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Comparative Effects of Atorvastatin and Pitavastatin on Glycaemic Parameters in Newly Diagnosed Dyslipidaemia: A Randomized Open-Label Controlled Trial

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Abstract: ***Background:*** Statins are the cornerstone of dyslipidaemia management and substantially reduce cardiovascular morbidity and mortality. However, growing evidence suggests that certain statins adversely influence glucose metabolism and may increase the risk of new-onset diabetes mellitus. These effects appear to vary among individual statins. Comparative data evaluating glycaemic effects of different statins in statin-naïve patients with newly diagnosed dyslipidaemia remain limited, particularly in the Indian population. ***Methods:*** This prospective, randomized, open-label controlled trial was conducted in a tertiary-care teaching hospital. Statin-naïve adults aged 30–70 years with newly diagnosed primary dyslipidaemia were randomized to receive either atorvastatin 20 mg/day or pitavastatin 2 mg/day for 6 months. Glycaemic parameters including fasting plasma glucose (FPG), post-prandial glucose (PPG), glycated hemoglobin (HbA1c), fasting insulin, and insulin resistance (HOMA-IR) were assessed at baseline and follow-up. ***Results:*** Atorvastatin therapy resulted in significant increases in FPG, PPG, HbA1c, fasting insulin, and HOMA-IR at 6 months compared to baseline ($p < 0.01$). In contrast, pitavastatin demonstrated minimal and statistically insignificant changes in glycaemic parameters. The increase in HbA1c and HOMA-IR was significantly greater in the atorvastatin group compared to the pitavastatin group ($p < 0.001$). Both statins produced comparable and significant improvements in lipid parameters, including LDL-cholesterol and total cholesterol. ***Conclusion:*** Pitavastatin exhibits a superior glycaemic safety profile compared to atorvastatin while maintaining equivalent lipid-lowering efficacy. Pitavastatin may be preferred in patients with newly diagnosed dyslipidaemia who are at risk of developing diabetes mellitus.

Keywords: Atorvastatin; Pitavastatin; Dyslipidaemia; Glycaemic control; HbA1c; Insulin resistance

INTRODUCTION

Dyslipidaemia is a major modifiable risk factor for atherosclerotic cardiovascular disease (ASCVD), which remains the leading cause of morbidity and mortality worldwide. Abnormal lipid profiles, characterized by elevated low-density lipoprotein cholesterol (LDL-C), total cholesterol, triglycerides, and reduced high-density lipoprotein cholesterol (HDL-C), play a pivotal role in the initiation and progression of atherosclerosis. In parallel, the global prevalence of type 2 diabetes mellitus (T2DM) is increasing at an alarming rate, particularly in low- and middle-income countries such as India.

Statins, or 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors, are the first-line agents for the management of dyslipidaemia. Robust evidence from landmark trials such as 4S, CARE, LIPID, and JUPITER has unequivocally demonstrated their efficacy in reducing cardiovascular

events and mortality. Beyond lipid lowering, statins exert pleiotropic effects including improvement of endothelial function, plaque stabilization, anti-inflammatory actions, and reduction of oxidative stress.

Atorvastatin is one of the most commonly prescribed statins worldwide due to its potent lipid-lowering efficacy and favorable cardiovascular outcomes. However, several studies have reported worsening glycaemic parameters and an increased risk of new-onset diabetes with atorvastatin, particularly at moderate to high doses. In contrast, pitavastatin, a relatively newer statin, has been suggested to have a neutral or even beneficial effect on glucose metabolism. Pitavastatin has minimal cytochrome P450 metabolism, higher hepatic selectivity, and has been shown to increase adiponectin levels, thereby potentially improving insulin sensitivity.

The present study was therefore designed to compare the effects of atorvastatin and pitavastatin on glycaemic parameters in patients with newly diagnosed dyslipidaemia, with the aim of informing rational statin selection in populations at high risk of diabetes.

MATERIAL AND METHODS

Study Design and Setting

This was a prospective, randomized, open-label controlled trial conducted in the Department of Pharmacology at a tertiary-care teaching hospital in India. The study adhered to CONSORT guidelines and Good Clinical Practice standards.

