

The lipid Status and linear relationship between TC and TG in Glycogen Storage Disease Ia

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Research

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Abstract

Background

Glycogen storage disease type I(GSDI) is a glucose metabolic disorder caused by glucose-6-phosphatase deficiency. GSDIa patients are characterized by hypoglycemia, hepatomegaly, hyperlipidemia and lactic acidemia. This study aims to review the lipid status in patients with GSDIa, explores the lipid treatment targets and preferable lipid-lowering drugs.

Methods

The clinical data of GSDIa patients characteristics were collected. Diet control, raw cornstarch were used to maintain normal blood glucose and lipid level. Some patients were given lipid-lowering drugs. We compared the lipid levels before and after each treatment.

Results

A total of 163 GSDIa patients were enrolled in this study and 773 times of lipid levels were detected. TG was normal in only 13 times of detection from 10 patients(2%). There were 26 patients who took atorvastatin or fibrates (fenofibrate or gemfibrozil) regularly for more than one year. The lipid levels could be improved after lipid-lowering drugs treatment. The therapeutic effect of atorvastatin was better than fibrates. The total cholesterol(TC) was positively correlated with total triglycerides(TG) after treatment. A regression equation was established for TC and TG, $TG = -2.86 + 1.63TC$. The complication of hyperlipidemia was mainly caused by TC. As long as TC maintained normal, TG did not have to be maintained normal and a certain degree of hypertriglyceridemia can be accepted. The lower bound of China Children's TC abnormal level (5.18 mmol/L) was substituted into the established regression equation to obtain $TG = 5.58$ mmol/L. We set a target that when the TG level was lower than 5.58 mmol / L after treatment, TC could maintain normally. There was no need for further increasing the dosage of lipid-lowering drug.

Conclusion

Patients with GSDIa had significant abnormalities in blood lipid metabolism. We found that there was a linear correlation between TC and TG, which was $TG = -2.86 + 1.63*TC$. We made a point that as long as the TC remained normal, a certain degree of hypertriglyceridemia could be accepted. We set a target that when the TG level was lower than 5.58 mmol / L after treatment, TC could maintain normally. This study found that the therapeutic effect of atorvastatin was better than fibrates.

1. Background

Glycogen storage disease type 1 (GSDI, OMIM 232200) is a glucose metabolic disorder caused by glucose-6-phosphatase (G6Pase) deficiency. The incidence of GSDI is about 1/100 000[1], of which GSDIa accounts for 80%[2]. Due to the last step of glycogenolysis and gluconeogenesis are affected, GSDI patients present with

severe hypoglycemia. Besides, patients also present with hyperlipidemia, hyperuricemia, hyperlactacidemia, growth and development retardation[3]. The main therapeutic methods are diet control and raw cornstarch treatment. The raw cornstarch can maintain normal glucose production rate, thus avoids hypoglycemia and reduces secondary metabolic complications.

G6Pase is mainly located in the liver, composed of G6PC and G6PT[4]. G6PC catalyzes the decomposition of G6P into glucose and phosphate. The G6PC active site is located in the endoplasmic reticulum, G6P is transported into the endoplasmic reticulum by G6PT[5][6]. Mutations in G6PC cause GSDIa. Patients with GSDIb, who have mutations in G6PT, have manifestations with neutropenia and inflammatory bowel disease.

Untreated GSDIa patients usually show significantly lipid metabolism disorder, which include elevated triglyceride(TG) and total cholesterol(TC), decreased low density lipoprotein-cholesterol(LDL-C) and high density lipoprotein-cholesterol(HDL-C)[7]. Although hyperlipidemia in GSDIa patients is prevalent and severe, the studies of lipid status in GSDIa patients are extremely rare. Most studies were case reports, ignoring treatment status and genotyping. Currently, there's neither recommendation of lipid-lowering drugs nor definite treating target for GSDIa patients.

This study is currently the largest retrospective single-center study of lipid metabolism in GSDIa patients. In this study, we reviewed the status of lipid metabolism in GSDIa patients, aimed to reviewed the lipid status in patients with GSDIa, explored the lipid treatment targets and preferable lipid-lowering drugs.

2. Methods

2.1 Patients

From July 1985 to April 2017, 163 GSDIa patients referred to the Pediatric Department of Peking Union Medical College Hospital. Most patients were followed-up once a year. All of the patients presented with development retardation, hepatomegaly, fasting hypoglycemia, hyperlipidemia, lactic acidemia and elevated liver enzymes. The patients were diagnosis by gene mutation was found in the *G6PC* gene. Diet control, raw cornstarch were used to maintain normal blood glucose and lipid level. Some patients were given lipid-lowering drugs. General guidelines for dosing raw cornstarch include 1.6 g of raw cornstarch per kilogram of body weight (ideal body weight) every 3–4 hours for young children, and 1.7–2.5 g raw cornstarch/kg every 4–5 hours (sometimes 6 hours) for older children, adolescents, and adults. Some patients with severe hyperlipidemia were treated with lipid-lowering drugs. There were 26 patients took atorvastatin or fibrates (fenofibrate or gemfibrozil) for more than one year regularly were included in the study. They were divided into atorvastatin group and fibrates group. According to the diagnostic criteria of hyperlipidemia in The NCEP Children's Experts Group in the United States[8], All data were divided into five groups by age: 0–4, 5–9, 10–14, 15–19, and greater than 20 years old.

