

# Study on Drug Harmful Events Caused by Adverse Reactions of Traditional Chinese Medicine Injections

Xinyuan Chen, Haiyang Sun, Hongxia Li

North China University of Science and Technology School of Pharmacy, Tangshan City, Hebei Province, 063210, China

## Abstract

**With the rapid development of medical technology, in order to comply with the trend of developing new drugs, we are striving for innovation in both drug composition and drug dosage forms. Among them, Chinese medicine injections are a class of innovative drugs in China, which are gradually widely used in clinical practice because of their advantages of rapid efficacy and reliable effect. Chinese medicine injections break the traditional way of administration of Chinese medicines and play an important role in first aid and patients who cannot take drugs orally. However, as the use of Chinese medicine injections continues to expand, and the number of reports of their adverse reactions is also increasing, resulting in safety issues becoming a top priority, making the development of Chinese medicine injections face unprecedented challenges. This paper further analyzes the causes and how to avoid the drug harmful events caused by the adverse reactions of Chinese medicine injections in recent years, hoping to provide certain help for the rational clinical application of Chinese medicine injections.**

## Keywords

**Traditional Chinese medicine injections (TCMIs); Adverse reactions (ADRs); Drug incidents.**

## 1. Foreword

According to the recommendations of the American Society of Health-System Pharmacists (ASHP), a drug hazard event is a risk or event associated with medication, including medication errors, adverse drug reactions, and adverse drug events [2]. In the 21st century, medical technology has developed rapidly, and various new drugs have emerged in an endless stream, helping human beings overcome diseases and maintain health, but at the same time, drugs are a double-edged sword, and repeated drug accidents have brought great pain to patients, and even endangered lives. Drug accidents have become a major problem that cannot be ignored in the entire pharmaceutical industry.

## 2. Status Quo

Traditional Chinese medicine injection is an aseptic preparation of a solution, emulsion, suspension and powder or concentrated solution formulated into a solution injected into the human body after the active ingredients of traditional Chinese medicine or natural medicine are extracted and purified under the guidance of the theory of traditional Chinese medicine and advanced preparation [3]. According to the survey, more than 400 enterprises across the country produce these 109 kinds of Chinese medicine injections with approval numbers, with annual sales of more than 20 billion yuan and annual use of more than 400 million person-times [4]. However, because Chinese medicine injections are new drugs independently studied in China, the promotion time is not long, and they have not been fully accepted by the public, and with the wide application of Chinese medicine injections in the clinic, the reports on the safety

of Chinese medicine injections have gradually increased, resulting in some patients questioning its safety [5].

The following is a summary of the occurrence of drug harm in Chinese medicine injections:

From 2001 to 2003, 77.2% of the adverse reactions caused by Chinese medicine were due to Chinese medicine injections. From 2004 to 2007, the proportion of adverse reactions caused by Chinese medicine injections increased to about 80%. From 2004 to 2012, the number of drug harmful events caused by the adverse reactions of Chinese medicine injections gradually increased, which caused widespread concern in society and public opinion [6].

The use of pueraria injection by 2004 had led to acute intravascular hemolysis in 18 patients; Due to the serious adverse reactions caused, in 2005, Chinese medicine injections such as Lianbizhi injection and Pushuning injection were required to revise the instructions for the use of the drug to strictly enforce their use standards; In 2006, the Houttuynia cordata allergy incident led to the death of more than 10 patients, and its use was stopped; In 2008, there were 3 cases and 1 death, respectively, caused by adverse reactions of Ingenia Yellow Injection and Eleutherococcus eleuthero injection. In 2009, there was a fatal incident of double huanglian injection; In 2012, the SFDA alerted Shengmai Injection, Shandan Injection, Xiyanning Injection and Chorunin Injection to severe allergic reactions. In November of the same year, it was announced that it was planned to eliminate 11 kinds of traditional Chinese medicine injections such as Pangshan Dragon Injection, Hepatic Xintai Injection, Liver Net Injection, Aconitum Injection [1], and many other cases appeared in clinical medication. Due to the continuous occurrence of drug damage incidents caused by Chinese medicine injections, people have doubts about the safety of Chinese medicine injections.

### 3. Cause

Allergic reactions that appear in symptoms such as anaphylactic shock and allergic asthma, and affect the respiratory system, digestive system, and nervous system function are all adverse reactions caused by traditional Chinese medicine injections, which cause unpredictable symptoms and lead to symptoms of various systems [9]. So what are the causes of adverse reactions to Chinese medicine injections?

There are many reasons for the adverse reactions of Chinese medicine injections, such as incomplete active ingredient research, lax raw material quality, incomplete preclinical research, too rough preparation process, limited clinical trials of new drugs, and non-attention to re-evaluation and follow-up studies after marketing.

First of all, the first aspect is the quality factor of raw materials, Chinese medicine injections are usually a compound composed of a variety of complex active ingredients of medicinal materials, and some of the active ingredients of Chinese medicines are not yet clear, so Chinese medicine injections are prone to problems in production. In addition, the quality of Chinese herbal medicines is greatly affected by the place of origin and harvest season, due to different places of origin, different growth environments, different harvesting times, different placement times, etc., so that the effective or toxic ingredient content of the same kind of medicinal materials is different. The most important thing is that the quality of raw materials and medicinal materials varies widely, and the quality control of the production department is not strict, resulting in the production of Traditional Chinese medicine injections, which are prone to safety problems [1].

