

# Efficacy of Shuxuening Injection in Treating Organophosphate Pesticide-Induced Myocarditis

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## Yuanwang *et al.*: Shuxuening Injection Efficacy in Treating Myocarditis

To observe the clinical efficacy of Shuxuening injection in treating organophosphorus pesticide-induced myocarditis. In this study, we enrolled a total of 200 patients with organophosphorus pesticide-induced myocarditis, who were admitted to Nanjing Pukou District Traditional Chinese Medicine Hospital from September 2020 to April 2023. Random allocation resulted in the formation of two groups, namely the control group and the observation group, each consisting of 100 cases. Routine treatment was administered to the control group, involving procedures like gastric lavage, detoxification, safeguarding of vital organs (heart, liver, and kidneys), and anti-acetylcholine interventions. On the other hand, the observation group underwent routine treatment combined with the administration of Shuxuening injection. Following a 10 d period of continuous treatment, a comparison was made between the two groups regarding clinical symptoms, improvement of physical signs, electrocardiogram readings, and myocardial enzyme profiles. Comparing the clinical efficacy between the two groups, the observation group exhibited a total effective rate of 97.00 %, whereas the control group demonstrated a rate of 88.00 % ( $p < 0.05$ ), indicating a notable difference. After the completion of treatment, the number of patients in the observation group exhibiting ST-T segment changes in the electrocardiogram was 3, which was notably lower than the number in the control group (7 cases). The control group, on the other hand, had 11 and 16 cases, respectively ( $p < 0.05$ ). After completion of the treatment, there was a notable enhancement in all indicators of the myocardial enzyme profile, demonstrating superior results in the observation group compared to the control group ( $p < 0.05$ ). The administration of Shuxuening injection exhibits remarkable efficacy in the treatment of organophosphorus pesticide-induced myocarditis.

**Key words:** Shuxuening injection, organophosphorus pesticide, myocarditis, clinical efficacy, heart failure

Commonly encountered in medical practice, Acute Organophosphorus Pesticide Poisoning (AOPP) carries the risk of toxic myocarditis<sup>[1-3]</sup>, which has implications for the prognosis of affected individuals. Respiratory and circulatory failure, and in extreme cases, sudden death, can arise as severe complications of AOPP<sup>[4,5]</sup>. The impact on cardiac function stems from the inhibitory effects of organophosphorus pesticides on acetylcholinesterase activity, leading to disrupted neural transmission<sup>[6,7]</sup>. Clinical presentations of toxic myocarditis, such as changes in Electrocardiogram (ECG) readings, heart failure, and myocardial infarction, are associated with the dosage and extent of organophosphorus pesticide exposure<sup>[8,9]</sup>. Shuxuening injection, a medication

obtained from the extraction of *Ginkgo biloba* leaves, is widely employed for treating cardiovascular diseases like myocardial infarction and coronary heart disease, suggesting promising therapeutic potential<sup>[10-12]</sup>. The key constituents of Shuxuening injection consist of *Ginkgo* flavone and Ginkgolide<sup>[13]</sup>. Extracted from *Ginkgo biloba* leaves, flavones possess diverse properties that encompass inhibiting myocardial cell necrosis, enhancing the survival capacity of cells in hypoxic conditions, reducing the extent of damage in myocardial cells, and regulating vascular tension. As a result, these actions contribute to the improvement of organ blood circulation and peripheral microcirculation<sup>[14,15]</sup>. Moreover, *Ginkgo* flavones can exert their effects by

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upregulating the expression of the B-Cell Lymphoma 2 (BCL-2) gene, which holds pivotal importance as an anti-apoptotic gene. The upregulation of this gene's expression augments the survival capabilities of myocardial cells in hypoxic conditions<sup>[16]</sup>, while concurrently promoting the production of bilirubin. Consequently, myocardial cells are shielded against oxidative damage arising from hemolytic lecithin<sup>[17]</sup>. Nevertheless, there is still a paucity of research on the extent of therapeutic benefits provided by Shuxuening in organophosphorus pesticide-induced myocarditis. Thus, the objective of this study is to assess the efficacy of Shuxuening in treating organophosphorus pesticide-induced myocarditis by comparing the divergence in clinical symptoms, ECG, and myocardial enzyme profiles between the Shuxuening treatment group and the control group. This study aims to broaden the treatment options for patients with organophosphorus pesticide-induced myocarditis, prioritizing their efficacy and safety. Simultaneously, it aims to serve as a valuable resource for clinicians, assisting them in creating more scientifically informed treatment protocols. In this study, we enrolled a total of 200 patients with organophosphorus pesticide-induced myocarditis, who were admitted to Nanjing Pukou District Traditional Chinese Medicine Hospital from September 2020 to September April 2023. Random allocation resulted in the formation of two groups. The observation group, comprised of 100 patients, consisted of 43 males and 57 females, aged between 17 y and 66 y, with an average age of  $(38.6 \pm 5.8)$  y. Among the individuals in the observation group, poisoning was induced by multiple factors, namely, 31 cases were attributed to malathion, 22 cases to parathion, 19 cases to methyl-parathion, 16 cases to dimethoate, and 12 cases to other causative agents. The average waiting time for treatment from admission ranged from 0.5 h to 4 h, with a mean duration of  $(2.4 \pm 1.3)$  h. The Acute Physiology and Chronic Health Evaluation (APACHE) score exhibited a range of 17 to 35, with a mean score of  $(25.4 \pm 3.3)$ . The control group encompassed 100 patients, comprising 48 males and 52 females, with an average age of  $(36.5 \pm 4.4)$  y and an age range of 19 y to 65 y. Among the individuals in the control group, poisoning incidents were classified into different categories; 34 cases of malathion

