

Delay in starting insulin therapy in patients with type 2 Diabetes Mellitus

Tip 2 diyabetes mellitus hastalarında insülin tedavisine geç başlama

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Abstract

Aim: There are many problems with insulin initiation though required in diabetes mellitus patients. This study aims to determine why patients are unable to receive insulin treatments on time.

Methods: Approval from the ethics committee and consent from the volunteers was obtained for this cross sectional, single center study, in which patients with type 2 diabetes mellitus over the age of 18 years were included. Pregnant women, patients with cirrhosis, and psychiatric disorders were excluded. A questionnaire was used for data collection. Statistical analysis was performed with SPSS 18.0.

Results: A total of 1062 patients were included in this study. Diabetes mellitus was regulated in 34% of the patients. The number of patients who did not use insulin even though they should was 105. While physicians did not recommend any insulin treatment to 34 patients, 33 patients did not want insulin treatment due to fear of injection and 32 patients did not start insulin treatment because they had incorrect information regarding insulin. When 36 patients who stopped insulin treatment while they were using were questioned for the reason, it was learnt that 8 patients' insulin treatment was stopped by their physicians. The remaining 28 patients, on the other hand, stopped their insulin treatments most frequently because of the difficulty of injection and incorrect information they heard about insulin. **Conclusions:** Providing outpatient conditions that increase patient-physician dialogue, ensuring that the injection pen and needle are seen and tested by the patient in person, and conferences for the patients and medical doctors to prevent getting the incorrect information would be the solution of the delay in starting insulin in diabetes mellitus.

Keywords: Diabetes Mellitus, Insulin, Early treatment

Öz

Amaç: Diyabetes mellitus hastalarında gerekmesine rağmen insülin başlatılmasıyla ilgili birçok sorun vardır. Bu çalışmanın amacı hastaların niçin zamanında insülin tedavilerini alamadıklarını saptamak ve bu sorunlara değinmektir.

Yöntemler: Tek merkezde kesitsel yapılan bu çalışma için etik kurul'dan izin ve gönüllülerden onam alındı. 18 yaşından büyük, tip 2 diyabetes mellituslu hastalar çalışmaya dahil edildi. Hamileler, 18 yaşından küçükler, dekompanse karaciğer hastalığı olanlar, psikiyatrik bozukluğu olanlar, Tip 1 diyabeti olanlar çalışmaya alınmadı. Veri toplanması için anket kullanıldı. İstatistiksel analiz SPSS 18.0'da yapıldı.

Bulgular: Toplam 1062 hasta çalışmaya alındı. Hastaların %34'ü regüle idi. İnsülin kullanması gerektiği halde kullanmayan hasta sayısı 105'di. 105 hastadan 34 hastaya hekimler hiç insülin tedavisi önermemişken 33 hasta enjeksiyon korkusu nedeniyle insülin istememiş ve 32 hasta ise insülin hakkında yanlış bilgileri olduğu için insülin kullanmaya başlamamıştı. İnsülin kullanırken insülin tedavisine son veren 36 hasta sorgulandığında 8 hastanın insülin tedavisi hekimleri tarafından durdurulmuştu. Kalan 28 hasta ise insülin tedavilerini en sık enjeksiyon zorluğu ve insülin hakkında duyduğu yanlış bilgiler nedeni ile kendileri bırakmıştı.

Sonuçlar: Hasta hekim diyalogunu artıran poliklinik şartlarının sağlanması, enjeksiyon kaleminin ve iğnesinin bizzat hasta tarafından görülüp denenmesi, yanlış bilgi edinilmesinden kaçınmak için hastalara ve doktorlara yönelik konferanslar diyabetes mellitus'ta insülinin geç başlanmasına çözüm olabilir.

