression (Yuan *et al*., 2017; Peter *et al*., 2020). Those with mild symptoms have decreased interest, poor appetite, worry and irritability, while those with severe symptoms also have insomnia, dreaminess, negativity and suicidal thoughts (De *et al*., 2020). In a negative mental state, the symptoms of CHD are aggravated, and in severe cases, it may lead to sudden

* Corresponding author: qiuming_65@21cn.com
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death (Rutledge *et al*., 2013).

β-receptor blockers and other drugs treat coronary heart disease, but long-term medication, heavy economic burdens and other factors often lead to anxiety and depression, leading to poor treatment results. Flupentixol and melitracen tablets is a compound preparation, its main components are flupentixol hydrochloride and melitracen hydrochloride. It is suitable for mild to moderate depression and anxiety. Some studies have shown that when flupentixol and melitracen tablets is added to the routine treatment of patients with chronic cardiovascular disease, it can effectively improve patients' cardiac function, angina pectoris symptoms and blood pressure fluctuation (Yang *et al*., 2017). For patients with heart disease, anxiety and depression, combined antidepressant therapy is particularly important to ensure effective treatment (Richards *et al*., 2017). Flupentixol and melitracen tablets is composed of two very effective compounds: low-dose fluguathiadihydrochloride and low-dose tetramethamphetamine hydrochloride. Low-dose fluguathiaton mainly acts on the dopamine autoregulatory receptor in the presynaptic membrane, promotes the synthesis and release of dopamine and increases the dopamine content in the synaptic cleft. Tetramethylanthrapromide inhibits the reuptake of norepinephrine and serotonin by the presynaptic membrane and increases the content of monoamine neurotransmitters in the synaptic gap to achieve an antidepressant effect and improve emotion (Meyer and Quenzer, 2013; Joint Formulary Committee, 2021).

The purpose of this study is to explore the clinical efficacy of treating patients with CHD and depression with flupentixol and melitracen tablets combined with psychological intervention, focusing on the improvement of clinical symptoms and psychological status.

MATERIALS AND METHODS

General information

From January 2019 to December 2020, 125 hospitalised patients for CHD related symptoms in the Department of Cardiology at the Union Hospital of Huazhong University of Science and Technology and the Department of Internal Medicine of Wuhan Wudong Hospital were selected and scored with the self-rating depression scale (SDS) and self-rating anxiety scale (SAS) by the convenience sampling method.

The inclusion criteria included (1) patients diagnosed with CHD; (2) patients with chest pain and tightness; (3) patients with stability of mind; and (4) patients and their families were aware of the contents of the study and (5) patients with an SDS score of ≥ 50 and an SAS score of ≥ 50, indicating clinically significant levels of depression and anxiety, respectively. Exclusion criteria included: (1) patients with poor compliance; (2) patients with adverse drug reactions; (3) other cardiovascular diseases; (4) patients with mental or consciousness disorders; and (5) patients with multiple organ failure, hypertensive emergency and severe renal insufficiency.

Treatment method

A total of 125 patients were evaluated psychologically, and 60 patients with depression and anxiety were identified. According to the random number table, 60 patients were randomly divided into study group and control group according to the order of admission, each consisting of 30 patients. Both the study group and the control group were given routine treatments of secondary prevention of CHD and individualised supportive psychotherapy. Aspirin 100 mg QD was given to prevent platelet aggregation; Lipitor 20 mg QN was given to reduce lipid and stabilise plaque; Betaloc 47 mg QD was given to slow down heart rate and improve heart function; and Shexiang Baoxin was given 2 bid, taken orally in the morning for 4 weeks / course of treatment.

For the study group, the participants were given one tablet of flupentixol and melitracen every day (each tablet contained 0.5 mg of droperidol and 10 mg of melitracen, Registration No.: h20171104, manufacturer: H. Lundbeck A/S).

Observation indicators

Before and after treatment, the following measurements were taken: NST (the number of leads of 12-lead conventional ECG ST segment depression, indicating the range of myocardial ischemia) and EST (the sum of 12 lead conventional ECG ST segment depression, indicating the degree of myocardial ischemia). The psychological status of the patients in the two groups was observed. SAS and SDS scales were used to evaluate the psychological status of the patients. The higher the score, the more serious the negative psychological emotion.

