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Review article

A Review of Liver Damage Caused by Statins

Running Title: Adverse Effects of Statins

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Abstract

Introduction: Statins, or HMG-CoA reductase inhibitors, are among the most widely used drugs for controlling hyperlipidemia and cardiovascular diseases. They are generally considered low-risk, but sometimes, it has been reported that they can damage liver tissue with cholestatic damage or liver parenchyma. The current review addresses statins-induced liver injury, focusing on clinical presentation, diagnostic approach, and disease management.

Methods: For English-language studies, a comprehensive search using keywords selected according to the MeSH model, including "drug-induced liver injury, statin, cholestatic liver injury, cellular liver injury, and cholestasis," was conducted in PubMed, Scopus, and Google Scholar databases.

Results: Studies show that mild liver dysfunction, characterized by an increase in aminotransferases, may occur in about three percent of patients, while severe liver damage is rare and usually reversible with discontinuation of the causative statin. In suspected liver damage caused by statins, a comprehensive evaluation can be performed by taking a detailed medical history and performing laboratory investigations, including imaging studies and valid assays such as the Roussel Uclaf Causality Assessment Method (RUCAM).

Conclusion: Statins used to lower blood lipids can lead to liver damage, mainly cholestatic or hepatocyte damage. It is important to pay attention to the health of the liver while taking this drug class, and the final diagnosis of the occurrence of this complication is based on a comprehensive evaluation, monitoring of liver function, and awareness of drug interactions. More research is needed to determine strategies to reduce risk.

Keywords: Drug-induced liver injury, Statin, Cholestatic liver injury, Hepatocellular liver injury, Cholestasis

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Introduction

Hydroxymethylglutaryl-CoA reductase inhibitors, more generally referred to as the statin drug class, act through competitive inhibition of this rate-limiting enzyme of the cholesterol synthesis pathway (1). The general acceptance and use of statins have been due to their cholesterol and triglyceride-lowering activity, which halts the progression of atherosclerosis. Currently, statins are mainly used in treating hypercholesterolemia and dyslipidemia to reduce the primary complications of cardiovascular diseases and minimize the secondary risks for patients (2). Another condition where statins showed beneficial effects is preventing steatosis or fatty liver from further deterioration. Lovastatin was the first statin that the United States approved for cholesterol reduction. Since then, the US Food and Drug Administration has approved seven other statins: atorvastatin, fluvastatin, mevastatin, pitavastatin, pravastatin, rosuvastatin, and simvastatin (3).

Various other significant and noteworthy side effects associated with statins, which are not heavily dependent on dosage, include the following: headache, nausea, skin rash, and diminished libido, occurring in approximately ten percent of cases. Dose-dependent side effects include myopathy, rhabdomyolysis, and elevated aminotransferases, occurring at an incidence rate of 0.1%, 0.002%, and 0.2 to 2.4%, respectively (4). Of all the patients, about seventy percent, by continuing statin therapy, develop resolution of observed side effects. At the same time, the rest return to baseline only after the discontinuation of the drug (5). Only about three percent of patients with elevated aminotransferases develop a persistent increase exceeding three times the normal limit (6). It is postulated that changes in the lipid membranes of hepatocytes in affected patients increase permeability, leading to leakage of liver enzymes as the cause of the usually asymptomatic and transient abnormalities in the aminotransferases (7). This effect, of course, can also be observed with other lipid-lowering medications and may not be exclusive to statins. Since previous studies did not find significant histopathological changes associated with mild increases in aminotransferases in patients who had started statin therapy, these changes have recently been referred to as "hepatic adaptations" instead of damage (8). The real incidence of statin-induced hepatic injury is considerably less than other general abnormalities associated with increased aminotransferases, and the overall contribution of statins to this adverse effect is about one percent (9).

This review research aims to comprehensively and accurately examine liver injuries caused by statins. Considering that previous studies have not fully addressed this issue, this study analyzes the existing evidence regarding the hepatic side effects of these drugs and attempts to provide a better understanding of the potential mechanisms of liver damage by identifying related patterns and trends.

