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ORIGINAL ARTICLE

Forty-eight weeks of statin therapy for type 2 diabetes mellitus patients with lower extremity atherosclerotic disease: Comparison of the effects of pitavastatin and atorvastatin on lower femoral total plaque areas

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ABSTRACT

Aims/Introduction: Type 2 diabetes mellitus is correlated with systemic atherosclerosis. Statin therapies have been proved to reduce low-density lipoprotein cholesterol (LDL-C) level, protecting type 2 diabetes mellitus patients from cardiovascular events. Recently, more interest has been focused on the regression of lower extremity atherosclerotic disease (LEAD) for the potential prevention of amputation. However, the effects of pitavastatin and atorvastatin on LEAD in type 2 diabetes mellitus patients have not been directly compared.

Materials and Methods: This study compared the effects of pitavastatin and atorvastatin on femoral total plaque areas (FTPA), and lipids and glucose metabolism in type 2 diabetes mellitus patients with elevated LDL-C level and LEAD. Type 2 diabetes mellitus patients with LDL-C level >2.6 mmol/L and LEAD were randomly assigned to receive either pitavastatin 2 mg/day or atorvastatin 10 mg/day for 48 weeks. FTPA were measured at baseline and the end of the study. Levels of glucose and lipids profile were measured periodically. The efficacy was evaluated in 63 patients.

Results: The percentage change in FTPA measurements was similar between the pitavastatin group and atorvastatin group (–17.79 ± 21.27% vs –14.34 ± 16.33%), as were the changes in LDL-C (–44.0 ± 18.0% vs –40.3 ± 18.2%) and triglyceride (17.6 ± 20.0% vs 16.2 ± 17.0%). However, the level of high-density lipoprotein cholesterol was significantly higher in the pitavastatin group compared with the atorvastatin group after 48 weeks of treatment (12.9 ± 10.3% vs 7.2 ± 11.7%, $P < 0.05$). There were no significant differences between groups for the measurements of glucose metabolism.

Conclusion: In type 2 diabetes mellitus patients with elevated LDL-C level and LEAD, 48 weeks of treatment with either pitavastatin or atorvastatin was associated with significant regression of FTPA. Pitavastatin treatment resulted in a significantly higher high-density lipoprotein cholesterol level compared with atorvastatin treatment.

INTRODUCTION

Lower extremity atherosclerotic disease (LEAD) is one of the major manifestations of diabetic macroangiopathy. LEAD affects approximately 15% of adults aged >70 years, reaching up to 200 million people around the world[1]. In the general population, patients with LEAD have increased risk of myocardial infarction, stroke and all-cause mortality[2]. The prevalence of LEAD is notably higher in individuals with diabetes mellitus[3,4]. Furthermore, diabetes mellitus patients are 15-fold more

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likely to suffer from amputation by LEAD than individuals without diabetes[5]. Despite its high prevalence, LEAD has often been under-recognized and under-treated[6,7].

Hydroxymethylglutaryl coenzyme A-reductase inhibitors (statins) have been proved to be effective in lowering the low-density lipoprotein cholesterol (LDL-C) level[8]. It is well established that statin therapy benefits cardiovascular and cerebrovascular diseases, particularly in reducing mortality in patients with coronary artery disease[9]. Statins are the first-line therapy to reduce lower limb complications in patients with LEAD as well, reported by current guidelines[10,11]. It might not only improve LEAD symptoms, but also slow down atherosclerosis progression of LEAD[12–15]. In addition, advantages in reducing systemic inflammation, lower-extremity amputation, in-hospital cardiovascular death and all-cause mortality have been observed in statins therapy[13,14,16,17]. However, evidence regarding the efficacy of statins treatment on LEAD in type 2 diabetes mellitus patients is still limited.

Unlike atorvastatin, pitavastatin is the third generation of statin, which shows a strong potential to reduce the LDL-C level with low doses[18]. Although previous studies have found some benefits of them in improving LEAD, further evidence is still required for the direct comparison of different statins on the improvement of LEAD in type 2 diabetes mellitus patients. Hence, the present study was undertaken to compare the effects of pitavastatin and atorvastatin on LEAD, and lipids and glucose metabolism in type 2 diabetes mellitus patients.