Anahtar kelimeler: Diyabetes Mellitus, İnsülin, Erken tedavi

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Ethics Committee Approval: This study was approved by the Ethics Committee of Prof. Dr. Cemil Taşcıoğlu City Hospital (Date: 9/25/2019, No:986). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Etik Kurul Onayı: Bu çalışma, Prof. Dr. Cemil Taşcıoğlu Şehir Hastanesi Etik Kurulu tarafından onaylanmıştır (Tarih: 25.09.2019, No: 986). İnsan katılımcıların katıldığı çalışmalarda tüm prosedürler, 1964 Helsinki Deklarasyonu ve daha sonra yapılan değişiklikler uyarınca gerçekleştirilmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

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

Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Published: 8/30/2020

Yayın Tarihi: 30.08.2020

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Introduction

Diabetes was first recognized by the ancient Egyptians 3500 years ago. The first clinical definition was made by Aretaeus, who lived in the Cappadocia region in about 120 years AD [1]. Diabetes Mellitus (DM) develops when the pancreas cannot produce enough insulin from beta cells or if the insulin produced cannot be used effectively.

DM is a chronic disease that can cause serious complications. Its complications can be macrovascular in the form of coronary, cerebral or peripheral artery disease, or microvascular, such as retinopathy, nephropathy, or neuropathy. The necessity of an effective treatment in preventing complications is an indisputable fact [2].

In addition to oral antidiabetic drugs, insulin also plays an important role in the treatment of DM. In the case of insulin deficiency, hyperglycemia and glucolipotoxicity due to increased fatty acids lead to apoptosis. In the pre-diabetes period, even during the impaired fasting glucose phase, more than 40% of pancreatic beta cells are lost. Therefore, insulin therapy is important in maintaining the beta-cell reserve [3-5].

Despite the long-term glycemic control and improving effects of insulin on the quality of life, the delay in starting insulin although treatment is indicated is due to various reasons. The reasons for this delay are associated with the physician, patient or both the physician and the patient [6].

This study aims to identify the main causes of delay in starting insulin treatment and provide solutions.

Materials and methods

Before starting this study, approval was obtained from the Ethics Committee of Prof. Dr. Cemil Taşcıoğlu City Hospital (9/25/2019/986) and informed consent was acquired from all patients who were willing to participate in the study before the data was received.

Patients with type 2 diabetes mellitus over the age of 18 years who applied to the internal medicine outpatient clinic of our tertiary hospital were included in this single center study. Pregnant women, those under the age of 18, patients with decompensated liver disease, or psychiatric disorders that prevent cognition or compliance, and those with Type 1 DM were excluded from the study.

All participants received a questionnaire specially designed by the physician. The survey included demographic information and personal diabetes treatment. Laboratory evaluations (fasting blood glucose, post prandial blood glucose, HbA1C) were performed at the hospital where the interviews were held. All laboratory parameters were measured using standard procedures.

Statistical analysis

Statistical analysis was performed with SPSS 18.0 (SPSS Inc., Chicago, IL, USA). Data were expressed as mean (SD) or continuous variables or as percentages for categorical variables. In the statistical evaluation of the data, *P*-value of <0.05 was considered significant.

Results

Within one year, 1062 patients with type 2 DM were included in the study. Among participants, 681 were female and 381 were male. The mean age of the study group was 59 (10) years, and the mean body mass index was 30 (5) kg/m². The mean fasting blood glucose level was 169 (70) mg/dl, the mean postprandial blood glucose, 234 (93) mg/dl, and the mean HbA1c, 8.1 (3.9) mg/dl. The mean diabetes duration was 9 (6) years, and the mean insulin usage period in patients under insulin treatment was 6 (5) years.

Considering that the HbA1c target was set at ≤7%, 330 patients (34%) were regulated, while 655 patients were not (Table 1). When the patients were divided into two groups according to HbA1c levels as ≤7% and >7%, it was seen that the group that was not regulated despite the treatment had diabetes for a significantly longer period.