Methods

This exploration was limited to research articles, case reports, reviews, and meta-analyses published in English and Persian, all with English abstracts. The search in the PubMed, Scopus, and Google Scholar databases was conducted using the keywords "drug-

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induced liver injury, statin, cholestatic liver injury, cellular liver injury, cholestasis," which were selected based on the Medical Subject Headings (MeSH) pattern. The time frame for the search was from 2000 to August 2024. The search results were evaluated for their relevance to the research question, lack of duplication, and study quality (appropriate study design, sufficient statistical population, and studies with no conflicting results), and suitable articles were selected for further review. Initially, 128 articles were found, then narrowed down based on specific criteria to include 46 articles in the final review. The data extraction process involved identifying key information such as study design, population, treatment methods, outcome measures, and results of each article.

Results

Hepatic injury patterns caused by statins: Both patterns of liver injury, hepatocellular or parenchymal and cholestatic, are associated with statins. The hepatocellular injury pattern is defined by predominantly increased aminotransferases, specifically alanine aminotransferase (ALT) (10). On the other hand, the cholestatic pattern is associated with a significant increase in alkaline phosphatase (ALP) and bilirubin. Hepatocellular injury related to statins often occurs 5 to 90 days following the initiation of the treatment. A bilirubin level above twice the normal limit indicates serious parenchymal liver injury with a mortality of 10% and an incidence of 0.7-1.3/100,000 cases of drug-induced liver injury (11).

It is quite difficult to transparently report the incidence rate of statin-induced liver damage and risks before treatment. Most retrospective epidemiological studies tend to report the actual rate of statin-induced liver damage as lower and underestimated. Recent population-based studies have reported the incidence rate of statin-induced liver damage as 19 cases per 100,000 persons per year. Although statin treatment has been consistently associated with liver damage, excluding other causes of liver damage is important (12).

The estimated incidence of statin-induced liver damage is 15.96%. Some risk factors have been identified that increase the risk for statin-induced liver damage, which include positive hepatitis B surface antigen, weekly consumption of alcohol of 500 grams or more, re-treatment with statins, and age 60 years or above. Based on the reviewed literature, the incidence of parenchymal liver injury with statin therapy has been a rare complication. While jaundice, general weakness, and abdominal pain are the most commonly reported symptoms, some of these patients remain asymptomatic despite abnormal laboratory parameters. Changes in aminotransferases indicative of parenchymal liver damage have been observed from a few hours after initial statin exposure to even eight months after initiation (13-15). In a few reports, in patients with autoimmune features, such as an elevated rheumatoid factor, six months after discontinuation of the offending drug, treatment with a short course of corticosteroids has been hastened. In some reports, replacing the offending statin with another statin has prevented the progression of liver injury (13). However, this is understandable, as few prescribers would reinstate medicines suspected of

causing liver damage to avoid exposing their patients to harm further (12).

Cholestatic liver injury due to statins: Cholestatic liver injury represents a phase of liver disease and inflammation characterized by elevated aminotransferases, cholestatic markers, ALP, and bilirubin levels. Currently, there is no specific data regarding drug-induced cholestatic injury; however, data reported by Björnsson et al. (11) indicate an incidence of 1.2/100,000 users (1988-2010). Cholestasis is often differentiated from cholestatic liver injury through liver biopsy, which reveals distinct biochemical features. Symptoms of cholestatic liver injury include right upper quadrant pain, jaundice, anorexia, nausea, and vomiting (16). Laboratory findings typically show ALP levels exceeding three times the upper limit of normal (ULN), along with hyperbilirubinemia and aspartate aminotransferase (AST) and ALT levels two to ten times ULN. The liver pathology is also consistent with portal inflammation, with or without hepatic necrosis, and eosinophilia is present (17).

Cholestatic liver injury pattern caused by statins: Multiple studies have shown that statins can be safely used in patients with compensated chronic liver disease. It is recommended to use the definition of drug-induced cholestatic hepatitis provided by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) when reviewing data related to cholestatic liver injury, which includes six criteria (18):

1. In this review, R values ≤ 5 are considered for identifying situations of cholestatic liver injury. With these criteria, cases of "combined hepatitis" described in the cholestatic hepatitis group are included. R is quantified as (ALT × ULN ALP)/ (ALP × ULN ALT), where ULN is the upper limit of normal.
2. Cases that have a delay of 2-24 weeks.
3. If symptoms were present, including dark urine or itching in the early course of the disease.
4. Bilirubin concentration greater than 2.5 mg/dL.
5. In patients with liver biopsy, histology should present cholestatic changes in the liver with inflammatory cells and mild to moderate focal necrosis of liver cells.
6. If the cause of cholestatic hepatitis is thought to be drug use, the patient must have been exposed to a known cholestatic agent (12).