METHODS

Patients

A total of 80 type 2 diabetes mellitus patients were recruited from the First Affiliated Hospital of Sun Yat-sen University (Guangzhou, Guangdong, China) and Jiangmen Central Hospital (Jiangmen, Guangdong, China) between October 2013 and April 2016. The participants were eligible if they were aged 40–75 years, had LDL-C levels >2.6 mmol/L, LEAD at stage Ⅰ of Fontaine's classification (asymptomatic stage) and stenosis >50% in all leg arteries. The exclusion criteria included contraindications to statins use (i.e., hepatic impairment, myopathy associated with creatine kinase levels higher than 10-fold or use of cyclosporine), secondary hyperlipidemia or hyperglycemia, use of steroid hormones, hormone replacement therapy or immunosuppressant, patients who had been taking statins or other lipid-lowering drugs before enrollment, patients with previous lower limb revascularization, patients with acute complications of diabetes mellitus or severe infections in the past 3 months, patients with autoimmune disease or other allergic diseases, heart failure (New York Heart Association class Ⅲ or higher), poorly controlled diabetes based on the study physician's treatment, and pregnant or lactating women. Patients with poor compliance could also be excluded. A total of 63 of the 80 consecutive LEAD patients completed the 48-week study.

Study design

After written informed consent was obtained, patients were randomly allocated to receive either atorvastatin 10 mg/day (ATV group) or pitavastatin 2 mg/day (PTV group) for 48 weeks using a computer-generated random number sequence. All patients entered a run-in phase of approximately 3 months, which encouraged them to engage in regular physical exercise and improve eating habits. Patients underwent regular follow-up clinical examinations at 12-week intervals, where responses to therapy (including side-effects) were evaluated at periodic clinical evaluations during follow up; when necessary, therapeutic adjustments were carried out on glucose or blood pressure management. The study protocol was reviewed and approved by the ethics committee of each participating institution.

Determination of variables

Baseline characteristics of patients were recorded at the first visit, including age; sex; anthropometric data; diabetes duration; smoking, drinking; history of diseases; medications for conditions, such as antiplatelet agents; and hypotensive drugs. Smoking was defined as at least 100 cigarettes consumed before the study. Drinking was defined as at least of 100 mL wine or spirits consumed per day before the survey.

Anthropometric data, including blood pressure, height and weight, were measured by recommended standard procedures. Briefly, blood pressure was the average value of two separate measurements taken at a 5-min interval. Weight and height were measured without shoes or bulky garments. Body mass index (kg/m^2) was determined by dividing the weight (kg) by height (m) squared.

Fasting blood samples were collected at baseline, and weeks 12, 24 and 48. Venous blood was drawn for determination of fasting plasma glucose (FPG; nmol/L), glycosylated hemoglobin A1c (HbA1c; %), serum creatinine (μmol/L), uric acid (μmol/L), aspartate transaminase (mmol/L), alanine transaminase (mmol/L), low-density lipoprotein cholesterol (LDL-C mmol/L), high-density lipoprotein cholesterol (HDL-C mmol/L), total cholesterol (TC; mmol/L) and triglyceride (TG; mmol/L). All serum parameters were detected on a Mindray (Mindray Medical International Limited, Shenzhen, China) automatic biochemistry analyzer.

To investigate the glycemic variability, parameters including the standard deviation of blood glucose (SDBG) and the coefficient of variation of fasting blood glucose (FBG-CV), were adopted. Patients had capillary glucose concentrations of both fasting or preprandial and postprandial determined for three consecutive days, which were documented based on those spontaneously reported. All patients had their portable glucose meters corrected according to the instructions. SDBG was calculated and used for assessing the intraday glycemic variability in the present study, whereas FBG-CV (%) was used for assessing the day-to-day variability.

Determination of LEAD

The sum of the plaque areas of both common femoral bifurcations (femoral total plaque areas [FTPA]) was measured at the first visit and the last visit. All scans were carried out using an ACUSON Sequoia 512 ultrasound system (Siemens, Erlangen, Germany), with a 5–13-MHz linear transducer and the on-screen calipers of the system. FTPA of all patients were examined by the same experienced sonographer unaware of the statins therapy.

Briefly, seven arteries in each lower limb, including the femoral artery, deep femoral artery, superficial femoral artery, popliteal artery, anterior tibial artery, posterior tibial artery and peroneal artery, were checked in order. LEAD was diagnosed according to the Mannheim consensus[19]. Atherosclerotic plaque was defined as the presence of a focal structure encroaching into the arterial lumen at least 0.5 mm, or at least 50% greater than the thickness of the surrounding vessel wall, or an intima-media thickness ≥1.5 mm. Each measurement (mean of three readings) was carried out on a frozen on-screen image in both longitudinal and transverse sections. Plaque area was measured offline on a PC using the 'Plaque Texture Analysis software' (LifeQMedical Ltd, Nicosia, Cyprus: www.lifeqmedical.com). The FTPA of both lower limbs was calculated (mm^2).

