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A pilot study of the effect of ezetimibe for postprandial hyperlipidemia

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Abstract

This study aimed to explore the feasible effect of ezetimibe for postprandial hyperlipidemia (PPHP).

Sixty participants were included in this study. Of these, 30 subjects in the intervention group received ezetimibe, while the remaining 30 participants in the control group did not undergo ezetimibe. All patients in intervention group were treated for a total of 2 weeks. Primary endpoints consisted of serum levels of total cholesterol (Total-C), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG). Secondary endpoints included apoB-48, remnant lipoprotein cholesterol (RLP-C), blood glucose, insulin, hemoglobin A1c (HbA1c), and monocyte chemotactic protein (MCP). All outcomes were measured before and after 2-week treatment.

After 2-week treatment, participants in the intervention group did not show better outcomes in primary endpoints of Total-C, LDL-C, HDL-C, and TG; and secondary endpoints of apoB-48, RLP-C, blood glucose, insulin, HbA1c, and MCP, compared with subjects in the control group.

The results of this study showed that ezetimibe may be not efficacious for participants with PPHP after 2-week treatment.

Abbreviations: HbA1c = hemoglobin A1c, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, MCP = monocyte chemotactic protein, PPHP = postprandial hyperlipidemia, RLP-C = remnant lipoprotein cholesterol, TG = triglyceride, Total-C = total cholesterol.

Keywords: effect, ezetimibe, postprandial hyperlipidemia

1. Introduction

Previous studies have found that postprandial hyperlipidemia (PPHP) account for the development of atherosclerosis and coronary heart disease.[1–3] It does not only impair reflex regulation of the cardiovascular system, but also injury this system.[4,5] However, a substantial number of cases with coronary heart disease are still not prevented, and these residual risk factors remain are tricky issues.[6–8] Of these risk factors, the levels of high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG) are regarded to be the most important and risk ones.[9–11]

Ezetimibe is a novel cholesterol-absorption inhibitor that selectively inhibits cholesterol absorption.[12–15] It is often used to treat dyslipidemia.[15–18] A recent clinical study reported that it can be applied to reduce LDL-C by about 18%, and cardiovascular events about 2%, compared with statin.[19] The other study has reported that it can help to improve fasting and PPHP.[20] It works by suppression of intestinal chylomicron production in patients with PPHP.[21] However, limit data regarding the effect of ezetimibe monotherapy on PPHP was available. Thus, the aim of this retrospective study was tried to further investigate the potential effect of ezetimibe monotherapy in participants with PPHP.

2. Methods

2.1. Design

This retrospective study was conducted between April 2016 and November 2017 at the People's Hospital of Yan'an. A total of 60 participants with PPHP were included. They were equally assigned to an intervention group and a control group. Subjects in the intervention group received ezetimibe for 2 weeks, while the participants in the control group did not receive ezetimibe during this period. The outcomes were measured before and after 2-week treatment.

This study was approved by the Medical Ethical Committee of the People's Hospital of Yan'an. Written informed consent was obtained from all included subjects in this study.

2.2. Participant eligibility

All included subjects aged above 18 years old. In addition, all of them did not receive lipid-lowering medications. Participants were excluded if they had cancers, concomitant inflammatory conditions, or major surgery 6 months before the study. Additionally, they were also excluded if they had psychological diseases and insufficient personal information. Furthermore, cases were excluded if they did not have sufficient information, such as outcome and characteristics data.

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2.3. Intervention

Participants in the intervention group underwent ezetimibe 10 mg/daily for a total of 2 weeks. The subjects in the control group did not administer ezetimibe during the treatment period. Participants continued their normal exercise and diet routines throughout the study period.

2.4. Outcome measurements

All the outcome data were measured by the laboratory tests. Primary endpoints included serum levels of total cholesterol (Total-C), TG, LDL-C, and HDL-C. Secondary endpoints consisted of apoB-48, remnant lipoprotein cholesterol (RLP-C), blood glucose, insulin, hemoglobin A1c (HbA1c), and monocyte chemotactic protein (MCP). All the outcomes were measured before and after 2-week treatment.