The participant's individual mean for the age period was used as the outcome. Since the change of lipid value of patients is relatively fast after treatment, the lipid value is basically stable after starting treatment for several months. Therefore, the same patient is counted as one case in each age group, which can be considered as reflecting the level of the last one or two years. We focused on the control level of each age group, so it can be considered that the data of the different age groups for one patient are independent of each other.

2.2 General Examination

Standardized protocols were used by trained examiners. All the participants were instructed to fast for 5 hours before venipuncture, and compliance was determined by interview on the morning of the examination. Laboratory evaluations including TC, TG, HDL-C and LDL-C were tested for patients.

2.3 Diagnostic criteria of hyperlipidemia

Lipid levels were related to age and gender. The US NCEP Children's Expert Group report had a high degree of recognition. The blood lipid levels were grouped by age in this article. The normal range of TC, TG, HDL-C, and LDL-C in our study was based on this standard[8]. For patients elder than 18 years old, the diagnostic criteria referred to 2016 Chinese guideline for the management of dyslipidemia in adults[9]. The normal range of TG, TC were listed in **Table 1**, the normal range of LDL-C, HDL-C were listed in **Table 2**.

In this article, we wanted to set a cut-off point for severe hypertriglyceridemia. Acute pancreatitis was the main complication of hyperlipidemia. In the GSD medical guidelines published by the American College of Medical Sciences in 2014, it was suggested that pancreatitis may occur in GSD patients with TG higher than 11mmol/L. Therefore TG \geq 11mmol/L was regarded as a cut-off point for severe hypertriglyceridemia[7].

2.4 Statistical methods

All data were divided into six groups by age: 0-1, 2-4, 5-9, 10-14, 15-19 and greater than 20 years. The data were analyzed with SPSS 24.0.0.0. Means and standard deviations were used to describe normally distributed quantitative variables. Medians and quartile ranges were used to describe nonnormally distributed quantitative variables. To avoid bias, each subject was weighted equally within every age group, the lipid levels of each patient in each age group were average numbers of multiple follow-up data.

Since the difference values were non-normally distributed, the lipids' levels before and after treatment were analyzed by Wilcoxon-ranktest. We analyzed the correlations between TC and TG by Pearson correlations. The liner regression relationship equation of TC with TG was computed using SPSS program. A *P* value <0.05 was considered to be significant in all instances.

3. Results

3.1 General Information

There were 163 GSDIa patients from 160 families were enrolled in this study, including 98 males and 65 females, with a male to female ratio of 1:0.66. All of the patients were from China. The age of first visit to hospital ranged from 4 months to 38 years old (mean 8.1 ± 7.2 years old). The followed up time was 0-29 years (mean 5.7 ± 5.4 years). The age of the last follow-up was 4 month to 43 years old (mean 13.8 ± 8.2 years old). All patients were treated with raw cornstarch. A total of 773 times of lipid levels were detected, among which 624 times were detected after intervention. TG was normal in only 13 times of detection from 10 patients(2%). There were 26 patients who took atorvastatin or fibrates (fenofibrate or gemfibrozil) regularly for more than one year. A total of 109 times of lipid levels were detected. There were 11 patients took statins and 11 patients took

fibrates. Four patients failed to respond to fibrates therapy and were switched to statins after six months of withdrawal. They were divided into both atorvastatin group and fibrates group.

3.2 The lipid level of GSDIa patients before intervention

The mean level of TC among 133 patients was 5.78 ± 3.07 mmol/L (Ranging from 2.78~18.77 mmol/L). The normal ratio was 41.7%.

The mean level of TG among 142 patients was 8.32 ± 8.51 mmol/L (Ranging from 1.81~73.96 mmol/L), The normal ratio was 1.4%.

The mean level of HDL-C among 92 patients was 0.92 ± 0.59 mmol/L (Ranging from 0.29~5.39 mmol/L), The normal ratio was 42.4%.

The mean level of LDL-C among 92 patients was 2.42 ± 1.36 mmol/L (Ranging from 0.26~6.26 mmol/L), The normal ratio was 88.9%.

3.3 The lipid level of GSDIa patients after raw cornstarch treatment

The TC level of 289 patients after raw cornstarch treatment was 5.84 ± 2.18 mmol/L (ranging from 1.71~22.79 mmol/L), The normal ratio was 41.9%.

