A practical “low-carbohydrate dietary care” model for elderly patients with type 2 diabetes

Yuwei Feng
Affiliated Hospital of Jiangnan University
Qinyue Wang
Affiliated Hospital of Jiangnan University
Jiao Hua
Hospital Infection-Control Dep, Affiliated Hospital of Jiangnan University
Yiran Liu
Affiliated Hospital of Jiangnan University
Xiaohui Zhong
Affiliated Hospital of Jiangnan University
Hong Cao
Affiliated Hospital of Jiangnan University
Yanping Xia
Affiliated Hospital of Jiangnan University
Feng Zhang (fengzhang@jiangnan.edu.cn)
Affiliated Hospital of Jiangnan University

Research Article

Keywords: low-carbohydrate dietary care, type 2 diabetes, compliance

Posted Date: May 16th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1629571/v1

Abstract

A randomized, double-blind, controlled experiment was conducted to observe how dietary care with restriction of carbohydrate absorption affects glucose and lipid metabolism in elderly patients with type 2 diabetes. Participants in the control group (Group C) were given standard treatment and in the experimental group (Group E) white common bean extract (WCBE) was given before meals. The trial was divided into two periods: intensive and maintenance intervention periods. Glucolipid metabolism was monitored in both groups during two intervention periods. Glycosylated hemoglobin (HbA1c) in Group E was lower than in Group C at the end of the 2- and 4-month, and significantly decline from baseline. The area under curve of oral glucose tolerance test (OGTT) glucose after 2- and 4-month intervention than baseline in Group E and were all significantly lower than in Group C after the intervention. Both High-density lipoprotein (HDL) and Low-density lipoprotein (LDL) also improved in group E ($P < 0.05$). In the clinical management of elderly patients with type 2 diabetes, this individualized model of care without restricting carbohydrate intake can effectively improve patients' glucose metabolism. The effect of this care model is similar to that of a low-carbohydrate diet care model. Therefore, this regimen could be a novel antidiabetic approach for patients with type 2 diabetes who are unwilling to restrict their carbohydrate intake.

Highlights

- α-amylase inhibitors purified from WCBE are beneficial for glycolipid control.
- A unique WCBE-based treatment option for elderly patients with type 2 diabetes.
- No restriction of carbohydrate intake in elderly people with type 2 diabetes.
- Functional foods improve patients' glycolipid metabolism in the short term.

Introduction

Diabetes has become one of the serious public health problems in the world. According to the latest IDF Diabetes Atlas (10th edition), the number of people with diabetes will reach 783 million by 2045. The proportion of people over the age of 60 with diabetes will continue to increase as the global population ages (1). In the vast majority of patients, the choice of medication to control blood glucose is the primary therapeutic approach. Based on drug control of blood glucose, how to improve the clinical efficacy of drugs through a scientific, practical, and reasonable care program is an ideal goal for the current treatment of diabetes.

In the treatment of diabetes, the American Diabetes Association believes that medical nutrition therapy (MNT) plays a vital role in preventing diabetes and its complications or delaying the rate of complications. The goals of MNT for the treatment of diabetes are to achieve the intensive management of blood glucose, blood lipid, and blood pressure; to prevent or slow down the occurrence of chronic complications; to satisfy the dietary problems required by individuals, and to consider personal and cultural factors and whether they are willing to change their dietary habits; to maintain a pleasant diet, and to limit the choice of food only when there is a clear scientific basis (2). Some researchers believe that dietary nursing education for elderly diabetic patients to allow patients to master the correct dietary knowledge and basic skills is the primary way to achieve an appropriate diet and promote health. Thus, dietary nursing education is one of the most economical and effective health care strategies (3). However, a report indicate that the level of knowledge and attitude towards nutrition health was low in the Chinese elderly, and misinterpretation of nutrition would increase the risk of chronic diseases such as diabetes in the elderly (4). It is well known that the dietary habits of the elderly are not easily changed.

Carbohydrates are an essential macronutrient that provides people with energy. However, carbohydrates become a health problem when rapidly digested and absorbed, especially when ingested in large amounts (5, 6). Type 2 diabetes (T2D) is becoming more prevalent in Asia, which can partly be attributed to carbohydrate-rich diets, including cereals or foods made from flour or starch alone. A prospective study showed that carbohydrate intake may increase the risk of T2D and may be associated with a lower intake of various nutrients and imbalanced macronutrient composition (7).

Diet control is an essential measure to prevent and control the disease during the natural course of diabetes and is an integral part of the self-management of diabetic patients. Since insulin resistance in patients with type 2 diabetes increases the eagerness for carbohydrate intake, dietary interventions that reduce dietary carbohydrate intake are thought to improve glycemic control and type 2 diabetes outcomes (8). A low-carbohydrate diet improves glycemic control in T2D patients without any harmful effects on cardiovascular system (9). Furthermore, compared to the low-fat diet, a low-carbohydrate diet can lower blood glucose levels and the economic burden of Chinese T2DM patients (10). However, dietary intervention requires patients to change their previous diet and living habits. For most patients, it is not easy to adhere to healthy dietary behaviors and form habits for a long time. The development of diabetes and complications and the stress triggered by long-term diet control significantly reduce patients' quality of life. The decrease in quality of life is one of the causes of poor patient compliance (11, 12).

