International Archives of Medical Research 12:2 (2020) 1-6

ORIGINAL RESEARCH PAPER

Evaluation of The Effect of Insulin Resistance on Pancreatic Exocrine Functions in Obese Patients With Fecal Elastase-1 Levels

Geliş Tarihi: 16.11.2020, Kabul Tarihi: 20.12.2020

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Abstract

Objective: *We aimed to show whether insufficiency develops in pancreatic exocrine functions since the insulin resistance period or not.*

Method: *We measured the anthropometric parameters, blood glucose profile parameters and fecal elastase-1 levels of a total of 65 obese patients with 35 insulin resistance and 30 without insulin resistance. Body mass indexes (BMI) Homeostasis of model assessment insulin resistance indexes (HOMA-IR) were calculated. Exocrine pancreatic insufficiency (EPI) was diagnosed with a fecal elastase-1 concentration (FE1) of less than 200 mg/g (ELISA).*

Results**:** *A statistically significant difference was not observed between the mean FE-1 levels between the groups. (p> 0.05). No statistically significant difference was observed between the distribution of mild and severe low FE-1 levels of the IR and Non-IR groups (p> 0.05) Table 3.*

Conclusion: *Our study revealed that the presence of insulin resistance does not cause any change in FE-1 levels in obese patients.*

Keywords: *pancreatic exocrine function, insulin resistance, fecal elastase-1*

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Introduction

While endocrine and exocrine functions are known as two separate functions of the pancreas, the possible link between these two functions within the same anatomy has always attracted attention among researchers[1]. Therefore, studies have been carried out to show that exocrine pancreatic insufficiency (EPI) may occur in patients with diabetes mellitus (DM)[2]. However, the mechanism has not been fully revealed.

There are studies showing the development of EPI in DM patients[2,3] as well as studies showing that DM develops secondary to physical damage in the pancreas after acute or chronic pancreatitis[4]. DM that develops after pancreatitis is even referred to as pancreatic DM[5].

In the diagnosis of EPI, which should be kept in mind in prolonged dyspeptic complaints, difficult and invasive methods were previously used. The diagnosis is made with low fecal elastastasis -1 (or pancreatic elastase-1) (FE-1) currently, which is a proteolytic enzyme that is checked by enzyme-linked immunosorbent assay (ELISA) method[6].

With the increasing prevalence of obesity all over the world, deterioration in blood glucose regulation and insulin resistance are more common in individuals. We determined that the relationship between DM and the development of EPI has been investigated many times, but there is no data for the period in which IR, also known as the pre-DM period, developed.

Our aim in this study was to show whether EPI developed during the insulin resistance period, which is known as the pre-DM period, and to show whether there is a connection between these two functions of the pancreas from the early damage period of the pancreas.

Method

Data of 65 obese patients aged 16-69 who applied to our internal medicine outpatient clinics with dyspeptic complaints between January 2018 and June 2019 and were evaluated for pancreas enzyme deficiency were retrospectively evaluated. These 65 patients were divided into two groups according to the presence of insulin resistance, as the insulin-resistant group (IR) and the non-insulin-resistant (Non-IR) group.

Patients with a history of acute or chronic pancreatitis, diabetes mellitus,malignancies, and pregnants were not included in the study. In addition, patients with a history of alcohol consumption of >20 g/day and those receiving hormone replacement therapy, kortikosteroid or antidiabetic medication were also excluded.

The study was approved by the Medipol University Ethics Committee (10840098-604.01.01-E.15454) and conducted in accordance with the Declaration of Helsinki.

Laboratory and clinical measurements

Blood samples taken from the patients after 10 to 12 hours of fasting were analyzed. Laboratory data, including the levels of serum glucose, insulin and HbA1c were recorded. Height, weight and waist circumference measurements of all participants were made. Fecal elastase was measured by using an enzyme-linked immunosorbent assay (ELISA) and the presence of fat in stool was assessed using the steatocrit.

Definitions

Diabetes mellitus

The diagnosis of diabetes mellitus was defined by the presence of any of the following items using the criteria updated in American Diabetes Association 2020[7].

1. Fasting blood glucose of 126 mg / dl or higher
2. HbA1c value of 6.5% or above
3. Random blood glucose> 200

Obesity

Body mass index (BMI) is calculated as measured body weight (kg) divided by measured height squared (m^2). A BMI over 30 was defined as obesity[8].

