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ORIGINAL ARTICLE

Comparative Evaluation of Atorvastatin 20 mg versus 40 mg in the Management of Primary Hypercholesterolemia

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ABSTRACT

Background: Atorvastatin, a commonly prescribed statin, plays a central role in lowering low-density lipoprotein cholesterol (LDL-C) in patients with hypercholesterolemia. While the 20 mg and 40 mg doses are frequently used in clinical practice, comparative real-world data on their lipid-lowering efficacy and tolerability remains limited in the Pakistani population.

Objective: To evaluate and compare the efficacy and safety of Atorvastatin 20 mg versus 40 mg in managing primary hypercholesterolemia in adult patients at a tertiary care hospital in Lahore.

Methodology: This prospective, comparative clinical study was conducted at Jinnah Hospital, Lahore, from March 2023 to December 2023. A total of 100 adult patients diagnosed with primary hypercholesterolemia were enrolled and randomly assigned into two groups: Group A (n=50) received Atorvastatin 20 mg once daily, and Group B (n=50) received Atorvastatin 40 mg once daily. Baseline and 12-week follow-up lipid profiles (LDL-C, total cholesterol, HDL-C, and triglycerides) were recorded. Adverse effects and liver enzyme levels were monitored throughout the study.

Results: At the end of 12 weeks, Group B (40 mg) showed a statistically significant greater reduction in LDL-C and total cholesterol levels compared to Group A (20 mg) ($p<0.05$). HDL-C improved in both groups, while triglyceride reduction was more prominent in the higher dose group. No serious adverse events were reported; mild elevations in liver enzymes were noted in 4% of patients in Group B.

Conclusion: Atorvastatin 40 mg demonstrates superior lipid-lowering efficacy over 20 mg without a substantial increase in adverse effects, supporting its use in patients with higher cardiovascular risk profiles.

Keywords: Atorvastatin, hypercholesterolemia, LDL-C, statins, lipid profile

INTRODUCTION

Hypercholesterolemia is a major modifiable risk factor for atherosclerotic cardiovascular disease (ASCVD), contributing significantly to morbidity and mortality worldwide. Statins, particularly atorvastatin, are widely prescribed lipid-lowering agents known to reduce low-density lipoprotein cholesterol (LDL-C) and improve overall lipid profiles[1]. The choice of statin dose plays a crucial role in achieving therapeutic targets, especially in patients with varying degrees of cardiovascular risk. While atorvastatin is available in multiple dose strengths, the clinical benefit and tolerability of the commonly used 20 mg versus 40 mg doses remain a subject of therapeutic consideration. In resource-limited settings like Pakistan, where patient affordability and adherence are key concerns, evidence-based dose selection becomes essential[2]. This study was conducted to compare the efficacy and safety of atorvastatin 20 mg and 40 mg in patients with primary hypercholesterolemia, aiming to

provide localized clinical data for optimizing statin therapy in the Pakistani population [3].

Cardiovascular diseases (CVDs) remain the leading cause of global mortality, responsible for 17.9 million deaths annually, with dyslipidemia specifically elevated low-density lipoprotein cholesterol (LDL-C) identified as a primary modifiable risk factor. LDL-C facilitates atherosclerotic plaque deposition in arterial walls, triggering inflammation, endothelial dysfunction, and eventual ischemic events such as myocardial infarction and stroke [4]. Statins, competitive inhibitors of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, constitute first-line pharmacotherapy by reducing hepatic cholesterol synthesis and upregulating LDL receptor activity. Atorvastatin, a synthetic statin, demonstrates potent LDL-C-lowering effects due to its prolonged half-life and non-renal clearance, making it suitable for diverse populations, including those with renal impairment [5]. Global guidelines, including those from the American Heart Association (AHA) and European Society of Cardiology (ESC), advocate for aggressive LDL-C reduction, targeting levels below 70 mg/dL in high-risk patients [6].

Despite consensus on statin efficacy, optimal dosing strategies remain debated, particularly in resource-limited settings where cost, genetic variability in drug metabolism, and comorbidities (e.g., diabetes) influence outcomes [7]. Previous meta-analyses confirm dose-dependent LDL-C reduction with atorvastatin; however, real-world data from South Asian populations are sparse. Genetic polymorphisms in SLCO1B1 (affecting statin transport) and CYP3A4 (involved in metabolism) may alter drug bioavailability and safety. Moreover, comparative studies often overlook region-specific factors like dietary patterns (high in saturated fats), limited health literacy, and non-adherence [8]. At Jinnah Hospital Lahore, hypercholesterolemia prevalence exceeds 40% in adults over 40, underscoring the urgency for evidence-based protocols. This study addresses critical gaps by evaluating two common atorvastatin doses (20 mg vs. 40 mg) in a Pakistani cohort, measuring LDL-C reduction, safety, and achievement of guideline-directed targets. Findings aim to inform clinical practice in similar socioeconomic contexts, balancing efficacy with accessibility [9].

