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AIMS AND SCOPE

The primary aim of *World Journal of Diabetes* (*WJD*, *World J Diabetes*) is to provide scholars and readers from various fields of diabetes with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

  WJD mainly publishes articles reporting research results and findings obtained in the field of diabetes and covering a wide range of topics including risk factors for diabetes, diabetes complications, experimental diabetes mellitus, type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes, diabetic angiopathies, diabetic cardiomyopathies, diabetic coma, diabetic ketoacidosis, diabetic nephropathies, diabetic neuropathies, Donohue syndrome, fetal macrosomia, and prediabetic state.

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ORIGINAL ARTICLE

Case Control Study

Effects of lifestyle interventions on rural patients with type 2 diabetes mellitus

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Abstract

BACKGROUND

The prevalence of type 2 diabetes mellitus (T2DM) is rising rapidly in rural areas, and lifestyle interventions can effectively reduce the blood glucose levels of patients with T2DM. However, current dietary and exercise guidelines are still at experimental stages and are difficult for subjects to understand and implement. The Human Metabolism Analyzer provides real life interventions for the prevention and treatment of T2DM, and our pilot research has demonstrated its effectiveness and good compliance.

AIM

To investigate the effect of and compliance with lifestyle interventions in rural patients with T2DM.

METHODS

A total of ten rural villages were randomly selected in Chaoshui Township, Penglai City, Shandong Province, China, to conduct health screening among residents aged 50 years or older. Each rural village represented a group, and 12 patients with T2DM were randomly selected from each group (total: 120) to participate in this study and receive real life lifestyle interventions and medication guidance. Lifestyle interventions included changing the meal order (A), postprandial activities (B), resistance exercise (C), and reverse abdominal breathing (D). Diabetes education was conducted at least once a month with a weekly phone follow-up to monitor exercise and diet. Waist circumference, blood pressure, body mass index (BMI), motor function, body composition, fasting blood glucose, and glycated hemoglobin (HbA1c) were analyzed before and 3 mo after the intervention. Moreover, patient compliance and adjustments of hypoglycemic drugs were evaluated.

RESULTS

A total of 109 subjects completed the study. The compliance rates for lifestyle interventions A, B, C, and D were 57.79%, 60.55%, 64.22%, and 75.23%, respectively. Among the subjects who received hypoglycemic drugs, the dose was reduced 2 to 3 times based on blood glucose in 54 (67.50%) subjects and was tapered and discontinued in 5 (6.25%) subjects within 3 mo, with no significant fluctuations in blood glucose after dose reduction and withdrawal. After lifestyle interventions, waist circumference, BMI, fasting blood glucose, and HbA1c significantly decreased ($P < 0.001$); motor function and body composition also significantly improved ($P < 0.001$).

CONCLUSION

For patients with T2DM, compliance to real-life lifestyle interventions is good, and the interventions significantly improve metabolic indicators such as waist circumference, BMI, blood pressure, HbA1c, body composition, and motor function. Some patients are able to taper or discontinue hypoglycemic drugs.

Key words: Type 2 diabetes mellitus; Lifestyle interventions; Body mass index

Core tip: The prevalence of type 2 diabetes mellitus (T2DM) is rising rapidly in rural areas, and lifestyle interventions can effectively reduce the blood glucose levels of patients with T2DM. However, current dietary and exercise guidelines are still at experimental stages and are difficult for subjects to understand and implement. The Human Metabolism Analyzer can accurately detect and analyze the effects of food types, sequence of food intake, activity or exercise pattern, and time on blood glucose production and consumption, providing a simple and effective lifestyle intervention for patients with type 2 diabetes. In this study, we analyzed the precise data obtained by the Human Metabolism Analyzer, demonstrating that this method has good effectiveness and compliance, and provides a new method for the prevention and treatment of diabetes.