The TG level of 293 patients after raw cornstarch treatment was 5.83 ± 5.63 mmol/L (ranging from 0.57~34.32 mmol/L), The normal ratio was 2.0%.

The HDL-C level of 253 patients after raw cornstarch treatment was 1.03 ± 0.30 mmol/L (ranging from 0.24~2.28 mmol/L). The normal ratio was 57.7%.

The LDL-C level of 253 patients after raw cornstarch treatment was 3.19 ± 1.14 mmol/L (ranging from 0.80~7.32 mmol/L). The normal ratio was 68%.

3.4 The lipid level of GSDIa patient after lipid-lowering drugs treatment

A total of 15 patients were treated with fibrates, the treatment time ranged from 1 to 3 years. The TC level of 15 patients after fibrates treatment was 6.27 ± 2.64 mmol/L, while the TG level was 6.33 ± 6.04 mmol/L. The HDL-C level of 8 patients after fibrates treatment was 0.87 ± 0.55 mmol/L, while the LDL-C level was 3.54 ± 2.48 mmol/L.

A total of 15 patients treated with atorvastatin, the treatment time ranged from 1 to 6 years. The TC level of 15 patients after atorvastatin treatment was 4.87 ± 1.41 mmol/L while the TG level was 5.05 ± 5.50 mmol/L. The HDL-C level of 9 patients after atorvastatin treatment was 1.01 ± 0.27 mmol/L while the LDL-C level was 2.69 ± 1.03 mmol/L.

3.5 The comparison of lipid levels between different treatment

3.5.1 The comparison of lipid levels before and after raw cornstarch treatment

The lipid levels of patients before and after raw cornstarch treatment were shown in Table 3-1. After treatment with raw cornstarch, the TG levels were significantly decreased by 30.50% ($P=0.00$), while the TC levels were not significantly decreased (Figure 1).

3.5.2 The comparison of lipid levels before and after lipid-lowering drugs treatment

The blood lipid levels of patients before and after fibrates treatment were shown in Table 3-2. TC and TG levels were slightly decreased after fibrates treatment but the difference was not significant. After treatment with fibrates, the TC level of 33.3% (5/15) patients and the TG level of 6.7% (1/15) patients decreased to normal (Figure 2).

The blood lipid levels of patients before and after atorvastatin treatment were shown in Table 3-3. After treatment with atorvastatin, TC, TG and LDL-C were significantly improved ($P<0.05$). The TC level of 73.3% (11/15) patients reach normal, but none of them reach normal TG level (Figure 3).

3.6 The linear correlation analysis between TC and TG

In our study, the TC and TG data were collected in patients with dietary control combined with raw cornstarch treatment. Pearson test was performed on TC and TG levels. The Pearson test results were shown in Table 3-4. The correlation coefficient of TC and TG was 0.514, $P=0.00$. It could be proposed that TG was positively correlated with TC. TC and TG were related with medium intensity.

3.7 The linear regression equation between TC and TG and blood lipid control target

It was reported in previous studies that there was a correlation between TC and TG [10]. The multiple linear regression equation for TC and TG had been established in some diseases [11].

The TC and TG data were collected in patients with dietary control combined with raw cornstarch treatment, and a total of 452 data were collected. A regression equation was established for TC and TG, and the regression standard error S_Y was recorded. The 95% predicted interval of TC level was represented by $Y_{0.05/2, (452-2)} S_Y$. Y represented the TG level and X represented the TC level in mmol/L. The regression equation was $Y = -2.86 + 1.63X$. The F regression test was performed on the overall regression coefficient, $P < 0.01$; the decision coefficient $R^2 = 0.264$; $S_Y = 4.48$.

In the 2014 GSDI guidelines published by the Genetics Society of the American Medical College, it was recommended to maintain the normal range of blood lipids to reduce the risk of arteriosclerotic cardiovascular disease (ASCVD) and pancreatitis [7]. However, previous studies had shown that hyperlipidemia could be improved but not cured in GSDI patients [12]. The incidence rate of hypertriglyceridemia was higher than the hypercholesterolemia obviously. After treatment with lipid-lowering drugs, TC could decrease to normal in most patients but TG was hard to decrease to normal. Because the complication of hyperlipidemia was mainly caused by TC, so a certain degree of hypertriglyceridemia could be allowed. Thereby, as long as the TC remains normal, we could set a TG target to allow a certain degree of hypertriglyceridemia.

The lower bound of China Children's TC abnormal level (5.18 mmol/L [13]) was substituted into the established regression equation, it could obtain that TG was 5.58 mmol/L, and the prediction interval at 95% confidence

level was -3.28×14.37 mmol/L. (Table 3-5).