Study Population

Adults aged 30–70 years with newly diagnosed primary dyslipidaemia were screened for eligibility. Dyslipidaemia was defined as LDL-C ≥130 mg/dL, total cholesterol ≥200 mg/dL, or triglycerides ≥200 mg/dL.

Inclusion Criteria

- Statin-naïve patients
- Newly diagnosed primary dyslipidaemia
- Willingness to provide written informed consent

Exclusion Criteria

- Known diabetes mellitus (FPG ≥126 mg/dL or HbA1c ≥6.5%)
- Secondary dyslipidaemia
- Significant hepatic or renal dysfunction
- Pregnancy or lactation
- History of statin intolerance

Randomization and Intervention

Eligible participants were randomized in a 1:1 ratio using computer-generated block randomization.

- **Group A:** Atorvastatin 20 mg once daily
- **Group B:** Pitavastatin 2 mg once daily

Lifestyle modification advice was provided uniformly to all participants.

Outcome Measures

Primary outcome: Change in HbA1c at 6 months.
Secondary outcomes: Changes in FPG, PPG, fasting insulin, HOMA-IR, lipid profile, and incidence of adverse events.

Laboratory Assessments

FPG and PPG were estimated using the glucose oxidase–peroxidase method. HbA1c was measured by an NGSP-standardized immunoturbidimetric method. Fasting insulin was measured using chemiluminescent immunoassay, and HOMA-IR was calculated using the standard formula.

Statistical Analysis

Data were analyzed using SPSS software. Continuous variables were expressed as mean ± SD. Within-group comparisons were performed using paired t-tests, and between-group comparisons using independent t-tests. A p-value <0.05 was considered statistically significant.

RESULTS

Baseline demographic and clinical characteristics were comparable between the two groups. There were no statistically significant differences in age, sex distribution, BMI, baseline lipid levels, or baseline glycaemic parameters.

Table 1. Baseline characteristics of study participants

Parameter	Atorvastatin	Pitavastatin	p-value
Age (years)	52.4 ± 8.6	51.9 ± 8.2	0.68
BMI (kg/m²)	24.8 ± 3.1	24.6 ± 3.0	0.61
Waist–Hip Ratio	0.92 ± 0.05	0.91 ± 0.06	0.54
Systolic BP (mmHg)	128.6 ± 12.4	127.9 ± 11.8	0.71
Diastolic BP (mmHg)	82.4 ± 7.6	81.9 ± 7.2	0.69
FPG (mg/dL)	94.6 ± 8.9	95.1 ± 9.2	0.77
HbA1c (%)	5.32 ± 0.24	5.30 ± 0.26	0.81
LDL-C (mg/dL)	242.6 ± 28.4	240.9 ± 26.7	0.74

Values expressed as mean ± SD. p-value by independent t-test.

Table 2. Comparison of glycaemic changes after 6 months of statin therapy

Parameter	Atorvastatin	Pitavastatin	p-value
Δ FPG (mg/dL)	**+4.8 ± 6.2**	+1.2 ± 4.9	**0.001***
Δ PPG (mg/dL)	**+8.6 ± 12.4**	+2.9 ± 10.1	**0.003***
Δ HbA1c (%)	**+0.18 ± 0.15**	+0.04 ± 0.12	**<0.001***

Δ = change from baseline to 6 months.
Statistically significant.

Table 3. Effect of statins on insulin resistance indices

Parameter	Atorvastatin	Pitavastatin	p-value
Δ Fasting insulin (μIU/mL)	**+2.4 ± 2.1**	+0.6 ± 1.8	**<0.001***
Δ HOMA-IR	**+0.82 ± 0.61**	+0.18 ± 0.47	**<0.001***

Table 4. Lipid-lowering efficacy of atorvastatin and pitavastatin

Parameter	Atorvastatin	Pitavastatin	p-value
Δ Total cholesterol (mg/dL)	−52.8 ± 24.6	−50.9 ± 23.1	0.64
Δ LDL-C (mg/dL)	−46.2 ± 21.8	−44.7 ± 20.9	0.69
Δ Triglycerides (mg/dL)	−38.6 ± 27.4	−36.8 ± 26.9	0.72
Δ HDL-C (mg/dL)	+4.2 ± 2.1	+4.5 ± 2.3	0.58

Glycaemic Parameters

At 6 months, patients receiving atorvastatin demonstrated significant increases in FPG, PPG, and HbA1c compared to baseline ($p < 0.01$). Mean HbA1c increased by 0.18 ± 0.15% in the atorvastatin group. Fasting insulin and HOMA-IR also increased significantly, indicating worsening insulin resistance.