Therefore, we need novel care models in the treatment of T2D that can reduce disruptions to patients' diets and lifestyles in order to improve their quality of life. Amylase inhibition can delay or hinder the breakdown of carbohydrates by inhibiting the activity of amylase or glycosidase, thereby decreasing glucose production. Among many portions of cereal and legumes, white common bean extract (WCBE) inhibits activity and biosafety, so it has a broader prospect in preventing and controlling diabetes and obesity (13). Here, we conducted a randomized, double-blind trial to apply WCBE to the diet of diabetic patients. On this basis, we did not overly influence the structure of the patient's diet. To investigate the effects of this new model of care on glucolipid metabolism in patients with type 2 diabetes and to explore individualized practice approaches to achieve low carbohydrate absorption without restricting carbohydrate intake.

Research Design And Methods

Inclusion exclusion criteria

Subjects were eligible if they met the following criteria: age 60–75 years, 6.5% ≤ HbA1c ≤ 13.0%. Exclusion criteria were: type 1 diabetes mellitus, malignant hypertension, severe heart disease, renal failure, inflammatory bowel disease, gastrointestinal ulceration, autoimmune disease, cancer, medical or surgical weight loss within 3 months, antibiotic therapy within 3 months; Subjects with a poor compliance or who violated the protocol or were unwilling to continue participation in the clinical trial were also asked to withdraw from the study.

Sample size estimates

In this study, the sample size was calculated using a comparison of two independent samples, by using PASS15.0 software and reviewing the literature of similar studies with $\alpha = 0.05$ and $\beta = 0.1$, the sample size was calculated as 21 cases in the control group and 32 cases in the experimental group, taking into account the 10% missed visit rate, the sample sizes of the two groups were determined to be at least 23 and 38 cases respectively. In the course of this study, 24 and 43 cases were eventually enrolled in the control group and experimental group respectively.

Methods

All subjects were randomized to an experimental group (Group E) and a control group (Group C). After enrollment, the demographic data of the issues were recorded, including gender, age, medication history, disease history, and lifestyle. Group C received the usual dietary instructions for diabetes. Referring to "*The dietary reference intakes for Chinese residents"* issued by the Chinese Nutrition Society, it is recommended that the carbohydrate energy supply ratio for Chinese adult residents is 50% – 65%. Patients in Group E underwent personalized dietary pattern intervention according to the characteristics of WCBE as a-amylase inhibition. Combined with the labor intensity, age, weight, and other factors of patients, they calculate patients' daily energy and nutrient content and develop the personalized nutritional formula to ensure that patients ingest enough carbohydrates and the proportion of nutrients is normal. Patients with a daily habitual carbohydrate intake of more than 65% should be supplemented with 3 grams of WCBE 15–30 minutes before the meal. Patients with a daily regular carbohydrate intake of between 50 and 65% received 1.5 g of WCBE. Glycosylated hemoglobin, OGTT blood glucose, and OGTT insulin levels were also monitored in participants. Patients' average carbohydrate intake was recorded weekly to change the use of WCBE dynamically.

The trial statistician created a computer-generated simple randomization scheme. The clinical trial is a double-blind trial in which subjects and investigators do not know to which group each issue is assigned. The statistician unblinds the grouping of all topics after completing the experiment. All participants underwent baseline biochemical measurements. All subjects underwent 2 phases of intervention: (1) 2 months of intensive intervention: All participants received daily telephone follow-up, self-monitoring of fasting blood glucose and 2-hour blood glucose every 3 days, weekly face-to-face interviews, and monthly nutritional evaluations. All subjects underwent biochemical investigations at the end of this period. We then randomly selected 19 participants in Group C and 26 participants in Group E to proceed to the subsequent intervention phase. (2) 2-Month Maintenance Phase: Participants were randomly selected from those who completed the first phase of the intervention to receive the intervention for an additional 2 months. During this period, they received only weekly telephone follow-ups. At the end of this period, participants underwent a third biochemical examination (Fig. 1). There was no harm to the subjects during the whole process.

During the intervention period, the primary outcome measures were changes in Glycosylated hemoglobin (HbA1c). Changing in fasting blood glucose (FBG) and HOMA-IR were the main secondary outcomes. Other secondary outcomes included changes in 0.5-h blood glucose (0.5-hPBG), 1-h blood glucose (1-hPBG), 2-h blood glucose (2-hPBG), 3-h blood glucose (3-hPBG), Cholesterol (CHOL), Triglycerides (TG), High-density lipoprotein (HDL), and Low-density lipoprotein (LDL).