3.8 Gene mutation test results

At least one mutation was found in the *G6PC* gene in all 163 patients. The gene data of 6 patients were incomplete. In the 157 patients with complete genetic analysis recorded, 143 patients detected two allelic mutations, 14 patients detected one single allelic mutation, and 299 alleles were detected totally. A total of 42 mutation types were detected, including 28 missense mutations, 9 deletion mutations, 4 nonsense mutations, and 1 splicing mutation; p.Leu216Leu (58.2%) and p.Arg83His (10%) were the most common mutations. A total of 58 genotypes are detected, the most common genotypes are p.Leu216Leu homozygous mutation (30.6%) and p.Leu216Leu/p.Arg83His (11.5%).

4. Discussion

GSDIa is a hereditary disease caused by G6Pase catalytic subunit defected. The typical metabolic disorder includes hypoglycemia, hyperlipemia, hyperuricemia and hyperlactacidemia. The blood lipid characteristics of GSDIa are high TC, high TG, high LDL-C, low HDL-C. Hyperlipemia is an important risk factor of cardiovascular and cerebrovascular diseases. With the progress of diagnosis and treatment of GSDIa, the life span of children is significantly extended. The long-term complication caused by hyperlipemia should be paid more attention.

The mechanism of hyperlipidemia in GSDIa patients is mainly due to increased acetyl-CoA and VLDL[14]. In the previous study, there was a lack of large epidemiological data on blood lipid levels in patients with GSDIa. There was no large-scale data about the serum lipid level after using lipid-lowering drugs for GSDIa patients. Currently, the largest report was reported by ESGSD I, 41.3% of 223GSDIa patients had high TC level and 12.1% had severe high TC level, while 18.6% had high TG level and 72.7% had severe high TG level[2].

4.1 The lipid level of GSDIa patient before intervention

The TC level of the normal newborns was 1.7 mmol/L, while the TG level was 0.4 mmol/L. They both rised gradually after birth and maintain about 4.3 mmol/L after 2 years old[15]. The normal value of blood lipid levels varied with age. The normal range of TC, TG, HDL-C, and LDL-C in this study was based on The US NCEP Children's Expert Group report.

The mean level of TC was 5.78 ± 3.07 mmol/L of 133 GSDIa patients in our research, 58.3% of the patients had hypercholesteremia. The mean level of TG was 8.32 ± 8.51 mmol/L of 142 GSDIa patients in our research, 98.6% of the patients had hypertriglyceridemia.

The incidence of hyperlipidemia is high in GSDIa patients. The previous study included 62 cases of GSDI patients (53 GSDIa and 9 GSDIb) revealed that the mean level of TC was 6.18 ± 2.47 mmol/L before treatment, while the mean level of TG was 11.17 ± 9.85 mmol/L[16]. Other study included 11 cases of GSDIa patients revealed the mean level of TC was 4.31–6.89 mmol/L, while the TG level was 16.26–69.09 mmol/L. But, the incidence of hyperlipemia was not reported in these research[17].

Thus, the level of hyperlipemia before treatment in our research was similar to the previous research. The incidence of hypertriglyceridemia was higher than the hypercholesteremia obviously.

4.2. The lipid level of GSDIa patient after raw cornstarch treatment

The TC level of 289 patients in our research after raw cornstarch treatment was 5.84 ± 2.18 mmol/L, 58.1% had hypercholesterolemia. The TG level of 293 patients after raw cornstarch treatment was 5.83 ± 5.63 mmol/L, 98% had hypertriglyceridemia. It showed that the incidence of hypercholesterolemia and hypertriglyceridemia were still high in GSDIa patients after raw cornstarch treatment.

In the previous ESGSDI study, 41.3% of 233 cases of GSDIa patients had hypercholesterolemia while 72.7% had hypertriglyceridemia[2]. Other two researches included 37 and 41 cases of GSDIa patients, the incidence of hypercholesterolemia ranged from 76 to 81.6%, the incidence of hypertriglyceridemia ranged from 85.3 to 100%[12, 18]. Similarly, the incidence of hypertriglyceridemia was higher than hypercholesterolemia in our research.

In the previous study, the TC and TG could be decreased significant after raw cornstarch treatment in 62 cases of GSDI patients(including 53 cases of GSDIa patients)[16]. The TC decreased from 6.18 ± 2.47 mmol/L to 5.61 ± 1.84 mmol/L after treatment, $P = 0.02$, and TG decreased from 11.17 ± 9.85 mmol/L to 6.81 ± 5.97 mmol/L, $P = 0.01$. Another study included 19 GSDI patients were treated with nocturnal gastric tube infusion since 1 years old, the lipid level decreased significantly but not completely normal [18] [19].

In our study, after treatment with raw cornstarch, the TG level was significantly decreased by $30 \pm 50\%$ ($P < 0.05$), while the TC level was not significantly decreased. Our research found that TG could be decreased significant after raw cornstarch treatment, which was similar to the previous research.