poisoning, 20 cases of parathion poisoning, 21 cases of methyl-parathion poisoning, 16 cases of dimethoate poisoning, and 9 cases originating from other causes. The average time from admission to treatment was  $(2.5 \pm 1.3)$  h, with the shortest duration being 0.5 h and the longest being 4 h. Regarding the APACHE score, it ranged from 18 to 33, with a mean score of  $(25.5 \pm 3.1)$ . The diagnostic criteria for toxic myocarditis were met in all cases, which included the following aspects<sup>[18,19]</sup>; a confirmed history of ingestion or dermal exposure to organophosphorus pesticides; no known history of heart disease; presence of symptoms ranging from chest tightness, chest pain, palpitations, to dyspnea with varying degrees of severity; elevation of myocardial enzyme levels exceeding twice the normal range; abnormal ECG findings indicative of ST-T changes, frequent premature ventricular contractions, and conduction disorders. Both criteria were compulsory for diagnosis, and the fulfillment of any two of criteria sufficed. The two groups exhibited no significant differences in terms of gender, age, causes of poisoning, APACHE score, and treatment duration ( $p > 0.05$ ), indicating their comparability. Routine treatment was implemented in both groups of patients, involving procedures such as gastric lavage, catharsis, administration of revitalizing agents (chlorpyrifos), anticholinergic drugs (atropine) for atropinization maintenance, respiratory support, application of vasodilators, high-dose vitamin C, polarizing fluid for myocardial nutrition, methylprednisolone for inflammatory response suppression, anti-infective therapy, and nutritional support. In conjunction with the routine treatment, the observation group was administered Shuxuening injection *via* intravenous infusion, consisting of a 10 ml dosage combined with 250 ml of 5 % glucose injection. Following a continuous 10 d treatment course, the therapeutic effects were assessed and compared. Clinical efficacy was determined through the evaluation of ameliorations in clinical symptoms and physical signs. ECG examinations were conducted. The myocardial enzyme profile was assessed, with Creatine Kinase Isoenzyme (CK-MB) measured using an immunosuppression method and Creatine Kinase (CK), Lactate Dehydrogenase (LDH), and Aspartate Transaminase (AST) measured *via* a rate method. In order to evaluate clinical efficacy, criteria were

established following the guidelines set by the "Diagnostic Criteria for Clinical Diseases and Standards for Cure and Improvement"<sup>[20]</sup>. In cure, complete elimination of symptoms and physical signs, accompanied by the normalization of ECG and myocardial enzyme levels. In significant improvement, substantial reduction or disappearance of symptoms and physical signs, along with ECG and myocardial enzyme levels returning to a near-normal state. In effective, partial improvement in symptoms and physical signs, accompanied by advancements in ECG and myocardial enzyme levels. And in ineffective, no improvement or deterioration of symptoms and physical signs was observed. 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 deviation, 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. The observation group exhibited an overall treatment effective rate of 97.00 %, which was remarkably higher than the 88.00 % rate observed in the control group ( $p < 0.05$ ) (Table 1). The number of patients in the observation group showcasing ST-T segment changes in the ECG prior to treatment was 88 and 81, respectively, similar to the control group's figures of 91 and 77 ( $p < 0.05$ ). Post-treatment, the number of patients in the observation group with ST-T segment changes significantly decreased to 3, while in the control group it decreased to 7, demonstrating a substantial decline ( $p < 0.05$ ) (Table 2). The initial myocardial enzyme profiles did not differ substantially between the two groups ( $p > 0.05$ ). However, following the treatment, substantial enhancements were observed in all indicators, with the observation group outperforming the control group ( $p < 0.05$ ) (Table 3). The widespread utilization of respiratory support techniques has resulted in a notable decline in the mortality rate of individuals suffering from organophosphorus pesticide poisoning, particularly when complicated by intermediate syndrome and respiratory failure. Multi-organ dysfunction resulting from severe organophosphorus pesticide poisoning, with a particular emphasis on cardiac damage, emerges