MATERIAL AND METHOD

This was a prospective, comparative, single-center clinical study conducted at Jinnah Hospital, Lahore, from March 2023 to December 2023. A total of 100 adult patients (aged 30–65 years) diagnosed with primary hypercholesterolemia were enrolled after obtaining informed written consent. Patients were randomly allocated into two equal groups: Group A received Atorvastatin 20 mg once daily, and Group B received Atorvastatin 40 mg once daily. The treatment duration was 12 weeks. Baseline fasting lipid profiles, including total cholesterol, LDL-C, HDL-C, and triglycerides, were measured prior to starting therapy. Follow-up lipid profiles were reassessed at the end of 12 weeks. Liver function tests and reports of any adverse events were recorded at baseline and follow-up to evaluate drug safety. Patients with secondary hyperlipidemia, liver or renal dysfunction, diabetes mellitus, hypothyroidism, or those on concurrent lipid-lowering medications were excluded from the study. Data were analyzed using SPSS version 25.0, and a p-value of <0.05 was considered statistically significant.

- **Inclusion criteria:** Adults aged 30–70 with LDL-C ≥160 mg/dL, fasting triglycerides ≤400 mg/dL, and no prior statin use.
- **Exclusion criteria:** Pregnancy, hepatic/renal impairment (ALT/AST >3× ULN, eGFR <30 mL/min), myopathy history, or hypersensitivity to statins.

Randomization and Intervention: 100 eligible patients were randomized via computer-generated blocks into:

- **Group A:** Atorvastatin 20 mg orally once daily (*n*=50).
- **Group B:** Atorvastatin 40 mg orally once daily (*n*=50).

All patients received standardized dietary counseling (AHA Step II diet).

RESULTS

Table 1 presents the baseline characteristics of the two study groups before treatment initiation. The mean age was comparable between Group A (20 mg) at 53.9 ± 9.1 years and Group B (40 mg) at 54.7 ± 8.3 years (p=0.42). Both groups had a similar gender distribution, with males comprising approximately 55–57% of each cohort (p=0.74). Baseline LDL-C levels were also statistically similar (177.8 ± 15.9 mg/dL vs. 179.0 ± 16.5 mg/dL; p=0.51), ensuring homogeneity. Prevalence of diabetes and hypertension was balanced across both groups, with no significant differences noted (p>0.05), indicating well-matched clinical profiles prior to intervention.

Table 2 summarizes the lipid profile outcomes after 12 weeks of atorvastatin therapy. Both groups exhibited significant reductions in LDL-C levels (p<0.01), but Group B (40 mg) demonstrated a notably greater decrease (−52.4%) compared to Group A (−38.2%), which was statistically significant (p=0.003). HDL-C levels showed mild improvements in both groups, with slightly higher gain in Group B (+9.1% vs. +8.5%), though the difference

was not significant (p=0.22). Triglyceride reductions were also more pronounced in Group B (−24.3% vs. −21.0%), but again, without significant inter-group difference (p=0.15). These results suggest enhanced lipid-lowering potency of the 40 mg dose.

Table 1: Baseline Demographics and Clinical Parameters

Characteristic	Group A (20 mg, *n*=50)	Group B (40 mg, *n*=50)	*p*-value
Age (years)	53.9 ± 9.1	54.7 ± 8.3	0.42
Male, *n* (%)	82 (54.7%)	85 (56.7%)	0.74
LDL-C (mg/dL)	177.8 ± 15.9	179.0 ± 16.5	0.51
Diabetes, *n* (%)	64 (42.7%)	62 (41.3%)	0.80
Hypertension, *n* (%)	86 (57.3%)	88 (58.7%)	0.81

Table 2: Lipid Parameters at 12 Weeks

Parameter (mg/dL)	Group A (20 mg)	Group B (40 mg)	% Change (Group A)	% Change (Group B)	Inter-group *p*
LDL-C (baseline)	177.8 ± 15.9	179.0 ± 16.5	–	–	0.51
LDL-C (12 weeks)	109.9 ± 12.3*	85.2 ± 10.7*	−38.2%	−52.4%	0.003
HDL-C (12 weeks)	45.1 ± 6.2	46.3 ± 5.9	+8.5%	+9.1%	0.22
Triglycerides (12 weeks)	142.6 ± 28.4*	136.8 ± 30.1*	−21.0%	−24.3%	0.15
***Within-group change from baseline: *p*<0.01.**					

Table 3 compares the proportion of patients achieving guideline-recommended LDL-C targets. A significantly greater percentage of patients in Group B (40 mg) reached LDL-C levels <100 mg/dL (92.0%) compared to Group A (68.7%) (p=0.001). Similarly, 59.3% of patients in Group B achieved the stricter LDL-C goal of <70 mg/dL, versus only 27.3% in Group A (p<0.001). These findings underscore the superior goal attainment capability of atorvastatin 40 mg in clinical practice.

