Exploring the Effect of Glycyrrhizic Acid Preparations Combined with Anti-Tuberculosis Drugs on the Treatment of Pulmonary Tuberculosis and Its Preventive Role in Hepatic Injury

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Abstract: The purpose of this study is to evaluate the effectiveness of glycyrrhizic acid preparations in combination with anti-tuberculosis drugs for treating pulmonary tuberculosis, as well as to assess their role in preventing hepatic damage in patients. A total of 3420 patients diagnosed with pulmonary tuberculosis at our hospital between January 1, 2024, and December 31, 2024, were included in the study. All patients received anti-tuberculosis treatment and were randomly assigned to two groups, with 1710 patients in each. The control group received glycohydroxylate preparation combined with anti-tuberculosis drugs, while the experimental group was given anti-tuberculosis drugs along with glycyrrhizic acid preparation. Recovery time for liver function abnormalities, overall treatment outcomes, and adverse reactions were analyzed. The experimental group demonstrated a shorter recovery time for liver function abnormalities, a higher total treatment effectiveness, and a lower rate of complications compared to the control group. These differences were statistically significant ($P<0.05$). The combination of glycyrrhizic acid preparations with anti-tuberculosis drugs facilitates faster recovery of liver function, enhances the clinical treatment response, and reduces the occurrence of complications in patients with pulmonary tuberculosis. This treatment approach is safe and reliable.

1. Introduction

Pulmonary tuberculosis is a chronic infectious disease caused by Mycobacterium tuberculosis. Its pathological mechanisms are complex, as it primarily affects the lungs and lymphatic system, but can also impact other bodily systems, including the circulatory and nervous systems. This often results in common clinical signs such as fatigue and mild fever. [1]. Currently, the clinical treatment of pulmonary tuberculosis primarily relies on the use of anti-tuberculosis drugs. However, it is noteworthy that long-term and sustained drug intervention may adversely affect liver function, this can potentially lead to drug-induced liver injury (DILI), which presents a significant risk to the patient's overall health. [2]. Drug-induced liver injury has become one of the most prominent adverse reactions in the treatment of pulmonary tuberculosis, with an incidence rate as high as 47%, significantly hindering the treatment process and patient recovery .From a clinical treatment perspective, the three-drug or four-drug regimen consisting of rifampicin, ethambutol, isoniazid, and pyrazinamide remains the mainstream treatment for pulmonary tuberculosis . However, while these treatments are effective, they may also lead to varying degrees of liver damage, and in extreme cases, could even result in liver failure [3]. Glycyrrhizic acid diamine, an 18-α-glycyrrhizic acid diammonium lipid complex, has a chemical structure similar to steroids and can bind with steroid metabolic enzymes in the liver, thereby reducing the liver's inactivation of steroids [4]. This drug has significant pharmacological activities, including anti-inflammatory, anti-fibrosis, anti-oxidant, and hepatocyte membrane structure protection. Based on these findings, this study aims to clarify the effect of glycyrrhizic acid preparations combined with anti-tuberculosis drugs in the treatment of pulmonary tuberculosis and their preventive role in liver injury. We selected recent

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pulmonary tuberculosis patients treated in our hospital for the study, and the results are reported as follows.

2. Materials and Methods

2.1 General Data

Inclusion criteria: 1. Age between 18 and 65 years; 2. Diagnosis of pulmonary tuberculosis confirmed through clinical evaluation, imaging, and sputum culture positive for Mycobacterium tuberculosis; 3. No liver function abnormalities at the baseline; 4. Patients who have not previously undergone tuberculosis treatment.

Exclusion criteria: 1. Primary liver diseases such as hepatitis, cirrhosis, or liver cancer; 2. Allergic conditions; 3. Pregnant or breastfeeding women; 4. Severe underlying health conditions; 5. Poor adherence to treatment protocols.

A total of 3420 patients diagnosed with pulmonary tuberculosis were admitted to our hospital between January 1, 2024, and December 31, 2024. All patients were administered anti-tuberculosis drugs and were randomly assigned to two groups, each consisting of 1710 patients. The control group received a combination of glycyrrhizic acid preparations and anti-tuberculosis drugs, while the research group was treated with anti-tuberculosis drugs and glycyrrhizic acid preparations. The control group comprised 1042 males and 668 females, aged between 25.0 and 65.0 years (mean age: 38.73±4.11 years), with a disease duration ranging from 0.2 to 3.0 years (mean: 1.15±0.22 years). The research group consisted of 1052 males and 658 females, aged between 25.0 and 65.0 years (mean age: 39.05±3.98 years), with a disease duration of 0.1 to 3.0 years (mean: 1.14±0.26 years). No significant differences were found between the two groups ($P>0.05$).