Statistical analysis

The predefined primary end-point of the present study was the change in FTPA after 48 weeks. Secondary end-points included lipids metabolism and glucose metabolism changes after 48 weeks.

Duration of diabetes mellitus, body mass index, height and diastolic pressure were among the baseline characteristics; uric acid, alanine transaminase and aspartate transaminase of both time points were non-normally distributed and were carried out on a Wilcoxon signed-rank test. Other normally distributed data were evaluated using a *t*-test. For percentage changes comparison, ANOVA analysis was carried out. The χ^2 statistic was used to compare the two groups regarding the proportion that showed baseline characteristics. All statistical analyses were carried out using SPSS software (version 19.0; SPSS Inc, Chicago, IL, USA). Values are reported as the mean ± standard deviation, except where indicated. A two-sided probability value of ≤0.05 was considered statistically significant.

RESULTS

Patients' characteristics

A total of 80 patients were enrolled and received allocated therapy (Figure 1). Of these, two patients discontinued treatment

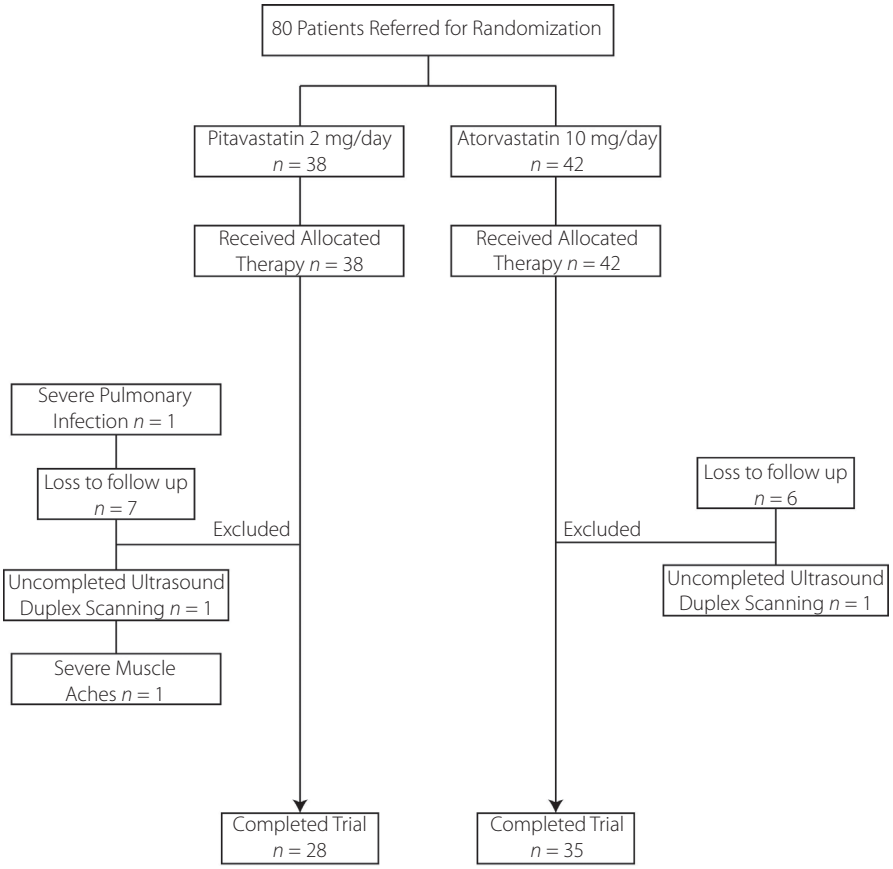

Figure 1 | Flow diagram of patients randomized and followed through the 48-week study.

because of severe pulmonary infection (follow up of 12 weeks) or muscle aches (follow up of 1 week) in PTV group. A total of 13 patients were not followed during the study, and two patients failed to complete ultrasound duplex scanning at the last visit. Thus, 63 patients (28 in the PTV group and 35 in the ATV group) were included in the end-point analysis.