Sample Collection and Laboratory Measurements

Blood samples were collected from subjects at month 0, at the end of 2 months of intervention, and the end of 4 months of intervention. Venous blood was taken from subjects fasted for 10–12 h. Serum was separated for laboratory tests. Clinical laboratory measurements were performed at the Affiliated Hospital of Jiangnan University. The blood cell measurements were conducted on the automated hematology analyzer (Sysmex K4500; Sysmex Corporation, Japan).

Statistical Analysis

Statistical Data were analyzed using Prism8 (GraphPadPrism, SanDiego, CA) statistical software. The Mann-Whitney test and Wilcoxon test were used for intra-group and inter-group comparisons in each phase, respectively. Mann-Whitney test was used for age, and chi-square test was used for sex. P values < 0.05 was considered statistically significant.

Results

General statement

This study enrolled 73 elderly patients with type 2 diabetes who met the inclusion criteria in the Affiliated Hospital of Jiangnan University from December 2017 to November 2018. All patients were randomized 2:3 into Group C (n = 28) and Group E (n = 45). Anthropometric and biochemical measurements were taken at 0, 2, and 4 months. A total of 67 patients (Group C=24/Group E=43) eventually completed the intensive phase intervention and 45 patients (Group C=19/Group E=26) completed the maintenance phase intervention. There were no statistically significant differences in age, sex, or medication regimen among the groups during the intensive and maintenance phases (Table 1).

Effects of a dietary care model to reduce carbohydrate absorption during an intensive intervention on glucose and lipid metabolism in elderly T2DM patients

Glucose metabolism

HbA1c is considered the gold standard for assessing long-term glycemic control in diabetic patients (14). The results of the within-group comparison showed that although there was no significant difference in HbA1c between Group E and Group C after dietary intervention for 2 months, there was a tendency to form a contrast. Group E showed a significant decrease in HbA1c after 2 months of dietary intervention compared to 0 months. However, it is worth noting that there was also a slight decrease in HbA1c in Group C, which may be related to our routine healthy diet education for patients in Group C, and patient compliance improved in the initial stage. The oral glucose tolerance test (OGTT) is a glucose load test used to understand islet cell function and the body's ability to regulate blood glucose. The results showed that FBG, 0.5-hPBG, 1-hPBG, 2-hPBG, and 3-hPBG decreased significantly compared with baseline after 2 months of dietary intervention. HOMA-IR is a measure used to evaluate an individual's level of insulin resistance, and the HOMA-IR index will gradually increase as the level of insulin resistance increases. The results showed no significant difference in HOMA-IR changes in Group E and Group C after 2 months of intervention. The area under the glucose curve in the OGTT showed a significant decreasing trend in Group E after 2 months, and it was different from Group C at 2 months .

Lipid metabolism

CHOL is an essential raw material for synthesizing adrenocorticotropic hormone, sex hormones, bile acids, vitamin D, and other physiologically active substances. It is also the main component of the cell membrane, and its serum concentration can be used as an indicator of lipid metabolism. The results showed no significant trend in CHOL after two months of the intervention diet. TG, a fatty substance in the blood, is mainly obtained from the diet and is lower in Group E than Group C at 2 months. HDL particles are small, can freely enter and exit the arterial wall, take up low-density lipoprotein, cholesterol, triglycerides, and other harmful substances immersed in the intimal layer of the vascular wall, and transport them to the liver for decomposition and excretion (15). The results showed that HDL levels showed a significant decreasing trend in Group C and an increasing trend in Group E at 2 months. LDL is a lipoprotein particle that carries cholesterol into peripheral tissue cells and can be oxidized to oxidized LDL. When LDL, significantly oxidatively modified LDL (OX-LDL), is in excess, the cholesterol it carries accumulates on the arterial wall and quickly causes arteriosclerosis (16).

The results showed that LDL levels increased in Group C and decreased significantly in Group E at 2 months. However, it is worth noting that due to the double-blind nature, we found a significant difference between the C and E groups at 0 months. HDL levels were significantly higher in Group C than in Group E, but LDL levels were significantly lower than in Group E. This difference may be related to the small sample size. With the intervention's progress, the difference between the two groups gradually narrowed at 2 months, and Group E developed better results, indirectly demonstrating that physical-based dietary intervention can regulate HDL and LDL in diabetic patients (Table 1).

Effects of a dietary care model to reduce carbohydrate absorption during maintenance on glucose and lipid metabolism in elderly T2DM patients

Glucose metabolism

We performed statistical analysis again for the patients who participated in the study (4 months). It was found that even if the frequency of follow-up was reduced at a later stage, the overall results showed that HbA1c was significantly lower in Group E than in Group C after 4 months of dietary intervention. HbA1c also decreased significantly from baseline in Group E. OGTT results showed that blood glucose levels were significantly lower in Group E than Group C after 4 months of dietary care. Comparison of the results within groups indicated a significant decreasing trend in 0.5-hPBG, 1-hPBG, 2-hPBG, and 3-hPBG compared with baseline, except for FBG, which was not significantly different from baseline. It is worth noting that FBG, 0.5-hPBG, and 2-hPBG in Group C showed an increasing trend after 4 months, which may be related to our randomized double-blind, patients in the general nursing intervention group subjectively perceived the effectiveness of this model as poor. Patients are no longer willing to strictly control their diet and are associated with reduced cooperation and compliance in subsequent phases. The HOMA-IR results showed no significant change in HOMA-IR from baseline in Group E after 4 months of intervention. Still, because of the increase in Group C, a difference was formed between the two groups at 4 months. The reason for elevated HOMA-IR in Group C we used above. The area under the glucose curve in the OGTT showed a significant decreasing trend after 4 months in Group E, and it was different from Group C at 4 months (Table 2).