Insulin resistance

Homeostasis model of assessment (HOMA) was used for the diagnosis of insulin resistance [9]. Insulin resistance index (HOMA-IR) was calculated according to the formula: fasting insulin (microU/L) x fasting glucose (mg/dL) /405. HOMA-IR> 2.5 was accepted as insulin resistance[9].

Pancreatic enzyme insufficiency

FE-1 test was used to evaluate exocrine pancreatic function. The reference concentration for FE-1 in feces was as follows[10]:

1. Normal exocrine pancreatic function: presence of enzyme> 200µg / g in stool
2. Exocrine pancreatic dysfunction: presence of enzyme <200µg / g in stool

Statistical analysis

The conformity of the data to normal distribution was tested with the Shaphiro wilk test, Student t test was used to compare normally distributed features in individuals with and without insulin resistance, and Mann Whitney u test was used to compare non-normally distributed features in individuals with and without insulin resistance. Relationships of categorical variables were analyzed

using Pearson and Exact Chi-square tests. As descriptive statistics, mean ± standard deviation for numerical variables, number and% values for categorical variables were given. SPSS Windows version 24.0 package program was used for statistical analysis and $p < 0.05$ was considered statistically significant.

Results

The demographic and anthropometric characteristics of the participants are presented in Table 1. There was no significant difference between the groups in terms of age, height and BMI ($p > 0.05$). However, a statistically significant difference was observed between the gender distributions of IR and Non-IR groups ($p = 0.024$). While the number of male patients is high in the IR group, the number of female patients is higher in the Non-IR group. The mean waist circumference and body weight of the IR group were statistically significantly higher than the Non-IR group (p values respectively; $p = 0.0001$, $p = 0.045$).

The mean glucose, insulin, HOMA-IR values of the IR group were found to be statistically significantly higher than the Non-IR group ($p = 0.0001$). The average HbA1c values of the IR group were found to be statistically significantly higher than the Non-IR group ($p = 0.014$) Table 1.

A statistically significant difference was not observed between the mean FE-1 levels between the groups. ($p > 0.05$) Table 1. In addition, no statistically significant difference was observed between the distribution of FE-1 levels of the IR and Non-IR groups ($p > 0.05$) Table 2.

The correlation coefficient between the level of FE-1 was examined. No statistically significant relationship was found ($p = 0.312$) (Figure 1).

Discussion

Simultaneous dysfunction can be seen in both functions of the pancreas, which has both endocrine and exocrine functions. As DM can be seen after pancreatitis[4], there have been studies showing that both type 1 and 2 DM patients develop EPI[1,3]. Many theories have been proposed regarding how EPI develops in DM[1].

In the study conducted by Yilmaztepe et al. with 32 diabetic patients and 12 healthy controls, it was found that 28% of type 2 diabetic patients had a decrease in exocrine function and no decrease was observed in control subjects[1]. In our study, although the rate of EPI in the IR group was determined to be 25.7%, there was no statistically significant difference between the rate of EPI in the Non-IR group (10%). This may be because both groups in our study included obese patients and were not

compared with patients with normal BMI. In previous studies, the incidence of EPI was reported to be between 5.4%[12] and 56.7%[13], consistent with our results (35.7%).

Since gender distributions were not homogeneous in both groups in our study, it should be considered that FE-1 levels may differ between genders. This may be the reason why there was no difference in FE-1 levels between the groups.

Since our study was not designed prospectively, there is no data regarding the presence of malabsorption in these patients. The gender distributions were not homogeneous in both groups in our study.

While there are many studies investigating EPI in DM, it is the first study evaluating EPI in insulin resistance known as the period of pre-DM. In this respect, it is the strength of our work that it sheds light on prospective studies.

In conclusion, our study revealed that the presence of insulin resistance does not cause any change in FE-1 levels in obese patients. However, larger studies should be planned in patients with insulin resistance and obesity in which pancreatic exocrine dysfunction could potentially be seen, compared with healthy controls with larger participation.

Authors' contributions: Both authors have contributed significantly to the conception, design, acquisition, analysis and interpretation of the data in this study. All of them were involved in the preparation of the article or its critical revision for important intellectual content, and everyone gave the final approval of the version to be published.

Ethical Statement: All authors declare that the study was conducted in accordance with the World Medical Association Helsinki "Ethical Principles for Medical Research Containing Human Subjects". The study was approved by the Medipol University Ethics Committee (10840098-604.01.01-E.15454) and conducted in accordance with the Declaration of Helsinki.

Conflict of Interest: The authors did not report any conflicts of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

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