CASE REPORT

Treating Severe Adverse Drug Reactions Caused by Ischemic Optic Neuropathy with Ginkgo Biloba Extract Injection: A Case Report

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ABSTRACT

Background • Ginkgo biloba extract preparations are commonly used in ophthalmology to improve circulatory disorders and provide neurotrophic support for the treatment of optic neuropathy. However, their use also carries a higher risk of adverse drug reactions (ADRs), some of which can be severe and even life-threatening, such as anaphylactic shock. This case report highlights the importance of recognizing and managing ADRs associated with ginkgo biloba extract in ophthalmology clinical practice. This report aims to emphasize the need for appropriate patient selection, adherence to prescribing guidelines, and proactive measures to reduce ADR occurrence.

Case Presentation • We present the case of a patient who experienced a severe ADR following the administration of Ginkgo biloba and Damo injection. The patient, a middle-aged individual without a history of allergies, developed anaphylactic shock within 30 minutes of medication initiation. Prompt medical intervention, including medication withdrawal, resuscitation, and intensive care unit transfer, led to symptom relief and successful recovery.

Conclusions • This case underscores the need for vigilance when prescribing ginkgo biloba extract, particularly in middle-aged and elderly patients. Despite no previous history of allergies and adherence to the prescribed dosage, severe ADR can still occur. Close monitoring of patients within the first 30 minutes of medication administration is crucial. Furthermore, strict adherence to drug instructions, proper TCM syndrome differentiation, appropriate choice of infusion solvents, and strict control of drip rates should be considered to enhance patient safety. Other factors such as patient age, allergy history, and initial medication were also identified as important considerations in preventing ADRs. This case report emphasizes the significance of early identification, immediate withdrawal of medication, vital sign monitoring, and timely administration of anti-allergy drugs in managing ADR. (*Altern Ther Health Med.* 2023;29(5):78-81).

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BACKGROUND

Ginkgo biloba extract is commonly used in ophthalmology to enhance ocular blood flow and address neurological disorders, particularly in treating optic nerve diseases. However, its utilization is not without risks, as it has been associated with a relatively high incidence of adverse drug reactions. According to previous studies, the reported incidence of adverse reactions to Ginkgo biloba extract can reach as high as 9.36%.[1] Adverse drug reactions (ADRs) are defined as harmful reactions that occur as a result of the normal usage and dosage of qualified drugs but are unrelated to the drug's intended purpose.[2] Severe ADRs encompass reactions that lead to death, pose life-threatening risks, or cause significant damage to organ function. Examples include anaphylactic shock, a clinically critical condition that can be fatal. However, ophthalmologists often have limited exposure to severe rescue situations in clinical practice. They may lack familiarity with relevant knowledge and have relatively weak proficiency in managing severe ADRs.[3] This knowledge gap poses significant medical safety risks when identifying and addressing severe ADRs.

This paper presents a case report and examines previous literature to summarize the clinical characteristics, diagnosis, and treatment strategies for ADRs associated with injection-based therapies. Furthermore, it discusses key preventive measures to enhance drug administration's safety in ophthalmology.[4,5]

CASE PRESENTATION

Patient Profile and Medical History

The patient, Mr Zhou, a 55-year-old male, was admitted to the hospital on 29 May 2020 with a diagnosis of ischemic optic neuropathy. He presented with sudden blindness and symptoms of qi deficiency and blood stasis. The patient reported experiencing mental sleep, loose stools, and normal urine. He had a history of diabetes for the past 4 months but did not adhere to regular medication. There was no history of other chronic diseases, drug allergies, or food allergies. Additionally, the patient had a 20-year history of alcohol consumption at a rate of half a catty per day.

Ocular Examination

Upon admission, the visual acuity of both eyes was measured as index/30cm, with no improvement upon correction. The intraocular pressure was recorded as 15mmHg in the right eye and 14mmHg in the left eye. There were no apparent restrictions in binocular eye movement, and the ocular position was positive. The conjunctiva of both eyes showed no signs of congestion, and the cornea was transparent. No keratic precipitates (KP) were observed, and the depth of the anterior chamber was approximately 1CT in the peripheral region. No signs of Tyndall effect Tyn (-) or cells (-) were detected. Both pupils were bilateral, round with a diameter of 5mm, and they exhibited direct light reflex. Mild lens opacity was observed in the pupil area, along with mild vitreous opacity.

Fundus Examination

Upon fundus examination, the color of the optic discs in both eyes appeared pale and clear, with a cup-to-disc (C/D) ratio of 0.5. The proportion of retinal vascular walking was roughly normal, with an arterial-to-venous (A/V) ratio of 2/3. The macular fovea was not clearly visible.