As shown in Table 1, the two experimental groups (PTV and ATV) had similar baseline characteristics. No differences between the two groups were observed for age, sex distribution, duration of diabetes, fasting plasma glucose, levels of low-density lipoprotein cholesterol or high-density lipoprotein cholesterol, measured FTPA variables and so on. Also, there were no differences between groups in the prevalence of smoking or drinking, the use of cardiovascular drugs or hypoglycemic agents and so on.

Effectiveness end-points

As expected, both pitavastatin and atorvastatin therapy resulted in significantly continued reductions in LDL-C concentrations (Figure 2c). Figure 2 summarizes the changes from the baseline in the primary and secondary effectiveness end-points after 48 weeks for the two experimental groups.

Femoral total plaque areas progressively decreased in both the PTV and ATV groups (Figure 2a,b), which were significantly different from the baseline levels (change in FTPA, -13.63 ± 15.27 mm^2 in the PTV group and -12.93 ± 14.67 mm^2 in the ATV group). FTPA regression was observed in 22 of 28 pitavastatin patients (78.6%), and 28 of 35 atorvastatin patients (80.0%; $P > 0.05$). The overall efficiency was 79.4%. There were no differences observed between the two groups in FTPA measurements at the end of the study ($-17.79 \pm 21.27\%$ vs $-14.34 \pm 16.33\%$).

Both pitavastatin and atorvastatin treatments showed increases in HDL-C levels; however, the PTV group was characterized by a higher level of HDL-C concentration compared with the ATV group (Figure 2d). At 48 weeks, the HDL-C concentration in PTV group was 1.32 ± 0.23 mmol/L ($12.9 \pm 10.3\%$ increase) compared with 1.22 ± 0.26 mmol/L ($7.2 \pm 11.7\%$ increase) in ATV group ($P < 0.05$; Figure 3). Also, both treatments resulted in a reduction in TG and TC

Table 1 | Baseline characteristics of 63 patients randomly assigned to either pitavastatin or atorvastatin

	PTV (n = 28)	ATV (n = 35)	P-value
Male, n (%)	14 (48.3)	18 (50.0)	1.000
Age (years)	59.92 ± 7.45	63.35 ± 9.32	0.129
Duration of diabetes mellitus (months)	96 (54–147)	96 (36–168)	0.964
Systolic blood pressure (mmHg)	135.46 ± 19.07	138.56 ± 24.56	0.597
Diastolic blood pressure (mmHg)	71 (61–81)	78 (70–85)	0.124
Height (m)	1.62 (1.52–1.68)	1.59 (1.55–1.68)	0.896
Weight (kg)	65 (59–70)	65 (60–72)	0.566
BMI (kg/m^2)	24.56 (23.10–26.67)	26.22 (23.73–27.29)	0.111
HbA1c (%)	8.53 ± 1.44	8.27 ± 1.63	0.511
FPG (mmol/L)	7.51 ± 1.45	7.17 ± 1.71	0.419
Cr (μmol/L)	83.33 ± 22.48	76.28 ± 25.12	0.264
UA (μmol/L)	392 (282–493)	322 (269–420)	0.232
AST (mmol/L)	20 (16–28)	20 (15–29)	0.800
ALT (mmol/L)	25 (20–32)	21 (16–29)	0.079
LDL-C (mmol/L)	3.55 ± 0.90	3.49 ± 1.04	0.802
HDL-C (mmol/L)	1.18 ± 0.24	1.14 ± 0.28	0.559
TC (mmol/L)	5.60 ± 1.09	5.52 ± 1.24	0.717
TG (mmol/L)	2.05 ± 1.28	2.05 ± 1.22	0.985
FTPA (mm^2)	75.04 ± 27.19	83.96 ± 27.29	0.202
Smoking, n (%)	9 (34.6%)	12 (35.3%)	1.000
Drinking, n (%)	6 (23.1%)	7 (20.6%)	1.000
Hypertension, n (%)	16 (61.5%)	24 (70.6%)	0.582
Cardiovascular disease, n (%)	5 (17.2%)	6 (16.7%)	0.603
Use of insulin therapy, n (%)	13 (50.0%)	21 (61.8%)	0.435
Use of hypoglycemic agents, n (%)	23 (88.5%)	25 (73.5%)	0.201
Use of cardiovascular medications, n (%)	17 (58.6%)	29 (80.6%)	0.062

Values are the mean ± standard deviation or median (lower quartile to upper quartile), or n (%) as indicated. ALT, alanine transaminase; AST, aspartate transaminase; ATV, atorvastatin group; Cr, serum creatinine; FPG, fasting plasma glucose; FTPA, femoral total plaque areas; HbA1c, glycosylated hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PTV, pitavastatin group; TC, total cholesterol; TG, triglyceride; UA, uric acid.