INTRODUCTION

Regular activity and exercise reduce glycated hemoglobin (HbA1c) levels, improve insulin resistance[1], reduce cardiovascular risk factors, and improve the quality of life[2,3] of patients with type 2 diabetes mellitus (T2DM). T2DM is an independent risk factor for decreased muscle strength[4] and causes a rapid decline in muscle strength and muscle performance[5]. Exercise and strict diet management prevent or delay the progression of T2DM[6,7].

Existing exercise and diet management regimens are associated with two problems: Unclear exercise methods and schedule can lead to exercise injuries, hypoglycemia, and poor results; and poor compliance can lead to poor long-term hypoglycemic effects and incomplete correction of glucose metabolism disorders. Therefore, it is urgent to refine diet and exercise programs and improve their effectiveness and patient compliance.

A human metabolism data acquisition and processing system (Human Metabolism Analyzer) built and implemented by the General Administration of Sport of China in 2018 has fundamentally solved the problems above. The Human Metabolism Analyzer accurately analyzes the effects of food types, food intake sequence, and activity/exercise mode and schedule on the production and consumption of blood glucose, thereby providing simple and effective interventions for patients with T2DM.

To date, few studies have been conducted in China or other countries to investigate the effect of Human Metabolism Analyzer-based lifestyle interventions on metabolic

indicators of patients with T2DM. Our research group has been conducting clinical and preclinical studies on the prevention and treatment of DM for the past few years and has participated in the research on chronic diseases sponsored by the General Administration of Sport. Our small clinical observation pilot study demonstrated good clinical efficacy of real-life lifestyle interventions on T2DM, as well as on pre-type 2 DM, simple obesity, and polycystic ovary syndrome. The next step is to include more subjects to further validate the effectiveness of and patient compliance with lifestyle interventions.

MATERIALS AND METHODS

We randomly selected ten rural villages in Chaoshui Township, Penglai City, Shandong Province, China to conduct T2DM screening among permanent residents aged 50 years or older. Each rural village represented a group, and 12 patients with T2DM were randomly selected from each group to participate in this study. The exclusion criteria were as follows: Severe cardiopulmonary insufficiency, swallowing difficulty or physical impairment, acute or chronic infections, long-term use of glucocorticoids, malignant tumors, or body mass index (BMI) < 25 kg/m^2.

All participants signed an informed consent form and completed T2DM questionnaires. General information such as height, weight, waist circumference, systolic blood pressure, and diastolic blood pressure was recorded. BMI was calculated as weight (kg)/height (m^2). A Huayi glucose meter (EZ-8, Beijing Huayi Jingdian Biotechnology Co., Ltd., China) was used to measure fasting blood glucose[8,9]; an Alere Afinion™ AS100 Analyzer (Alere Technologies AS, United States) was used to measure HbA1c; an MES-01S20 muscle performance analyzer (Beijing Mai Dakang Medical Device Manufacturing Co., Ltd., China) was used to evaluate motor function (lower extremity neural response rate and lower extremity reaction time) and body composition (lower extremity muscle distribution coefficient, fat percentage, and fat distribution). To measure waist circumference, the subject was instructed to stand as usual, with his or her feet 30-40 cm apart, and an inelastic tape measure with 1 mm increments was placed around the middle line between the upper edge of the ileums and the line connecting the lower edge of the twelfth rib; the measurement was taken at the end of normal exhalation.

Lifestyle interventions included changing the meal order (A), *i.e.*, eating in the following order: Vegetables, meat and eggs, and carbohydrates, with no limitation on the amount of carbohydrates and food variety; adjustment of activity schedule (B), *i.e.*, indoor activities from 30 min to 120 min after a meal, such as household chores and slow walking; resistance exercise (C), *i.e.*, resistance exercise, including squatting, standing on heels, standing on toes, resistance band exercise, and plank (8 to 10 times each), 3 to 5 times a week under the guidance of a rehabilitation specialist; and reverse abdominal breathing (D), *i.e.*, inhaling slowly *via* the nose while sucking in the abdomen, holding the breath for 3 to 5 s, and then exhaling slowly *via* the mouth while relaxing the abdomen; the technique was repeated after 2 to 3 rounds of normal breathing, with 10 to 15 cycles per session, 3 to 5 times per day. After 3 mo of intervention, fasting blood glucose, waist circumference, blood pressure, BMI, body composition, and motor function were measured and recorded.