Lipid metabolism

Analysis of lipid metabolism results showed no differences in CHOL or TG between the E and C groups at 4 months. HDL showed an upward trend in Group E and a downward trend in Group C at 4 months of intervention. LDL decreased in Group E but increased in Group C at 4 months of intervention. However, there were differences in HDL and LDL results between the C and E groups at baseline, with higher HDL levels and lower LDL levels in Group C than in Group E. With the progress of the intervention, there was a changeover phenomenon between the two groups at 4 months. Group E developed better results, indirectly demonstrating that physical-based dietary intervention can regulate HDL and LDL in diabetic patients (Table 2).

Compliance analysis

In the intensive intervention phase, we conducted dietary health education for the patients once a day according to their actual conditions without much influence on diet structure. Some patients will experience increased satiety and reduced carbohydrate intake later. It is necessary to assess the average carbohydrate intake of patients dynamically and timely adjust the dosage of WCBE promptly. At the end of the intensive intervention phase, 24 subjects in Group C (males 8 and females 16) and 43 subjects in Group E (males 25 and females 18) completed the second biochemical examination. 10.5% of patients in Group C were weaned from the experiment, compared with only 4% of patients in Group E (Table 1) . We then randomly selected 19 Group C participants (males 6 and females 13) and 26 Group E participants (males 13 and females 13) to continue the final phase of the intervention. To investigate the applicability and autonomy of patients to this dietary pattern, in the second stage, we reduced the frequency of follow-up and followed patients once a week. 13.7% of patients in Group C were taken off from the experiment, compared with only 7% of patients in Group E (Table 2) .

Patients in Group C dropped out of the investigation because of prolonged diabetic diet control, resulting in a sense of burnout. The patient's autonomy became less controlled, and his diet was not following the diabetic dietary requirements. And the patient subjectively did not want to continue the experiment. We did not interfere excessively with the structure of the diet of the patients in Group E. The patients in Group E did not want to continue the experiment because of the production of bloating.

In summary, patients in Group C had worse compliance and higher dropout rates than those in Group E due to continuous dietary control. Long-term dietary management is not easy for elderly diabetic patients.

Discussion

We adopt a personalized dietary care model, which is similar to the effect of a low-carbohydrate diet in reducing carbohydrate absorption. Notably, this new model does not restrict carbohydrate intake. Overall, this dietary care has a significant ameliorating effect on glucose metabolism in elderly T2DM patients. Even when the frequency of follow-up decreased in the second stage, the overall trend of glucose metabolism indicators was better in Group E than in Group C. After 2 and 4 months of intervention, there was no significant difference in the changes of CHOL and TG between the two groups, but the HDL levels in Group E after 2 and 4 months of intervention was higher than that of Group C. In addition, participants in Group C had a higher dropout rate due to their inability to adhere to long-term dietary control, whereas this outcome was not observed in Group E.

At present, several studies have demonstrated that the implementation of diet nursing education for diabetic patients and nutritional intervention can effectively control patients' blood glucose levels and improve the metabolic homeostasis of patients, such as lipid metabolism. At the same time, diet nursing intervention can also prevent or delay the occurrence and development of diabetes-related complications and reduce the mortality of patients (17, 18). In addition, dietary care treatment can also reduce medical costs (19). Steven *et al.* (20) performed an 8-week very-low-calorie diet intervention followed by a 6-month normal caloric diet in 30 patients with type 2 diabetes and found fasting blood glucose, and HbA1c returned to normal in 13 patients. Several studies have also shown that early strict dietary control can play a reversal role for some patients with newly diagnosed type 2 diabetes and result in complete remission of the disease (21, 22). Throughout the process of diabetes prevention and treatment, it is therefore important to provide effective dietary nursing interventions for patients.