An ECG was taken before and one day after the flupentixol and melitracen tablets treatment. A doctor measured the electrocardiogram. NST and EST scores were performed by two associate chief physicians of cardiology, and then the average value was taken. A double-blind method was used for scoring. The higher the score, the worse the cardiovascular function.

During the hospitalization of patients, the monitoring of adverse reactions is obtained through the clinical observation and detection of medical staff.

Efficacy evaluation

The following ratings were used in the evaluation:

Significantly effective: The clinical symptoms disappeared, and the ECG returned to normal, and the SAS and SDS scores reduced by ≥70%.

Effective: Most clinical symptoms disappeared, and the ECG results improved, and the SAS and SDS scores reduced by ≥50%.

Improved: The clinical symptoms partially disappeared, and the ECG results improved, and the SAS and SDS scores reduced by <50%.

Ineffective: The clinical symptoms and ECG results did not change or worsen, or the SAS and SDS scores did not reduce by at least 50%.

Clinical symptoms: Common CBD-related symptoms such as chest tightness, chest pain, nausea and vomiting.

The total effective rate of treatment = (significantly effective + effective + improved)/ total number of cases × 100%.

The SAS and SDS score reduction rate of ≥ 50% is effective and <50% is ineffective.

Statistical methods

SPSS 23.0 statistical software was used to process the data. The measurement data were in line with the positive distribution through the Shapiro-Wilktest test. The measurement data were expressed as mean ± standard deviation (x ± s), and the t-test was used; the counting data were expressed in percent using the chi-square test. If $P < 0.05$, the difference was statistically significant.

RESULTS

Essential information

Table I shows the basic information of the patients. Among the 125 patients, 60 patients had an SDS score ≥50 (an SDS score less than 50 is considered normal; the higher the score, the more severe the depressive symptoms). Among them, 27 were male and 33 were female. Their ages ranged from 54 to 73 years, with an average of 64.1 ± 7.4. The 60 patients were randomly divided into a study group and a control group (30 cases in each group). In the study group, the average age of the participants was 64.8±7.9. The course of the disease (in years) was 10.1 ± 4.2. The number of participants rated with grades I, II, III and IV of angina pectoris were 7, 14 and 9, respectively. The left ventricular ejection fraction was 0.41 ± 0.14. For the control group, the average age was 63.5 ± 6.7. The course of disease (in years) was 10.4 ± 4.3 years. The grades I, II, III and IV of angina pectoris were 7, 16, and 7, respectively. The left ventricular ejection fraction was 0.42 ± 0.12. The difference was not statistically significant.

Incidence of depression and anxiety symptoms

Of the 125 patients with CHD, there were 60 cases with SDS and SAS scores ≥ 50 points. The incidence of depression and anxiety symptoms in this study was 48.0%.

Effect of flupentixol and melitracen on SAS and SDS

After four weeks of treatment, the SAS and SDS scores of patients with CHD in the study group decreased significantly more than the scores for the control group ($t = 6.609$, $P = 0.001$). The decrease in SDS scores of patients with CHD in the study group was significantly higher than for those in the control group ($t = 7.424$, $P = 0.003$) (Table II).

Effect of flupentixol and melitracen NST and EST

Before treatment, there was no significant difference in NST and EST scores between the study group and the control group. After treatment, the cardiac function of the study group and the control group improved, and the NST and EST scores decreased significantly. The NST and EST scores of patients with CHD in the study group were significantly lower than that in the control group (Table III).

Comparison of treatment effects

Table IV shows comparison of effective rate of study and control groups. The total effective rate of treatment in the study group was 93.3% and in the control group it was 83.3%.

Table I. Basic information of patients.