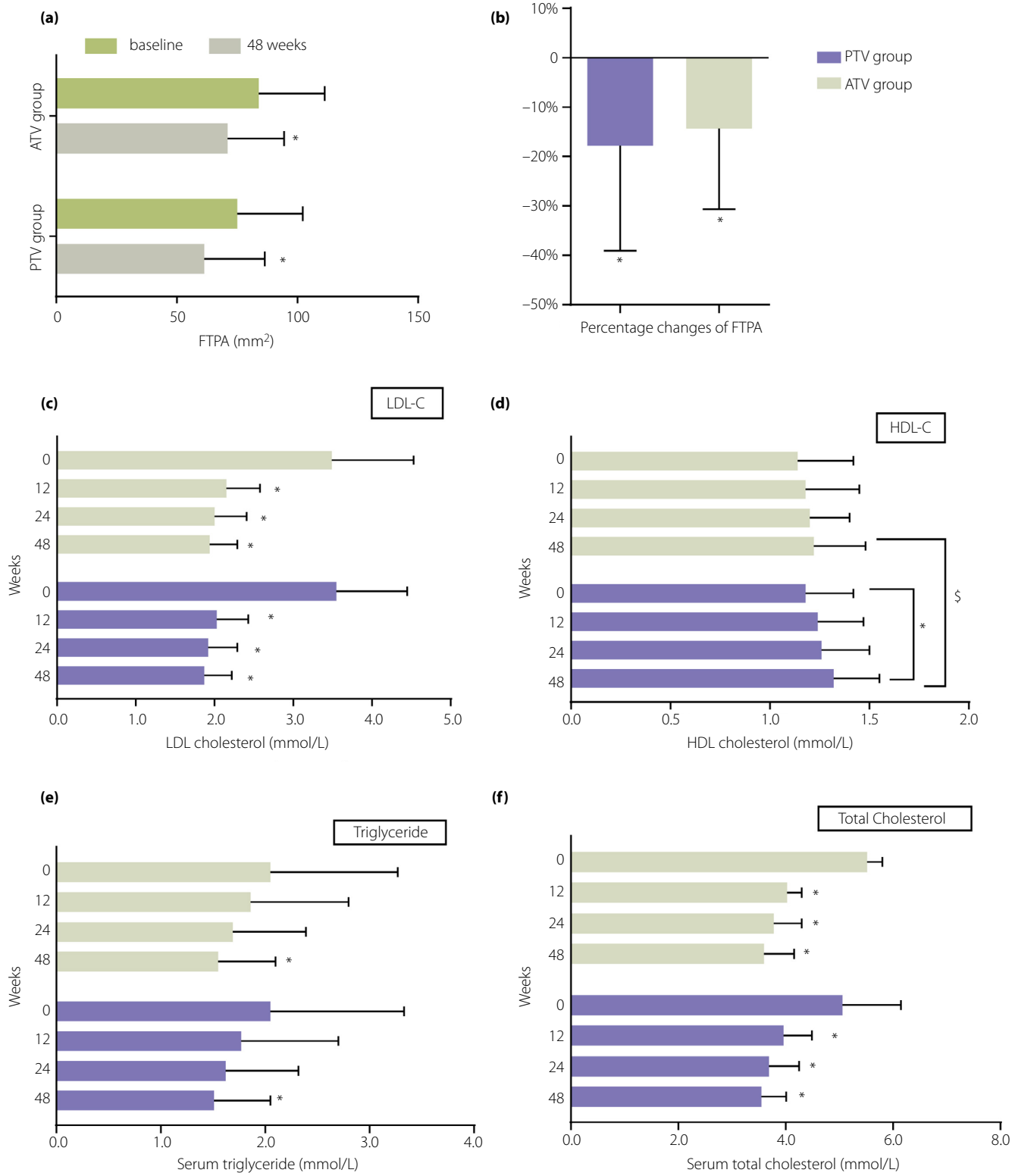

Figure 2 | Changes in femoral total plaque areas (FTPA), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol and serum triglyceride over the course of the study. (a) FTPA levels and (b) the percentage change of FTPA from the baseline levels in the indicated group. (c) LDL-C, (d) HDL-C, (e) serum triglyceride and (f) serum total cholesterol levels during the visits of the study. *$P < 0.05$ compared with the baseline level. $^{\$}P < 0.05$ compared with the atorvastatin (ATV) group. PTV group, pitavastatin group.