In Asia, high consumption of refined grains such as fine rice and wheat flour has led to a shift in an unhealthy dietary pattern, contributing to one of the critical factors in the high incidence of type 2 diabetes worldwide (23). To better achieve the ideal blood glucose level, diabetic patients need to adhere to long-term healthy dietary behaviors for life, which is undoubtedly a great challenge for most patients. Lack of nutritional awareness and difficulty in changing dietary habits in elderly patients with type 2 diabetes reduces their compliance with dietary interventions. Therefore, there is a need for other care models to reduce excessive intervention in patients' dietary patterns. We incorporate WCBE into usual dietary instructions for patients with T2DM, which can be used to restrict carbohydrate absorption without limiting their carbohydrate intake. We don't tamper too much with the patient's dietary habits because of this, and we adjust the WCBE dose to match the patient's daily carbohydrate intake. Because of its high level of safety and maneuverability, as well as its capacity to regulate glucose and lipid metabolism in older patients with T2DM, this unique dietary care model seems promising. In addition, we will limit the impact of the intervention on the patient's diet structure and suitably advise patients who have lowered carbohydrate intake due to WCBE-induced satiety to raise their carbohydrate intake. This type of dietary pattern, which increases carbohydrate consumption, not only prevents glucose absorption but also regulates the gut microbiota. The mechanism of action of WCBE is similar to that of acarbose, which is extensively employed as a glycosidase inhibitor and has a carbohydrate catabolism inhibitory effect in the small intestine. As a result, when additional carbohydrates enter the large intestine, acarbose can kickstart the gut microbiota's glucose metabolism. Acarbose modulates the gut microbiota and stimulates GLP-1 release, which can help to increase insulin secretion and lower blood sugar levels (24). In the future, we can also focus on the role of gut microbiota to investigate whether this dietary pattern without limiting carbohydrate intake can promote blood glucose homeostasis through intestinal mechanisms.

Overall, this novel model can bring out the co-benefit for patients and nurses. On the one hand, it can overcome the burnout of diabetic patients due to long-term dietary control and increase their compliance. On the other hand, the encouragement of patients will significantly promote the practicability of nursing, the progress of nursing education, and the efficiency of nursing care for patients.

Conclusion

In conclusion, in the clinical treatment of elderly patients with type 2 diabetes, using a personalized care model that limits carbohydrate absorption can effectively improve the level of glucose metabolism in patients. In addition, this model can reduce the patient dropout rate, improve treatment compliance, and reduce the difficulty of care.

Abbreviations

WCBE	White common bean extract
MNT	Medical nutrition therapy

T2D	Type 2 diabetes
HbA1c	Glycosylated hemoglobin
FBG	Fasting blood glucose
0.5-hPBG	0.5-h blood glucose
1h-PBG	1-h blood glucose
2-hPBG	2-h blood glucose
3-hPBG	3-h blood glucose
CHOL	Cholesterol
TG	Triglycerides
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
OGTT	Oral glucose tolerance test

Declarations

Ethical Approval and Consent to participate

This double-blind, randomized controlled trial was conducted in the Affiliated Hospital of Jiangnan University, Wuxi, China from December 2017 to November 2018. The trial was approved by the Ethics Review Committee of the Affiliated Hospital of Jiangnan University (ID: IEC201711001) and registered as ChiCTR-IOR-17013656 in the China Clinical Trial Registry. Written informed consent was obtained from all participants before the intervention.

Consent for publication

All authors agree to publish.

Data avail ability statement

Data is available on request from the authors.

Conflict of interests

The authors declare that there is no conflict of interest.

Funding

There is no financial support for this manuscript

Author contributions

Yuwei Feng and Qinyue Wang were responsible for designing the protocol, writing the protocol and report, extracting and analysing the data, and interpreting the results.Jiao Hua, Yiran Liu and Xiaohui Zhong were responsible for designing the review protocol and screening potentially eligible studies, and arbitrating on potentially eligible studies. Hong Cao and Yanping Xia were involved in data extraction and provided feedback on the report. Feng Zhang provided feedback on the report.

