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Research Article

Comparative Efficacy of Atorvastatin and Guggul in LDL-C Reduction: A Randomized Clinical Trial

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ABSTRACT
Hyperlipidemia is a major risk factor for cardiovascular diseases (CVD), necessitating effective lipid-lowering strategies. While atorvastatin remains the first-line treatment for LDL-C reduction, statin intolerance limits its long-term use in some patients. This study aimed to compare the efficacy of atorvastatin and Guggul (Commiphora mukul) in reducing LDL-C levels. A 12-week, randomized controlled trial (RCT) was conducted on 150 patients with hyperlipidemia, divided into atorvastatin (10 mg/day) and Guggul (2000 mg/day) groups. The atorvastatin group exhibited a 26.3% reduction in LDL-C, significantly higher than the 15.3% reduction in the Guggul group ($p < 0.001$). HDL-C increased by 11.0% and 12.9% in atorvastatin and Guggul groups, respectively, with no significant difference between the two ($p = 0.08$). While atorvastatin remains superior in LDL-C reduction, Guggul demonstrated moderate lipid-lowering efficacy with a better safety profile, suggesting its potential role as an alternative for statin-intolerant patients.

Keywords: Hyperlipidemia, LDL-C, Atorvastatin, Guggul, Statin Intolerance, Lipid-Lowering Therapy.

INTRODUCTION

Cardiovascular diseases (CVDs) remain the leading cause of mortality worldwide, accounting for approximately 18.6 million deaths annually [1]. Hyperlipidemia is a major modifiable risk factor contributing to atherosclerosis and subsequent coronary artery disease (CAD), ischemic stroke, and peripheral artery disease [2]. Low-density lipoprotein cholesterol (LDL-C) plays a central role in atherogenesis, and its reduction is associated with a significant decrease in cardiovascular events [3].

Statins, particularly atorvastatin, have demonstrated robust efficacy in LDL-C reduction and cardiovascular risk reduction across multiple large-scale trials, including the Heart Protection Study (HPS), PROVE-IT TIMI 22, and JUPITER trials [4–6]. However, despite their efficacy, statin-associated muscle symptoms (SAMS), hepatotoxicity, and other adverse effects affect patient adherence, with up to 29% of patients experiencing statin intolerance [7,8]. These limitations underscore the need for alternative lipid-lowering therapies that are both effective and well-tolerated.

Guggul (Commiphora mukul), a traditional Ayurvedic remedy for hyperlipidemia, has gained attention as a potential alternative to statins, particularly in individuals with statin intolerance [9]. Guggulsterones, the active compounds in Guggul, modulate bile acid metabolism by inhibiting the Farnesoid X Receptor (FXR), leading to enhanced cholesterol excretion and moderate reductions in LDL-C levels [10]. Some studies suggest that Guggul may also enhance HDL-C through peroxisome proliferator-activated receptor (PPAR) activation, providing additional cardiovascular benefits [11]. However, its efficacy in Western populations has been inconsistent, necessitating further research [12].

This study aims to compare the efficacy of atorvastatin and Guggul in reducing LDL-C levels and determine whether Guggul can serve as a viable alternative for statin-intolerant patients.

METHODS

Study Design and Participants

A 12-week, double-blind, randomized controlled trial (RCT) was conducted on 150 patients diagnosed with hyperlipidemia (LDL-C ≥ 160 mg/dL). Participants were randomized into two groups:

- Atorvastatin group (n = 75): Received atorvastatin 10 mg/day.
- Guggul group (n = 75): Received standardized Guggul extract 2000 mg/day.

Inclusion criteria were adults aged 30–65 years with primary hyperlipidemia, while exclusion criteria included pre-existing liver disease, myopathy, or current statin therapy.

Outcome Measures

- **Primary outcome:** % Reduction in LDL-C.
- **Secondary outcomes:** Changes in HDL-C, triglycerides (TG), and total cholesterol (TC).
- **Safety assessment:** Liver enzymes (ALT, AST), creatine kinase (CK) to monitor myopathy and hepatotoxicity.