as the primary cause of fatality<sup>[21,22]</sup>. Antagonizing the toxic myocardial injury caused by organophosphorus pesticides on the basis of improving myocardial blood supply is an important aspect in managing cardiac complications<sup>[23,24]</sup>. Evidence suggests that Shuxuening injection exhibits beneficial effects on cerebral blood circulation, cerebral blood vessel dilation, cerebral blood flow enhancement, and the augmentation and protection of brain cells<sup>[25,26]</sup>. The purpose of this study was to figure out the effectiveness of Shuxuening in managing organophosphorus pesticide-induced myocarditis. The results revealed notable enhancements in clinical symptoms, physical signs, myocardial enzyme profiles, and ECG in the observation group, surpassing those observed in the control group. These findings indicate the potential effectiveness of Shuxuening as a viable treatment alternative. Regarding improvements in clinical symptoms and physical signs, the observation group exhibited a superior overall effective rate of 97.00 %, in contrast to the control group's rate of 88.00 %. These results emphasize the significant influence of Shuxuening in ameliorating clinical symptoms, alleviating cardiac strain, and enhancing cardiac function. In terms of myocardial enzyme profiles, the absence of a remarkable difference was observed between the two groups prior to treatment ( $p > 0.05$ ). However, following treatment, all indicators exhibited substantial improvements, with the observation group showing superior results compared to the control group ( $p < 0.05$ ). Moreover, ECG examination serves as a crucial measure for evaluating cardiac function. Significantly, there were no remarkable differences detected in the number of patients displaying ST-T segment changes in the ECG between the observation and control groups prior to treatment. Nevertheless, following treatment, a significant reduction in the number of patients demonstrating ST-T segment changes was observed in the observation group compared to the control group, pointing towards the cardio protective effect of Shuxuening. Thus, the findings of this study provide compelling evidence for the marked clinical efficacy of Shuxuening in treating myocarditis induced by organophosphorus pesticides. The use of Shuxuening leads to noteworthy improvements in clinical symptoms, myocardial enzyme profiles, and ECG indices. It

is also likely that Shuxuening works through mechanisms such as protecting myocardial tissue, improving cardiac function, and reducing cardiac load. However, several limitations should be considered when interpreting the findings of this study. Firstly, the study was conducted at a single center with a relatively small sample size, which may compromise the generalizability of the results due to potential selection bias. Additionally, the relatively short study duration necessitates further long-term follow-up to assess the extended efficacy and safety of Shuxuening. Furthermore, as Shuxuening is a complex herbal preparation, its

precise pharmacological mechanisms remain incompletely understood and warrant further comprehensive investigation. In conclusion, this study preliminarily confirms the efficacy of Shuxuening in managing organophosphorus pesticide-induced myocarditis. Shuxuening emerges as a potential therapeutic avenue, serving as a valuable reference for clinicians seeking to address this particular disease. Nonetheless, to establish the efficacy and safety of Shuxuening definitively, as well as to thoroughly unravel its mechanisms of action, it is imperative to conduct extensive, large-scale, multicenter, and long-term clinical studies.

**TABLE 1: CLINICAL EFFICACY**

Group (n=100)	Cure	Marked Improvement	Improvement	Ineffectiveness	Overall effective rate
Observation	72 (72.00)	18 (18.00)	7 (7.00)	3 (3.00)	97 (97.00)
Control	56 (56.00)	21 (21.00)	11 (11.00)	12 (12.00)	88 (88.00)
$\chi^2$			5.838		
p			0.016		

**TABLE 2: ECG ABNORMALITY**

Group (n=100)	ST-T changes		Arrhythmia	
	Before	After	Before	After
Observation	88 (0.88)	3 (0.03)	81 (0.81)	7 (0.07)
Control	91 (0.91)	11 (0.11)	77 (0.77)	16 (0.16)
$\chi^2$	0.479	4.916	0.482	3.979
p	0.489	0.027	0.487	0.046

**TABLE 3: CHANGES OF MYOCARDIAL ENZYME PROFILE AND CHOLINESTERASE**

Group (n=100)	CK (u/l)		CK-MB ( $\mu$ /l)		LDH ( $\mu$ /l)		AST ( $\mu$ /l)	
	Before	After	Before	After	Before	After	Before	After
Observation	523.44±59.79	142.77±27.46*	45.34±9.22	16.46±3.88*	303.98±48.89	133.60±36.61*	126.99±51.37	25.20±6.05*
Control	514.51±62.76	226.93±36.59*	45.16±9.23	27.55±5.03*	317.89±56.03	226.72±54.53*	138.52±49.46	78.53±20.48*
t	-1.030	18.397	-0.141	-17.459	1.871	14.178	1.618	24.976
p	0.304	0.000	0.888	0.000	0.063	0.000	0.107	0.000

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

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