The number and distribution of medications according to the drug active substances used by the patients were as follows: Metformin 842 (79.3%), Sulfonylurea 233 (21.9%), Acarbose 20 (1.9%), Glitazone 84 (7.9%), Glinides 6 (0.6%), Gliptins 430 (40.5%), SGLT-2 inhibitors 103 (9.7%), GLP-1 agonists 9 (0.8%), rapid-acting insulins 210 (19.8%), basal insulins 340 (32%), ready-mix analog insulins 68 (6.4%) (Table 2).

Table 1: Demographic data

	HbA1c ≤7 (n=330)	HbA1c ≥7 (n=655)	Total (n=1062)	<i>P</i> -value
Gender (F/M)	207/123	426/229	681/381	0.609
Age (years)	59 (10)	60 (11)	59 (10)	0.300
BMI (kg/m ²)	30 (5)	29 (5)	30 (5)	0.400
FBG (mg/dl)	118 (23)	194 (72)	169 (70)	0.001
PPBG (mg/dl)	163 (43)	270 (91)	234 (93)	0.001
Diabetes duration (years)	7 (5)	10 (6)	9 (6)	0.001
Insulin usage period (years)	5 (4)	6 (5)	6 (5)	0.307

BMI: Body mass index, FBG: Fasting Blood Glucose, PPBG: Postprandial Blood Glucose

Table 2: Distribution of patients included in the study according to the drug active substances they used

Drug active substances	n	%
Metformin	842	79.3
Gliptins	430	40.5
Sulfonylurea	233	21.9
SGLT-2 inhibitors	103	9.7
Glitazone	84	7.9
Acarbose	20	1.9
GLP-1 agonists	9	0.8
Glinides	6	0.6
Basal insulins	130	32
Ready-mix analog insulins	68	6.4
Rapid-acting insulins+basal insulins	210	19.8

Metformin was the most commonly used agent (n=239, 22.5%), which was followed by a combination of metformin and gliptin (n=109, 10.3%). Among insulin treatments, the combination of basal-acting insulin and fast-acting insulin was the most preferred (n=92, 8.7%) compared to all treatment options (Table 3).

Considering the patients who were using four or more oral antidiabetic agents or had HbA1c ≥9, 105 (9.9%) of the patients were not using insulin although it was indicated. When those 105 patients were asked why they did not use insulin, 34 (32.7%) stated that physicians did not recommend any insulin treatment so far, 33 (31.7%) rejected insulin because of fear of injection, and 32 (30.8%) did not start insulin because of the dreadful comments they had heard about insulin before. These dreadful comments included that insulin became habitual and caused kidney failure. Remaining three of our patients had not switched to insulin due to insufficient educational status, two

patients thought they would have hypoglycemia and one patient was afraid of gaining weight (Table 4).

Patients who interrupted insulin treatment while using insulin were questioned what the reason was. Based on the responses, they were divided into two as physician-induced and patient-induced to stop insulin treatment. In 8 (22%) of our patients, the treatment of insulin was stopped by the physician while 28 (78%) of our patients had stopped their insulin treatments themselves. In patients who interrupted their insulin treatment with the physicians' advice, the mean age (years), fasting blood sugar (mg/dl), postprandial blood sugar (mg/dl), HbA1c (mg/dl), diabetes duration (years), insulin usage period (years) and body mass index (kg/m²) were 51, 174, 184, 7.8, 6, 8, and 24, respectively. In the same order, the values of the patients who quit insulin treatment on their terms were 57, 251, 308, 11, 9, 3, and 28 (Table 5). Reasons for physicians to stop insulin treatment in 8 patients included regulation of blood glucose in 6 patients and hypoglycemia in 2 patients. On the other hand, the reasons for 28 patients interrupting their insulin treatment were insufficient information on insulin in 10 (35%) patients, difficulty in injection in 9 (32%) patients, inadequate educational level and lack of helpers in 4 (14%) patients, hypoglycemia in 4 (14%) patients, and weight gain in one patient.