4.3 The comparison of lipid levels after lipid-lowering drugs treatment

In the previous study, there was no large-scale data focus on the lipid levels about the lipid-lowering drugs for GSDIa patients. The lipid-lowering drugs used in this study were fibrates (fenofibrate and gemfibrozil) and atorvastatin. Fibrates could improve the expression of LPL, thus increased the hydrolyzation of TG. They could also elevate the secretion of ApoA-1 and HDL-C. Previous studies had shown the secretion of VLDL was normal but the decomposition rate was decreased in 2 GSDIa patients, which might reflect the LPL activity was decreased. In these two patients, TG was decrease by fibrates for 50%[20].

The rate-limiting enzyme of cholesterol synthesizing was HMG-CoA reductase. Atorvastatin could inhibited HMG-CoA reductase and decreased LDL-C in the liver cells, thus the number of LDL receptors on the liver cytomembrane was increased and the elimination of VLDL and LDL was improved. Previous studies showed that the dyslipidemia of GSDIa patients characterized by increased VLDL levels and decreased LDLR metabolism. Furthermore, statins had been shown to have strong effects on lipid-lowering treatment in multiple studies, mainly by lowering VLDL remnants through the uptake of the LDL receptors. Thus, the lipid levels could be substantially decreased by statins [21].

This study analysed the lipid metabolism of 30 GSDIa patients. The TC and TG were improved after fibrates treatment, but it had no significant difference. While the TC and TG could be improved significantly after

atorvastatin treatment. The TC level of 73.3%(11/15) patients could decrease to normal. It was suggested that lipid metabolism could be improved after lipid-lowering drugs treatment. The therapeutic effect of atorvastatin was better than fibrates. The TC could achieve normal in most patients after diet control, raw cornstarch treatment and atorvastatin treatment.

4.4 The linear regression equation between TC and TG

The Pearson correlation test suggested that there was a positive correlation between TC and TG. TC and TG were related with medium intensity. A regression equation was established for TC and TG, $TG = -2.86 + 1.63TC$. The F regression test was performed on the overall regression coefficient, $P < 0.01$. The regression coefficient was statistically significant. The decision coefficient $R^2 = 0.264$.

The incidence of hyperlipidemia is high, but the incidence of its complication pancreatitis is low. The TC was considered a key factor leading to ASCVD. It is important to decrease the level of TC [22]. Therefore, the TC level was the mainly target of lipid control for GSD patients. As long as TC was maintained normally, TG did not have to be maintained normal and a certain degree of hypertriglyceridemia could be accepted. There was no need for further increasing the dosage of lipid-lowering drug. We wanted to set a target to allow a certain degree of hypertriglyceridemia. The lower bound of China Children's TC abnormal level (5.18 mmol/L[13]) was substituted into the established regression equation to obtain $TG = 5.58$ mmol/L. We set a target that when the TG level was lower than 5.58 mmol / L after treatment, TC could maintain normally.

Many studies had showed that the lipid levels were unable to control normal in GSDIa patients. As long as the TC maintain normal, the TG level derived from this regression equation could be used as a reference for clinical treatment. Moreover, this study was a retrospective study. So, a long time of follow-ups were needed to observe the difference of atherosclerosis incidence between patients with $TG > 5.58$ mmol/L and ≤ 5.58 mmol/L. More long-term treatment researches were needed to confirm the feasibility of this control target.

The blood lipid levels in the NCEP standard were grouped by age. If we substituted the normal values of TC of different ages into this regression equation, we could get the TG value of each allowable hypertriglyceridemia for different ages period.

5. Conclusion

Patients with GSDIa had significant abnormalities in lipid metabolism. We found that there was a linear correlation between TC and TG, which was $TG = -2.86 + 1.63 * TC$. We made a point that as long as the TC remains normal, a certain degree of hypertriglyceridemia could be accepted. We suggested that when the TG level was lower than 5.58mmol / L after treatment, TC could maintain normally. This study found that lipid metabolism could be improved after lipid-lowering drugs treatment. The therapeutic effect of atorvastatin was better than fibrates.

List Of Abbreviations

Glycogen storage disease type Ia(GSDIa)

Total cholesterol(TC)

Total triglycerides(TG)

Low density lipoprotein-cholesterol(LDL-C)

High density lipoprotein-cholesterol(HDL-C)

Glucose-6-phosphatase (G6Pase)

National Cholesterol Education Program (NCEP)

Arteriosclerotic cardiovascular disease(ASCVD)

Declarations

- **Ethics approval and consent to participate**

Because of the retrospective nature of the study, the ethics approval and consent to participate is not needed in this study. We will do our best to protect patients' privacy.

- **Consent for publication**

Not applicable

- **Competing interests**

The authors disclose no conflicts.