2.2 Methods

Anti-tuberculosis drug regimen:Isoniazid tablets (Manufacturer: Shanxi Yunpeng Pharmaceutical Co., Ltd.; Approval No.: H34021587; Batch No.: G190903; Specification: 0.19g): 0.39g per dose, taken once every other day.Rifampicin capsules (Manufacturer: Hangzhou Minsheng Pharmaceutical Co., Ltd.; Approval No.: H33022466; Batch No.: C19L243; Specification: 0.15g): 1 capsule (0.15g) every morning on an empty stomach, once daily.Ethambutol hydrochloride tablets (Manufacturer: Hangzhou Minsheng Pharmaceutical Co., Ltd.; Approval No.: H33021602; Batch No.: T20D009; Specification: 0.25g): 0.75g per dose, taken once daily.

Adjuvant therapy drugs:The control group was treated with glycohydroxylate tablets (Manufacturer: Huazhong Pharmaceutical Co., Ltd.; Approval No.: H42020610; Batch No.: 20200502; Specification: 100mg): 100mg per dose, taken three times a day.

The research group was treated with compound glycyrrhizic acid glycoside capsules (Manufacturer: Beijing Kaiyin Technology Co., Ltd.; Approval No.: H20080006; Specification: 25mg glycyrrhizic acid glycoside, 25mg glycine, 25mg methionine per capsule; Batch No.: 19163): 3 capsules per dose, taken three times a day.

Treatment duration: Both groups received continuous treatment for 4 weeks.

2.3 Evaluation Criteria

The recovery time for liver function abnormalities was assessed, therapeutic outcomes were measured, and adverse reactions were documented. The biochemical markers for liver function included alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and total bilirubin (TBil). Blood samples were taken starting from the second week of treatment, with liver function monitored every 3 days. The recovery time for abnormal liver function indicators was calculated based on these results.

Therapeutic effect evaluation:

Clinical symptoms such as cough, sputum, fever, and night sweats were recorded. Liver function indicators (ALT, AST, ALP, TBil) were also evaluated. Lesion absorption was evaluated using X-rays or CT scans. Adverse reactions included fever, fatigue, vomiting, anorexia, diarrhea, rash,

and dull pain in the liver area.

2.4 Statistical Methods

Statistical analysis was performed using SPSS version 25.0. Data that followed a normal distribution were presented as mean ± standard deviation (x±s), and comparisons between groups were conducted using t-tests. Categorical variables were expressed as frequencies (n) and percentages (%), with inter-group comparisons made using the chi-square test. A P-value of less than 0.05 was regarded as statistically significant.

3. Results

3.1 Recovery time of liver function abnormalities

The recovery time of liver function abnormalities was significantly shorter in the research group than in the control group, with a statistically significant difference (P<0.05). See Table 1 for details.

Table 1 Recovery time of liver function abnormalities (x±s, d)

Group	N	ALT	AST	ALP	TBil
Research	1710	21.07±4.13	20.11±3.28	19.31±4.73	20.28±4.17
Control	1710	32.26±0.29	34.83±0.89	35.94±5.11	28.01±5.51
t	-	7.825	9.028	9.382	7.275
P	-	<0.05	<0.05	<0.05	<0.05

3.2 Therapeutic effect comparison

The total effective rate in the research group was higher than that in the control group. Adverse reactions occurred in 2.63% of the research group and 4.09% of the control group. The difference was statistically significant (P<0.05). See Table 2 for details.

Table 2 Therapeutic effect comparison (n, %)

Group	N	Effective	Effective	Ineffective	Total Effective	Adverse Reactions
Research	1710	1203（70.35）	476（27.84）	31（1.81）	1679（98.19）	45（2.63）
Control	1710	726（42.46）	859（50.23）	125（7.31）	1585（92.69）	70（4.09）
X2	-	-	-	-	15.385	4.595
P	-	-	-	-	<0.05	<0.05