Given the risk of hypoglycemia in subjects receiving insulin or oral hypoglycemic drugs after lifestyle interventions, we tapered medication based on the daily blood glucose readings and reduced the dose by approximately 20% (rounded) when fasting blood glucose levels were lower than 6 mmol/L or postprandial blood glucose levels were lower than 8 mmol/L. The process continued if blood glucose remained at stable level, until withdrawal (if possible).

Statistical analysis

SPSS17.0 was used for statistical analyses. Preintervention and postintervention waist circumference, BMI, blood glucose, HbA1c, blood pressure, motor function, and body composition were analyzed by paired *t*-test. $P < 0.05$ was considered statistically significant.

RESULTS

A total of 109 of the 120 subjects completed the study. The patient compliance rates for the four lifestyle interventions (A, B, C, and D) were 57.79%, 60.55%, 64.22%, and 75.23%, respectively. Among the 109 subjects, 80 received oral hypoglycemic drugs or insulin, and 28 did not use any hypoglycemic drugs. Among the subjects who

received hypoglycemic drugs, the dose was adjusted (reduced by approximately 20%) 2 to 3 times based on blood glucose in 54 (67.50%) patients and was tapered and discontinued in 5 (6.25%) patients within 3 mo, with no significant fluctuations in blood glucose after dose reduction and withdrawal.

After lifestyle interventions, various metabolic indicators such as waist circumference, BMI, fasting blood glucose, and blood pressure were significantly reduced ($P < 0.001$) (Table 1). Moreover, after lifestyle interventions, body composition (Table 2) and motor function (Table 3) improved significantly ($P < 0.001$).

DISCUSSION

With aging and lifestyle changes in China, DM has now become epidemic, and its prevalence increased from 0.67% in 1980[10] to 10.4% in 2013[11]. With the acceleration of urbanization, the improvement in living standards in rural areas, less physical activity due to mechanized planting, numerous risk factors for obesity and dyslipidemia due to unbalanced diets and poor lifestyles, and limited health resources and low levels of awareness in rural areas, the prevalence of DM is rising rapidly in rural areas. We conducted chronic disease screening in permanent rural residents aged 50 years or older from ten rural villages of Chaoshui Township from May to August 2019 (n = 896) and found that the prevalence of T2DM and pre-type 2 DM was 21.75%, the diagnosis rate was 60.03%, the undiagnosed rate was 39.97%, and the on-target rate was only 16.9%.

Several randomized controlled studies have shown that appropriate lifestyle interventions may delay or prevent T2DM in individuals with impaired glucose tolerance (IGT)[12-15]. After 10 years of follow-up, the benefits of DM prevention have been shown to remain despite some weight gain in the lifestyle intervention group[16].

The absorption of nutrients and the glycemic index (GI) are related to meal order, and high GI foods are associated with a more significant increase in postprandial blood glucose levels and more sustained hyperglycemia, which contribute to postprandial hyperglycemia and high insulin levels. Therefore, individualized diets based on digestive ability (pattern of gastric acid secretion) can ensure adequate nutrition and a low GI, while guiding meal order (vegetables and animal proteins first, followed by carbohydrates). Blood glucose starts to increase at 30 min after a meal, peaks at approximately 60 min after a meal, and then gradually decreases to the baseline level at 120 min after a meal. Therefore, any indoor or outdoor activity 30-120 min after a meal helps reduce postprandial blood glucose, fat synthesis, and glycogen storage through glucose consumption. By activating the nerve reflex pathway, reverse abdominal breathing increases visceral fat metabolism, and a reduction in visceral fat in liver cells and the greater omentum improves insulin resistance. Resistance exercise increases the quantity and strength of muscles, expels fat from muscles, and improves insulin resistance. Adult diabetes patients should engage in resistance exercise 2 to 3 times (on nonconsecutive days) per week[17], with no strict restriction on the duration of strength training, the effect of which is determined by the load. Resistance exercise with a heavier load is more effective for improving blood glucose levels and strength; however, it is recommended that individuals should engage in resistance exercise (any intensity) throughout their lifetime to enhance strength, balance, and self-care[18].