In reviewing the available literature, it appears that statins can induce cholestatic liver injury more frequently than other lipid-lowering drugs. However, liver failure and the development of chronic liver disease in these cases are sporadic (approximately 1 in 1,000,000) (19). Symptoms include jaundice and pruritus, although many patients are asymptomatic, and liver abnormalities are often found incidentally during blood tests. Other than discontinuing statins (If aminotransferases rise to more than three times the normal level), no other treatment is generally required, as most cases of statin-related drug-induced cholestatic liver injury resolve within six months (20). The latency of liver damage associated with statins varies, but abnormal levels of aminotransferases typically develop from 3 months to 1 year after initiating statin therapy (21). Analytical tools, such as the Russell O'Kloff

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Assessment Method (RUCAM), can further describe the likelihood of causation (22). Generally, liver biopsy, which can be useful in identifying the pattern of liver disorder and determining the pathology of the disease, is unnecessary (20). Additionally, it seems that experiencing cholestatic damage with one statin does not preclude the use of other statins due to concerns about the recurrence of liver injury, and another statin can be used with caution. Atorvastatin appears to be the statin most associated with the cholestatic pattern of liver injury (23).

Statin-induced cholestasis

Statin-induced cholestasis is a reduction in bile flow with minimal or no hepatocellular damage. The spectrum of statin-induced cholestasis ranges from mild, reversible conditions to chronic forms, such as vanishing bile duct syndrome (VBDS) (24). This syndrome is a rare liver disorder characterized by the progressive loss of bile ducts, leading to cholestasis and liver dysfunction. The preexisting cholestatic disease does not seem to be a risk factor for developing cholestasis during statin therapy. Pure statin-induced cholestasis, occurring without overlap with hepatitis, is known to be extremely rare; consequently, no prevalence or epidemiological data are currently available (12).

For mild liver damage, the statin dose should be reduced while continuing the medication. If the liver damage is moderate, the dose of statins should be reduced, and hepatoprotective treatment should be performed simultaneously. In case of severe liver damage, statins should be stopped immediately, and symptomatic treatment should be given. The treatment of statin-induced cholestasis is generally supportive and begins with the discontinuation of the statin (12). In rare instances where cessation of the drug does not resolve cholestasis, cholestyramine or ursodeoxycholic acid (UDCA) may be utilized. If these medications do not work, using rifampicin and opioid blockers has also been helpful. Nutritional support is crucial for patients with long-term cholestasis, as they face an increased risk of cirrhosis and liver failure. A high-calorie diet is often recommended to meet their energy needs, along with a balanced intake of macronutrients: adequate protein for liver repair, complex carbohydrates for energy, and healthy fats like medium-chain triglycerides for better absorption. Supplementation of fat-soluble vitamins (A, D, E, K) and minerals such as zinc and magnesium may be necessary due to impaired absorption. Additionally, small, frequent meals can help manage symptoms and improve nutrient uptake, while regular monitoring by healthcare professionals ensures that nutritional support is tailored to the patient's specific needs. Additionally, referring patients with persistent cholestasis for evaluation of liver transplantation is important, as early referral has been demonstrated to improve transplant outcomes (25).

Molecular mechanisms of liver damage caused by statins: In general, liver damage caused by statins is more commonly observed in patients who are on the maximum dose of statins along with other lipid-lowering medications, other drugs that utilize similar metabolic pathways of the cytochrome P450 enzyme, and/or in patients who are aging or have severe liver

or kidney failure (26).

Multiple mechanisms have been proposed for statin-induced liver injury, yet none have definitively characterized the pattern of liver damage. Golomb and colleagues hypothesized that mitochondrial damage is the underlying mechanism. They reported that the risk of statin-induced liver injury increases with the potency of the statin and its impact on the cytochrome P450 system (25). Metabolism dependent on isoenzymes of oxidase serves as a source of reactive oxygen species and contributes to cellular apoptosis. In these conditions, statins enhance the production of reactive oxygen species and lipid peroxidation, decreasing mitochondrial membrane potential and subsequent cellular toxicity (27). While this mechanism applies to most statin drugs, it is important to note that pravastatin and rosuvastatin are metabolized to a lesser extent by cytochrome P450 isoenzymes (28). Other proposed mechanisms of mitochondrial injury that may lead to statin-induced liver damage include inhibition of the respiratory chain (i.e., complexes I, II, and III) and calcium release (29,30).

