تأثير بذور الحلبة في المقاومة للأنسولين لدى مرضى الداء السكري من النمط 2 المعالجين بالميتفورمين والغليبورايد

رفاه منافيخي

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مُلخَّص

يُعدّ الدَّاء السكَّري من النَّمط 2 مرضاً استقلابياً يتَّسم بالفشل في استتباب الغلوكوز مع اضطراب في استقلاب الكربوهيدارت، الدّهون والبروتينات ناتج عن المقاومة للأنسولين. بالرغم من توفر الأدوية اللازمة للعلاج إلا أنّ الاهتمام بالعلاجات الطبيعيَّة ازداد في السنوات الأخيرة بهدف دراسة تأثير العلاج الطبيعي في تعديل استجابة المريض للعلاج. الهدف من هذه الدراسة هو تقييم تأثير الحلبة في خفض المقاومة للأنسولين من خلال حساب مستويات مُشعر TG:HDL-C عند مرضى السكَّري من النمط 2 المُعالَجين بالميتفورمين والغليبورايد. استمرّت الدراسة لمدّة 8 أسابيع، حيث تمَّ تقسيم المرضى عشوائياً إلى مجموعتين: المجموعة F تمَّ إعطاؤهم بذور الحلبة بشكلها المنقوع في الماء المغلي بالمُشاركة مع معالجتهم الدَّوائيَّة، والمجموعة الشَّاهدة C تمَّ إعطاؤهم المُعالجة الدَّوائيَّة بمفردها. قمنا بحساب مشعر TG:HDL-C في بداية الدراسة وفي نهاية الدراسة. أظهرت النتائج انخفاضاً في مستويات مشعر TG :HDL-C في الأسبوع 8 بالمقارنة مع الأسبوع 0 دون وجود دلالة إحصائية، وبالتَّالي فإنَّ بذور الحلبة قد تساهم في خفض المقاومة للأنسولين عبر خفض مشعر TG:HDL-C ولذا فقد تلعب دوراً جيداً في تدبير الدَّاء السكَّري من النَّمط 2، كما قد تُنقص خطر الإصابة بالمرض القلبي الوعائي.

الكلمات المفتاحية :الحلبة، الداء السكَّري من النمط 2، المقاومة للأنسولين، مشعر TG:HDL-C.

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Effect of Fenugreek Seeds on Insulin Resistance in Type 2 Diabetics Receiving Metformin and Glyburide

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Abstract

Type 2 diabetes mellitus is a metabolic disorder characterized by failure of glucose homeostasis with disturbance of carbohydrate, fat and protein metabolism caused by Insulin Resistance (IR). To overcome this disturbance, management plans have been developed based on several foundations which involved changing lifestyle and treating with antidiabetic agents. In recent years, the interest in natural remedies increased and recently the researches were headed to study the effect of drug - herbs interactions in modifying the patient's response to treatment, that these herbs may improve the effects of some medications.

The aim of this study was to evaluate the effects of fenugreek seeds on the assessment of Insulin Resistance by calculating an index depending on lipid profile of patients with type 2 diabetes who were treated with metformin and glyburide. The study lasted for 8 weeks, and the patients were divided randomly into 2 groups. Group F was given fenugreek seeds soaked in boiled water in combination with their treatment, and the control group (C) received their treatment alone. Triglyceride (TG) and high-density lipoprotein cholesterol (HDL-C) were measured. The IR index (TG:HDL-C ratio) was calculated at the beginning of the study (week 0) and at the end of the study (week 8).

Our results showed an insignificant decrease in TG:HDL ratio, in group F at week 8 in comparison with the baseline values at week 0.

Conclusively, fenugreek seeds may help in decreasing insulin resistance by reducing the value of IR index (TG:HDL-C ratio) or may improve the cell in response to insulin, so fenugreek may be a good addition in the management of patients with type 2 diabetes, and could decrease the risk of coronary heart disease (CHD).

Keywords: fenugreek, Insulin resistance, lipid profile, TG/HDL ratio, type 2 diabetes.

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1- INTRODUCTION

Diabetes mellitus is a metabolic disorder of multiple etiology characterized by chronic hyperglycemia resulting from defects in insulin action due to phenomena of Insulin resistance (IR). Abnormalities in the metabolism of carbohydrate, protein, and fat are also present [1, 2]. If blood glucose levels remain high over a long period of time, this can result in long term damage of organs such as kidneys, eyes, nerves, heart and blood vessels. Complications in some of these organs can lead to death [3-5].

Management of diabetes mellitus constitutes lifestyle management, exercise, weight control and antihyperglycemic drugs like sulfonylureas, biguanides, alpha-glucosidase inhibitors, thiazolidinediones, and meglitinide [1]. The prevalence of type 2 diabetes (T2D) is increasing globally [6, 7]. It is anticipated that by the year 2025, over 75% of all people with diabetes will belong to the developing countries. In Syria, diabetes mellitus is one of the most common diseases, as the diabetic patients comprise 10% of population [8].