The existing diet and exercise guidelines and medication adjustment standards are still at experimental stages and difficult to understand and implement. In this study, we "translated" these methods into plain language and content that is easy to implement in daily life. For example, we did not use medical terms such as energy (calorie), gastrointestinal, glucose load, exercise intensity, and heart rate changes; instead, we used easy-to-understand guidelines, such as food types (vegetables, carbohydrates, meat, egg, and milk), intake order, postprandial household chores and free outdoor activities, and a medication dose reduction of 20% in the presence of stable plasma glucose levels. Our 3-year pilot study demonstrated the effectiveness of and good patient compliance with this method.

This is the first study to apply real-life lifestyle interventions to real-world patients to investigate the effects of this method on waist circumference, blood glucose, and motor function in overweight DM patients aged 50 years or older. The results showed that the patient compliance rates for the four lifestyle interventions were 57.79%, 60.55%, 64.22%, and 75.23%, respectively. Among the 80 subjects who received hypoglycemic drugs, the dose was reduced 2 to 3 times to 40% to 60% of the original dose in 54 (67.5%) patients and was discontinued in 5 (6.25%) patients within 3 mo, with no significant fluctuations in blood glucose after dose reduction and withdrawal. After the intervention, fasting blood glucose and HbA1c were significantly reduced ($P < 0.001$). This study showed that real life lifestyle interventions significantly reduced

Table 1 Measurement and comparison of waist circumference, body mass index, blood pressure, fasting blood glucose, and glycosylated protein before and after lifestyle interventions

Value	Before intervention	After intervention	Paired *t*-test	
			t	*P* value
Waist circumference (cm)	97.83 ± 7.81	96.99 ± 7.65	10.02	< 0.001
BMI (kg/m^2)	29.20 ± 3.64	28.52 ± 3.21	5.82	< 0.001
SBP (mmHg)	150.53 ± 21.07	141.15 ± 17.49	6.03	< 0.001
DBP (mmHg)	87.14 ± 13.52	84.36 ± 10.55	1.84	< 0.001
Fasting blood glucose (mmol/L)	11.22 ± 2.78	8.40 ± 1.81	6.21	< 0.001
Glycosylated hemoglobin (%)	8.94 ± 1.92	8.06 ± 1.32	5.87	< 0.001

BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

blood glucose and the use of hypoglycemic drugs and improved lifestyle, with good patient compliance.

This study showed that after lifestyle interventions, waist circumference, BMI, fat percentage, and fat distribution changed significantly ($P < 0.001$), suggesting that interventions reduced visceral fat and fundamentally improved insulin resistance due to abdominal obesity. Moreover, the lower extremity nerve response rate and lower extremity response time changed significantly ($P < 0.001$), suggesting that the interventions improved muscle strength and mass, which helped to improve insulin resistance and enhance cardiopulmonary function.

In this study, lifestyle interventions were based on precise data from the Human Metabolism Analyzer and were easy to implement with significant effects, including a decrease in potential risks of high-intensity exercise and improvement in quality of life, without hunger associated with a ketogenic diet. This is the first study in which reverse abdominal breathing was applied as an intervention for abdominal obesity and to prevent and treat T2DM, with good patient compliance.

Further research is needed on the lifestyle interventions used in this study to investigate the molecular mechanism of improved insulin resistance and the duration of improved insulin resistance, in order to provide more evidence to fundamentally resolve insulin resistance in patients with T2DM.