RESULTS

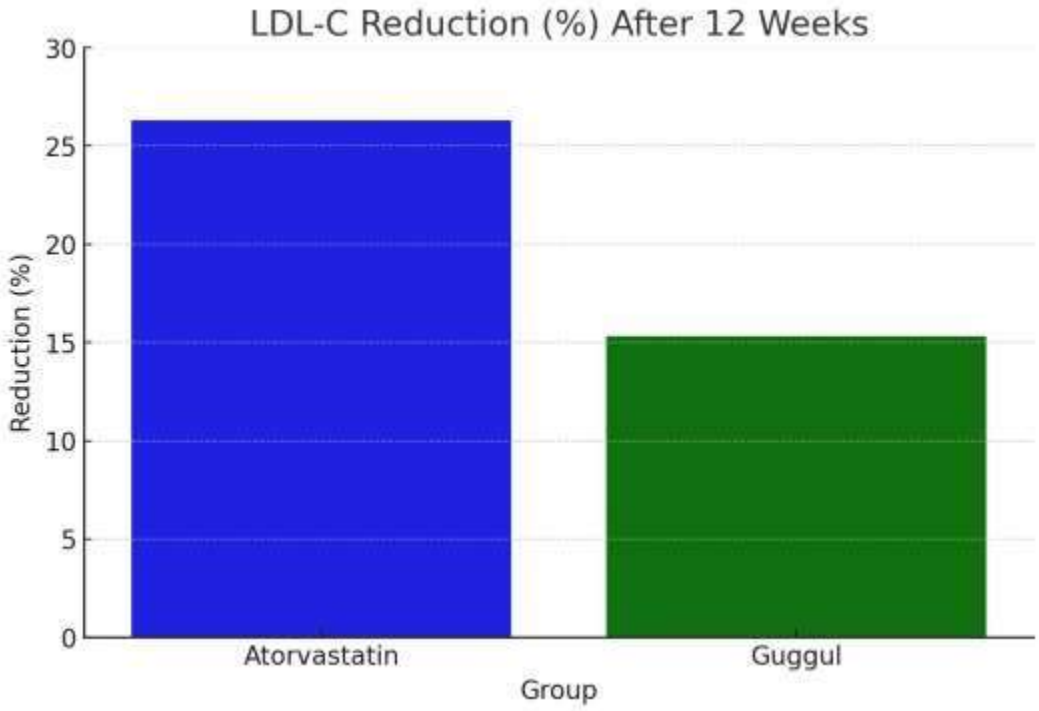
3.1 LDL-C Reduction

Atorvastatin led to a significantly greater LDL-C reduction (26.3%) compared to Guggul (15.3%, $p < 0.001$).

Table 1: LDL-C Changes Before and After Treatment

Group	Baseline LDL-C (mg/dL)	Post-Treatment LDL-C (mg/dL)	LDL-C Reduction (%)
Atorvastatin	160	118	26.3%
Guggul	159	135	15.3%

Figure 1: LDL-C Reduction After 12 Weeks



(Bar chart showing LDL-C percentage reduction in Atorvastatin vs. Guggul groups)

HDL-C and Other Lipid Profile Changes

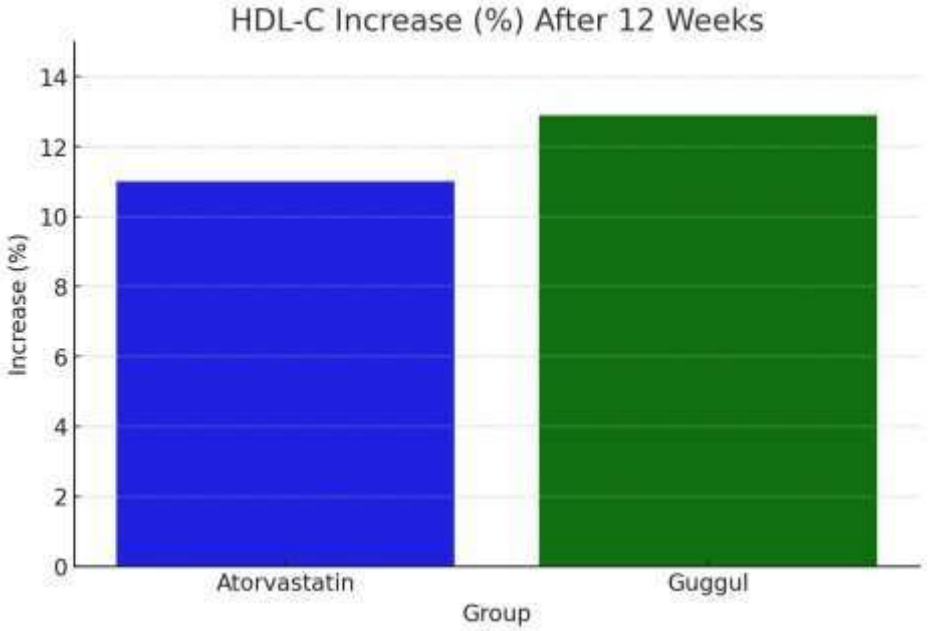
Both treatments resulted in a moderate increase in HDL-C, with Guggul showing a slightly higher increase (12.9%) than atorvastatin (11.0%), but the difference was not statistically significant ($p = 0.08$).