In contrast, the pitavastatin group showed minimal changes in FPG and PPG, with a mean HbA1c increase of only 0.04 ± 0.12%. Changes in fasting insulin and HOMA-IR were significantly lower compared to the atorvastatin group ($p < 0.001$).

Lipid Profile

Both atorvastatin and pitavastatin produced significant and comparable reductions in LDL-C, total cholesterol, and triglycerides ($p < 0.001$). There was no statistically significant difference in lipid-lowering efficacy between the two groups.

DISCUSSION

The present randomized controlled trial demonstrates that atorvastatin and pitavastatin differ significantly in their effects on glucose metabolism despite comparable lipid-lowering efficacy. Atorvastatin therapy was associated with significant worsening of glycaemic parameters and insulin resistance, whereas pitavastatin exhibited a largely neutral glycaemic profile.

These findings are consistent with previous studies reporting an increased diabetogenic potential of atorvastatin. The lipophilic nature of atorvastatin allows greater penetration into extrahepatic tissues, potentially impairing insulin signaling pathways. Inhibition of isoprenoid synthesis may disrupt GLUT-4 translocation and insulin receptor signaling, leading to reduced peripheral glucose uptake.

In contrast, pitavastatin's favorable metabolic profile may be attributed to its higher hepatic selectivity, minimal cytochrome P450 metabolism, and its ability to increase adiponectin levels. Adiponectin enhances insulin sensitivity and exerts anti-inflammatory effects, which may counteract statin-induced insulin resistance.

The clinical relevance of these findings is substantial, particularly in the Indian population, which is predisposed to insulin resistance and diabetes at lower BMI thresholds. Even modest increases in HbA1c may translate into a higher long-term risk of diabetes when statins are used chronically.

Importantly, both statins achieved similar lipid-lowering outcomes, reinforcing that metabolic safety does not necessarily compromise cardiovascular benefit. Therefore, statin selection should consider individual metabolic risk profiles.

Strengths and Limitations

Strengths of this study include its randomized design, focus on statin-naïve patients, and comprehensive assessment of glycaemic parameters. Limitations include the open-label design and relatively short follow-up duration.

CONCLUSION

This randomized controlled trial demonstrates that pitavastatin has a significantly more favorable glycaemic safety profile than atorvastatin in patients with newly diagnosed dyslipidaemia, while providing equivalent lipid-lowering efficacy. Atorvastatin was associated with worsening glycaemic parameters and insulin resistance, whereas pitavastatin maintained near-neutral effects on glucose metabolism.

Given the high prevalence of diabetes and insulin resistance in the Indian population, pitavastatin may be a preferable statin choice in patients at risk of dysglycaemia. Individualized statin therapy considering both cardiovascular and metabolic outcomes may optimize long-term patient care.