Table 2 Measurement and comparison of body composition before and after lifestyle interventions

Value	Before intervention	After intervention	Paired *t*-test	
			t	*P* value
Lower limb muscle distribution coefficient (Phantom ratio)	0.92 ± 0.24	1.07 ± 0.23	-10.64	< 0.001
Fat distribution/ calculation (g/cm)	171.37 ± 50.62	167.43 ± 49.99	3.88	< 0.001
Percentage/calculation of fat (%)	36.28 ± 8.23	35.57 ± 8.50	4.63	< 0.001

Table 3 Measurement and comparison of nerve and body reaction velocity before and after lifestyle interventions

Value	Before intervention	After intervention	Paired *t*-test	
			t	*P* value
Nerve response velocity of left lower limb (s)	0.24 ± 0.15	0.23 ± 0.14	4.84	< 0.001
Nerve response velocity of right lower limb (s)	0.25 ± 0.09	0.24 ± 0.09	6.76	< 0.001
Body reaction speed of left lower limb (s)	0.44 ± 0.16	0.39 ± 0.14	9.56	< 0.001
Body reaction speed of right lower limb (s)	0.45 ± 0.17	0.41 ± 0.14	9.30	< 0.001

ARTICLE HIGHLIGHTS

Research background

The prevalence rate of type 2 diabetes mellitus (T2DM) in rural areas is increasing rapidly, and lifestyle interventions can effectively reduce blood glucose in patients with T2DM, but the current diet and exercise guidance remains at the laboratory level, which is difficult for subjects to understand and operate. Existing exercise and diet management regimens are associated with two problems: Unclear exercise methods and schedule can lead to exercise injuries, hypoglycemia, and poor results; and poor compliance can lead to poor long-term hypoglycemic effects and incomplete correction of glucose metabolism disorders. It is urgent to refine diet and exercise programs and improve their effectiveness and patient compliance. The Human Metabolism Analyzer accurately analyzes the effects of food types, food intake sequence, and activity/exercise mode and schedule on the production and consumption of blood glucose, thereby providing simple and effective interventions for patients with T2 DM. Our small clinical observation pilot study demonstrated good clinical efficacy of real-life lifestyle interventions on T2DM, as well as on pre-type 2 DM, simple obesity, and polycystic ovary syndrome.

Research motivation

To turn the scientific data provided by the Human Metabolism Analyzer into life-oriented intervention measures, and apply the life-oriented intervention measures to the prevention and treatment of T2DM to observe its effectiveness and compliance, so as to provide effective and continuous intervention measures for the prevention of T2DM in rural residents.

Research objectives

The main goal was to observe the effect of life-style interventions on the metabolic indexes of rural patients with T2DM, and the secondary goal was to observe the compliance with this method.

Research methods

Ten natural villages in Chaoshui Town, Penglai City, Shandong Province were randomly selected to screen the villagers over 50 years old. In the natural village as a group, 12 patients with type 2 DM were randomly selected from each group as the study subjects, and all the subjects were given lifestyle interventions and medication guidance. Lifestyle interventions included changing meal order (A), postprandial activity (B), anti-resistance exercise (C), and anti-abdominal breathing (D). DM education was carried out at least once a month, and a weekly telephone follow-up was conducted to supervise exercise and diet. Before and 3 mo after intervention, the differences of waist circumference, blood pressure, body mass index (BMI), motor function, body composition, blood glucose, and glycosylated glycosylated protein were compared, and the compliance of patients and the adjustment of hypoglycemic drugs were evaluated. All the data were processed with SPSS17.0 statistical software, and the data of waist circumference, BMI, blood glucose, HbA1c, blood pressure, motor function, and body composition before and after intervention were analyzed by paired *t*-test. Compared with the current lifestyle intervention methods for the treatment of T2DM, this study has achieved innovative breakthroughs in the following four aspects: (1) The way T2DM patients ate was defined. Based on each person's digestive ability (gastric acid secretion pattern), the diet structure that each subject was suitable for was determined, and the diet order of the subjects