The second aspect is the reason for the stability of the active ingredient in Chinese medicine, for drugs such as Chinese medicine, which are mainly derived from natural products, physical factors and chemical factors will have an impact on the stability of its active ingredient. When one or more factors affect the injection of traditional Chinese medicine, it may lead to the degradation of its active ingredients, and the formation of impurities or deterioration and mold, resulting in adverse reactions.

The third aspect is the influence of the preparation method, different Chinese medicines use different processing methods, and different processing methods may also make Chinese medicines exert different medicinal effects. At present, the level of process for preparing Chinese medicine injections is not high, and it is an important task to improve the standardization of the production process of Chinese medicine injections, and there are also instabilities in the control process technology. Due to different production processes, there are some differences in the toxic components and active ingredients of the preparation. While these differences have an impact on the efficacy of the injection, they may also cause adverse reactions.

#### 4. Method

After analyzing the causes of adverse reactions of Chinese medicine injections, how to avoid them in the future drug research and development and use, so as to reduce the occurrence of drug harmful events?

The most important thing is to put the quality of good drugs, from the raw materials of the drug to the excipients used for preparation, we must strictly ensure the quality. Whether it is the procurement and use of the correct raw materials and accessories or the selection of suitable packaging materials for pharmaceutical manufacturers is a basic requirement, but also should be raw materials, packaging materials, intermediate products, to be packaged finished products and finished product identification, inspection and content determination must have relevant records, the material and finished products should be left samples for inspection or inspection. At the same time, it is necessary to strengthen the supervision of drugs.

Secondly, it is necessary to ensure the correct production process of drugs and standardize the daily storage of drugs. Article 25 of the Drug Administration Law of the People's Republic of China specifically proposes that "when examining and approving drugs, the drug supervision and administration department under the State Council shall review and approve chemical raw materials together, and review relevant excipients, packaging materials and containers that directly contact drugs" [10].

Finally, it is necessary to pay attention to the rational use of new drugs such as traditional Chinese medicine injections, strictly grasp the indications, and reasonably choose the route of administration; Strictly control the dosage and course of treatment; It is strictly forbidden to mix and match, cautiously combine drugs, and strengthen drug monitoring. In addition, improve the basic equipment for emergency treatment, strengthen the training of medical personnel's emergency response ability, and take timely countermeasures when suspicious adverse events are found, so as to effectively prevent the occurrence of drug hazards.

#### References

- [1] TAN Lejun, WANG Meng, ZHU Yan. Research progress on adverse reactions of Chinese medicine injections [J]. Chinese Journal of Chinese Materia Medica, 2014, 39(20): 3889-3898.
- [2] Hou Kelu, Huang Lin, Feng Yufei. Retrospective analysis of drug hazards related to drug quality in China [J]. Chinese Journal of Hospital Pharmacy, 2020, 40(06): 640-643. DOI:10.13286/j.1001-5213.2020.06.09.
- [3] Zhao Feiyan, Qin Yuanyuan, Shen Xikun, Huang Yuyu, Tang Liang, Tang Qiuyue, Xu Liwei." The establishment of the scoring classification method and its application in the evaluation of the function of traditional Chinese medicine injections [J]. Modern Applied Pharmacy of China, 2022, 39(02): 224-230. DOI:10.13748/j.cnki.issn1007-7693.2022.02.014.
- [4] LI Yanlin. Characteristics of sensitization reactions and sensitization markers of Shuanghuanglian injection [D]. Peking Union Medical College, 2016.

- [5] Zheng Na. The effect of key monitoring on the rational clinical use of Chinese medicine injections based on the review of doctors's orders [J]. Journal of Chinese Medicine Management, 2021, 29(23): 175-176. DOI: 10.16690/j.cnki.1007-9203.2021.23.099.
- [6] WANG Chenxiao. Safety of Clinical Application of Chinese Medicine Compatibility and Chinese Medicine Injection [C] //Proceedings of the 2nd Clinical Chinese Medicine Conference. [Publisher unknown], 2018: 20-23.
- [7] Ma Hui. Research on medical damage liability in the context of basic medical treatment [M]. Chinese Min University Press:, 201808.247.
- [8] Meng Xiangying. Adverse reactions of traditional Chinese medicine injections and their research progress [J]. China Health Nutrition, 2012, 22(06): 599-600.
- [9] Zhao Baosheng, Li Chunna, Fan Bingruo, Wei Qian, Xu Tunhai, Wu Jiarui. Research status and countermeasures of safety of chinese medicine injections [J]. Journal of Clinical Drug Therapy, 2013, 11(05): 15-18.
- [10] Ma Guanglin,Zhao Yuxin,Zhang Wei. Study and implement the newly revised Drug Administration Law to strengthen the status and role of drug standards [J]. China Food and Drug Administration, 2020(01): 18-31.