References

1. Federation. ID. IDF Diabetes Atlas, 10th edn. Brussels,Belgium: International Diabetes Federation. Brussels,Belgium: International Diabetes Federation. 2021.
2. Pastors J, Warshaw H, Daly A, Franz M, Kulkarni K. The evidence for the effectiveness of medical nutrition therapy in diabetes management. Diabetes care. 2002;25(3):608–13.
3. Miller C, Edwards L, Kissling G, Sanville L. Nutrition education improves metabolic outcomes among older adults with diabetes mellitus: results from a randomized controlled trial. Preventive medicine. 2002;34(2):252–9.
4. Foundation CDR. Nutrition and health report of the elderly in China. China Development Press. 2015.
5. Waldhart A, Muhire B, Johnson B, Pettinga D, Madaj Z, Wolfrum E, et al. Excess dietary carbohydrate affects mitochondrial integrity as observed in brown adipose tissue. Cell reports. 2021;36(5):109488.
6. Wee M, Henry C. Reducing the glycemic impact of carbohydrates on foods and meals: Strategies for the food industry and consumers with special focus on Asia. Comprehensive reviews in food science and food safety. 2020;19(2):670–702.
7. Ha K, Joung H, Song Y. Inadequate fat or carbohydrate intake was associated with an increased incidence of type 2 diabetes mellitus in Korean adults: A 12-year community-based prospective cohort study. Diabetes research and clinical practice. 2019;148:254–61.
8. Volek J, Fernandez M, Feinman R, Phinney S. Dietary carbohydrate restriction induces a unique metabolic state positively affecting atherogenic dyslipidemia, fatty acid partitioning, and metabolic syndrome. Progress in lipid research. 2008;47(5):307–18.
9. Gram-Kampmann E, Hansen C, Hugger M, Jensen J, Brønd J, Hermann A, et al. Effects of a six-month low-carbohydrate diet on glycemic control, body composition and cardiovascular risk factors in patients with type 2 diabetes: an open-label RCT. Diabetes, obesity & metabolism. 2022.
10. Han Y, Cheng B, Guo Y, Wang Q, Yang N, Lin P. A Low-Carbohydrate Diet Realizes Medication Withdrawal: A Possible Opportunity for Effective Glycemic Control. Frontiers in endocrinology. 2021;12:779636.
11. Bradley C, Speight J. Patient perceptions of diabetes and diabetes therapy: assessing quality of life. Diabetes/metabolism research and reviews. 2002:S64-9.
12. Huang E, Brown S, Ewigman B, Foley E, Meltzer D. Patient perceptions of quality of life with diabetes-related complications and treatments. Diabetes care. 2007;30(10):2478–83.
13. Shaban E, Elbakry H, Ibrahim K, El Sayed E, Salama D, Farrag A. The effect of white kidney bean fertilized with nano-zinc on nutritional and biochemical aspects in rats. Biotechnology reports (Amsterdam, Netherlands). 2019;23:e00357.
14. Kaur J, Jiang C, Liu G. Different strategies for detection of HbA1c emphasizing on biosensors and point-of-care analyzers. Biosensors & bioelectronics. 2019;123:85–100.
15. Kontush A. HDL and Reverse Remnant-Cholesterol Transport (RRT): Relevance to Cardiovascular Disease. Trends in molecular medicine. 2020;26(12):1086–100.
16. Mitra S, Goyal T, Mehta J. Oxidized LDL, LOX-1 and atherosclerosis. Cardiovascular drugs and therapy. 2011;25(5):419–29.
17. Cucuzzella M, Riley K, Isaacs D. Adapting Medication for Type 2 Diabetes to a Low Carbohydrate Diet. Frontiers in nutrition. 2021;8:688540.
18. Franz M, Warshaw H, Daly A, Green-Pastors J, Arnold M, Bantle J. Evolution of diabetes medical nutrition therapy. Postgraduate medical journal. 2003;79(927):30–5.
19. Rizkalla S, Taghrid L, Laromiguiere M, Huet D, Boillot J, Rigoir A, et al. Improved plasma glucose control, whole-body glucose utilization, and lipid profile on a low-glycemic index diet in type 2 diabetic men: a randomized controlled trial. Diabetes care. 2004;27(8):1866–72.
20. Steven S, Hollingsworth K, Al-Mrabeh A, Avery L, Aribisala B, Caslake M, et al. Very Low-Calorie Diet and 6 Months of Weight Stability in Type 2 Diabetes: Pathophysiological Changes in Responders and Nonresponders. Diabetes care. 2016;39(5):808–15.
21. Gow M, Baur L, Johnson N, Cowell C, Garnett S. Reversal of type 2 diabetes in youth who adhere to a very-low-energy diet: a pilot study. Diabetologia. 2017;60(3):406–15.
22. Sarathi V, Kolly A, Chaithanya H, Dwarakanath C. High rates of diabetes reversal in newly diagnosed Asian Indian young adults with type 2 diabetes mellitus with intensive lifestyle therapy. Journal of natural science, biology, and medicine. 2017;8(1):60–3.
23. Ley S, Hamdy O, Mohan V, Hu F. Prevention and management of type 2 diabetes: dietary components and nutritional strategies. Lancet (London, England). 2014;383(9933):1999–2007.

24. Zhang M, Feng R, Yang M, Qian C, Wang Z, Liu W, et al. Effects of metformin, acarbose, and sitagliptin monotherapy on gut microbiota in Zucker diabetic fatty rats. BMJ open diabetes research & care. 2019;7(1):e000717.

Tables

Table 1
Differential analysis of glucose and lipid metabolism in elderly patients with T2DM during intensive intervention