	Gender (cases)		Age (years)	Degree		Angina grades				LVEF normal value (55%-65%)	Course of disease (years)
	Male	Female		NST	EST	I	II	III	IV		
Study group	13	17	64.8±7.9	6.49±2.12	7.56±1.35	7	14	9	0	41%±14%	10.1±4.2
Control group	14	16	63.5±6.7	6.51±1.94	7.58±1.47	7	16	7	0	42%±12%	10.4±4.3
X^2/t	0.218		0.541	0.223	0.379	0.237				0.436	0.782
P	0.841		0.129	0.624	0.574	0.579				0.648	0.318

NST, The number of leads with ST depression in 12-lead conventional electrocardiogram, indicating the range of myocardial ischemia; EST, the sum of ST-segment depression in 12-lead conventional electrocardiogram, indicating the degree of myocardial ischemia; CHD, Coronary heart disease. left ventricular ejection fraction.

Table II. Effect of flupentixol and melitracen on SAS and SDS scores before and after treatment of CHD with depression.

Group	Number of cases	SAS		t value	P value	SDS		t value	P value
		Before treatment	After treatment			Before treatment	After treatment		
Study group	30	53.77±9.62	39.17±7.34	9.54	0.000*	58.75±9.28	42.62±7.45	2.97	0.006
Control group	30	53.92±9.48	50.66±7.39	6.90	0.000*	58.14±8.95	54.27±8.43	1.22	0.233
t value	-	0.732	6.609			0.464	7.424		
P value	-	0.451	0.001			0.372	0.003		

SDS, self-rating depression scale; SAS, self-rating-rating anxiety scale. *, The difference was statistically significant.

Table III. Effect of flupentixol and melitracen on NST and EST scores before and after treatment of CHD with depression.

Group	Number of cases	NST		t value	P value	EST		t value	P value
		Before treatment	After treatment			Before treatment	After treatment		
Study group	30	6.49±2.12	4.03 ±1.72	6.681	0.000*	7.56±1.35	5.85±1.43	5.866	0.003*
Control group	30	6.51±1.94	5.77±1.69	3.388	0.037*	7.58±1.47	6.93±1.36	3.055	0.016*
t value	-	0.737	4.652			0.924	3.384		
P value	-	0.657	0.001*			0.647	0.006*		

NST, The number of leads with ST depression in 12-lead conventional electrocardiogram, indicating the range of myocardial ischemia; EST: the sum of ST-segment depression in 12-lead conventional electrocardiogram, indicating the degree of myocardial ischemia. *, The difference was statistically significant.

Table IV. Comparison of treatment effects between the study and the control groups.

	Significantly effective (case)	Effective (case)	Improved (case)	Ineffective (case)	Total effective rate (%)	χ^2	P
Study group	12	13	3	2	93.3	1.456	0.228
Control group	8	12	5	5	83.3		

Adverse reactions

Both groups of patients completed four weeks of observation and treatment. Throughout this period, heart rate and blood pressure were monitored regularly using standard clinical techniques. Heart rate was typically monitored through the use of electrocardiograms (ECGs) and pulse measurement, while blood pressure was checked using a sphygmomanometer.

Potential neurotoxic side effects were evaluated through regular neurological examinations and patient self-reports. Neurological examinations included a range of tests assessing both central and peripheral nervous system function, such as mental status evaluations, cranial nerve examinations, motor strength assessments, coordination evaluations, and sensory testing.

Based on this systematic monitoring and evaluation, there were no obvious abnormalities in heart rate and blood pressure during treatment with flupentixol and melitracen tablets, and no obvious mental and neurological toxic side effects were observed.

DISCUSSION

The results of this study show that: (1) the scores of the self-rating depression scale and the self-rating anxiety scale after treatment for the study group were significantly lower than those of the control group, and the difference was statistically significant ($P < 0.05$); (2) the scores of NST and EST after treatment for the study group were significantly lower than the control group, and the difference was statistically significant ($P < 0.05$); (3) the effective rate (93.3%) of the study group after treatment was significantly higher than that of the control group (83.3%).

The results of studies on flupentixol and melitracen tablets suggest that, except for angina pectoris events, there were significant reductions in cardiovascular events, such as myocardial infarction, premature ventricular contractions and ventricular tachycardia (Sun *et al.*, 2017). This paper investigates the current situation and

psychological assessment of inpatients with CHD and studies the efficacy of flupentixol and melitracen tablets treatment in improving anxiety and depression in patients with CHD.