2.5. Statistical analysis

SPSS software (SPSS V.15.0, IBM Corp, Armonk, NY) was applied to analyze all the data. Continuous variables were analyzed by Mann–Whitney *U* test; categorical data were conducted by Fisher exact test. $P < .05$ was defined as the statistical significance.

3. Results

The characteristics of patient cases in both groups are showed in Table 1. There were no significant differences in all patient characteristics before the therapy between the intervention group and the control group.

Table 1

Patient characteristics.

Characteristics	Intervention group (n = 30)	Control group (n = 30)	*P*
Age, y	37.5 (8.7)	38.3 (9.2)	.73
Race (Asian China)	30 (100.0)	30 (100.0)	—
Sex			
Male	21 (43.9)	18 (53.7)	.42
Female	9 (56.1)	12 (46.3)	—
BMI, kg/m^2	26.9 (2.2)	27.2 (2.4)	.61
Medical history			
Myocardial infarction	0 (0)	1 (3.3)	.49
Angina	0 (0)	2 (6.7)	.29
Stroke	1 (3.3)	0 (0)	.49
Other	2 (6.7)	1 (3.3)	.56
Comorbidity			
Diabetes	2 (6.7)	3 (10.0)	.64
Hypertension	3 (10.)	5 (16.7)	.45
Thyroid disease	0 (0)	1 (3.3)	.49
Other	1 (3.3)	2 (6.7)	.56
Waist circumference, cm	87.5 (10.1)	88.2 (9.8)	.79
Blood pressure			
Systolic	125.6 (13.4)	127.2 (14.1)	.65
Diastolic	70.3 (8.9)	72.1 (9.3)	.44
Heart rate, beats/min	65.1 (9.1)	66.4 (8.8)	.57
Smoking history			
Yes	11 (36.7)	13 (43.3)	.60
No	19 (63.3)	17 (56.7)	—
Dyslipidemia	14 (46.7)	16 (53.3)	.61
Glucose intolerance	2 (6.7)	4 (13.3)	.40
Metabolic syndrome	1 (3.3)	2 (6.7)	.56

Data are present as mean ± standard deviation or number (%).
BMI = body mass index.

Table 2

Comparison of primary endpoints before the treatment.

Laboratory tests, mg/dL	Intervention group (n = 30)	Control group (n = 30)	*P*
Total-C	218.5 (14.3)	212.9 (13.7)	.12
HDL-C	62.2 (13.5)	59.6 (12.4)	.44
LDL-C	131.7 (18.3)	127.9 (19.7)	.43
TG	115.1 (36.6)	113.7 (38.2)	.88

Data are present as mean ± standard deviation.
HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, TG = triglyceride, Total-C = total cholesterol.

Before the treatment, there were no significant differences regarding the primary endpoints of Total-C, LDL-C, HDL-C, and TG (Table 2); and secondary endpoints of apoB-48, RLP-C, blood glucose, insulin, HbA1c, and MCP (Table 3) between 2 groups.

After 2-week treatment, the comparison of primary endpoints (Total-C, $P = .33$; LDL-C, $P = .67$; HDL-C, $P = .45$; and TG, $P = .29$; Table 4), and secondary endpoints (apoB-48, $P = .61$; RLP-C, $P = .44$; blood glucose, $P = .89$; insulin, $P = .30$; HbA1c, $P = .11$; and MCP, $P = .36$; Table 5) still did not differ significantly between 2 groups.

4. Discussion

A previous study has explored the efficacy of ezetimibe on PPHP and lipemia-induced endothelial dysfunction.[22] It included 20 participants with PPHP, and these subjects were divided into 2 groups equally.[22] Ten participants in the treatment group received ezetimibe, while the other 10 subjects in the control group did not receive ezetimibe. It found that PPHP is closely correlated with transient endothelial dysfunction.[22] Additionally, it found that ezetimibe enhances PPHP and its induced endothelial dysfunction.[22] However, the sample size of that study is too small, with 10 subjects each group only, to draw a confirm conclusion.[22] Thus, it cannot provide strong evidence for the clinic as well as for further study.

The results of a previous study demonstrate that ezetimibe may be utilized to reduce levels of fasting and postprandial TG, PLP-C, and apoB-48 after fat loading test.[22] The other studies explored the effect of ezetimibe and also found that it could reduce levels of apoB-48 in male participants with mixed hyperlipemia.[23] Furthermore, another study also showed that

Table 3

Comparison of secondary endpoints before the treatment.