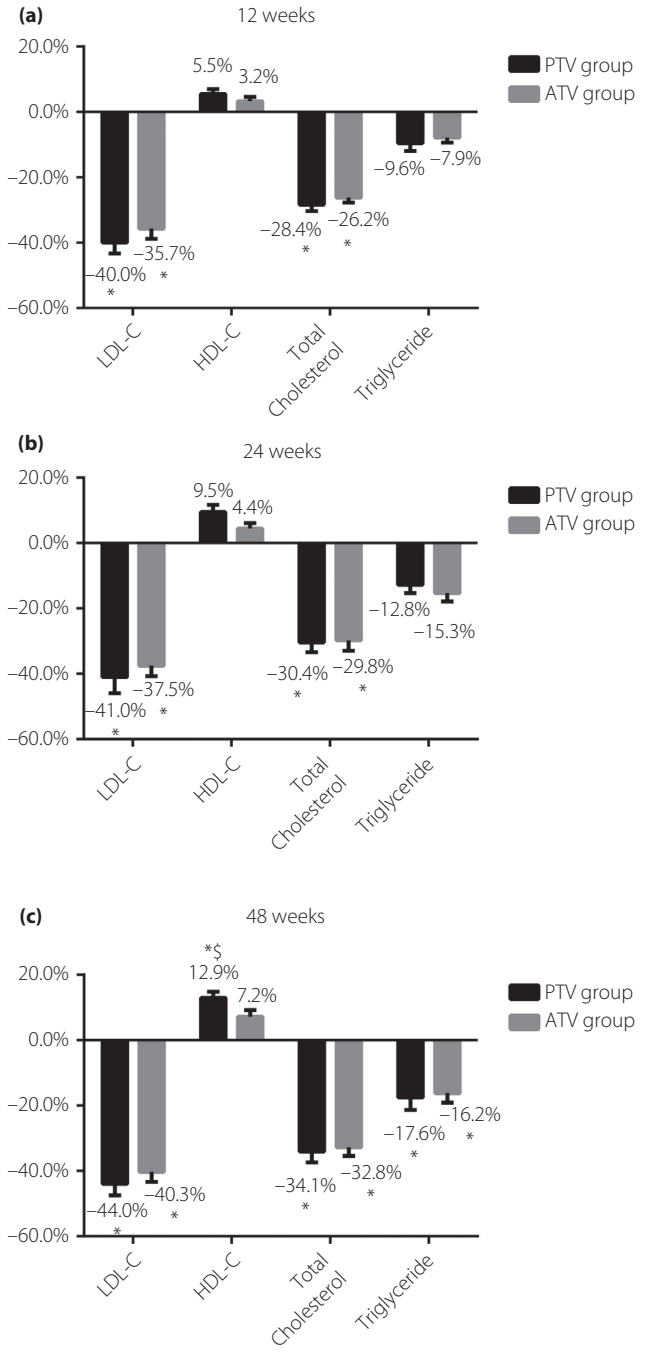

Figure 3 | Percentage changes of low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), total cholesterol and serum triglyceride from the baseline levels at indicated time points. Percentage changes in (a) 12 weeks, (b) 24 weeks and (c) 48 weeks. *$P < 0.05$ compared with the baseline level. $^{\$}P < 0.05$ compared with the atorvastatin group (ATV) group.

levels, which did not differ between groups at any time point (Figure 2e,f). The percentage change in TC levels on completion of treatment was −34.1% in the pitavastatin group and −32.8% in the atorvastatin group, and in TG levels was −17.6% in the pitavastatin group and −16.2% in the atorvastatin group (Figure 3).

HbA1c, FPG, SDBG and FBG-CV (%) levels were summarized in Table 2. No significant differences were found between groups in HbA1c, FPG, SDBG and FBG-CV at any time point during the study period. However, HbA1c showed continuous decreases in both experimental groups.

Tolerability

Adverse events considered related to the use of drugs were found in the pitavastatin group, where one patient failed to continue using pitavastatin for severe muscle aches. In the present study, we did not find other reported adverse events for statin use. There was no significant difference in the changes of aspartate transaminase, alanine transaminase, uric acid and serum creatinine at the end of the study compared with the baseline levels (Table 3).