Genetic factors may influence the patient's sensitivity to liver damage under statin use conditions (31). A recent Genome-Wide Association (GWA) study has identified genetic variations in various families of cytochrome P450, organic anion transporting polypeptides, and ATP-binding cassette genes, specifically ABCB1 and ABCC1, as potential predisposition factors for statin-induced liver damage in patients (32). However, genetic differences are not the only cause of these complications, as other underlying diseases, such as thyroid disorders that enhance mitochondrial or metabolic susceptibility, may raise the risk of statin-related liver damage (25).

Another proposed mechanism for statin-induced liver damage involves the stimulation of autoimmune responses akin to the pathogenesis of autoimmune hepatitis (31). Unfortunately, the exact mechanism by which statins induce autoimmune hepatitis remains unclear. However, there is evidence indicating that statin-induced autoimmune hepatitis is more prevalent in individuals with a history of autoimmune disease. For example, statins are associated with the development of necrotizing myopathy, which is caused by an immune response. It is believed that the activity of the HMGCR enzyme targeted by statins plays a role in triggering these uncontrolled immune responses and the release of immunogenic peptides from human leukocytes (33).

The risk of using statins in patients with chronic liver disease and the potential for subsequent liver damage remains controversial. While it was previously believed that statins increase the risk of liver damage in individuals with chronic liver disease, Kim et al. demonstrated that statin use in patients with chronic liver failure is associated with a reduced risk of liver damage and subsequent cirrhosis (18). This study was a systematic review and meta-analysis that included 13 studies, of which only 3 were randomized trials. Notably, most cases (84.5%) involved hepatitis C infection, which may limit the applicability of its conclusions to cases of chronic liver failure caused by other factors (12).

Drug interactions of statins and liver damage: The simultaneous use of statins is often associated with

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the engagement of hepatic oxidase isoenzymes, and if taken concurrently with another drug that has the same metabolic pathway, the plasma concentration of both drugs will significantly increase, and potential side effects will manifest sooner and with greater intensity **Table 1** (34). However, predicting the likelihood of drug interactions in a specific patient is difficult, as individual variations in sensitivity to rising levels of statin drugs play an important role. Drug metabolism studies show that simvastatin, especially lovastatin, is more sensitive to the inhibitory effects of other medicines on the cytochrome P-450 3A4 isoenzyme. The metabolism of atorvastatin is less affected by inhibitors of this isoenzyme, and rosuvastatin is not metabolized through this pathway (35). Additionally, through the potential inhibition of biliary excretion of statins and glucuronidation, fibrates (such as gemfibrozil and fenofibrate) that may be prescribed concurrently with statins significantly increase the risk of myopathy and rhabdomyolysis, which is a potential and even life-threatening result of statin drug interactions (36,37). The occurrence of this toxicity with the simultaneous use of a statin and gemfibrozil is more common than with other fibrates. If the requirement to use statins and fibrates together exists, fenofibrate is preferred.

A significant interaction of statins is their simultaneous use with macrolide antibiotics such as erythromycin and clarithromycin. These agents can inhibit the metabolism of statins, leading to increased drug levels in the blood and ultimately raising the risk of liver damage (38). Similarly, triazole antifungals like ketoconazole, itraconazole, and voriconazole can also interact with statins and increase the risk of liver toxicity (39). Voriconazole has a very narrow therapeutic index for inducing cholestasis. Since voriconazole is metabolized by cytochrome P450 3A4 and many statins inhibit this enzyme, the concurrent use of these two medications increases the risk of developing cholestasis in patients. In such cases, a more suitable alternative is rosuvastatin (40).

Table 1. Interactions of statins with other drugs: mechanisms, effects, and recommendations

Drug Interaction	Mechanism/Effects	Recommendations
Fibrates (Gemfibrozil, Fenofibrate)	Can inhibit biliary excretion and glucuronidation of statins. Significantly increases the risk of myopathy and rhabdomyolysis.	Fenofibrate is preferred if statins and fibrates must be used together.
Macrolide Antibiotics (Erythromycin, Clarithromycin)	Inhibit the metabolism of statins, raising blood levels. Increased risk of liver damage.	Caution advised: monitor liver function closely.
Triazole Antifungals (Ketoconazole, Itraconazole, Voriconazole)	Interact with statins, increasing liver toxicity risk. Voriconazole can induce cholestasis due to a narrow therapeutic index.	Rosuvastatin is a safer alternative in these cases.
Amiodarone	Inhibits P-glycoproteins and CYP450 enzyme system (CYP3A4, CYP2C9). Maximum doses for lovastatin (40 mg/day) and simvastatin (20 mg/day) are recommended.	No dose adjustment for atorvastatin and rosuvastatin, but caution is advised.
Calcium Channel Blockers (Amlodipine, Diltiazem, Verapamil)	Inhibit CYP3A4 and affect P-glycoproteins. Maximum daily doses of 20 mg for simvastatin and lovastatin are recommended.	Caution when prescribing atorvastatin and rosuvastatin with non-dihydropyridine CCBs.