Flupentixol and melitracen tablets is a commonly used drug to regulate mood and treat depression. It can regulate the function of the central nervous system, exert strong anti-anxiety and depression effects and can also antagonise the side effects of drugs. Its constituent flupentixol reduces the adverse effects of melitracen, such as increased heart rate and blood pressure, and melitracen antagonises the extrapyramidal symptoms that may be caused by flupentixol (Ji *et al*., 2017; Li and Jia, 2018).

The incidence of anxiety and depression symptoms in patients with CHD is 48%, and nearly half of the patients have anxiety and depression symptoms, which is consistent with the reports in the literature (Yuan *et al*., 2017; Peter *et al*., 2020). Its occurrence is related to genetic, psychological and social factors, neuroendocrine disorders and other causes. Many patients found cognitive changes after CHD, such as decreased self-esteem, decreased professionalism and decreased anti-stress ability (Elamragy *et al*., 2019). The negative mental state interacts with corresponding physiological factors to form a certain vicious circle that seriously affects the cure rate of CHD and its prognosis. The two are mutually causal. Therefore, active anti-anxiety and anti-depressant treatment for patients with CHD complicated by anxiety and depression can achieve better therapeutic effects and reduce the occurrence of malignant events of cardiovascular and cerebrovascular diseases (Cheng *et al*., 2018; Zhang *et al*., 2018). SAS and SDS scales were used to assess efficacy. SAS is mainly used to evaluate the severity of adult anxiety symptoms and their changes in treatment. SDS is a four-level self-rating scale composed of 20 items. It is mainly used for severe symptoms of depression in adults and the changes in the course of treatment. Both can be used for psychological consultation outpatient, psychiatric outpatient or inpatient psychiatric patients. SDS is not as effective in assessing depression in patients with severe blockage. SAS has little effect on the identification of neurosis.

This study included a small number of subjects and did not explore the long-term effect of flupentixol and melitracen tablets in CHD complicated with depression. Next, we will follow up the patients and conduct a multi-centre, large-sample study.

CONCLUSION

Flupentixol and melitracen tablets can significantly reduce anxiety, alleviate depression, improve the clinical efficacy of CHD treatment and improve the quality of life of CHD patients with anxiety and depression. Throughout the four-week observation and treatment period, patients were monitored regularly for heart rate, blood pressure, and potential neurotoxic side effects using standard clinical techniques. No obvious abnormalities or toxic side effects were observed. This study is worthy of clinical application.

DECLARATIONS

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IRB approval

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Wuhan Wudong Hospital, and all patients signed an informed consent form.

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Wuhan Wudong Hospital, and all patients signed an informed consent form.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Statement of conflict of interest

The authors have declared no conflict of interest.

REFERENCES

Barquera, S., Pedroza-Tobías, A., Medina, C., Hernández-Barrera, L., Bibbins-Domingo, K., Lozano, R. and Moran, AE., 2015. Global overview of the epidemiology of atherosclerotic cardiovascular disease. *Arch. med. Res*., **46**: 328-338. https://doi.org/10.1016/j.arcmed.2015.06.006

Chen, H., Lu, W., Liu, L., Liu, H., Xu, G., Yan, X., Tan, X. and Hu, Y., 2020. Influencing factors of coronary heart disease and its correlation with bone-related proteins. *Guangxi med. Sci*., **42**: 1477-1480.

Cheng, F., Lin, P. and Yu, H., 2018. The relationship between anxiety and depression and coronary plaque stability in patients with coronary heart disease. *J. Nurs. Sci*., **33**: 1-4.

