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Comparison of the effects of impaired fasting glucose and impaired glucose tolerance on diabetic development risks on HbA1c levels: A retrospective study

Bozulmuş açlık glukozu ve bozulmuş glukoz toleransının diyabet gelişim riski üzerine etkilerinin HbA1c düzeyleri üzerinden karşılaştırılması: Retrospektif çalışma

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Abstract

Aim: The process between normal glucose metabolism and diabetes is called the prediabetes period. This period is impaired fasting glucose (IFG), impaired glucose tolerance (IGT) or glycosylated hemoglobin A1c (HbA1c) level of 5.7-6.5%. IFG, IGT or IFG+IGT, shows increased risk of developing diabetes. The aim of this study is to compare the risk levels of diabetes development between glucose metabolism disorders.

Methods: Patients who underwent oral glucose tolerance test (OGTT) and whose HbA1c values were measured before and after the test on a quarterly basis and did not have diabetes in 2016, were scanned through the automation system and taken into study. Patients with HbA1c levels between 5.7 and 6.4% were evaluated as pre-diabetic, and an increase in the HbA1c levels in these patients from 5.7% to 6.4% was considered to increase the risk of developing diabetes. Patients were divided into three groups according to the presence of isolated IFG, isolated IGT and IFG + IGT. Patients with IFG were group 1, patients with IGT were group 2, and patients with IFG + IGT were group 3. Correlation analysis was performed between the groups on HbA1c levels.

Analyzes were performed using the SPSS 22.0 program. Mann Whitney U Test was used for descriptive statistical methods as well as for non-normal distribution of measured values. Significance was evaluated at $p < 0.05$.

Results: In the study period, 706 patients who had OGTT in our hospital and who had HbA1c levels before and after OGTT on a quarterly basis were determined. The number of patients in Group 1 was 272; in group 2 was 222 and in group 3 was 212. Compared to the HbaA1c levels of groups, the risk of diabetes development in Group 1 was statistically low compared to group 2 and 3 ($p<0.001$). No statistically significant differences were detected between group 2 and 3 ($p=0.381$).

Conclusions: As a result of our study, patients with isolated IGT and IFG+IGT were found to be significantly higher than patients with an isolated IFG of diabetes development risks. There was no apparent difference between those with an isolated IGT and the IFG+IGT.

Keywords: Prediabetes, Impaired Fasting Glucose, Impaired Glucose Tolerance

Öz

Amaç: Normal glukoz metabolizması ile aşikar diyabet arasındaki süreç prediyabetik dönem olarak adlandırılır. Bu dönem bozulmuş açlık glukozu (BAG), bozulmuş glukoz toleransı (BGT) veya glikozillenmiş hemoglobin A1c (HbA1c) düzeyinin %5,7-%6,5 olmasıdır. BAG, BGT veya BAG+BGT artmış diyabet gelişim riskini gösterir. Bu çalışmanın amacı glukoz metabolizması bozukluklarının diyabet gelişim risk düzeylerini karşılaştırmaktır.

Yöntemler: 2016 yılı içinde oral glukoz tolerans testi (OGTT) yapılan, test öncesi ve sonrası üç aylık dönemde HbA1c değerleri ölçülen ve diyabet tanısı almamış hastalar, otomasyon sistemi üzerinden tarandı ve çalışmaya alındı. HbA1c düzeyi %5,7-6,4 arasında olan hastalar prediyabetik olarak değerlendirildi ve bu hastaların kendi içinde HbA1c düzeylerinin %5,7'den %6,4'e doğru artışı diyabet gelişim riskinde de artış kabul edildi. Çalışma hastaları izole BAG, izole BGT ve BAG+BGT varlığına göre üç gruba ayrıldı. İzole BAG saptanan hastalar grup 1'i, izole BGT saptanan hastalar grup 2'yi ve BAG+BGT saptanan hastalar grup 3'ü oluşturdu. Gruplar arasında HbA1c düzeyleri üzerinden korelasyon analizi yapıldı.

Çalışmada elde edilen bulgular değerlendirilirken istatistiksel analizler için SPSS 22.0 programı kullanıldı. Çalışma verileri değerlendirilirken tanımlayıcı istatistiksel metodların yanı sıra ölçüm değerlerinin normal dağılım göstermeyen karşılaştırmalarında Mann Whitney U Test kullanıldı. Anlamlılık $p<0,05$ düzeylerinde değerlendirildi.