The secretion of insulin into the blood in response to the blood glucose concentration is the primary mechanism of glucose homeostasis. Insulin binds to its receptor, which starts many protein activation cascades. These include translocation of Glut-4 transporter to the plasma membrane and influx of glucose, glycogen synthesis, glycolysis and triglyceride synthesis.

Insulin resistance (IR) is the major cause of type 2 diabetes, so the Homeostasis Model Assessment for Insulin Resistance (HOMA-IR) index is widely used as a measure of insulin resistance in adults and has also been validated in children and adolescents. However, the HOMA calculations require measurement of plasma fasting glucose and insulin, which is expensive and very delicate. Therefore, there is a need for a diagnostic test for predicting insulin resistance (IR) that is easy to carry out, offers good precision and is of low cost. Determination of triglyceride (TG) and High Density Lipoprotein-Cholesterol (HDL-C) levels is routine tests which are inexpensive compared to insulin assay, and they also can be tested using portable analyser in clinical setting [9]. Previous studies reported conflicting findings on the usefulness of the triglyceride to HDL-C ratio (TG:HDL-C ratio) as index of IR and it is ethnicity-dependent. In individuals with insulin resistance, TG levels increased while HDL-C

levels decreased. A higher ratio would represent a poorer health status because there is a large amount of circulating fats in the blood stream and/or a low amount of healthy cholesterol. A TG:HDL-C ratio of ≥ 3 has been shown to be closely correlated to insulin resistance. The TG:HDL-C ratio has also been shown to be an independent risk factor for coronary heart disease (CHD) [9].

According to the global tendency for using natural remedies in order to reduce the side effects associated with drugs, we investigated in this study the role of fenugreek in combination with antidiabetic agents in controlling various bioclinical parameters in patients with T2D [10]. The use of natural substances has become more extensive over the past few years, motivated certainly by the faith that they may have fewer side effects as compared to pharmaceuticals and by their effortless accessibility to the populace without prescriptions or visits to the health providers [11], and more interestingly as the natural substances may enhance the effect of some medications leading to reducing their doses when they are taken concurrently [12].

More than 400 traditional plant treatments for diabetes mellitus have been recorded, but only a small number of these have received scientific and medical evaluation to assess their efficacy [13].

There are many active substances in fenugreek that are responsible for its various effects. The most important of these active ingredients are: soluble fibers, 4-hydroxy isoleucine, saponins and comarins [14].

2- AIM of RESEARCH

The present study is focusing on the effects of fenugreek on lipid profile by calculating TG:HDL ratio in order to evaluate the insulin resistance in T2D patients receiving both metformin and glyburide, and this is the first time that the fenugreek is studied to assess the TG:HDL ratio along with the combination of two antidiabetic agents (metformin and glyburide).

3- MATERIALS AND METHODS

Kits used in this study: Kits for the assay of HDL cholesterol and TG were purchased from BioSystems (Reagents & Instruments) Barcelona, Spain and fenugreek seeds were purchased from local market.

3-1- Inclusion criteria of patients

- Patients with diagnosed type 2 diabetes mellitus who were receiving metformin and glyburide

- Patients of both sexes
- Patients aged between 30 to 70 years

3-2- Exclusion criteria of patients

- Patients with type 1 diabetes mellitus
- Patients having a history of myocardial infarction
- Patients with a history of hepatic or renal failure
- Pregnant or lactating women

This study lasted for 8 weeks. The research protocol has been approved by the University of Aleppo, Syria. Patients with previously diagnosed type 2 diabetes mellitus (n = 98), visiting the Center of Comprehensive Medical Clinics in Aleppo, were divided randomly into two groups: F and C. Group F (fenugreek group) was comprised of 53 patients who were given fenugreek seeds soaked in boiled water at a dose of 10 g/day after main meal in combination with their treatment (500 mg metformin once a day and 4 mg glyburide twice a day). Group C (control group) was comprised of 45 patients who were given only the treatment that they were previously receiving (500 mg metformin once a day and 4 mg glyburide twice a day).

On the first day of the study (week 0), venous blood was taken. After centrifugation, plasma was used to quantify: triglyceride (TG) using the enzymatic method and high-density lipoprotein cholesterol (HDL-C) using the precipitation method. Then the TG:HDL-C ratio was calculated. On the final day of the study (week 8), venous blood was taken and the previous mentioned steps were followed.