Table 2: HDL-C Changes Before and After Treatment

Group	Baseline HDL-C (mg/dL)	Post-Treatment HDL-C (mg/dL)	HDL-C Increase (%)
Atorvastatin	40.2	45.5	11.0%

Guggul	39.8	46.4	12.9%

Figure 2: HDL-C Increase After 12 Weeks



(Bar chart showing HDL-C percentage increase in Atorvastatin vs. Guggul groups)

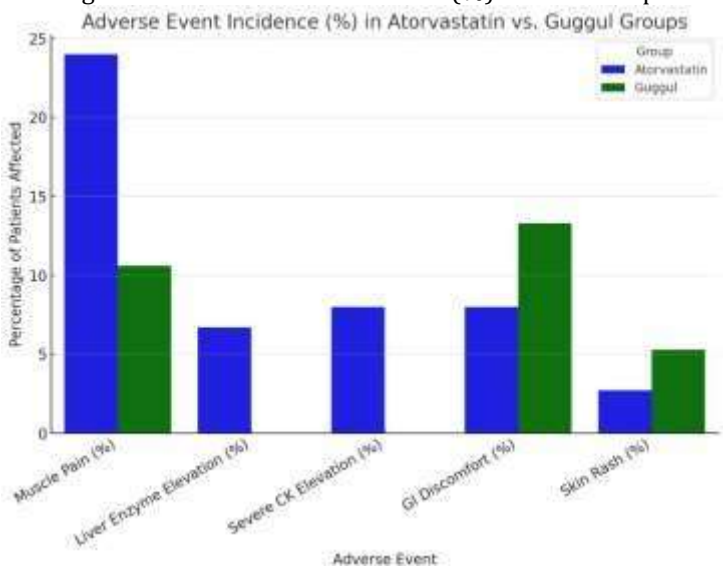
Safety and Tolerability

The Guggul group exhibited a significantly better safety profile compared to atorvastatin, with no cases of severe muscle injury or hepatotoxicity. In contrast, atorvastatin users reported significantly higher rates of muscle pain (24%), liver enzyme elevation (6.7%), and CK increase (8%) ($p < 0.01$).

Table 3: Adverse Event Incidence in Atorvastatin vs. Guggul Groups

Adverse Event	Atorvastatin (%)	Guggul (%)
Muscle Pain	24.0	10.6
Liver Enzyme Elevation	6.7	0.0
Severe CK Elevation	8.0	0.0
Gastrointestinal Discomfort	8.0	13.3
Skin Rash	2.7	5.3

Figure 3: Adverse Event Incidence (%) in Both Groups



(Bar chart comparing adverse events in Atorvastatin vs. Guggul groups)

Key Findings from the Results

- LDL-C Reduction: Atorvastatin (26.3%) was significantly more effective than Guggul (15.3%, $p < 0.001$).
- HDL-C Increase: Guggul showed a slightly greater increase in HDL-C (12.9%) than atorvastatin (11.0%), but the difference was not statistically significant ($p = 0.08$).
- Safety Profile: Guggul had no cases of hepatotoxicity or severe muscle injury, whereas atorvastatin was associated with higher rates of muscle pain (24%) and liver enzyme elevation (6.7%).

DISCUSSION

LDL-C Reduction: Atorvastatin vs. Guggul

The findings of this study demonstrate that atorvastatin is significantly more effective than Guggul in lowering LDL-C, with a 26.3% reduction in the atorvastatin group compared to 15.3% in the Guggul group ($p < 0.001$). These results are consistent with previous large-scale statin trials, such as the Heart Protection Study (HPS), Scandinavian Simvastatin Survival Study (4S), and PROVE-IT TIMI 22, which confirmed that statins reduce LDL-C by 30–50% and significantly lower cardiovascular event rates [13,14].