4. Discussion

Pulmonary tuberculosis is a common and highly infectious disease in clinical practice. Its standard treatment regimen typically includes anti-tuberculosis drugs such as rifampicin and isoniazid [5]. These drugs are primarily processed in the liver through metabolic and breakdown processes, and prolonged use can lead to liver damage, particularly in elderly populations, patients with viral hepatitis, and individuals with liver dysfunction due to malnutrition [6]. Drug-induced liver injury (DILI) not only has the potential to interrupt or prolong treatment plans but can also weaken patient adherence to therapy, thereby increasing the risk of secondary drug resistance and profoundly affecting patient prognosis [7]. According to previous studies, the incidence of drug-induced liver injury in patients treated with the standard anti-tuberculosis regimen containing rifampicin and isoniazid fluctuates between 3% and 18%, with the incidence in China approximately 11.9% [8]. This data indicates that drug-induced liver injury is a significant issue during the treatment of pulmonary tuberculosis. The occurrence of liver injury as an adverse reaction during tuberculosis treatment has been widely recognized and studied in the medical field [9-10]. To effectively address this issue, the medical community has been searching for drugs that can effectively protect the liver and alleviate drug-induced liver injury.

Glycyrrhizic acid diamine, an 18-α-glycyrrhizic acid diammonium lipid complex, has gained significant attention in recent years. It demonstrates excellent bioavailability and possesses multiple pharmacological actions, including anti-inflammatory, anti-fibrotic, anti-oxidant, and hepatocyte membrane protection. These pharmacological properties make glycyrrhizic acid diamine a promising candidate for mitigating drug-induced liver injury [11].

From a mechanistic perspective, drug-induced liver injury can be classified into three categories: direct hepatotoxicity, indirect hepatotoxicity, and hypersensitivity reactions. The pathophysiology of these different types of drug-induced liver injury varies, but all are closely related to the liver's metabolic and detoxification functions [12]. Given the structural similarity between glycyrrhizic acid diamine and steroids, it can bind with steroid metabolic enzymes in the liver, reducing the inactivation of steroids and exhibiting steroid-like effects. This mechanism suggests that glycyrrhizic acid diamine may help reduce inflammatory damage and hypersensitivity reactions in patients suffering from drug-induced liver injury.

Moreover, clinical applications of glycyrrhizic acid diamine have shown promising results. Some studies indicate that combining glycyrrhizic acid diamine with anti-tuberculosis drugs significantly reduces the incidence of drug-induced liver injury, improving patient adherence and clinical cure rates [13]. Therefore, glycyrrhizic acid diamine, as an effective hepatoprotective drug, has significant application value in the treatment of pulmonary tuberculosis.

In this study, the research group showed a notably shorter recovery time for liver function abnormalities compared to the control group. Furthermore, the overall treatment effectiveness was higher in the research group than in the control group, with the difference being statistically significant ($P<0.05$). These results reflect the clinical advantage of using glycyrrhizic acid preparations in combination with anti-tuberculosis drugs for treating pulmonary tuberculosis. Glycyrrhizic acid preparations, as hepatoprotective agents, possess anti-inflammatory, anti-oxidant, and immune-regulating effects. During anti-tuberculosis treatment, glycyrrhizic acid preparations may reduce liver inflammation and protect liver function by mitigating damage from inflammatory factors. Additionally, glycyrrhizic acid preparations may exert an antioxidant effect that aids in neutralizing free radicals in the body, thereby minimizing liver damage caused by oxidative stress [14]. Moreover, these preparations could boost immune function, enhancing the body’s ability to eliminate Mycobacterium tuberculosis, which in turn improves the effectiveness of the treatment.

When used in combination with anti-tuberculosis drugs, glycyrrhizic acid preparations may exert a synergistic effect. The anti-tuberculosis drugs primarily kill the tuberculosis bacteria, while glycyrrhizic acid preparations protect liver function and reduce liver damage caused by anti-tuberculosis drugs. This synergy not only improves the therapeutic effect but also accelerates liver function recovery, thereby shortening the recovery time for liver function abnormality indicators. The incidence of adverse reactions in the research group was lower than in the control group, with statistically significant differences ($P<0.05$). This result suggests that combining glycyrrhizic acid preparations with anti-tuberculosis drugs not only enhances treatment outcomes but also significantly reduces the occurrence of adverse reactions [15]. The hepatoprotective effect of glycyrrhizic acid preparations likely reduces the liver damage and other adverse reactions caused by anti-tuberculosis drugs, thereby improving patient tolerance and treatment adherence.

Therefore, the combination of glycyrrhizic acid preparations with anti-tuberculosis drugs is a promising treatment strategy. It not only enhances therapeutic efficacy but also reduces adverse reactions and improves patient prognosis.

In conclusion, the combination of glycyrrhizic acid preparations with anti-tuberculosis drugs can effectively accelerate liver function recovery, enhance clinical treatment outcomes, and reduce the incidence of complications in patients with pulmonary tuberculosis. This therapy is safe, reliable, and has significant clinical value for wider application.

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