Table 3: The distribution of patients according to the drugs they use most frequently and the ratio of these treatments to the treatment combinations

Treatment choices	n	%
Barely Metformin	239	22.5
Barely Gliptin	18	1.7
Barely Sulfonylurea	14	1.3
Metformin+Gliptin	109	10.3
Metformin+Sulfonylurea	56	5.3
Metformin+Gliptin+SGLT-2	29	2.7
Metformin+Glitazone	14	1.3
Metformin+Sulfonylurea+Gliptin	72	6.8
Metformin+Glitazone+Gliptin	15	1.4
Metformin+Sulfonylurea+Glitazone	11	1
Barely Basal Insulin	14	1.3
Basal Insulin+Metformin	23	2.2
Basal Insulin+Metformin+Gliptin	31	2.9
Basal Insulin+Metformin+SGLT-2	12	1.1
Basal Insulin+Metformin+Sulfonylurea +Gliptin	14	1.3
Basal Insulin+Rapid-acting insulin	92	8.7
Basal Insulin+Rapid-acting insulin+Metformin	33	3.1
Basal Insulin+Rapid-acting insulin+Gliptin	12	1.1
Basal Insulin+Rapid-acting insulin+Metformin+Gliptin	45	4.2
Mix Insulin +Metformin	19	1.8
Mix Insulin+Metformin+Gliptin	13	1.2

Table 4: Distribution of reasons for not using insulin among patients using four or more oral antidiabetic drugs or HbA1c greater than 9 mg/dl

Reasons for not using insulin (n=105)	n	%
Physicians have not recommended	34	32.3
Fear of injection	33	31.4
Dreadful comments they had heard about insulin	32	30.4
Insufficient educational status	3	2.8
Fear of hypoglycemia	2	1.9
Afraid of gaining weight	1	0.9

Table 5: Comparison of patients whose insulin therapy was discontinued by the physician and those who discontinued their insulin treatments themselves

Patients whose insulin therapy was discontinued (n:36)	by the physician (n:8)	by themselves (n:28)	P-value
Age (years)	51 (9)	57 (9)	0.43
FBG (mg/dl)	174 (42)	251 (84)	0.01
PPBG(mg/dl)	184 (30)	308 (86)	0.10
HbA1c (mg/dl)	7.8 (1)	11 (2)	0.38
Diabetes duration (years)	6 (5)	9 (5)	0.69
Insulin usage period (years)	8 (9)	3 (5)	0.28
BMI (kg/m ²)	24 (13)	28 (3)	0.03

FBG: Fasting Blood Glucose, PPBG: Postprandial Blood Glucose, BMI: Body mass index

Discussion

Type 2 DM has an increasing prevalence worldwide. This brings both increased treatment costs and complications of diabetes together with increased morbidity and mortality. Blood glucose regulation is important to prevent the development of

complications of diabetes, and compliance with treatment algorithms is tremendously essential.

When looking at the insulin regimens used by patients, mixed insulins are the least preferred by physicians in treatment with a ratio of 16%, while basal + bolus treatment is administered with a rate of 51%. However, in parallel with the previous studies, in our study, we observed that we are still not at the desired point in the treatment of diabetes. In the recent TEMD study on this subject, Sonmez et al. [7] determined the mean HbA1c level as 7.7% in Type 2 diabetic patients followed in the endocrinology outpatient clinic, while in two separate studies conducted by Ilkova et al. [8] and Satman et al. [9] the HbA1c levels were reported as 8.1% and 8.6%, respectively. In our study, the mean HbA1c level was 8.1% in patients who visited the internal medicine outpatient clinic. Again, in the TEMD study, it was reported that only 40% of patients with Type 2 diabetes were achieving HbA1c targets. These rates were 29% and 23% in the studies of Ilkova et al. and Satman et al., respectively. The differences in the two ratios probably result from different HbA1c targets and the 5-year interval between the two study periods. In our study, when we accepted HbA1c ≤7 as the regulation criteria, we found that only 34% of our patients who visited the internal medicine outpatient clinic reached target HbA1c levels [10].