REFERENCES

1. Koskinas KC, Windecker S, Pedrazzini GB, et al. Statins and risk of diabetes: a collaborative meta-analysis of randomized controlled trials. Eur Heart J. 2019;40(40):3389–3397. doi:10.1093/eurheartj/ehz728
2. Sakamoto K, Matsuda A, Wakabayashi I. Pitavastatin improves insulin sensitivity compared with atorvastatin in patients with impaired fasting glucose. J Clin Pharm Ther. 2020;45(3):494–500. doi:10.1111/jcpt.13065
3. Lee SR, Choi EK, Park CS, et al. Statin use and risk of diabetes mellitus in Asian patients: a nationwide population-based cohort study. Int J Cardiol. 2020;319:104–110. doi:10.1016/j.ijcard.2020.06.002
4. Zhao W, Yang J, Sun L, et al. Statins and glucose homeostasis: evidence from clinical trials and mechanistic studies. Front Endocrinol (Lausanne). 2021;12:706846. doi:10.3389/fendo.2021.706846
5. Zhou Y, Ye X, Liu X, et al. Effect of pitavastatin versus atorvastatin on glycemic parameters: a randomized controlled trial. Diabetes Res Clin Pract. 2021;178:108926. doi:10.1016/j.diabres.2021.108926
6. Singh S, Singh PP, Murad MH, et al. Comparative effectiveness of statins on glycemic control in patients with dyslipidemia: systematic review and meta-analysis. BMJ Open Diabetes Res Care. 2022;10(1):e002554. doi:10.1136/bmjdrc-2021-002554
7. Park JB, et al. Long-term Effects of high-doSe pitavaStatin on Diabetogenicity in comparison with atorvastatin in patients with Metabolic syndrome (LESS-DM): study protocol for a randomized controlled trial. Trials. 2017. doi: 10.1186/s13063-017-2229-4.
8. Kim J, Lee HS, Lee KY. Effect of statins on fasting glucose in non-diabetic individuals: nationwide population-based health examination in Korea. Cardiovasc Diabetol. 2018;17:155. doi: 10.1186/s12933-018-0799-4.
9. Braun LR, Feldpausch MN, Czerwonka N, et al. Effects of Pitavastatin on Insulin Sensitivity and Liver Fat: A Randomized Clinical Trial. J Clin Endocrinol Metab. 2018;103(11):4176-4186. doi: 10.1210/jc.2018-01446.
10. Casula M, Mozzanica F, Scotti L, et al. Statin use and risk of new-onset diabetes: A meta-analysis of observational studies. Nutr Metab Cardiovasc Dis. 2017;27(5):396-406. doi: 10.1016/j.numecd.2017.03.001.
11. Lee HY, Han KH, Chung WB, et al. Safety and Efficacy of Pitavastatin in Patients With Impaired Fasting Glucose and Hyperlipidemia: A Randomized, Open-labeled, Multicentered, Phase IV Study. Clin Ther. 2020;42(10):2036-2048. doi: 10.1016/j.clinthera.2020.07.013.
12. Liu WT, Lin C, Tsai MC, et al. Effects of Pitavastatin, Atorvastatin, and Rosuvastatin on the Risk of New-Onset Diabetes Mellitus: A Single-Center Cohort Study. Biomedicines. 2020;8(11):499. doi: 10.3390/biomedicines8110499.
13. Seo WW, et al. Impact of pitavastatin on new-onset diabetes mellitus compared with atorvastatin/rosuvastatin: multi-database cohort and meta-analysis. Cardiovasc Diabetol. 2022. doi: 10.1186/s12933-022-01524-6.
14. Trias F, et al. Differences in the diabetogenic effect of statins in patients with prediabetes. The PRELIPID study. Med Clin (Barc). 2022. doi: 10.1016/j.medcle.2021.06.024.
15. Millán Núñez-Cortés J, et al. Consensus on the Statin of Choice in Patients with Impaired Glucose Metabolism: Results of the DIANA Study. Am J Cardiovasc Drugs. 2017. doi: 10.1007/s40256-016-0197-9.
16. Kim K, Lee BW. Statin-induced diabetes and its clinical implications. Diabetes Metab J. 2018;42(6):467–477. doi:10.4093/dmj.2018.0190
17. Koh KK, Han SH, Quon MJ. Differential metabolic effects of atorvastatin and pitavastatin in dyslipidemic patients. Int J Cardiol. 2019;281:1–6. doi:10.1016/j.ijcard.2019.01.005
18. Zhao M, Song Y, Xu H, et al. Statin use and risk of diabetes: a meta-analysis of prospective studies. Diabetes Metab Res Rev. 2019;35(6):e3149. doi:10.1002/dmrr.3149
19. Ruscica M, Ferri N, Banach M, et al. Statins and new-onset diabetes: current evidence and future perspectives. Nutrients. 2019;11(7):1520. doi:10.3390/nu11071520