De, H.E.W., Palacios, J.E., Adèr, H.J., van, Marwijk, H.W.J., Tylee, A. and van, der. Feltz-Cornelis, C.M., 2020. Chest pain, depression and anxiety

in coronary heart disease: Consequence or cause? A prospective clinical study in primary care. *J. Psychosom. Res*., 129: 109891. https://doi.org/10.1016/j.jpsychores.2019.109891

Elamragy, A.A., Abdelhalim, A.A., Arafa, M.E. and Baghdady, Y.M., 2019. Anxiety and depression relationship with coronary slow flow. *PLoS One*, **14**: e0221918. https://doi.org/10.1371/journal.pone.0221918

Ji, X., Shen, Q. and Cai, W., 2017. Efficacy analysis of Flupentixol and Melitracen Tablets in the treatment of elderly hypertensive patients with coronary heart disease complicate with anxiety and depression. *Cardiovasc. Dis. Electron. J. Integr. Trad. Chin. Western Med*., **5**: 36-37.

Joint Formulary Committee, 2021. *British National Formulary (BNF) (80th ed.)*. Pharmaceutical Press, London.

Li, A. and Jia, C., 2018. Analysis of the treatment of flupentixol and melitracen tablets combined with doxepin on coronary heart disease complicated with depression. *Northern Pharma*., **15**: 20-21.

Meyer, J.S. and Quenzer, L.F., 2013. *Psychopharmacology: Drugs, the brain and behavior (2nd ed.)*. Sinauer Associates, Inc., Sunderland, MA.

Moran, A.E., Forouzanfar, M.H., Roth, G.A., Mensah, G.A., Ezzati, M., Murray, C.J. and Naghavi, M., 2014. Temporal trends in ischemic heart disease mortality in 21 world regions, 1980 to 2010: The Global Burden of Disease 2010 study. *Circulation*, **129**: 1483-1492. https://doi.org/10.1161/CIRCULATIONAHA.113.004042

Nowbar, AN., Gitto, M., Howard, JP., Francis, DP., Al-Lamee, R., 2019. Mortality from ischemic heart disease. *Circ. Cardiovasc. Qual. Outcomes*, **12**: e005375. https://doi.org/10.1161/CIRCOUTCOMES.118.005375

Peter, R.S., Meyer, M.L., Mons, U., Schöttker, B., Keller, F., Schmucker, R., Koenig, W., Brenner, H. and Rothenbacher, D., 2020. Long-term trajectories of anxiety and depression in patients with stable coronary heart disease and risk of subsequent cardiovascular events. *Depress Anxiety*, **37**: 784-792. https://doi.org/10.1002/da.23011

Richards, S.H., Anderson, L., Jenkinson, C.E., Whalley, B., Rees, K., Davies, P., Bennett, P., Liu, Z., West, R., Thompson, D.R. and Taylor, R.S., 2017. Psychological interventions for coronary heart disease. *Cochrane Database Syst. Rev*., **4**: CD002902. https://doi.org/10.1002/14651858.CD002902.pub4

Rutledge, T., Redwine, L.S., Linke, S.E. and Mills, P.J., 2013. A meta-analysis of mental health treatments and cardiac rehabilitation for improving clinical outcomes and depression among patients with coronary heart disease. *Psychosom. Med*., **75**: 335-349. https://doi.org/10.1097/PSY.0b013e318291d798

Sun, X., Zhang, C., Lin, Q., Qiu, G. and Liang, J., 2017. Flupentixol and melitracen improve anxiety, depression and prognosis of patients after percutaneous coronary intervention. *Anhui Med*., **21**: 147 -150.

Yang, Y., Chen, W. and Ren, M., 2017. Efficacy analysis of Flupentixol and melitracen tablets in the treatment of chronic cardiovascular disease complicated with anxiety and depression. *Grassroots Med. Forum*, **21**: 3961-3963.

Yuan, J., Hong, H. and Zou, F., 2017. The clinical effect of flupentixol and melitracen tablets in the treatment of coronary heart disease with mood disorders and its influence on mental state. *China Pract. Med.*, **12**: 140-141.

Zhang, L., He, D., Yang, Y., Pu, L., Xu, L., Zhou, Y. and Liu, M., 2018. Clinical study of stress-induced myocardial ischemia in patients with stable coronary heart disease complicated with depression and anxiety. *Chin. J. Intern. Med*., **57**: 494-499.