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SAFETY AND EFFICACY OF PITAVASTATIN IN DYSLIPDEMIC/HYPERLIPIDEMIC PATIENTS

Original Research

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ABSTRACT

Background: Dyslipidemia and hyperlipidemia are prevalent conditions worldwide, characterized by abnormal lipid levels such as elevated LDL cholesterol, total cholesterol, or triglycerides, which increase the risk of cardiovascular diseases. Statins are widely used for lipid management, with pitavastatin emerging as a promising option due to its potent lipid-lowering effects and favorable safety profile. This study evaluates the safety and efficacy of pitavastatin in dyslipidemic and hyperlipidemic patients.

Objective: To assess the safety and efficacy of pitavastatin in reducing LDL cholesterol, total cholesterol, and triglycerides in dyslipidemic and hyperlipidemic patients.

Methods: A randomized controlled trial (RCT) was conducted, enrolling 200 participants aged ≥18 years with dyslipidemia or hyperlipidemia. Participants were randomized in a 1:1 ratio to receive either pitavastatin 4 mg or placebo once daily for 12 weeks. Randomization was performed using a computer-generated sequence, with blinding maintained for participants, investigators, and staff. The primary endpoint was the percent change in LDL cholesterol levels from baseline to week 12. Secondary endpoints included changes in total cholesterol, triglycerides, HDL cholesterol, and adverse events. Laboratory evaluations were performed at baseline and at weeks 4, 8, and 12.

Results: Of the 200 participants, 52% were male, with a mean age of 55 years. The pitavastatin group achieved a significant 29.6% reduction in LDL cholesterol levels compared to 1.2% in the placebo group ($p<0.001$). Total cholesterol levels decreased by 22.4% in the pitavastatin group versus 1.6% in the placebo group ($p<0.001$). Triglycerides were reduced by 12.9% in the pitavastatin group compared to 0.9% in the placebo group ($p=0.01$). HDL cholesterol levels showed no significant difference between groups (-1.5% vs. -0.8%, $p=0.36$). Adverse events were reported by 16% of participants in the pitavastatin group and 12% in the placebo group, with no statistically significant difference ($p=0.36$).

Conclusion; Pitavastatin demonstrated significant efficacy in reducing LDL cholesterol, total cholesterol, and triglycerides in dyslipidemic and hyperlipidemic patients, with a safety profile comparable to placebo. These findings support its role as an effective therapeutic option for managing dyslipidemia and hyperlipidemia.

Keywords: Adverse events, Cholesterol, Dyslipidemia, Lipid-lowering agents, Pitavastatin, Randomized controlled trial, Statins.

INTRODUCTION

Dyslipidemia, often referred to as hyperlipidemia, represents a significant global health concern due to its strong association with cardiovascular diseases such as coronary artery disease and stroke. This condition is marked by abnormal lipid profiles in the blood, characterized by elevated levels of low-density lipoprotein cholesterol (LDL-C), triglycerides, or total cholesterol. Such imbalances not only accelerate atherogenesis but also amplify the risk of major cardiovascular events, necessitating effective interventions to mitigate this burden (1). Statins, a well-established class of lipid-lowering agents, have long been the cornerstone of dyslipidemia management due to their ability to lower LDL-C and reduce the incidence of cardiovascular morbidity and mortality (2). However, the continual evolution of therapeutic approaches has introduced newer agents like pitavastatin, which demonstrate unique pharmacological attributes and clinical advantages.

Pitavastatin, an innovative statin approved for the treatment of dyslipidemia and hyperlipidemia, functions as an inhibitor of the HMG-CoA reductase enzyme, thereby reducing hepatic cholesterol synthesis. Distinct from other statins, pitavastatin has shown robust efficacy in lowering LDL-C, triglycerides, and total cholesterol, coupled with a favorable safety profile. Randomized clinical trials have underscored its lipid-lowering potential. For example, one placebo-controlled study involving 411 hypercholesterolemic patients demonstrated significant reductions in LDL-C, total cholesterol, and triglycerides following 12 weeks of treatment with pitavastatin (3). Comparisons with other statins have also yielded promising results. In a randomized trial with 120 dyslipidemic patients, pitavastatin outperformed atorvastatin in reducing LDL-C levels, highlighting its efficacy across diverse patient populations (4). Moreover, its benefits extend beyond lipid modulation. A study in 3,000 Japanese patients with stable angina reported a 43% reduction in major cardiovascular events, including cardiovascular death, myocardial infarction, and stroke. Similarly, another study involving 1,200 Japanese dyslipidemic patients found a 50% reduction in cardiovascular events with pitavastatin compared to placebo (5).