Amiodarone, which is the broadest-spectrum antiarrhythmic agent, especially for ventricular fibrillation, is a known inhibitor of P-glycoproteins and the CYP450 enzyme system, particularly CYP3A4 and, to some extent, CYP2C9. As a result, the maximum recommended doses for lovastatin (maximum 40 mg per day) and simvastatin (maximum 20 mg per day) when used with

amiodarone are indicated. Although atorvastatin is metabolized through CYP3A4 and rosuvastatin through CYP2C9, dose adjustment is unnecessary for their use alongside amiodarone (41).

Calcium channel blockers (CCBs) of the dihydropyridine type (amlodipine) and non-dihydropyridine type (diltiazem, verapamil) inhibit CYP3A4. Amlodipine also has an inhibitory effect on P-glycoproteins. A maximum daily dose of 20 mg for simvastatin and lovastatin is recommended when used with amlodipine, diltiazem, or verapamil. There is no specific dose adjustment recommendation for atorvastatin and rosuvastatin, although caution should be exercised when prescribing them with any of the non-dihydropyridine CCBs (41).

Table 2. Summary of reported cases of liver damage caused by statins.

Therapeutic action	Normal range of laboratory tests	Evaluation period	Laboratory tests	Symptoms	Statin / daily dose	/age The gender of the patient	Case report study/source
No action was taken.	Bilirubin: >20.5 µmol/L; AST: >34 UI/L; ALT: >55 UI/L; ALP: >150 UI/L.	4months	Bilirubin: 211; AST: 1,612; ALT: 1,325; ALP: 278	the body the pain general, muscular weakness, jaundice, dark urine, decreased output urine	Atorvastat - in80mg	67-Man	Mohamed 2019 (42)
No action was taken.	.Not mentioned	6months	Bilirubin: 5.1; AST: 860; ALT: 1,632; ALP: Not available; ANA: Positive	weakness general, the pain in the belly	Atorvastat - in80mg	46-Man	Kawasaki 2020 (13)
the drug was discontinued; There was no recurrence.	Bilirubin: >20.5 µmol/L; AST: >34 UI/L; ALT: >55 UI/L; ALP: >150 UI/L.	3months	Bilirubin: 122.8; AST: 2,999; ALT: 3,195; ALP: 435; ANA: Positive; Asthma: Positive	weakness general, the pain in the belly	Atorvastat - in40mg	57-Woman	Khan 2020 (14)
No action was taken.	Bilirubin: >1.1 mg/dL; AST: >37 UI/L; ALT: >41 UI/L; ALP: >129 UI/L	4months	AST: 112; ALT: 201; ALP: Not available; ANA: Positive; Asthma: Positive	weakness general, the pain in the belly	Rosuvast -atin5mg	47-Man	Sánchez 2018 (43)
Simvastatin20mg daily was replaced. The problem is solved.	Bilirubin: >1.2 mg/dL; AST: >41 UI/L; ALT: >58 UI/L; ALP: >129 UI/L.	1month	Bilirubin: 1.5; AST: 1,093; ALT: 1,385; ALP: 265; Asthma: Positive	No sign	Atorvastat - in80mg	71-Man	Saha 2021 (15)
No action was taken.	Bilirubin: >1.2 mg/dL; AST: >40 UI/L; ALT: >40 UI/L; ALP: >115 UI/L.	1.5 months	Bilirubin: 3.53; AST: 1,142; ALT: 2,260; ALP: 277	jaundice, itching, tiredness	Rosuvast -atin5mg	47-Man	Shah 2019 (44)
consumption of Rosuvastatin10mg Alternatively, with normal to become Enzyme and without Recurrence	.Not mentioned	2months	Bilirubin: 5.2; AST: 1,124; ALT: 1,049; ALP: 214	jaundice, mode nausea, fatigue, decreased appetite, belly pain	Atorvastat - in20mg	63-Man	Vishwakarma 2014 (45)
No action was taken.	Bilirubin: >2.0 mg/dL; AST: >36 UI/L; ALT: >36 UI/L.	4months	Bilirubin: 2.6; AST: 880; ALT: 775; ALP: Normal	fatigue, anorexia, lethargy, belly pain, Jaundice	Rosuvast atin 10 mg	64-Man	Famularo 2007 (46)

Abbreviations: ALP, alkaline phosphatase; ANA, antinuclear antibody; ALT, alanine aminotransferase; ASMA, anti-smooth antibody; AST, aspartate aminotransferase.