Bulgular: Çalışma döneminde hastanemizde OGTT yapılan ve OGTT öncesi ve sonrası üç aylık dönemde HbA1c düzeyleri bakılan 706 hasta tespit edildi. Grup 1'deki hasta sayısı 272; grup 2'deki hasta sayısı 222, grup 3'deki hasta sayısı 212 olarak saptandı. Grupların HbaA1c düzeyleri karşılaştırıldığında Grup 1'de diyabet gelişim riskinin grup 2 ve 3'e göre istatistiksel olarak anlamlı düzeyde düşük olduğu görüldü ($p<0,001$). Grup 2 ve 3 arasında istatistiksel olarak anlamlı bir farklılık saptanmadı ($p=0,381$).

Sonuç: Çalışmamız sonucunda izole BGT'si ve BAG+BGT'si olan hastaların diyabet gelişim riskleri izole BAG'si olan hastalara göre anlamlı oranda yüksek bulunmuştur. İzole BGT'si olanlarla BAG+BGT'si olanlar arasında ise belirgin bir farklılık saptanmamıştır.

Anahtar Kelimeler: Prediyabet, Bozulmuş Açlık Glukozu, Bozulmuş Glukoz Toleransı

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Introduction

Diabetes mellitus is a health problem that increases day by day because of the incidence and widespread complications around the world. The number of diabetic patients is rapidly increasing, especially due to unhealthy and irregular diet in developed societies, diminished amount of daily physical activity, obesity and increase in elderly population. As of 2015, 193 million have not yet been diagnosed, with a total of approximately 415 million diabetics, and this number is projected to rise to 642 million by 2040 [1].

Diabetes is a chronic metabolic disease that requires continuous medical care in which the organism cannot make good use of carbohydrates, fats and proteins due to insulin deficiency or insulin deficiency defects. Diagnostic criteria for other disorders of diabetes and glucose metabolism are as follows.

Fasting plasma glucose (FPG)>126 mg/dl, plasma glucose>200 mg/dl on the 2nd hour in oral glucose test, randomized PG>200 mg/dl at any time and diabetic symptoms, >6.5% HbA1c levels may be diagnosed as apparent diabetes mellitus. The diagnosis of isolated impaired fasting glucose (IPG) can be made by measuring the FPG at 100-125 mg/dl with the second hour postprandial PG <140 mg/dl. The diagnosis of isolated impaired glucose tolerance (IGT) is FPG<100 mg/dl while second hour postprandial PG is between 140-199 mg/dl. In IFG+IPG FPG is 100-125 mg/dl and second hour postprandial PG is 140-199 mg/dl [2].

IFG and IGT are now considered prediabetes. The International Committee of Experts on Diabetes, HbA1c reported that individuals in the range of 5.7-6.4% (39-46 mmol/mol) were at high risk for diabetes and should be included in protection programs. Studies conducted in various societies have shown that the high risk group identified by HbA1c levels covers people with a higher glucose metabolism disorder than isolated IFG and IGT. Similar studies in the literature also support this opinion [2].

In this study; we aimed to evaluate whether there is any difference in the risk of developing diabetes among these patient groups by looking at HbA1c levels of patients with isolated IFG, isolated IGT and IFG+IGT who did not have diabetes.

Material and methods

A retrospective observational study was planned. The study was made in accordance with the Helsinki decoration. Patients who performed oral glucose tolerance test (OGTT) between 2016–2017 in our hospital were scanned through hospital automation system. Patients who had measured in HbA1c values before and after OGTT three month period and had not diagnosed with diabetes were taken in the study.

Patients with HbA1c levels between 5.7% and 6.4% were prediabetes evaluated and an increase in the HbA1c levels in these patients from 5.7% to 6.4% was considered to increase the risk of developing diabetes. Patients were divided into three groups according to the presence of isolated IFG, isolated IGT and IFG+IGT. Patients with IFG were group 1, patients with IGT were group 2, and patients with IFG+IGT were group 3. Correlation analysis was performed between the groups on HbA1c levels.

Analyzes were performed using the SPSS 22.0 (Statistical Package for the Social Sciences, Power IBM Software) program. When evaluating the study data, the descriptive statistical methods (mean, standard deviation) as well as the comparison of the measured values do not show the normal distribution of the Mann Whitney U Test were used. Significance was evaluated at $p < 0.05$.

Results

In the study period, 706 patients who had OGTT in our hospital and who had HbA1c levels before and after OGTT on a quarterly basis were determined. The number of patients in Group 1 was 272; in group 2 was 222 and in group 3 was 212. The mean HbA1c of the patients in group 1 was 5.84%, 6.03% of patients in group 2, 6.02% of patients in group 3.

