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Abstract

The objective of this paper was to investigate the characteristics and general rules of domestic safflower injection causing allergic shock, to retrieve the medical journals published domestically, and to make statistical analysis on the cases of allergic shock caused by safflower injection. Results showed that the incidence of allergic shock caused by safflower injection in patients above 40 years old was high: females were more than males. It occurred within 30min after medication, and no patient died after emergency treatment. The study concluded that allergic shock caused by safflower injection is related to many factors, and clinical care personnel should pay more attention to it.

Keywords: safflower injection; allergic shock; literature analysis

Introduction

Safflower is the dried flower of *Carthamus tinctorius* L. plant in the family Compositae. It is pungent and warm in nature, and enters the channels of heart and liver. Its main functions are promoting blood circulation, removing blood stasis and stopping pain (State, 2010). Safflower injection is yellowish red to brownish red sterilised water solution extracted from safflower, containing safflower uranidin, safflower quinone glycoside and other ingredients. It is clinically applied in gynaecology. For example, it can promote coronary arterial blood flow increase, inhibit platelet aggregation, prevent thrombosis, and treat reproductive diseases. It also has good and fast efficacy in the treatment of other aspects in clinical, such as occlusive cerebrovascular disease, coronary heart disease, myocardial infarction, vasculitis, etc. With a wide range of clinical applications, its adverse reactions are significantly increased (Cheng et al., 2011; Rong et al., 2004; Guo, 2005; Zhang et al., 2004; Dong, 2003), in which, the most serious one is allergic shock. This paper makes statistics and analysis on the literature reports of allergic shock caused by safflower injection to provide references for rational and safe clinical drug use.

Data and methods

We retrieved CNKI Chinese Academic Journal Web publishing pool with “safflower injection” and “allergic shock” as the keywords, rejected the repeated reports of same cases, excluding relevant literature reviews, and found a total of 14 conforming literatures (Zhao et al., 2011; Song et al., 2006; Wang et al., 2004; Yang et al., 2011; Pan., 2005; Han., 2003; Yang et al., 2008; Ji, 2003; Du et al., 2005; Fan et al., 2007; Yu., 2004; Zhang et al., 2006; Guo et al., 2007; Liu., 2005), that is, a total of 14 cases. Bibliometrics was adopted to assort and summarise patient gender, age, primary diseases, allergic history, allergic shock occurring time, usage, dosage, drug combination, clinical manifestations, prognosis, and other information in case data.

Results

Gender and age distribution

The 14 cases have gender and age records, including 5 males (35.71%) and 9 females (64.29%). The youngest is 24 years old and the oldest is 76 years old, as shown in Table 1.

Table 1: Gender and age distribution for allergic shock caused by safflower injection (case, %)

| Gender | Age (years old) | | | | Total |
|--------|-----------------|----------|----------|----------|----------|
| | <18 | 18-40 | 41-60 | >60 | |
| Male | 0 | 3 | 2 | 0 | 5(35.71) |
| Female | 0 | 2 | 5 | 2 | 9(64.29) |
| Total | 0(0.00) | 5(35.71) | 7(50.00) | 2(14.29) | 14(100) |

Primary diseases and past medical history

In the 14 cases of allergic shock, the primary diseases are mostly different, as shown in Table 2.

Table 2: Primary diseases and past medical history

| Primary disease | n | Literature |
|---|---|-------------------------------------|
| Diabetes mellitus complicated with neurovascular disease | 1 | Dong, 2003 |
| Idiopathic pulmonary interstitial fibrosis | 1 | Zhao et al., 2011 |
| Chronic Renal Insufficiency | 1 | Song et al., 2006 |
| Limb numbness, with past hypertension and allergic rhinitis history | 1 | Wang et al., 2004 |
| Chronic hepatitis B | 1 | Yang et al., 2011 |
| Lacunar cerebral infarction in right frontal medulla | 1 | Pan, 2005 |
| Basilar arterial insufficiency, Lacunar cerebral infarction | 1 | Han, 2003 |
| Ocular fundus arteriosclerosis, ocular fundus hemorrhage, with more than 10 years of hypertension | 1 | Yang et al., 2008 |
| Coronary heart disease, myocarditis, anteroseptal myocardial infarction | 3 | Ji, 2003; Du et al., 2005; Yu, 2004 |
| Fracture of nasal bone | 1 | Fang, 2007 |
| Protrusion of cervical disc | 1 | Zhang et al., 2006 |
| Automobile crushes lateral malleolus and foot | 1 | Guo et al., 2007 |

Past allergic history

In the 14 cases of allergic shock, 6 cases have no allergic history, only 2 cases have allergic history (one case is allergic to salvia miltiorrhizae injection, and the other is allergic to penicillin), and the other 6 cases have unclear allergic history (but not indicating no allergic history).

Allergic shock occurring time distribution

Allergic shock mostly occurs within 10min after drug administration. The fastest is about 2min, and the slowest is continuous intravenous infusion till 16d, discontinue till 28d, and at about 5min on 29d. The other 2 cases exceeding 30min occur respectively at the second and fourth (once a day) infusion. It is shown in Table 3.

Table 3: Allergic shock occurring time distribution

| Time (min) | <5 | 5-10 | 11-30 | >30 |
|----------------|-------|-------|-------|-------|
| N | 4 | 4 | 3 | 3 |
| Proportion (%) | 28.57 | 28.57 | 21.43 | 21.43 |

Usage and dosage of safflower injection

The usage and dosage specified in the Instructions of Safflower Injection (Shanxi Yabao Pharmaceutical Co., Ltd): for the treatment of occlusive cerebrovascular disease, we used intravenous infusion with 15ml each time; we diluted it with 250~500ml 10% glucose injection, once a day, 15~20 times for a course. For the treatment of coronary heart disease, we used intravenous infusion, 5~20ml each time; we diluted it with 250~500ml 5%~10% glucose injection, once a day, 10~14 times for a course, and the course interval is 7~10 days. For the treatment of vasculitis, we used intramuscular injection, 2.5~5ml each time, 1~2 times a day. All the 14 cases of allergic shock are for intravenous administration. Except one case that has unclear dosage, the dosage for the other cases is within the common range. In 4 cases, normal saline is used to dilute safflower injection, different from the instructions. It is shown in Table 4.