Insulin therapy has an important place in the treatment of diabetes mellitus. Achieving desired goals and maintaining pancreatic cell reserves should be the primary goals by ensuring the regulation of blood glucose levels in patients. There are more than one study showing the effectiveness of insulin therapy and early blood glucose regulation slowing the progression from prediabetes to diabetes and preventing its complications. The UKPDS study showed that while early glucose control reduces the risk of both macrovascular and microvascular complications, late control of diabetes is of little benefit to macrovascular complications [11-13].

In the study of Pennartz et al. [14] on patients with type 2 diabetes mellitus, who were not controlled sufficiently with metformin, a significant improvement in residual pancreatic cell function with early use of basal insulin was demonstrated.

However, when necessary, the delay in the transition to insulin therapy may be due to the physician, the patient or both the physician and the patient. The two most important reasons that emerged in our study were the patients' fear of injections and their dreadful ideas about insulin. Contrary to the expectations, lack of education is no longer an obstacle to starting insulin therapy. Besides, when the patients were divided into three classes according to HbA1c levels, the group with the highest HbA1c had the lowest rate of insulin offered by the physician, which suggests that the physicians had difficulty in changing the ossified misconceptions of the diabetic patients and they have stopped repeating their proposal.

Barriers to insulin initiation or continuation are worldwide problems. The main obstacles encountered after starting insulin therapy were determined by Lee et al. [15] as fear, misperception, and side effects. Insulin follow-up programs, multidisciplinary diabetes care teams, making glucometers and more easily accessible strips have become necessary to overcome these obstacles.

On the other hand, Karter et al. [16] attributed the reasons for the failure of starting insulin usually to the misinterpretations of the patients like the insulin itself has side effects such as blindness, kidney failure, causing amputation, increasing the risk of a heart attack, causing stroke or premature death, to their injection phobia, anxiety of hypoglycemia, negative impact on social life and work, and insufficient literacy.

The more difficult it is to start insulin for the patient who needs insulin treatment, the more difficult it is for the patient to continue the treatment. Oliveria et al. [17] reported that 86% of patients who required insulin treatment had never been recommended it by healthcare professionals, and 46% of patients who started insulin treatment had stopped. In this study, the average time between the patients' first and last prescriptions was 4.9 years. The most common causes of discontinuation of insulin were injection difficulty and the physicians' advice to no longer continuing. In their study, Khunti et al. [18] also emphasized the graveness of the delays to start insulin treatment and increase the dosages.

Yavuz et al. [19] reported that having negative perceptions about insulin treatment and basal-bolus insulin treatment regimen, young age, and starting new treatment were the most common difficulties for conformity to treatment.

In our study, when the reasons for quitting insulin were questioned, incorrect information previously obtained about insulin (45%) and fear of injection (47%) were the foremost patient reasons. Also, when the causes of insulin discontinuation associated with the physician or the patient are compared, the fasting blood glucose and BMI of the group in which the physicians stopped insulin treatment were statistically significantly lower than the other group. It is observed that physicians stop insulin treatment when they reach moderate HbA1c values with moderate postprandial glucose levels in young and thinner patients with near-normal fasting glucose levels. It is noteworthy that the patients who quit insulin by themselves were older, fatter, with a history of older diabetes, having poorly controlled diabetes, and having more newly started insulin therapy. Contrary to the expectations, only 14% of patients who quit insulin reveal the cause as hypoglycemia, while hypoglycemia was the reason for 25% of physicians to quit insulin. Therefore, it is possible to say that the fear of experiencing hypoglycemia resides in the physician rather than the patient.

Limitation

One potential limitation of this study is that it is based on data from a single center; therefore, composition of population, departmental protocols, resources, and staffing characteristics are potential limits to the generalizability of our results.

Conclusion

The most important physician-induced reasons of delay starting insulin are not to adequately inform the patient about insulin therapy and fear of hypoglycemia that the patient will experience. The most common patient-induced causes are fear of injections and dreadful ideas about insulin. The educational meetings for hypoglycemia and injection fears and enough time in outpatient clinic for patients can solve the problem of delay starting insulin in diabetes mellitus.

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