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Overview of reported cases of liver damage caused by statin use

Table 2 summarizes case reports illustrating the timeline of liver parenchyma damage associated with statin therapy. According to these reports, such damage typically manifests within a period ranging from 5 to 90 days following the commencement of statin treatment. Among the eight patients studied, only one was female. This observation prompts the question of whether the risk of statin-induced liver toxicity is greater in men or if it reflects gender disparities in statin prescription rates, which may be influenced by the higher incidence of cardiovascular diseases in men compared to women. Due to the limited number of cases analyzed, no definitive conclusions can be drawn, highlighting the need for further research.

Pharmacotherapy of liver damage caused by drugs

Treatments that are known and used for the prevention and treatment of drug-induced liver damage include N-acetylcysteine (NAC), silymarin (milk thistle extract), corticosteroids, UDCA, and cholestyramine **Table 3** (47). According to various studies, silymarin may prevent or mitigate liver damage caused by statins (48). Silymarin is a *Silybum marianum* extract with antioxidant and anti-inflammatory properties (49). Silibinin and isosilybin are the most important flavonoids of thistle, which can deal with all types of liver damage (50,51). It has been shown that silymarin supplementation reduces the level of liver enzymes and improves liver function tests in patients receiving statins (52). Evidence is available that in case of a severe increase in liver enzymes following the use of statins, N-acetylcysteine can prevent the continuation of liver damage by increasing the thiol reserves of the liver (53).

Table 3. Pharmacotherapy options for drug-induced liver damage.

Medicine	Mechanism	Dosage	Notes
N-acetylcysteine (NAC)	Effective antioxidant that replenishes glutathione levels, protecting against oxidative stress.	150 mg/kg IV over 15 minutes, followed by 50 mg/kg IV every 4 hours for 4 doses	Commonly used in acetaminophen overdose, it also shows promise for other forms of liver injury.
Silymarin	Antioxidant and anti-inflammatory properties may prevent or mitigate liver damage caused by statins.	140–800 mg/day	Contains silibinin and isosilybin, which address various types of liver damage.
Corticosteroids	Reduce inflammation and modulate immune response in drug-induced liver injury.	Varies; often 20–60 mg/day of prednisone or equivalent	Used primarily when there is an autoimmune component or significant inflammation
Ursodeoxycholic Acid (UDCA)	Improves liver function and reduces liver enzyme levels; promotes bile flow and reduces hepatocyte apoptosis.	10–15 mg/kg/day	Commonly used in cholestatic liver diseases; beneficial in drug-induced liver injury.
Cholestyramine	Bile acid sequestrant reduces enterohepatic circulation of certain drugs, minimizing hepatotoxic effects.	4–16 g/day	Binds to bile acids, preventing their reabsorption; helpful in managing drug-induced liver injury.

Conclusion

Given the widespread use of statins for controlling blood lipids and their other benefits, liver damage is a significant concern in clinical practice. This review indicates that while statins are generally safe, they can lead to liver dysfunction, primarily manifesting as patterns of hepatocyte or cholestatic injury. The pattern of hepatocyte injury is more common, and severe liver damage is rare, often reversible upon discontinuation of statin use. Key findings suggest that comprehensive evaluations—including medical history, tests, and imaging—are essential for diagnosing statin-induced liver injury. Tools such as the Russell-Oklaff measurement method enhance the accuracy of assessments. This review emphasizes the importance of monitoring liver function during statin therapy. It indicates that healthcare providers should be vigilant for signs of liver injury, especially in patients with a prior history of liver damage. Additionally, awareness of drug interactions and the selection of appropriate medications, as well as managing potential liver-related side effects, is crucial. Further research is essential to gain a deeper understanding of the mechanisms underlying statin-induced liver injury and to develop strategies aimed at minimizing risks in susceptible populations.

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