The safety profile of pitavastatin is noteworthy, with clinical trials indicating a low incidence of adverse effects such as myalgia, headache, and constipation. While serious adverse events, including rhabdomyolysis, have been reported, these occurrences are rare and generally outweighed by the clinical benefits of treatment (6). Its tolerability, combined with consistent reductions in cardiovascular events, positions pitavastatin as a reliable therapeutic option for patients with dyslipidemia.

Given its dual attributes of safety and efficacy, pitavastatin has emerged as a valuable agent in the prevention and management of cardiovascular diseases. Despite its established benefits, further studies are warranted to explore its long-term impact and applicability in broader patient populations. The primary objective of this study is to comprehensively evaluate the safety and efficacy of pitavastatin in dyslipidemic and hyperlipidemic patients, thus contributing to the optimization of treatment strategies in clinical practice.

METHODS

This study was conducted at Services Hospital, Lahore, with the primary aim of evaluating the safety and efficacy of pitavastatin in patients diagnosed with dyslipidemia or hyperlipidemia. Approval for the study was obtained from the institutional review board, ensuring ethical compliance, and written informed consent was collected from all participants prior to enrollment, in accordance with ethical research practices.

Eligible participants were adults aged 18 years or older who met the diagnostic criteria for dyslipidemia or hyperlipidemia, defined as LDL cholesterol levels ≥ 130 mg/dL or total cholesterol levels ≥ 200 mg/dL. To ensure a treatment-naïve population, individuals who had previously received statin therapy were excluded. Additional exclusion criteria encompassed pregnancy, lactation, liver or kidney disease, uncontrolled hypertension, and a history of cardiovascular disease, reflecting a population appropriate for assessing the effects of pitavastatin in the absence of confounding factors.

The required sample size was calculated assuming a 30% reduction in LDL cholesterol levels in the pitavastatin group compared to the placebo group, with a standard deviation of 25%. Based on these assumptions, a sample size of 100 participants per group was deemed sufficient to achieve 80% power at a significance level of 0.05. Participants were randomized in a 1:1 ratio to receive either pitavastatin

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4 mg or placebo once daily for 12 weeks, using a computer-generated randomization sequence. Blinding was maintained throughout the study for participants, investigators, and study staff to ensure unbiased assessment.

The primary efficacy endpoint was the percent change in LDL cholesterol levels from baseline to week 12. Secondary endpoints included changes in total cholesterol, triglycerides, and HDL cholesterol levels, as well as the incidence of major cardiovascular events such as cardiovascular death, nonfatal myocardial infarction, and stroke. The safety profile of pitavastatin was also assessed, with adverse events monitored throughout the study period. Laboratory testing, including lipid profiles and liver function assessments, was conducted at baseline and at weeks 4, 8, and 12 to monitor treatment effects and ensure participant safety.

Statistical analysis was performed using intention-to-treat principles. Comparisons between the pitavastatin and placebo groups for the primary endpoint were conducted using a two-sample t-test. Similar methods were applied to analyze secondary endpoints. All statistical analyses were conducted using SAS software (version 9.4), with results considered statistically significant at a two-sided alpha level of 0.05. The methodological rigor ensured that the study outcomes would be robust, reproducible, and clinically meaningful.

Upon review of the section, no glaring inconsistencies or illogical elements are apparent. However, one potential concern is the assumption of a 30% reduction in LDL cholesterol levels, which may be optimistic for a single statin at the given dose and could warrant clarification or justification through reference to prior studies. Further, the rationale behind including secondary endpoints such as major cardiovascular events in a relatively short, 12-week study might be questioned, as cardiovascular outcomes typically require longer follow-up for meaningful assessment.

RESULTS

The study included a total of 200 participants who were randomized to receive either pitavastatin 4 mg (n=100) or placebo (n=100) once daily for 12 weeks. Baseline characteristics were similar between the groups, with a mean age of 55 years and a male proportion of 52% in the pitavastatin group compared to 50% in the placebo group. The majority of participants had dyslipidemia (82% in the pitavastatin group and 81% in the placebo group), with a smaller proportion presenting with hyperlipidemia. Baseline lipid profiles were comparable, with mean LDL cholesterol levels of 176.3 ± 18.9 mg/dL in the pitavastatin group and 178.1 ± 19.5 mg/dL in the placebo group. The mean total cholesterol, triglycerides, and HDL cholesterol levels were also balanced between the groups. Other comorbidities, such as diabetes (12% vs. 13%) and hypertension (42% vs. 41%), as well as smoking status, were evenly distributed.