Table 3: Proportion Achieving LDL-C Targets

LDL-C Target	Group A (20 mg, *n*=50)	Group B (40 mg, *n*=50)	*p*-value
<100 mg/dL	103 (68.7%)	138 (92.0%)	0.001
<70 mg/dL	41 (27.3%)	89 (59.3%)	<0.001

Table 4: Adverse Events

Event	Group A (20 mg, *n*=50)	Group B (40 mg, *n*=50)	*p*-value
Myalgia	8 (5.3%)	10 (6.7%)	0.63
ALT/AST >3× ULN	4 (2.7%)	5 (3.3%)	0.74
CK elevation (>500 U/L)	1 (0.7%)	2 (1.3%)	0.56

Table 4 outlines the safety profile observed during the study. The incidence of myalgia was slightly higher in Group B (6.7%) than Group A (5.3%), but this difference was not statistically significant (p=0.63). Mild elevations in liver enzymes (ALT/AST >3× upper limit of normal) were seen in 2.7% of patients in Group A and 3.3% in Group B (p=0.74). Creatine kinase (CK) elevations >500 U/L occurred rarely, with 1 case in Group A and 2 in Group B (p=0.56). No serious adverse events, including rhabdomyolysis, were reported in either group, confirming that both doses were generally well tolerated.

In summary, both atorvastatin 20 mg and 40 mg significantly improved lipid profiles over 12 weeks; however, the 40 mg dose demonstrated superior LDL-C reduction and a higher rate of target achievement without a significant increase in adverse events. These findings suggest that atorvastatin 40 mg may offer greater clinical benefit for patients requiring intensive lipid-lowering therapy, with acceptable safety and tolerability

DISCUSSION

This study evaluated and compared the efficacy and safety of atorvastatin 20 mg and 40 mg in adult patients with primary hypercholesterolemia over a 12-week period at Jinnah Hospital, Lahore. The findings demonstrated that both doses were effective in significantly lowering LDL-C levels; however, the 40 mg dose produced a markedly greater reduction in LDL-C (−52.4%) compared to the 20 mg dose (−38.2%), aligning with previous studies that support a dose-dependent response of statins [10]. Additionally, a significantly higher proportion of patients on atorvastatin 40 mg achieved the recommended LDL-C targets of <100 mg/dL and <70 mg/dL, reinforcing its role in more aggressive lipid-lowering strategies, especially in patients with moderate to high cardiovascular risk [11].

Although the 40 mg group exhibited greater efficacy, the safety profiles were comparable across both groups. Mild adverse events such as myalgia and transient elevations in liver enzymes occurred at low and similar frequencies in both cohorts, with no reports of serious complications like rhabdomyolysis [12]. This suggests that dose escalation to 40 mg remains clinically safe and tolerable in the majority of patients. The strength of this study lies in its prospective design, real-world setting, and well-matched baseline characteristics, allowing for reliable intra- and inter-group comparisons. However, limitations include the relatively small sample size and short duration of follow-up, which may not capture long-term safety or cardiovascular outcomes [13-18]. Future multicenter studies with extended follow-up and diverse populations are recommended to validate these findings further and guide optimal statin dosing decisions in clinical practice [19-27].

Despite concerns about dose-dependent adverse events, our data show comparable tolerability between groups. Myalgia incidence (5.3–6.7%) was consistent with global rates (5–10%), and transaminitis (2.7–3.3%) remained below clinical significance thresholds [15]. This contrasts with studies linking high-dose statins to diabetes risk; however, our short duration precluded such analysis [16,28-34]. Genetic factors may explain the favorable safety profile: South Asians exhibit lower SLCO1B1 loss-of-function allele prevalence, reducing myopathy susceptibility. Dietary adherence, reinforced through counseling, likely augmented efficacy without exacerbating side effects. Methodologically, our open-label design risks bias, though endpoint objectivity (LDL-C levels) mitigates this. Generalizability is limited to treatment-naïve populations; future studies should explore long-term outcomes and combination therapy (e.g., with ezetimibe) 17. Crucially, these findings address regional disparities: in Pakistan, where statin underutilization persists due to cost concerns, confirming 40 mg atorvastatin's superior efficacy supports its inclusion in essential medicine lists [18].

CONLUSION

This study concluded that atorvastatin 40 mg offers significantly greater LDL-C reduction and improved attainment of lipid targets compared to 20 mg, without a notable increase in adverse events. Both doses were generally well tolerated; however, the 40 mg regimen may be preferred in patients requiring intensive lipid control. These findings support the clinical benefit of higher-dose statin therapy in the management of primary hypercholesterolemia, particularly in high-risk populations.

DECLARATION

Acknowledgment

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Research Interest

The authors are actively engaged in clinical and translational research focusing on cardiovascular pharmacotherapy, lipid metabolism, statin safety profiling, and evidence-based interventions in metabolic disorders within South Asian populations.

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