DISCUSSION

The present study compared the effects of pitavastatin and atorvastatin on FTPA, lipids and glucose control in type 2 diabetes mellitus patients. It was shown that either pitavastatin (2 mg/day) or atorvastatin (10 mg/day) treatment led to

Table 2 | Glucose monitoring during the study in the two experimental groups

	PTV (n = 28)	ATV (n = 35)
HbA1c (%)		
Baseline	8.53 ± 1.44	8.27 ± 1.63
12 weeks	7.69 ± 0.62	7.46 ± 0.78*
24 weeks	7.04 ± 0.44*	6.94 ± 0.52*
48 weeks	6.89 ± 0.90*	6.91 ± 1.19*
SDBG		
Baseline	1.51 ± 0.30	1.45 ± 0.28
12 weeks	1.29 ± 0.29	1.38 ± 0.37
24 weeks	1.13 ± 0.23	1.20 ± 0.20
48 weeks	1.58 ± 0.31	1.66 ± 0.23
FPG (mmol/L)		
Baseline	7.51 ± 1.45	7.17 ± 1.71
12 weeks	7.46 ± 1.68	6.66 ± 1.29
24 weeks	6.69 ± 0.89	7.13 ± 1.13
48 weeks	7.14 ± 1.17	6.72 ± 1.78
FBG-CV (%)		
Baseline	17.30 ± 7.45	19.79 ± 6.92
12 weeks	18.58 ± 6.82	20.34 ± 8.23
24 weeks	15.31 ± 7.26	16.72 ± 7.95
48 weeks	18.36 ± 6.21	20.51 ± 7.99

Values are mean ± standard deviation. ATV, atorvastatin; FBG-CV, the coefficient of variation of fasting blood glucose; FPG, fasting plasma glucose; HbA1c, glycosylated hemoglobin A1c; PTV, pitavastatin group; SDBG, standard deviation of blood glucose. *$P < 0.05$ compared with the baseline levels.

Table 3 | Blood chemistry parameters during the study in the two experimental groups

	Baseline	48 weeks	*P*-value
PTV			
Cr (μmol/L)	83.33 ± 22.48	93.39 ± 39.29	0.131
UA (μmol/L)	392 (282–493)	409 (299–500)	0.672
AST (mmol/L)	20 (16–28)	21 (14–30)	0.697
ALT (mmol/L)	25 (20–32)	25 (19–31)	0.680
ATV			
Cr (μmol/L)	76.28 ± 25.12	85.65 ± 32.75	0.191
UA (μmol/L)	322 (269–420)	385 (317–431)	0.360
AST (mmol/L)	20 (15–29)	25 (15–33)	0.437
ALT (mmol/L)	21 (16–29)	23 (17–30)	0.481

Values are mean ± standard deviation or median (lower quartile to upper quartile). ALT, alanine transaminase; AST, aspartate transaminase; ATV, atorvastatin group; Cr, serum creatinine; PTV, pitavastatin group; UA, uric acid.

significant regression of FTPA in type 2 diabetes mellitus patients with elevated LDL-C levels. When the effects on glucose and lipid metabolism were compared, similar decreases of LDL-C, TG and TC levels were observed in both groups, except for a more significant increase in HDL-C levels in the pitavastatin group. The HbA1c, FPG, SDBG and FBG-CV (%) levels were also similar in the two groups.

LEAD is one of the several manifestations of diffuse atherosclerosis, which implies a high cardiovascular risk[16]. In the population of people with diabetes, the prevalence of LEAD is notably higher than that in the population of people without diabetes[5]. Furthermore, type 2 diabetes mellitus patients with LEAD have increased risk of cardiovascular and cerebrovascular events, or lower extremity amputation[20,21]. Although with high prevalence, the early stage of LEAD has always been unnoticed because of the absence of symptoms. Therefore, timely scanning and prompt treatment of LEAD is essential for all type 2 diabetes mellitus patients.