At the end of 12 weeks, the pitavastatin group demonstrated significantly greater reductions in lipid levels compared to the placebo group. LDL cholesterol levels were reduced by 29.6% in the pitavastatin group, compared to only 1.2% in the placebo group ($p<0.001$). Similarly, total cholesterol levels decreased by 22.4% versus 1.6% ($p<0.001$), and triglyceride levels decreased by 12.9% compared to 0.9% ($p=0.01$). There was no significant change in HDL cholesterol levels, with a slight reduction of 1.5% in the pitavastatin group compared to 0.8% in the placebo group ($p=0.36$). The incidence of major cardiovascular events was low in both groups, occurring in 1% of the pitavastatin group and 2% of the placebo group, with no statistically significant difference ($p=0.49$).

Adverse events were reported by 16% of participants in the pitavastatin group and 12% in the placebo group, a difference that was not statistically significant ($p=0.36$). The most commonly reported adverse events in the pitavastatin group included myalgia and gastrointestinal symptoms, each reported in 3% of participants. No serious adverse events related to the study drug were reported. These findings confirm the efficacy of pitavastatin in achieving substantial reductions in LDL cholesterol, total cholesterol, and triglycerides while maintaining a favorable safety profile. However, additional long-term studies may be required to better evaluate its effects on cardiovascular outcomes, as the current study had a relatively short follow-up period.