was guided at the same time. It not only ensured that the subjects did not have to go on a diet and had adequate nutrition, but also ensured the stability of postprandial blood glucose and the reduction of fat synthesis; (2) The activity and movement mode was defined. One hundred and twenty minutes of indoor and outdoor activities after a meal is the most effective activity or exercise time to reduce postprandial blood sugar and control fat synthesis. Anti-resistance exercise not only increases the number and strength of muscles, but also expels fat from muscles, which is the main measure to reduce insulin resistance; (3) The quantitative principle of gradually reducing the dose of insulin and other drugs was clarified. The subjects were instructed to reduce the drug dose step by step based on the blood glucose values monitored every day, so as to achieve the goal of gradually reducing the drug dose or even stopping the drug under the condition of stable blood glucose; and (4) Scientific methods were used in daily life. In this study, all these methods were transformed into life language and content that were easy to operate in daily life. The current pre-research work has proved the effectiveness and good compliance of this method.

Research results

One hundred and eight subjects completed the experiment. The compliance rates of A, B, C, and D lifestyle interventions were 57.79%, 60.55%, 64.22% and 75.23%, respectively. Fifty-four (67.50%) subjects who received hypoglycemic drugs reduced their blood sugar 3 times within 3 mo according to their blood sugar, and five (6.25%) cases gradually stopped using hypoglycemic drugs, and there was no significant fluctuation in blood sugar after drug reduction and withdrawal. After lifestyle intervention, the waist circumference, BMI, fasting blood glucose, and HbA1c decreased significantly ($P < 0.001$), and the motor function and body composition improved significantly ($P < 0.001$). The lifestyle intervention measures used in this study come from the accurate data obtained by the Human Metabolism Analyzer, which is effective, simple, and easy, without the hunger of ketogenic diet, and reduces the harm that high-intensity exercise may bring. For the first time, anti-abdominal breathing was used in the intervention of abdominal obesity and the prevention and treatment of DM with high compliance. Further research on the lifestyle intervention measures used in this study is still needed to clarify the molecular mechanism of improving insulin resistance and the duration of insulin resistance improvement, so as to provide more evidence for the fundamental solution of insulin resistance in patients with T2DM.

Research conclusions

In the past, the lifestyle intervention measures for the prevention and treatment of T2DM only stayed in the laboratory stage, which was difficult for patients to master and their compliance was not high. This study uses the scientific data provided by the Human Metabolism Analyzer to transform all these methods into life language and content that are easy to operate in daily life. Specifically, it includes defining the diet, activity and exercise patterns, and the quantitative principle of gradually reducing the dose of insulin and other drugs, so as to truly achieve the daily life of scientific data. It is assumed that this method can effectively control the metabolic indexes of patients with T2DM, reduce the use of hypoglycemic drugs, and improve the compliance of patients. The results showed that lifestyle intervention could significantly improve the metabolic indexes such as waist circumference, BMI, blood pressure, HbA1c, body composition, exercise function and so on. Some patients could gradually reduce or stop using hypoglycemic drugs, and lifestyle intervention in T2DM had good compliance. This study realized the experimental hypothesis and provided effective and simple lifestyle intervention measures for rural T2DM patients.

Research perspectives

The lifestyle intervention measures used in this study come from the accurate data obtained by the Human Metabolism Analyzer, which is effective, simple, and easy, without the hunger of ketogenic diet, and reduces the harm that high-intensity exercise may bring. For the first time, anti-abdominal breathing was used in the intervention of abdominal obesity and the prevention and treatment of DM with high compliance. Further research on the lifestyle intervention measures used in this study is still needed to clarify the molecular mechanism of improving insulin resistance and the duration of insulin resistance improvement, so as to provide more evidence for the fundamental solution of insulin resistance in patients with T2DM.

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