	E Group			**C Group**			**P Value**	
Gneral Information	Month 0	Month 2	P Value	Month 0	Month 2	P Value	Month 0	Month 2
Age(years)	67.791 ± 3.625	/	/	66.580 ± 3.581	/	/	0.2193[a]	/
Gendre(Females/Males)	18/25	/	/	16/8	/	/	0.0515[k]	/
Plasma glucose homeostasis								
HbA1c (%)	8.049 ± 1.316	7.293 ± 1.104	< 0.0001****	7.871 ± 0.766	7.633 ± 0.778	0.0150*	0.7577	0.0822
Fasting Blood Glucose ($mmol{\cdot}L^{-1}$)	8.851 ± 2.138	7.864 ± 1.886	< 0.0001****	7.818 ± 1.68	7.993 ± 1.734	0.8334	0.0874	0.4648
OGTT_0.5h PBG ($mmol{\cdot}L^{-1}$)	13.100 ± 2.633	10.727 ± 2.213	< 0.0001****	10.740 ± 2.502	10.809 ± 2.139	0.8553	0.0011##	0.6378
OGTT_1h PBG ($mmol{\cdot}L^{-1}$)	17.580 ± 2.219	14.447 ± 2.556	< 0.0001****	16.035 ± 3.230	15.278 ± 2.279	0.1621	0.1394	0.0598
OGTT_2h PBG ($mmol{\cdot}L^{-1}$)	20.020 ± 3.357	16.660 ± 3.679	< 0.0001****	18.032 ± 3.375	18.955 ± 3.640	0.1280	0.0674	0.0161#
OGTT_3h PBG ($mmol{\cdot}L^{-1}$)	17.484 ± 4.126	14.839 ± 4.378	< 0.0001****	16.962 ± 4.102	17.384 ± 4.029	0.7469	0.8002	0.0217#
OGTT_Glucose_AUC ($mmol{\cdot}L^{-1}{\cdot}min^{-1}$)	3042.581 ± 465.946	2534.674 ± 496.165	< 0.0001****	2751.750 ± 500.406	2790.417 ± 464.533	0.9944	0.0644	0.0227#
HOMA-IR	21.380 ± 12.899	19.930 ± 11.847	0.0957	22.581 ± 13.699	22.123 ± 12.534	0.5297	0.6877	0.6347
Plasma lipid homeostasis								
CHOL ($mmol{\cdot}L^{-1}$)	4.811 ± 0.864	4.696 ± 0.849	0.2170	4.865 ± 0.892	4.555 ± 1.021	0.0907	0.9096	0.5921
TG ($mmol{\cdot}L^{-1}$)	1.669 ± 1.433	1.360 ± 0.597	0.5922	1.741 ± 0.822	1.847 ± 0.893	0.3941	0.1194	0.0155#
HDL ($mmol{\cdot}L^{-1}$)	1.225 ± 0.348	1.539 ± 0.699	0.0033**	2.593 ± 0.962	1.147 ± 0.234	< 0.0001****	< 0.0001####	0.0101#
LDL ($mmol{\cdot}L^{-1}$)	2.919 ± 0.775	2.569 ± 0.950	0.0018**	1.573 ± 0.808	2.760 ± 0.861	< 0.0001****	< 0.0001####	0.4221

The Mann-Whitney test (#) and Wilcoxon test (*) were used for intra-group and inter-group comparisons in each phase, respectively. Mann-Whitney test was used for age (a), and chi-square test was used for sex (k). *P* values < 0.05 was considered statistically significant.

Table 2
Differential analysis of glucose and lipid metabolism in elderly patients with T2DM during maintenance

	E Group			C Group			P Value	
Gneral Information	Month 0	Month 4	P Value	Month 0	Month 4	P Value	Month 0	Month 4
Age(years)	67.308 ± 3.232	/	/	66.320 ± 3.908	/	/	0.4388^{a}	/
Gendre(Females/Males)	13/13	/	/	13/6	/	/	0.2166^{k}	/
Plasma glucose homeostasis								
HbA1c (%)	7.947 ± 1.428	7.135 ± 0.800	0.0002***	7.879 ± 0.600	7.879 ± 1.027	0.7901	0.3010	0.0095$^{\#\#}$
Fasting Blood Glucose (mmol·L^{-1})	8.692 ± 2.173	8.055 ± 1.434	0.1814	7.628 ± 1.536	9.921 ± 1.866	0.0017**	0.0682	0.0014$^{\#\#}$
OGTT_0.5h PBG (mmol·L^{-1})	12.725 ± 2.797	10.600 ± 2.027	0.0039**	10.632 ± 2.365	12.715 ± 2.281	0.0039**	0.0259$^{\#}$	0.0086$^{\#\#}$
OGTT_1h PBG (mmol·L^{-1})	17.295 ± 2.080	14.889 ± 2.364	0.0003***	16.080 ± 2.955	18.089 ± 2.933	0.0602	0.3017	0.0015$^{\#\#}$
OGTT_2h PBG (mmol·L^{-1})	19.915 ± 3.361	16.284 ± 4.078	< 0.0001****	18.009 ± 2.893	21.031 ± 3.988	0.0095**	0.0925	0.0005$^{\#\#\#}$
OGTT_3h PBG (mmol·L^{-1})	17.335 ± 4.696	14.181 ± 4.240	0.0001***	17.092 ± 3.483	19.271 ± 4.073	0.1042	0.9728	0.0004$^{\#\#\#}$
OGTT_Glucose_AUC (mmol·L^{-1}·min^{-1})	3005.423 ± 479.846	2511.346 ± 481.070	< 0.0001****	2750.211 ± 436.241	3184.211 ± 544.963	0.0124*	0.1826	0.0002$^{\#\#\#}$
HOMA-IR	21.350 ± 12.840	19.800 ± 11.620	0.7467	22.560 ± 12.250	35.920 ± 26.490	0.0107*	0.4928	0.0290$^{\#}$
Plasma lipid homeostasis								
CHOL (mmol·L^{-1})	4.952 ± 0.863	4.898 ± 0.971	0.9842	4.852 ± 0.946	4.619 ± 0.822	0.1572	0.5274	0.2582
TG (mmol·L^{-1})	1.841 ± 1.630	1.395 ± 0.553	0.2962	1.741 ± 0.892	1.750 ± 1.010	0.5476	0.5349	0.5125
HDL (mmol·L^{-1})	1.205 ± 0.363	2.328 ± 1.153	< 0.0001****	2.804 ± 0.864	1.256 ± 0.279	< 0.0001****	< 0.0001$^{\#\#\#\#}$	0.0006$^{\#\#\#}$
LDL (mmol·L^{-1})	2.884 ± 0.974	2.129 ± 1.013	< 0.0001****	1.304 ± 0.518	2.891 ± 0.736	< 0.0001****	< 0.0001$^{\#\#\#\#}$	0.0039$^{\#\#}$