Compared to the HbaA1c levels of groups, the risk of diabetes development in patients with IFG was statistically low compared to in patients with IGT and IFG+IGT ($p<0.001$). No statistically significant differences were detected between in patients with IGT and IFG+IGT ($p=0.381$) (Table 1).

Table 1: Comparison of HbA1c levels between groups

Patients with Isolated IFG and Isolated IGT			
	IFG	IGT	p [b]
HbA1c [a]	5.8 (4.8-7.0)	6.1 (5.0-7.8)	<0.001
Patients with Isolated IFG and IFG+IGT			
	IFG	IFG+IGT	p [b]
HbA1c [a]	5.8 (4.8-7.0)	6.0 (4.9-7.8)	<0.001
Patients with Isolated IGT and IFG+IGT			
	IGT	IFG+IGT	p [b]
HbA1c [a]	6.1 (5.0-7.8)	6.0 (4.9-7.8)	0.381

[a] mean (min-max), [b] Mann-Whitney U test

Discussion

As a result of our study, patients with isolated IGT and IFG+IGT were found to be significantly higher than patients with an isolated IFG of diabetes development risks. There was no apparent difference between those with an isolated IGT and the IFG+IGT.

The process between normal glucose metabolism and apparent diabetes is termed as the preterm period. The risk of developing diabetes increased significantly in this period. Cases that have been entered into a prediabetes; IFG, IGT and HbA1c levels are between 5.7% and 6.5% [3].

The IGT was first described in 1979, replacing borderline diabetes. For the first time in 1985, as a class of clinical glucose intolerance, it has taken its place in the World Health Organization (WHO) classification [4,5]. Finally, in 1997 and 1999, WHO and the American Diabetes Association (ADA) described carbohydrate metabolism disorders as one of the developmental processes, describing non-diabetic fasting hyperglycemia as IFG [6,7]. IFG has been described as not being sufficient for the diagnosis of diabetes, even though glucose is above normal glucose levels. This metabolic condition has been

adopted as a transition between normal glucose levels and the IGT. In people with IGT and IFG, HbA1c is usually found at normal levels or very mildly normal [8]. In our study; the HbA1c levels were found to be close to the lower limit in the pre-diabetic range in patients with isolated IFG, while isolated IGT and IFG+IGT were found to be significantly higher in the pre-diabetic range.

Prediabetes is an intermediate table showing that the risk of developing diabetics is high and poses a high risk not only for diabetes also for various other diseases. The IFG and IGT are associated with obesity, dyslipidemia and hypertension. Studies have shown that 5-10% of the pre-diabetic patients have passed the diabetic stage per year, although it varies according to the population characteristics and the prediabetes definition. The annual diabetes incidence for IFG is 6-9%, 4-6% for the IGT and 15-19% in the case of both [9]. In our study, this evaluation was not possible because the patients had no follow-up data. The incidence of diabetes in individuals with IGT and IFG+IGT can be interpreted as higher because the high risk of diabetes development will affect the incidence.

The IFG and the IGT are not equaled in metabolic and they also demonstrate different prevalence characteristics in societies. In different studies, the IGT was observed more frequently than the IFG. In our study, the number of IFG patients was found to be higher than the number of patients with IGT, in contrast to the patients who had OGTT within one year. The fact that our study was made in a limited number of people and only in people with OGTT may have resulted in this outcome. IFG and IGT can be observed separately, and can be observed together. In a study conducted in 2007; it has been observed that IFG and IGT disorders are rarely associated with each other in patients aged 40-74 years who were not previously diagnosed with diabetes [10]. In our study; the incidence of IFG+IGT is low compared to isolated IFG and isolated IGT, but is relatively close. It is not surprising that the incidence of IFG and IGT coincidence is high because we consider that our study experience is only for patients with OGTT and that the expectation of prediabetes and diabetes mellitus is high in these patients.

People in the pre-diabetic stage often advance go on type 2 diabetes, and these patients carry an important risk for various complications, such as in diabetics. When the insulin resistance in the liver and muscle tissue is not met with adequate insulin release from the beta cells of the pancreas, the hyperglycemia table emerges. So; the primary responsibility for the progression of prediabetes to diabetes is a progressive decrease in beta cell function. But; increasing insulin resistance also contributes to the reduction of beta cell backup, as it indirectly increases the need for insulin release from beta cells [11,12]. Therefore, treatments for prediabetes and diabetes should be protect beta cell function and can reduce insulin resistance.