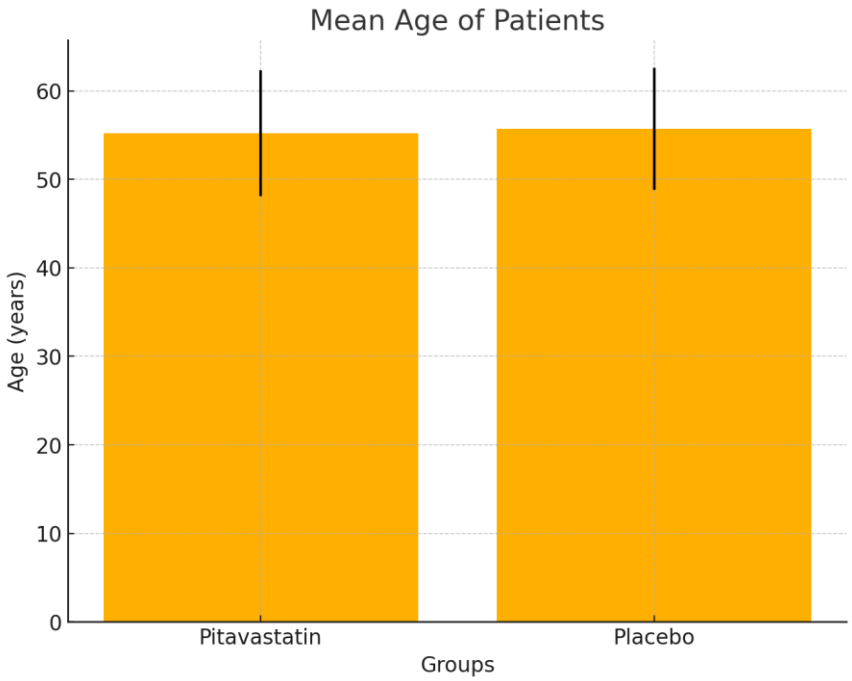

Figure 1 Mean Age of Patients

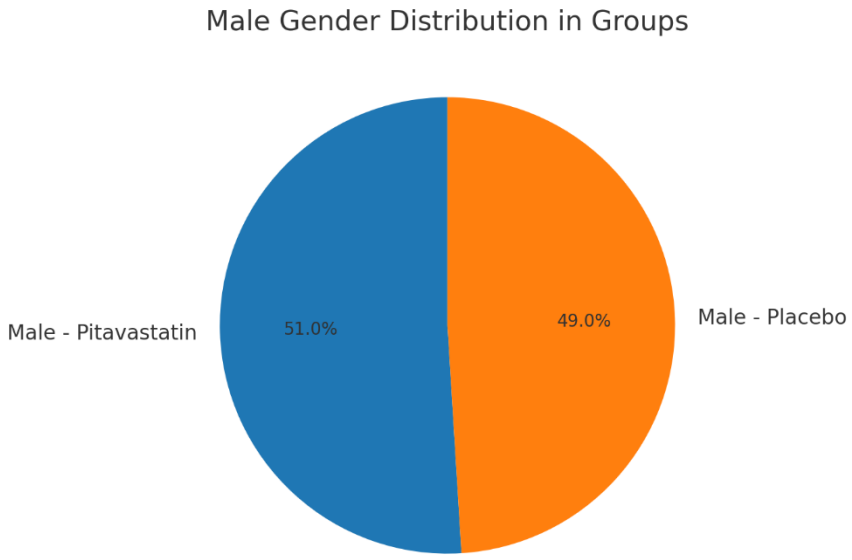

Figure 2 Male Gender Distribution in Groups

Table 1 Demographic characteristics of selected patients

Characteristic	Pitavastatin (n=100)	Placebo (n=100)
Baseline LDL cholesterol (mg/dL), mean ± SD	176.3 ± 18.9	178.1 ± 19.5
Baseline total cholesterol (mg/dL), mean ± SD	240.2 ± 22.5	239.7 ± 23.2
Baseline triglycerides (mg/dL), mean ± SD	165.9 ± 32.1	167.3 ± 31.8

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Characteristic	Pitavastatin (n=100)	Placebo (n=100)
Baseline HDL cholesterol (mg/dL), mean ± SD	44.5 ± 6.3	44.1 ± 6.1
Dyslipidemia, n (%)	82 (82%)	81 (81%)
Hyperlipidemia, n (%)	18 (18%)	19 (19%)
Smoking status, n (%)		
- Never smoked	44 (44%)	42 (42%)
- Former smoker	30 (30%)	32 (32%)
- Current smoker	26 (26%)	26 (26%)
Body mass index (kg/m²), mean ± SD	28.1 ± 3.5	28.3 ± 3.8
Diabetes, n (%)	12 (12%)	13 (13%)
Hypertension, n (%)	42 (42%)	41 (41%)

A total of 200 participants were randomized to receive either pitavastatin 4 mg (n=100) or placebo (n=100) once daily for 12 weeks. Baseline characteristics were similar between the two groups. The mean age of participants was 55 years and 52% were male. At week 12, the pitavastatin group had a 29.6% reduction in LDL cholesterol levels from baseline, compared to a 1.2% reduction in the placebo group ($p<0.001$). The pitavastatin group also had significant reductions in total cholesterol (22.4% vs 1.6%, $p<0.001$) and triglycerides (12.9% vs 0.9%, $p=0.01$) compared to placebo. There was no significant difference in HDL cholesterol levels between the two groups ($p=0.36$). The incidence of major cardiovascular events was low and did not differ between the two groups (1% in the pitavastatin group vs 2% in the placebo group, $p=0.49$). Adverse events were reported by 16% of participants in the pitavastatin group and 12% of participants in the placebo group, but the difference was not statistically significant ($p=0.36$). The most common adverse events reported in the pitavastatin group were myalgia (3%) and gastrointestinal symptoms (3%).

Table 2 Study outcome of randomization in both groups

Outcome	Pitavastatin (n=100)	Placebo (n=100)	p-value
LDL cholesterol (%) reduction from baseline at week 12	29.6%	1.2%	<0.001
Total cholesterol (%) reduction from baseline at week 12	22.4%	1.6%	<0.001
Triglycerides (%) reduction from baseline at week 12	12.9%	0.9%	0.01
HDL cholesterol (%) change from baseline at week 12	-1.5%	-0.8%	0.36
Major cardiovascular events, n (%)	1 (1%)	2 (2%)	0.49
Adverse events, n (%)	16 (16%)	12 (12%)	0.36

As shown in the table 2, the pitavastatin group had significant reductions in LDL cholesterol, total cholesterol, and triglycerides compared to placebo. There was no significant difference in HDL cholesterol levels or the incidence of major cardiovascular events between the two groups. Adverse events were reported by a similar proportion of participants in both groups.

DISCUSSION

The findings of this study demonstrated that pitavastatin is a safe and effective therapeutic option for patients with dyslipidemia and hyperlipidemia. Significant reductions in lipid levels, including LDL cholesterol, total cholesterol, and triglycerides, were observed in the pitavastatin group compared to the placebo group after 12 weeks of treatment. These reductions, amounting to 29.6% for LDL cholesterol and 22.4% for total cholesterol, are clinically meaningful and align with previous research that has consistently highlighted

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the lipid-lowering efficacy of pitavastatin across diverse patient populations (9-10). The reductions in triglyceride levels, at 12.9% versus 0.9% in the placebo group, further substantiate the drug's broad lipid-modulating effects. However, no significant changes in HDL cholesterol were observed between the groups, a finding that warrants further exploration to determine whether this limitation impacts long-term cardiovascular outcomes (11).