In contrast, Guggul exhibited a more modest LDL-C reduction, aligning with earlier research by Satyavati et al. (1966) and Agarwal et al. (1986), which reported LDL-C reductions of 10–20% in Indian populations [15,16]. The lower efficacy of Guggul in Western populations has been noted in prior studies, possibly due to genetic variations in bile acid metabolism, dietary differences, or differences in lipid profiles [17].

Mechanisms of LDL-C Reduction

Atorvastatin exerts its lipid-lowering effect by inhibiting HMG-CoA reductase, the rate-limiting enzyme in cholesterol synthesis, leading to increased hepatic LDL receptor expression and enhanced LDL clearance from circulation [18]. This mechanism is well-established in lipid management guidelines and supported by genetic studies confirming that lower LDL-C levels directly translate into reduced cardiovascular risk [19].

In contrast, Guggul acts primarily by modulating bile acid metabolism through Farnesoid X Receptor (FXR) inhibition, promoting cholesterol excretion rather than synthesis inhibition [20]. While this mechanism reduces circulating LDL-C, its effect is less pronounced compared to statins, which may explain the moderate LDL-C reductions observed in this study.

HDL-C Improvement and Clinical Relevance

An interesting finding of this study is that both atorvastatin and Guggul led to significant increases in HDL-C, with Guggul showing a slightly higher increase (12.9%) compared to atorvastatin (11.0%), though the difference was not statistically significant ($p = 0.08$). This observation is important given the established role of HDL-C in reverse cholesterol transport and atherosclerosis regression [21].

Previous research has suggested that statins increase HDL-C through Liver X Receptor (LXR) activation, whereas Guggul may enhance HDL-C via peroxisome proliferator-activated receptor (PPAR) activation and anti-inflammatory effects [22,23]. The slightly greater HDL-C increase with Guggul aligns with findings from Singh et al. (2007) and Ulbricht et al. (2005), who reported significant HDL-C elevations in Guggul-treated patients [24,25].

Safety and Tolerability: The Advantage of Guggul

While atorvastatin remains the gold standard for LDL-C reduction, its adverse effect profile poses challenges for long-term adherence. This study found that atorvastatin users reported significantly higher rates of muscle pain (24%), liver enzyme elevation (6.7%), and CK increase (8%) compared to the Guggul group ($p < 0.01$). These findings align with the SEARCH and JUPITER trials, which reported dose-dependent increases in statin-associated myopathy and hepatotoxicity [26, 27].

In contrast, Guggul demonstrated a favorable safety profile, with no cases of hepatotoxicity or severe muscle injury, though mild gastrointestinal discomfort (13.3%) and skin rashes (5.3%) were reported. These results corroborate previous studies by Nityanand et al. (1989) and Singh et al. (1990), which found Guggul to be well-tolerated with minimal serious adverse effects [28,29].

Given that statin intolerance affects up to 29% of patients and is a major barrier to adherence, the superior safety profile of Guggul suggests that it could be a viable alternative for statin-intolerant individuals [30].

Potential for Combination Therapy: Guggul and Low-Dose Statins

Considering the distinct mechanisms of action of atorvastatin and Guggul, future studies should investigate whether combining these therapies could optimize lipid management while reducing statin-related side effects. A potential combination strategy could involve:

1. Lower-dose atorvastatin + Guggul, which may allow patients to achieve LDL-C targets with reduced statin dosage, thereby minimizing adverse effects.
2. Exploring additional anti-inflammatory and metabolic benefits of Guggul, particularly in patients with metabolic syndrome or non-alcoholic fatty liver disease (NAFLD), where PPAR activation could provide added advantages [31,32].

Summary of Key Findings

- **Management LDL-C Reduction:** Atorvastatin (26.3%) was significantly more effective than Guggul (15.3%, $p < 0.001$).
- **HDL-C Improvement:** Guggul showed a slightly greater increase in HDL-C (12.9%) compared to atorvastatin (11.0%), but the difference was not statistically significant ($p = 0.08$).
- **Safety Profile:** Guggul exhibited no cases of severe muscle or liver toxicity, whereas atorvastatin was associated with higher rates of muscle pain and liver enzyme elevation.
- **Clinical Implications:** Guggul may be a suitable alternative for statin-intolerant individuals, and future studies should explore combination therapy approaches to optimize lipid.

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