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- **Authors' contributions**

Zhenjie Zhang (Formal analysis; Investigation; Methodology; Writing– original draft)

Yuheng Yuan (Data curation; Formal analysis)

Mingsheng Ma (Conceptualization; Investigation; Resources)

Yuehui Hong (Data curation; Formal analysis; Investigation)

Zhixing Sun (Software; Supervision; Validation)

Mengqi Zhang (Investigation; Methodology; Project administration)

Zhengqing Qiu (Funding acquisition; Writing – review & editing)

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- **Availability of data and materials**

All data generated or analysed during this study are included in this published article

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Tables

		TC[mg/dl(mmol/L)]					TG[mg/dl(mmol/L)]				
ear-old)	Gender	0-4	5-9	10-14	15-19	>20	0-4	5-9	10-14	15-19	>20
priate	M	<176(4.56)	<180(4.66)	<178(4.61)	<170(4.40)	<200	<69(0.78)	<67(0.76)	<80(0.90)	<94(1.06)	<150
	F	<177(4.58)	<184(4.77)	<179(4.64)	<177(4.58)	(5.20)	<79(0.89)	<73(0.82)	<93(1.05)	<90(1.02)	(1.70)
il	highM	177□209	181□209	179□208	171□203	200□240	69□102	67□104	80□129	94□152	150□250
	F	178□206	185□211	180□207	178□209		79□115	73□108	93□135	90□136	
lipidemia	M	>209(5.41)	>209(5.41)	>208(5.39)	>203(5.26)	≥240	>102(1.15)	>104(1.18)	>129(1.46)	>152(1.72)	≥200
	F	>206(5.34)	>211(5.46)	>207(5.36)	>209(5.41)	(6.20)	>115(1.30)	>108(1.22)	>135(1.53)	>136(1.54)	(2.30)

Table 1 The classification standard of TG and TC in patients of all ages in this study

The normal range of TC and TG in children are reference The NCEP Children's Experts Group in the United States

The normal range of TC and TG in patients aged 18 or over are reference 2016 Chinese guideline for the management of dyslipidemia in adults

Age(year-old)	Gender	LDL-C[mg/dl(mmol/L)]				HDL-C[mg/dl(mmol/L)]			
		5-9	10-14	15-19	>20	5-9	10-14	15-19	>20
Inappropriate level	M	<106(2.75)	<112(2.90)	<112(2.90)	<130(3.40)	>50(1.30)	>47(1.22)	>40(1.04)	-
	F	<118(3.06)	<113(2.93)	<114(2.95)		>48(1.24)	>46(1.19)	>44(1.14)	
Critical high level	M	106~133	112~136	112~134	130~160	39~50	38~47	31~40	-
	F	118~144	113~140	114~141		37~48	38~46	36~44	
Hyperlipidemia	M	>133(3.44)	>136(3.52)	>134(3.47)	≥160(4.10)	<39(1.01)	<38(0.98)	<31(0.80)	<40(1.0)
	F	>144(3.73)	>140(3.63)	>141(3.65)		<37(0.96)	<38(0.98)	<36(0.93)	

Table 2 The classification standard of LDL-C and HDL-C in patients of all ages in this study

The normal range of HDL-C/ LDL-C in children are reference The NCEP Children's Experts Group in the United States

The normal range of HDL-C/ LDL-C in patients aged 18 or over are reference 2016 Chinese guideline for the management of dyslipidemia in adults

Index	Number of patients	before treatment	after treatment	Decrease ratio [before treatment-after treatment]	P value
TC(mmol/L)	97	5.92 2.98	5.82 1.97	0 30%	0.39
TG(mmol/L)	101	8.37 7.23	5.39 5.29	30 50%	0.00
HDL-C(mmol/L)	65	0.96 0.63	1.10 0.34	-6	0.32
LDL-C(mmol/L)	64	2.40 1.36	2.96 1.38	-21 54%	0.00

Table 3-1 The comparison of blood lipids levels before and after raw cornstarch treatment [M±Q] The mean values of blood lipids and lipoproteins before and after raw cornstarch treatment were non-normal distribution, and the rank sum test was performed.

Index	Number of patients	raw cornstarch	fibrates	Decrease ratio [raw cornstarch -drug]	P value
TC(mmol/L)	15	6.66 3.65	6.27 2.64	-6 48%	0.36
TG(mmol/L)	15	7.96 6.60	6.33 6.04	21 101%	0.41
HDL-C(mmol/L)	8	0.95 0.23	0.87 0.55	10 17%	0.14
LDL-C(mmol/L)	8	2.39 1.66	3.54 2.48	-30 83%	0.07

Table 3-2 The comparison of blood lipids levels before and after fibrates treatment [M±Q] The mean values of blood lipids and lipoproteins before and after fibrates treatment were non-normal distribution, and the rank sum test was performed.