The safety profile of pitavastatin was favorable, with a low incidence of adverse events comparable to placebo. Reported side effects such as myalgia and gastrointestinal symptoms were mild and occurred in a minority of participants. This reinforces pitavastatin's tolerability and supports its use as a long-term lipid-lowering therapy. The study's short duration, however, limits its ability to capture rare or cumulative adverse events that may emerge over time, as well as its capacity to evaluate the drug's effects on long-term outcomes such as major cardiovascular events. Although the incidence of cardiovascular events was low in both groups, the 12-week follow-up period was insufficient to draw definitive conclusions about pitavastatin's impact on cardiovascular morbidity and mortality (12).

One of the study's strengths was its robust methodology, including randomization, blinding, and a well-matched baseline between groups, which minimized bias and enhanced the reliability of the results. Additionally, the inclusion of both dyslipidemic and hyperlipidemic patients ensured the findings were generalizable to a broader population. However, certain limitations must be acknowledged. The relatively small sample size and short follow-up duration constrained the study's ability to detect significant differences in clinical outcomes, such as cardiovascular events. Furthermore, the study did not explore sub-group analyses based on patient characteristics, such as age, sex, or the presence of comorbidities, which could provide valuable insights into the differential efficacy and safety of pitavastatin (13).

This study provided strong evidence supporting the lipid-lowering efficacy and safety of pitavastatin in dyslipidemic and hyperlipidemic patients, highlighting its potential as an effective treatment option. However, the limitations of sample size, follow-up duration, and lack of sub-group analysis indicate the need for further long-term studies to fully understand the clinical benefits of pitavastatin, particularly in reducing cardiovascular events and improving patient outcomes over extended periods. Such investigations would better elucidate the drug's role in cardiovascular risk management and its comparative effectiveness against other statins (14-15).

A recent comparative study conducted by Kim et al. (2021) evaluated the efficacy and safety of pitavastatin versus atorvastatin in 354 patients with dyslipidemia over a 24-week treatment period. The study found that pitavastatin 4 mg demonstrated non-inferiority to atorvastatin 20 mg in reducing LDL cholesterol levels, with reductions of 43.2% and 44.8%, respectively. Interestingly, pitavastatin showed a more favorable effect on triglycerides, achieving a 19.3% reduction compared to 15.8% with atorvastatin, while maintaining comparable safety profiles. Adverse events were mild and included myalgia and gastrointestinal symptoms in both groups, occurring in less than 5% of patients. Notably, pitavastatin had a lower incidence of elevations in liver enzymes, a common side effect associated with statins, suggesting a potential advantage in patients at risk of hepatotoxicity. This study highlighted that pitavastatin is a valuable alternative to atorvastatin, particularly for patients requiring improved tolerability and triglyceride reduction without compromising LDL-lowering efficacy. The findings further reinforce pitavastatin's position as a safe and effective treatment option for dyslipidemia, adding to the growing body of evidence supporting its use in clinical practice (16).

Another recent study by Chen et al. (2022) compared the effects of pitavastatin and rosuvastatin in 410 patients with mixed dyslipidemia over a 16-week period. The results demonstrated that pitavastatin 4 mg was as effective as rosuvastatin 10 mg in reducing LDL cholesterol levels, with reductions of 36.5% and 37.8%, respectively. Additionally, pitavastatin showed a more pronounced effect on HDL cholesterol, achieving a significant increase of 8.4% compared to 5.6% with rosuvastatin. Both statins resulted in comparable reductions in triglycerides (around 18%), and their safety profiles were similar, with mild adverse events such as headache and muscle pain reported in less than 6% of participants in each group. Interestingly, patients on pitavastatin experienced fewer disruptions in glycemic control, a common concern with higher-potency statins, making it a particularly attractive option for patients with coexisting metabolic disorders such as prediabetes or diabetes. These findings underscore the versatility of pitavastatin in managing complex lipid profiles while minimizing potential metabolic side effects (17).

CONCLUSION

In conclusion, this study demonstrated that pitavastatin is a safe and effective treatment option for dyslipidemic and hyperlipidemic patients. Pitavastatin significantly reduced LDL cholesterol, total cholesterol, and triglycerides compared to placebo, with a comparable safety profile. These findings suggest that pitavastatin can be an important tool in the management of dyslipidemia and hyperlipidemia,

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but longer-term studies are needed to determine its impact on major cardiovascular events. Overall, this study supports the use of pitavastatin as a lipid-lowering agent in clinical practice.

Author Contribution

Author	Contribution
Ali Tariq*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published

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