Clinical Examination

The patient's body temperature was recorded as 36°C, heart rate as 76 beats per minute, respiratory rate as 18 breaths per minute, and blood pressure as 126/78mmHg. No significant cardiopulmonary abnormalities were detected. The tongue appeared dark red with tooth marks, and there was a thin white coating and fine veins.

Treatment Protocol

After stabilizing the patient's blood sugar levels, traditional Chinese medicine (prescribed in the outpatient setting) was continued, and acupuncture treatment was administered. The patient received a static infusion of 70mg ginkgo leaf extract injection in 0.9% sodium chloride solution (250 ml) once daily, at a drip rate of approximately 60 drops per minute.

Development of Anaphylactic Shock

On the sixth day, the patient experienced symptoms of palpitations, chest tightness, lip cyanosis, cold sensation, and generalized skin flushing, which were indicative of anaphylactic shock.

Treatment Response

The medication was immediately discontinued. The patient's body temperature was recorded as 36°C, heart rate as 161 beats per minute, blood pressure as 66/37mmHg, blood glucose as 4.6 mmol/L, and the electrocardiogram showed no obvious abnormalities. Following urgent consultation with the cardiology and critical care departments, double venous access was established, and a full-speed static expansion of 1000 ml of sodium chloride injection was administered. The patient received a static dose of 10mg of dexamethasone, a 0.3 g muscle injection of adrenaline for an anti-allergic effect, and a static dose of 2 g of calcium gluconate. A dopamine pump was initiated to stabilise circulation, and the patient was provided with oxygen. Subsequently, the patient was transferred to the intensive care unit (ICU) for further treatment. The patient's symptoms were relieved, and their vital signs recovered smoothly. Even in the absence of a history of allergies and with no abnormalities observed after several days of continuous medication, vigilance should not be relaxed, and continued monitoring of medication should be ensured.

DISCUSSION

The patient exhibited typical symptoms of anaphylactic shock, including chest tightness, cyanosis, skin flushing, increased heart rate, and sudden changes in blood pressure.[5] The primary diagnosis was ischemic optic neuropathy, which aligned with the indications for the drug administered. The patient had no history of drug or food allergies, and there were no contraindications for the medication.[6] The prescribed dosage of 70mg/day and a drip rate of 60 drops per minute were within the recommended usage and dosage. The medication was reviewed, and confirmed that it was a qualified drug within its shelf life. It suggests that anaphylactic shock is a severe adverse drug reaction that poses a life-threatening risk and is unrelated to the drug's intended purpose and normal dosage.[7]

ADR should be differentiated from the effects of concomitant medication, disease progression, and other treatments.[8] In this case, the patient did not receive any other injectable medications, and there was a history of using oral hypoglycemic drugs for many years without any previous adverse reactions.[9] The patient's ischemic optic neuropathy does not directly affect blood pressure or heart rate, and no cardiovascular diseases were detected in previous or admission physical examinations. Therefore, it can be concluded that the severe ADR observed, in this case, is attributable to the injection of ginkgo biloba extract.[10]

Ginkgo biloba leaf contains over 160 components, including flavonoids, phenols, terpenoids, trace elements, and various amino acids.[11] These components have the potential to delay or prevent the apoptosis of retinal ganglion cells by improving impaired nerve microcirculation,

scavenging free radicals, and providing neurotrophic support. However, due to the complexity of its components and the multitude of targets, ginkgo biloba extract is more likely to induce ADRs during clinical applications. One study reported an incidence of ADRs with ginkgo biloba extract at 9.36%, with severe ADRs accounting for approximately 18%.[12]

By conducting a comprehensive search and analysis of previous literature on Ginkgo biloba extract from databases such as Wanfang, CNKI, and Wip from 1996 to the present,[13] the following clinical features of ADRs caused by ginkgo biloba extract have been identified: (1) Predominantly affects middle-aged and elderly patients, with 70% of patients being over 50 years old; (2) 87% of the patients have no history of allergies; (3) ADRs mainly occur within 30 minutes of administration, with the earliest onset observed between 1 to 2 minutes, and the latest after more than 10 days of continuous medication; (4) ADRs may involve multiple organs or systems of the body, with the circulatory system being the most commonly affected (20.62%), followed by general malaise, and skin damage.[14] Other systems that may be affected include facial features, the nervous, respiratory, digestive, and reproductive systems.