Index	Number of patients	raw cornstarch	atorvastatin	Decrease ratio [raw cornstarch -drug]	P value
TC(mmol/L)	15	6.96	4.87 1.41	35	0.00
TG(mmol/L)	15	8.80 5.37	5.05 5.50	33 48%	0.02
HDL-C(mmol/L)	9	0.96 0.27	1.01 0.27	3 26%	0.89
LDL-C(mmol/L)	9	3.42 1.42	2.69 1.03	40 32%	0.01

Table 3-3 The comparison of blood lipids levels before and after atorvastatin treatment [M±Q] The mean values of blood lipids and lipoproteins before and after atorvastatin treatment were non-normal distribution, and the rank sum test was performed.

	TG and TC
Number of detections	452
Pearson correlation	0.514
P value	0.00

Table 3-4 The linear correlation analysis between TG and TC

[Please see the supplementary files section to view Table 3-5.]

Figures

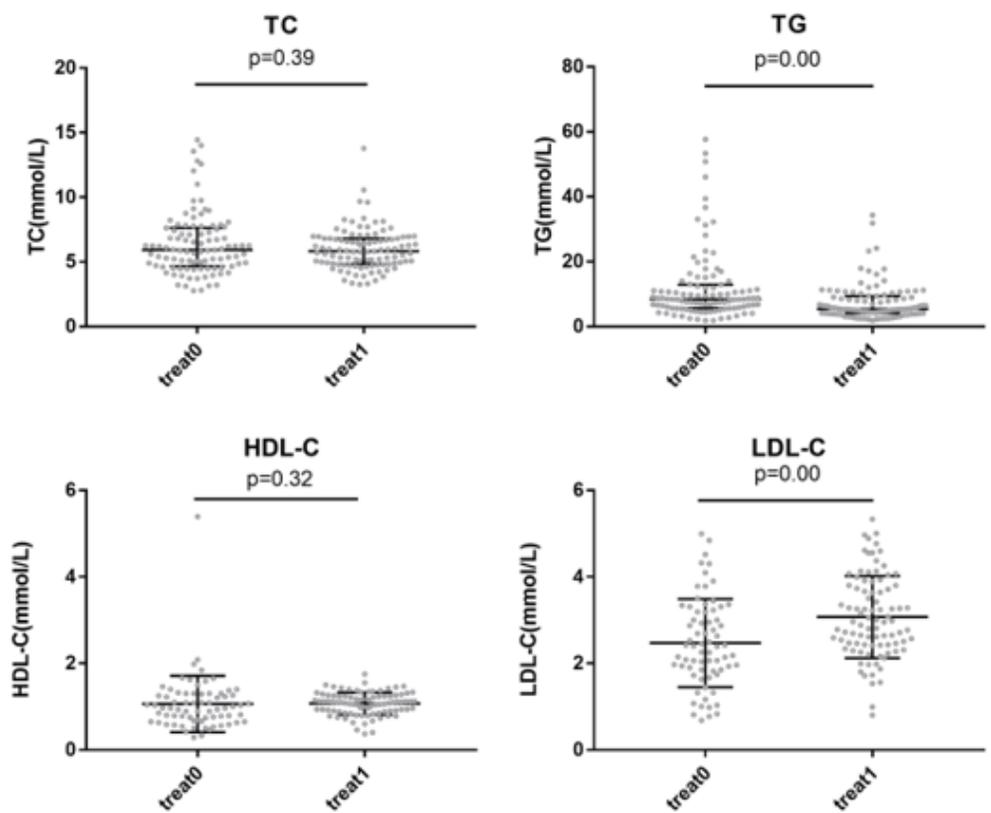


Figure 1

The distribution of lipids level in patients before and after raw starch treatment, The horizontal lines are shown as the median and the upper and lower quartiles.. Treat0, untreated; treat1, simple diet combined with raw cornstarch treatment patients