The basis of treatment in pediatric patients should be to prevent development of diabetes, protect beta cells, prevent or delay micro and macrovascular complications. In many clinical trials, it is emphasized that the changes in lifestyle can prevent the progression of preterm diabetes. These lifestyle changes aim mainly; to regulate the nutrition, increase physical activity and gain weight control [13].

Various nutritional styles are known to have health benefits and thought that nutritional style changes can be effective in preventing diabetes growth. Some studies have been conducted to investigate the effect of nutrition on diabetes development. In one of these studies, a diet supplemented with olive oil was proposed for some of the patients and a diet rich in oil seeds was proposed for another group, while the third group was fed on a low-fat diet. After four years of follow-up, it was determined that the number of newly developed diabetes in the first two groups was lower than in the third group. In this study no weight difference was detected between the groups. Although these results suggest that the nutritional style may reduce the risk of diabetes development, there are some limitations that may disrupt the interpretation of the results. Moreover, it is not clear which content of nutrition is beneficial in this study [14,15].

Although an important part of insulin resistance and secretion is associated with genetic factors, it can be significantly changed by environmental and behavioral arrangements. Exercise is also one of them and various studies have shown that exercise can be beneficial in the prevention of diabetes [16]. In a meta-analysis, the risk of developing type-2 diabetes with physical activity has been examined and the mid-level physical activities such as walking in these studies have been compared with sedentary lifestyle. The result of these studies is that the risk of developing diabetes in physically active groups decreases considerably. This result suggests that exercise has a weight-independent effect on glucose metabolism [17]. A prospective study examined the effects of aerobic exercises with weight exercises. Patients; for 18 years, at least 150 minutes a week, they have applied a weight exercise or aerobic exercise. In the study, the patient group with sedentary lifestyle is included. In the group that performs both the weight exercise and the aerobic exercise, a significant decrease in the risk of diabetes development, according to the control group, has been recorded, in patients who combine both exercises, is observed to be the most significant decrease in the risk of diabetes development. This study; primarily has confirmed the positive effects of exercise in reducing the risk of diabetes development, also has shown that both weight exercises and aerobic exercises are effective in this respect [18].

In patients with diabetes, it is well known that permanent weight loss has a positive effect on glycemic control. Similarly in patients with prediabetes diet, exercise and weight loss is shown to prevent progression [19]. One of the most important studies is Finnish Diabetes Prevention study. In this study, patients with an average age of 55, body mass index of around 33 kg/m2 and isolated impaired glucose tolerance were attended. These patients were taken to a weight loss program through diet and exercise. At the end of two year, patients in the weight loss program that average 3.5 kg, the patients in the control group are 0.8 kg lost and at the end of 4 years, the cumulative diabetes incidence of study group was significantly lower than the control group. This finding has shown that the risk of diabetes is reduced by 58% with lifestyle arrangements. In this study, patients who have not developed diabetes have been observed for 3 years and have not been offered a lifestyle

changes in the follow-up period. At the end of this period; in this group of patient's diabetes incidence was still lower than the control group. This work has shown that after the measures have been discontinued, the anti-diabetic effect of lifestyle arrangements has been decreased but continued. In analyses, the most important factor affecting diabetes risk reduction has been observed to be weight loss [20]. In another study proving the effectiveness of lifestyle arrangements, patients with glucose tolerance disorder have been randomized to diet, exercise, diet + exercise and control group and after 6 years of follow-up, the incidence of diabetes was higher in the control group than in all the prevention groups. When patients were evaluated again 17 years after the study, diabetes incidence was still lower compared to those involved in any of the control groups. More importantly, cardiovascular and all-reason mortality in patients in this group has been significantly lower than control [21]. Lifestyle regulation in pre-diabetic patients prevents type 2 diabetes. From this point, both the physical activity and dietary arrangements are effective. These measures have the strongest effect in preventing diabetes if it provides weight loss [22].

In our study, pre-diabetic patients were studied and their risk of developing diabetes was assessed through their HbA1c levels. According to the results, the patients with IFG and IFG+IGT are considered to be more closely monitored than other groups and need to be taken to diet programs for lifestyle change, exercise and weight loss purposes. We think it should be a more stringent approach than patients with IFG.

When evaluating the results of our study, it would be useful to consider the limitations of the number of patients, the deficiency of standardization required for the use of HbA1c as a diagnostic criterion in our country, and the fact that patients cannot participate in the evaluation of other variables in terms of risk of developing diabetes. In terms of diabetes development, the risk of the population to be evaluated with more extensive studies and the appropriate lifestyle models and treatment options must be reviewed.

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