4- RESULTS AND DISCUSSION

4-1- Effect of administration of fenugreek seeds with metformin and glyburide on IR index (TG:HDL-C ratio):

Due to the disturbed levels of glucose in T2D patients, hyperlipidemia could occur as a secondary complication [15]. So we measured the parameters of lipid profile of T2D patients. Table 1 shows the change in triglyceride and HDL-C levels in week 0 and week 8 in fenugreek group (F) and in control group (C). The results showed significant decrease in triglyceride levels in group F from 215.82 ± 20.67 mg/dl at week 0 to 152.58 ± 13.53 mg/dl at week 8 ($p < 0.05$). This decrease was more in fenugreek group than in control group where the triglyceride concentration was decreased from 181.65 ± 9.39 mg/dl at week 0 to 146.96 ± 14.08 mg/dl at week 8, and this reduction was not statistically significant ($p > 0.05$). The comparison

between both groups showed that fenugreek seeds could contribute to antidiabetic agents (metformin and glyburide) in lowering TG levels.

Table 1. also shows the change in HDL cholesterol levels at week 0 and week 8 in fenugreek group (F) and in control group (C). The results showed no significant change in HDL-C levels ($p > 0.05$) at week 0 and week 8 in both groups [16].

To assess the IR in T2D patients we considered the IR index (TG:HDL-C ratio) of ≥ 3 as insulin resistance [9]. The measurements of TG:HDL-C ratio showed that in both groups IR was (TG:HDL-C ratio ≥ 3). There was a decrease in TG:HDL-C ratio in fenugreek group (F) without statistical significance ($p > 0.05$) (Fig 1).

Table 1. Changes in mean TG, HDL and TG:HDL-C ratio in week 0 and week 8 in patients receiving fenugreek seeds with metformin and glyburide (group F), and patients receiving only metformin and glyburide (group C).

	Group F		Group C	
	Mean ± SEM Week 0	Mean ± SEM Week 8	Mean ± SEM Week 0	Mean ± SEM Week 8
TG mg/dl	215.82± 20.67	152.58±13.53*	181.65 ± 9.39	146.96 ±14.08
HDL-C mg/dl	44.68 ± 2.41	42.40 ± 2.70	46.47 ± 2.46	43.10 ± 3.13
TG/HDL-C	5.67±0.92	3.92±0.48	4.91±0.5	3.52±0.49

* $P < 0.05$

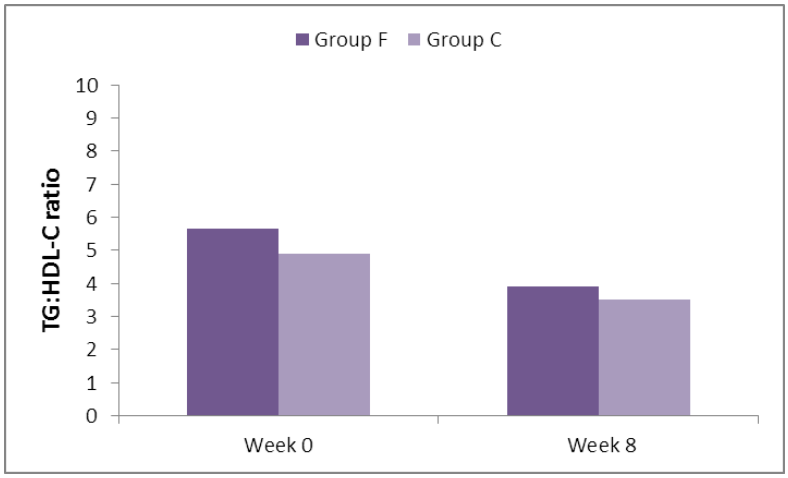

Figure 1. Changes in mean TG:HDL-C ratio in week 0 and week 8 in patients receiving fenugreek seeds with metformin and glyburide (group F), and patients receiving only metformin and glyburide (group C).

Our results are in agreement with other clinical trials as TG levels were significantly reduced [17], and no change was observed in HDL-C levels [18].

The difference in effect intensity of fenugreek seen in different studies may be attributed to the differences in fenugreek preparation, doses or duration of study.

The probable mechanism of the antilipidemic effect of fenugreek could be contributed to galactomannan compound (soluble fiber in fenugreek), which is believed to act as selective inhibitor of intestinal lipase and steroidal saponins interacting with bile salts in the G tract [19].

These results demonstrate that fenugreek could improve the lipid profile, which is frequently affected in patients with T2D and may help in decreasing insulin resistance, thus it could improve patients' response to their treatment.

5- CONCLUSION

Clinical studies which evaluate the effects of fenugreek on patients with T2D treated with antidiabetic agents are limited. Our study is supporting these studies, and the present results showed that fenugreek seeds had positive effect on improving lipid profile in patients with T2D and may help in decreasing insulin resistance and the risk of coronary heart disease (CHD).

More clinical studies about the role of fenugreek with antidiabetic agents in patients with T2D are recommended to confirm the positive effects of fenugreek in order to obtain potential reduction in drugs doses, thus reducing side effects associated with them and delaying the shift to insulin treatment in type 2 diabetics.

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