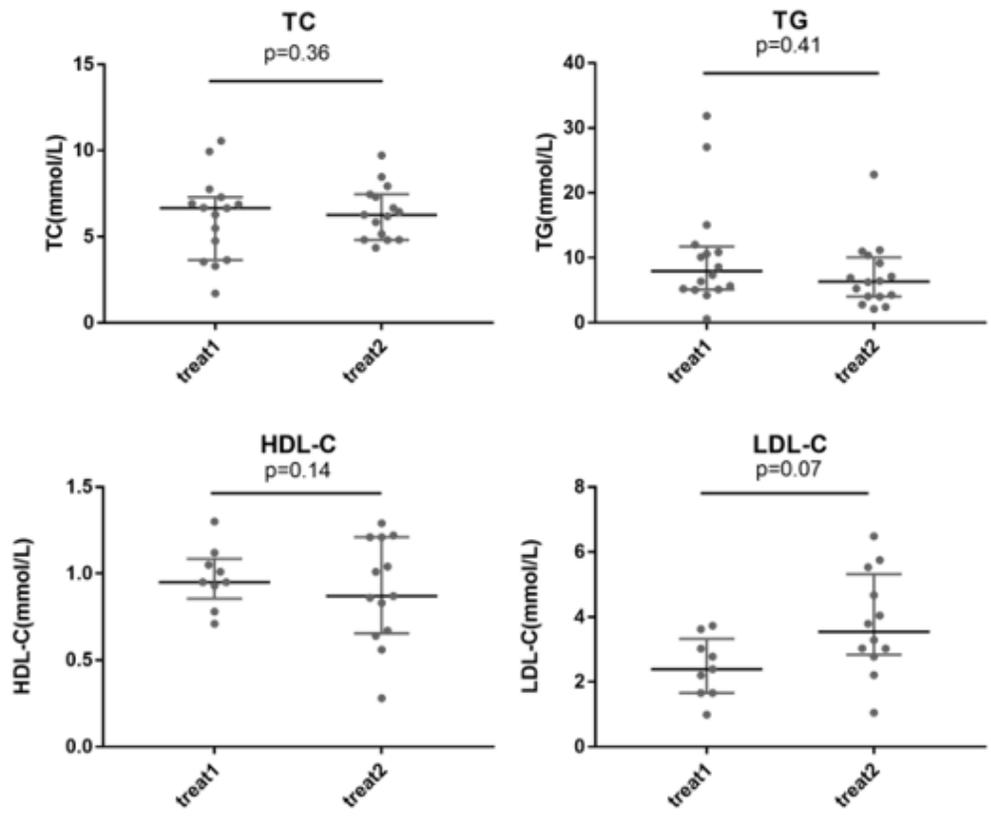


Figure 2

The distribution of lipids level in patients before and after fibrates treatment, The horizontal lines are shown as the median and the upper and lower quartiles. treat1, simple diet combined with raw cornstarch treatment patients. treat2—fibrates treatment.

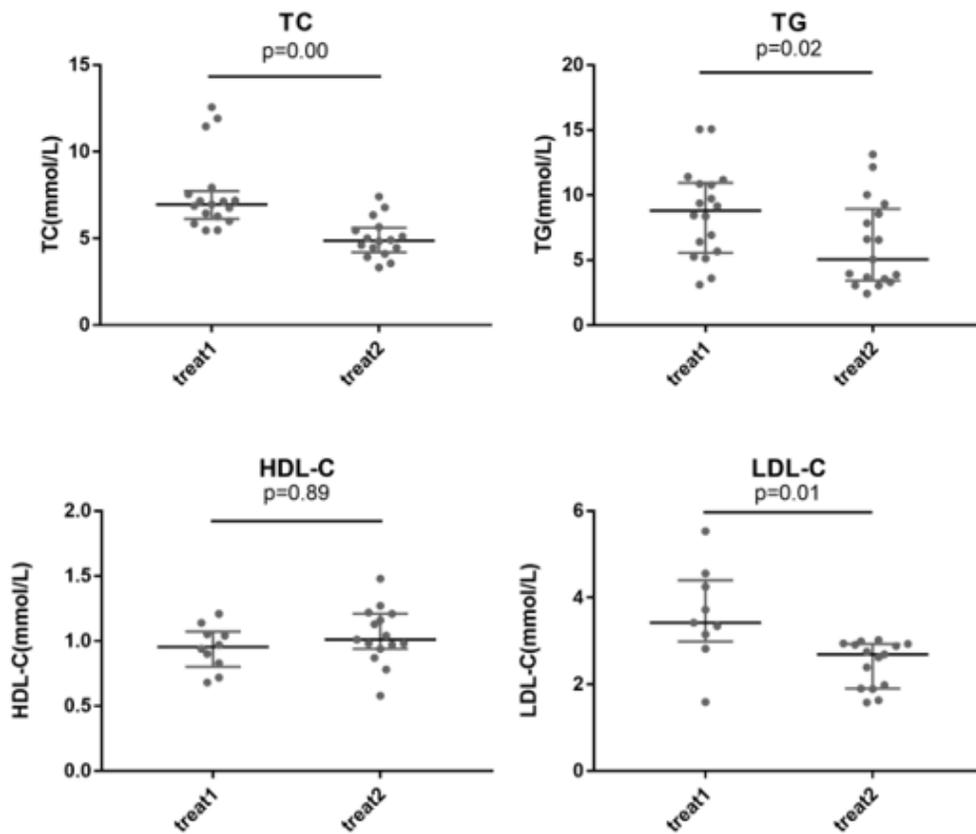


Figure 3

The distribution of lipids level in patients before and after atorvastatin treatment, The horizontal lines are shown as the median and the upper and lower quartiles. treat1, simple diet combined with raw cornstarch treatment patients. treat2atorvastatin treatment.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Table35.PNG](#)