Secondary endpoints	Intervention group (n = 30)	Control group (n = 30)	*P*
ApoB-48, μg/mL	4.5 (2.1)	4.4 (2.5)	.87
RLP-C, mg/dL	5.1 (1.8)	5.0 (2.0)	.84
Blood glucose, mg/dL	92.3 (10.4)	94.1 (11.3)	.52
Insulin, μIU/mL	6.6 (2.2)	6.3 (2.5)	.62
HbA1c, %	5.0 (0.2)	5.0 (0.3)	1.00
MCP-1, pg/mL	320.4 (42.8)	299.5 (50.7)	.08

Data are present as mean ± standard deviation.
Apo = apolipoprotein, HbA1c = hemoglobin A1c, MCP = monocyte chemotactic protein, RLP-C = remnant lipoprotein cholesterol.

Table 4

Comparison of primary endpoints after the treatment (change from before treatment).

Laboratory tests, mg/dL	Intervention group (n = 30)	Control group (n = 30)	Difference	P
Total-C	−16.5 (−24.7, −7.9)	−7.4 (−16.4, −3.2)	−9.1 (−13.5, −5.4)	.33
HDL-C	0.4 (0.1, 0.8)	0.8 (0.3, 1.2)	−0.3 (−0.6, −0.1)	.67
LDL-C	−15.3 (−21.6, −8.4)	−6.9 (−9.1, −3.0)	−8.3 (−10.2, −5.9)	.45
TG	−12.1 (−16.0, −8.1)	−2.5 (−4.7, −1.0)	−9.4 (−12.9, −6.6)	.29

Data are present as mean ± range.
HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, TG = triglyceride, Total-C = total cholesterol.

Table 5

Comparison of secondary endpoints after the treatment (change from before treatment).

Secondary endpoints	Intervention group (n = 30)	Control group (n = 30)	Difference	P
ApoB-48, μg/mL	−0.9 (−1.4, −0.5)	−0.3 (−1.4, −0.5)	−0.5 (−0.8, −0.2)	.61
RLP-C, mg/dL	−0.6 (−1.0, −0.2)	−0.2 (−0.5, −0.1)	−0.4 (−0.7, −0.2)	.44
Blood glucose, mg/dL	1.3 (0.5, 1.9)	0.4 (0.1, 0.8)	0.7 (0.3, 1.1)	.89
Insulin, μIU/mL	−0.5 (−0.9, −0.2)	0.2 (0.1, 0.3)	−0.6 (−1.0, −0.3)	.30
HbA1c, %	−0.1 (−0.4, −0.1)	−0.2 (−0.3, −0.1)	−0.1 (−0.2, −0.1)	.11
MCP-1, pg/mL	−10.1 (−13.5, −7.2)	−6.6 (−8.4, −3.7)	−3.5 (−4.7, −2.2)	.36

Data are present as mean ± range.
Apo = apolipoprotein, HbA1c = hemoglobin A1c, MCP = monocyte chemotactic protein, RLP-C = remnant lipoprotein cholesterol.

ezetimibe may be decrease the TG and apoB-48 containing lipoproteins formation in the small intestine.[24]

To our best knowledge, this is the study to investigate the feasible effect of ezetimibe alone for PPHP among Chinese population. The results of this study are inconsistent with the previous study.[22] In the present study, the results did not show greater effect in both primary endpoints and secondary endpoints. It indicated that ezetimibe may not show promising effect for PPHP after 2-week treatment. However, it may work after longer intervention.

This study has 3 limitations. First, the sample size is still relatively small in this pilot study, although it included more subjects than the previous study.[22] Second, the treatment duration of this study is quite short, with only 2 weeks, which may affect the results of this study. Third, this study was conducted at 1 hospital only. Thus, it may impact the generalization of the results to the other hospitals. Future studies should avoid these limitations.

5. Conclusion

The results of this study demonstrated that ezetimibe may be ineffective for subjects with PPHP after 2-week treatment. Further studies should extend the treatment period to further investigate its effect.

Author contributions

Conceptualization: Chun-Li Liu, E-Zhong Xue, Ming-Hui Zhang.
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