The Mann-Whitney test ($^{\#}$) and Wilcoxon test (*) were used for intra-group and inter-group comparisons in each phase, respectively. Mann-Whitney test was used for age (^{a}), and chi-square test was used for sex (^{k}). *P* values < 0.05 was considered statistically significant.

Figures

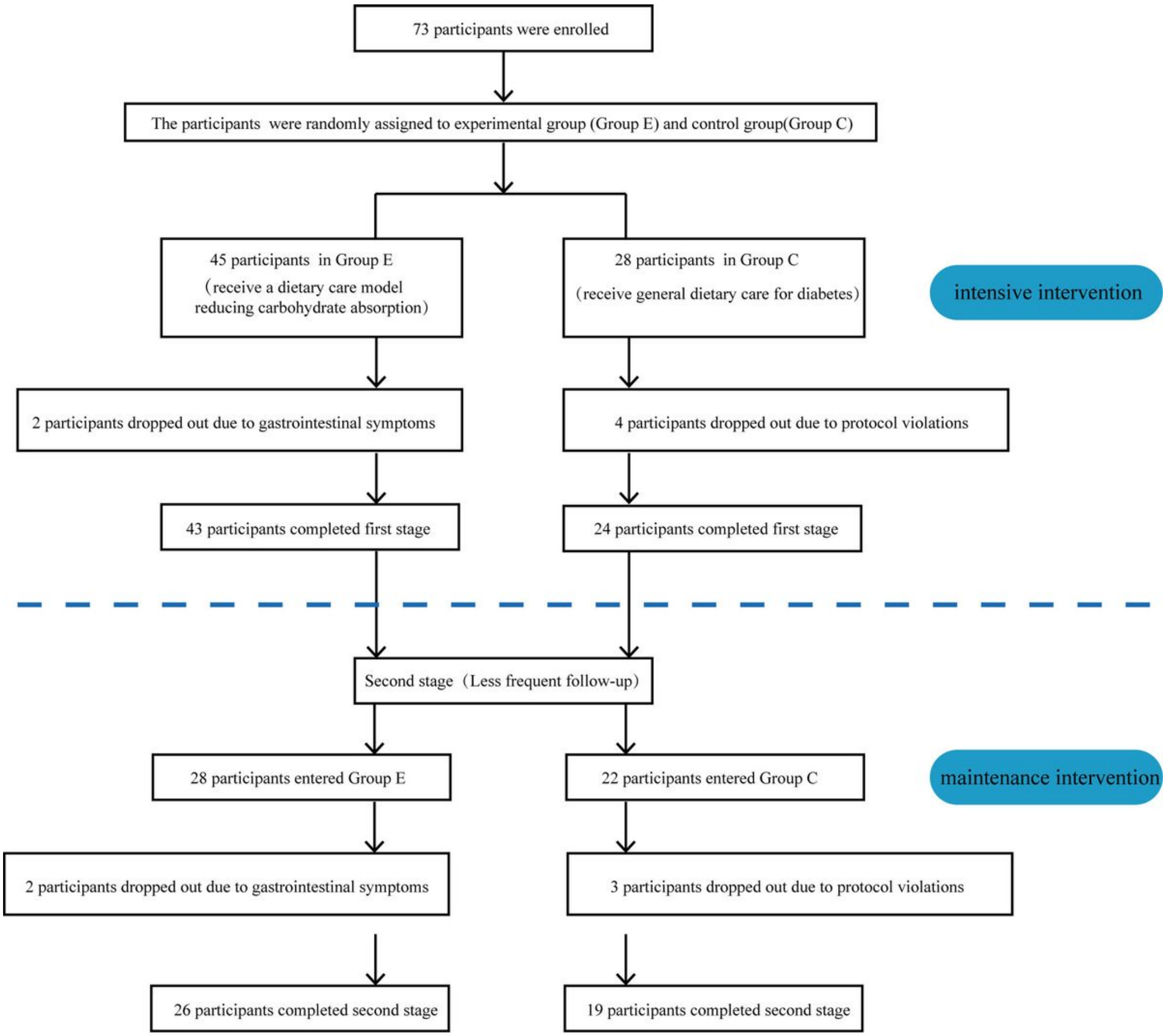

Figure 1

Experimental procedure