Table 4: Usage and dosage of safflower injection

| Usage and dosage | n |
|---|---|
| 250ml normal saline + 20ml safflower injection for intravenous infusion | 4 |
| 250ml 5% glucose + 20ml safflower injection for intravenous infusion | 5 |
| 250ml 5% glucose + 15ml safflower injection for intravenous infusion | 1 |
| 250ml 5% glucose + 40ml safflower injection for intravenous infusion | 1 |
| 250ml 10% glucose + 20ml safflower injection for intravenous infusion | 1 |
| 300ml 5% glucose + 10ml safflower injection for intravenous infusion | 1 |
| Unclear, only know 40ml safflower injection for intravenous infusion | 1 |

Drug combination

In the 14 cases, 5 cases have drug combination, in which, one case takes short-acting insulin, 1 case takes Beijing No. 0 anti-hypertension tablets, 1 case takes Suxiao Jiuxinwan, 1 case takes other drugs (detailed drug is not recorded) and 1 case takes traditional Chinese medicine for heart disease (detailed drug is not recorded). 2 cases have no drug combination, and the other 7 cases are unclear (not indicating no drug combination).

Producers and batch numbers of safflower injections causing allergic shock

In the 14 cases of allergic shock, 5 cases have unclear producers and batch numbers, and the other cases are shown in Table 5.

Table 5: Producers and batch numbers of safflower injections causing allergic shock

| Producer and batch number | n |
|--|---|
| Jilin Weiwei Pharmaceutical Co., Ltd, Batch No.: 2004010, 20030502 | 2 |
| Shanxi Hengda Pharmaceutical Co., Ltd, Batch No.: 05040401 | 2 |
| Shanxi Yabao Pharmaceutical Co., Ltd, Batch No.: 20010601 | 1 |
| Taiyuan Huawei Pharmaceutical Co., Ltd, Batch No.: 20021230 | 1 |
| Yaan 999 Pharmaceutical Co., Ltd, Certificate No.: 251020673 | 1 |
| Wanrong 999 Pharmaceutical Co., Ltd, Batch No.: 0607021 | 1 |
| LOKIS (Jilin) Pharmaceutical Co., Ltd, Certificate No.: Z22023866, Batch No.: 20041102 | 1 |
| Unclear producers and batch numbers | 5 |

Emergency measures and prognosis

When allergic shock occurred, the safflower injection was stopped immediately. Patient was made to lie on their back, to inhale high-flow

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oxygen, to accept ECG life care, and to intravenously take epinephrine, dexamethasone, metaraminol, etc. The patients accompanied by sharp decline in blood pressure were given dopamine, diphenhydramine and other vasopressors. Patient's blood pressure, pulse, respiration and heart rate were closely monitored, and patient's consciousness, pupil, skin and mucous membrane conditions were also observed. 6 patients recovered within 30min of rescue, 5 patients recovered within 2 hours, the other 3 patients recovered after 1 day, and no patient died.

Discussion

Relationship between allergic shock and gender and ages

It can be seen from the age distribution that the cases are mainly distributed in >40 years old, but not <18 years old, because, on one hand, the indications of safflower injection are the diseases for elderly people, leading to increase of drug use frequency and probability as well as the occurrence of adverse reactions. On the other hand, elderly patients have drug sensitivity and tolerance different from young patients. The efficacy threshold turns narrow, metabolic capacity decreases, leading to drug accumulation (Zhang et al., 1995) and adverse reactions. It can be seen from gender distribution that females (64.29%) are significantly more than males (35.71%). It is likely that safflower injection more easily cause allergic shock in female patients, but due to limited data collection, it needs further observation, study and verification in clinical.

Relationship between allergic shock and primary diseases

It can be seen from Table 2 that safflower injection is applied in heart cerebrovascular diseases and some orthopaedic diseases, but the incidence of allergic shock in patients with heart cerebrovascular diseases is much higher. In addition, in patients with liver and kidney diseases, the drug may affect the body's metabolism, reduce the body's tolerance, and increase the probability of adverse reactions.

Relationship between allergic shock and past allergic history

In the 14 cases, 6 cases have unclear past allergic history, indicating that clinical staff did not pay full attention to patients' allergic history or that the quality of ADR reports needs to be improved (Bian et al., 2010). In general, patients with allergic history are more prone to allergic shock, but due to limited data collection, it needs further observation, study and verification in clinical.

Relationship between allergic shock and occurring time

The probability for safflower injection to cause allergic shock within 10min after drug administration reaches up to 57.14%, and that within 30min is even as high as 78.57%. So, medical care staff should closely observe the patients' conditions in the infusion process and immediately stop infusion when abnormalities are found. Three patients have allergic shock after the second infusion, suggesting that medical care staff should be vigilant at the application of safflower injection.

Relationship between allergic shock and drug usage and dosage and drug combination

The drug instruction recommends to use 250~500ml 5% or 10% glucose injection as the dilution solvent, and some literatures report that the combination of two injections caused increase of pH value and insoluble particles, suggesting that safflower injection should not be combined with 0.9% sodium chloride injection for use. Chinese medicine injection contains relatively complex active ingredients and is prone to adverse reactions, and the combination with western medicine is more likely to cause adverse reactions (Zhang et al., 2010).

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