Statin has been strongly recommended for patients with cardiovascular and peripheral vascular disease, including LEAD[22]. Currently, five available statins possess a wide range of efficacy for the reduction of LDL-C, possible minor differences in affecting HDL-C levels and wide variability in other non-lipid modification effects[23]. It has been shown that treatment with atorvastatin is associated with a reduction in stiffness of the lower limb arteries and lowering the risk of lower extremity amputation in type 2 diabetes mellitus patients[17,24]. However, data of the optimal statin for diabetes patients with LEAD are still limited. In the present study, we, for the first time, compared the efficacy of pitavastatin and atorvastatin in early-stage LEAD. We found that either pitavastatin (2 mg/day) or atorvastatin (10 mg/day) was effective in preventing the progression of LEAD, indicating that the current dose of pitavastatin or atorvastatin was suitable in the management of early-stage LEAD in Chinese diabetes patients.

Hyperlipidemia is one of the main risk factors of atherosclerosis. The benefits of statin treatment on atherosclerosis are based on their efficacy in hyperlipidemia[25–27]. In the present study, we found that both pitavastatin and atorvastatin markedly reduced TC, LDL-C and TG levels after 12 weeks of treatment, followed by a further moderate reduction. The reduction rates of TC were 17.6% in the pitavastatin group and 32.8% in the atorvastatin group, respectively. Even though pitavastatin and atorvastatin showed similar effects on the TC and TG reduction, we noticed a significant 12.9% increase of HDL-C level in the pitavastatin group, but no significant changes were observed in the atorvastatin group after 48 weeks of treatment.

HDL-C is a lipoprotein that plays key roles in the reverse transportation of excess cholesterol into the liver for further degradation[28]. Previous studies found that HDL-C levels were inversely correlated with the risk for cardiovascular events, even in patients with low LDL-C levels under statin treatment[29,30]. Furthermore, the statins' function for regression of coronary artery plaque volume was associated with HDL-C elevation, irrespective of LDL-C lowering effects[31]. Although we did not find a significant relationship between the elevation of HDL-C levels and the regression of FTPA (data was not shown), we assumed that a superior effect of pitavastatin on FTPA would be found with the expansion of the sample size and extension of the study period.

Statins might increase HDL-C levels through various mechanisms, which is independent of their abilities in decreasing LDL-C levels[32,33]. The degree of the increase of HDL-C levels varies among statins, and it has been under debate in recent years. The diversity might be correlated with different treatment periods and different statin doses used. For example, 52 weeks of treatment with pitavastatin (2 mg/day) produced a significantly higher HDL-C level compared with atorvastatin (10 mg/day)[9]. However, in another study, pitavastatin (1 mg/day) failed to increase HDL-C levels, whereas atorvastatin (10 mg/day) significantly increased HDL-C levels after 12-week treatment[34]. At present, it is recognized that clinically used doses of pitavastatin could effectively increase HDL-C levels with ranges from 8.2% to 10%[9,18,35]. Our research presented similar results after 48 weeks of treatment.

Steps for HDL-C formation in the liver include apolipiprotein A-I catabolism, ABCA1 transportation of cholesterols, and LCAT esterification *etc*[32,36]. Statins may affect HDL-C metabolism through the activation of these genes' expression[35,36]. Outside the liver, statins might influence cholesterol efflux from peripheral cells and transport of cholesterol esters[32,37,38]. However, the exact mechanisms of different statins in influencing HDL-C synthesis are controversial, which needs to be further studied.

In recent years, increasing evidence has shown that the use of statins was associated with a higher risk of new-onset diabetes both in the European and Asian populations[25,39]. Some studies have reported that pitavastatin has less influence on glucose metabolism[40], giving the expectation that pitavastatin might be a priority in the management of dyslipidemia in diabetes patients. In our current study, we did not find significant

differences between the two groups in either FPG, FBG-CV or HbA1c at the beginning as well as at the end of the study, suggesting that influence of statins on glucose control in diabetes patients was limited with the co-use of glucose-lowering medicine.

There were some limitations to the present study. First, the study was carried out with a small sample size. Therefore, additional larger clinical studies are required to confirm the statins' beneficial effects in treating early-stage LEAD. Second, the study population was mainly elderly or aged type 2 diabetes mellitus patients. It remains unclear if a similar benefit of statins is attributable to young patients. However, to some extent, the present study is useful, as the target population is representative of patients seen in actual clinical practice.

In conclusion, treatment with both pitavastatin and atorvastatin were shown to be effective for FTPA regression in type 2 diabetes mellitus patients with elevated LDL-C levels. Pitavastatin also proved to significantly increase HDL-C levels compared with atorvastatin. In summary, we proposed that pitavastatin might be superior in the control of dyslipidemia among diabetes patients with LEAD.

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DISCLOSURE

The authors declare no conflict of interest.

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