In the case of this patient, who was over 50 years old and had no history of allergies, the ADR occurred on the 6th day of medication. This highlights the importance of closely monitoring the medication response in middle-aged and elderly patients within 30 minutes.[15] Even in the absence of a history of allergy and no abnormalities observed after several days of continuous medication, vigilance should not be relaxed, and continued monitoring of medication is necessary.[16]

It has been suggested that allergic reactions caused by Ginkgo biloba injection are primarily attributed to the presence of impurities, such as tannins, that are not adequately removed during the extraction process. Once injected into the body, these impurities can form larger molecular complexes by binding to plasma proteins, leading to allergic reactions. Additionally, the patient's allergic constitution and the intensity, concentration, and infusion rate of the drug can also contribute to such reactions. Previous literature analysis has identified common factors contributing to ADRs: the absence of syndrome differentiation and treatment records. Ginkgo biloba leaves possess a taste that is sweet, bitter, and flat, and they belong to the heart and lung meridians. They are known to promote blood circulation, relieve pain, and are suitable for conditions such as wind-phlegm flow in the meridians and blood stasis or obstruction. These conditions should be accompanied by evidence of damp stasis.[17]

In the present case, the patient had a long history of alcohol consumption, which can lead to dampness and heat accumulation in the body, damaging the spleen and stomach and resulting in spleen deficiency. It can hinder the promotion of essence, qi, and blood to the eyes, leading to unknown divine light. The patient's tongue exhibited characteristics such as dark red color, tooth marks, thin white coating, fine veins, and stringy appearance, which are consistent with the pattern of deficiency in temper, dampness, and blood stasis, supporting the diagnosis.[18-19]

However, the previous literature did not include information regarding TCM syndrome and the type of patients, which contradicts the fundamental principles of TCM syndrome differentiation and treatment. This omission poses a hidden risk to the safe and rational use of drugs. Secondly, the choice of intravenous infusion solvent is inappropriate. According to the instructions for Shuxuening injection, a 5% glucose injection should be used as the diluent. When sodium chloride injection containing ionic components is used, it can lead to the formation of insoluble particles due to salt precipitation, thereby increasing the risk of ADRs. Studies have shown that the incidence of ADRs was 2.62% with 5% glucose and 5.60% with 0.9% sodium chloride, which was statistically significant ($P < .05$).[19]

Improper selection of sodium chloride as the diluent was observed in 35% of previous cases. Thirdly, the intravenous drip rate is excessively fast.[20] The injection manual for ginkgo biloba extract recommends a drip rate of 15-30 drops per minute for adults. Drip rates that are too fast can result in the rapid infusion of a large amount of medication into the vein, increasing the likelihood of ADRs. In this case, and 80% of cases in the previous literature, the drip rate exceeded 40 drops per minute. These three factors highlight the importance of adhering to the principles of syndrome differentiation, selecting the appropriate diluent, and strictly controlling the drip speed.

The key aspects of managing ADR include early identification, immediate discontinuation of the medication, monitoring of vital signs, and providing symptomatic treatment. Prompt administration of anti-allergy drugs and necessary life support measures is crucial. Consulting a physician for diagnosis and treatment assistance is essential in critical situations. In this particular case, the patient's condition was critical.[21-22] Fortunately, the onset occurred during regular working hours when the ward director conducted rounds. Thanks to the coordinated efforts of doctors and nursing staff at all levels, the patient was successfully stabilized, and no serious adverse consequences occurred.

CONCLUSION

As a Chinese patent medicine preparation, the high incidence of ADRs, particularly severe ADRs, associated with ginkgo biloba extract poses significant safety risks in ophthalmology clinical treatment. When prescribing Ginkgo biloba and Damo injections, it is essential to carefully select the appropriate patient population based on their functional indications. Medical advice should be provided in accordance with the instructions, and the pharmacy department should effectively communicate drug usage information and precautions to clinical practitioners. It is crucial to strengthen the review process of medical advice and actively collect and

report any adverse drug reactions to enhance safety. It also emphasizes the need to summarize and analyze drugs that have shown adverse reactions regularly. These measures aim to reduce the occurrence of adverse reactions, promote rational medication, and improve patient outcomes.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Consent was obtained or waived by all participants in this study.

PAYMENT/SERVICES INFO

All authors have declared that no financial support was received from any organization for the submitted work.

FINANCIAL RELATIONSHIPS

All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

OTHER RELATIONSHIPS

All authors have declared that no other relationships or activities could appear to influence the submitted work.

CONFLICTS OF INTEREST

The authors declared no conflicts of interest.

AUTHORS' CONTRIBUTIONS

All authors contributed equally to this work.

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