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Research

Personalized Treatment Selection and Its Effects on Glycemic Control in Older Adults with Diabetes: A Single Center Experience

Yaşlı Diyabetli Yetişkinlerde Kişiye Özel Tedavi Seçimi ve Glisemik Kontrol Üzerine Etkileri: Tek Merkez Deneyimi

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ABSTRACT

Objective: As society ages, managing people with diabetes gains importance and becomes difficult because of accompanying diseases and complications. This study examined the effects of treatment changes in people with diabetes over 65.

Methods: The data of patients aged ≥65 who were followed up in the İstanbul University, İstanbul Faculty of Medicine between 2010 and 2017 were retrospectively analyzed. Demographic data, comorbidities, complications, and metabolic effects of treatment changes were evaluated.

Results: The study included 250 patients with a mean age of 72.0±6.6 years. Of the patients, 78.8% had hypertension, 58.4% had dyslipidemia, 32% had coronary artery disease, and 10% had chronic renal failure. The frequency of diabetic neuropathy was 26%, nephropathy 22.8%, and retinopathy 20.8%. The incidence of hypoglycemia was 16.4%. While oral antidiabetic drugs (OAD) alone decreased by 19%, 14% of these patients switched to OAD + basal insulin therapy and 4% to basal-bolus therapy during the follow-up period. With the addition of basal insulin to OAD, an additional 0.9% reduction in glycated hemoglobin (HbA1c) was achieved, and a further 1.2% reduction was achieved by switching to basal-bolus insulin.

Conclusion: Our study has shown that continuing the use of metformin in older adults with diabetes with preserved renal functions and adding insulin to their existing treatments when needed, despite all the reservations, provides an effective treatment by decreasing the HbA1c level. However, the lower-than-expected hypoglycemia frequency in our study may be due to the progressive age of diabetes and hypoglycemia unawareness due to accompanying autonomic neuropathy. Education of patients gains importance in this regard.

Keywords: Older adults with diabetes, glycemic control, hypoglycemia, personalized treatment

ÖZ

Amaç: Toplum yaşlandıkça, eşlik eden hastalıklar ve komplikasyonlar nedeniyle şeker hastalarının yönetimi önem kazanmakta ve zorlaşmaktadır. Bu çalışma 65 yaş üstü şeker hastalarında tedavi değişikliklerinin etkilerini incelemeyi amaçlamıştır.

Gereç ve Yöntem: İstanbul Üniversitesi, İstanbul Tıp Fakültesi'nde 2010-2017 yılları arasında izlenen 65 yaş ve üzeri hastaların verileri retrospektif olarak incelendi. Demografik veriler, komorbiditeler, komplikasyonlar ve tedavi değişikliklerinin metabolik etkileri değerlendirildi.

Bulgular: Çalışmaya ortalama yaşları 72,0±6,6 yıl olan 250 hasta dahil edildi. Hastaların %78,8'inde hipertansiyon, %58,4'ünde dislipidemi, %32'sinde koroner arter hastalığı ve %10'unda kronik böbrek yetmezliği vardı. Diyabetik nöropati sıklığı %26, nefropati %22,8, retinopati %20,8 idi. Hipoglisemi görülme sıklığı %16,4 olarak belirlendi. Tek başına oral antidiyabetik ilaçların (OAD) kullanımı %19 azalırken, bu hastaların %14'ünün takip döneminde OAD + bazal insülin tedavisine ve %4'ünün bazal bolus tedavisine geçtiği gözlendi. Glikozillenmiş hemoglobinde (HbA1c) OAD'ye bazal insülin ilavesiyle ek bir %0,9'luk azalma ve bazal-bolus insüline geçilmesiyle ise ilave %1,2'lik azalma sağlandı.

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Sonuç: Çalışmamız, böbrek fonksiyonları korunmuş yaşlı diyabetlilerde tüm çekincelere rağmen metformin kullanımına devam edilmesinin ve gerektiğinde mevcut tedavilerine insülin eklenmesinin HbA1c değerini düşürerek etkili bir tedavi sağladığını göstermiştir. Ancak hipoglisemi sıklığının beklenenden düşük bulunması, ilerleyen diyabet yaşı ve eşlik eden otonom nöropatiye bağlı hipoglisemi farkındasızlığından kaynaklanıyor olabilir. Bu noktada hastaların eğitimi önem kazanmaktadır.

Anahtar Kelimeler: Yaşlılıkta diyabet, glisemik kontrol, hipoglisemi, kişiselleştirilmiş tedavi

INTRODUCTION

Diabetes, which is currently considered a global epidemic, affected 382 million people worldwide in 2013, and this number is expected to reach 592 million by 2035 (1). In the United States of America, while the diabetes rate in older adults over 65 years old is around 22-33%, it is estimated that this rate will increase with the aging of the current population (2). According to the TURDEP-I study conducted in 1997, the frequency of type 2 diabetes in all age groups in our society was found to be 7.2%, and in the TURDEP-II study completed in 2010, this rate increased to 13.7% (3,4). For individuals aged 65 years and over, it increased from 20% to 35% in these 13 years. In the period between these two studies, the onset of diabetes five years earlier will increase both diabetes and diabetes complications in the population aged 65 and over in the coming years. Diabetes in old age is closely related to cardiovascular diseases, macrovascular and microvascular complications, the risk of hypoglycemia causing increased mortality, and hospitalization rates. Both diagnosis and treatment are problematic in this age group because of functional impairments and different comorbidities of older adults (5). There are very few studies on diabetes management in older adults. The main reason for this is that physiological changes that occur with aging are difficult to adapt to studies involving young populations (6). This study aimed to examine the general approach to treatment and the clinical effects of changes for treating patients aged 65 years and over who applied to the Diabetes Polyclinic of İstanbul University, İstanbul Faculty of Medicine, Department of Endocrinology and Metabolic Diseases.

METHODS

Study Design

For this study, outpatient follow-up files of all patients who applied to the Diabetes Policlinic of İstanbul University, İstanbul Faculty of Medicine Endocrinology and Metabolic Diseases Department between 2010 and 2017 were retrospectively scanned with the diagnosis of type 2 diabetes. The data of patients aged 65 years and over who came for follow-up visits at least three times after their first admission and had treatment arrangements were evaluated. Data from patients who applied for two or fewer follow-up visits and who were younger than 65 years were not assessed. This study was approved by the Ethics Committee of İstanbul University, İstanbul Faculty of Medicine (decision no: 08, date: 02.04.2021) and was conducted in accordance with the Declaration of Helsinki Principles. Written informed consent was obtained from each participant.

Study Variables

Patients' age, gender, educational status, marital status, employment status, smoking and alcohol use habits, duration of diabetes, diabetes diagnosis type, comorbidities, drugs preferred for diabetes treatment and treatment of micro- and macrovascular complications, treatment changes made at each control, and changes in weight and biochemical parameters were collected.

According to the Turkish Endocrinology and Metabolism Association 2018 diabetes guideline, in older adults with diabetes, the A1C target should be <7.0-7.5% in healthy patients with a low risk of hypoglycemia, considering complications, comorbid diseases, and other risks. On the other hand, it is recommended to aim for A1C <8.0-8.5% in patients with high hypoglycemia and other risks and need of care (7). In the American Association of Clinical Endocrinology 2018 guideline, the glycated hemoglobin (HbA1c) target is recommended as ≤6.5% for most healthy older adults, especially those with intact cognitive and functional status. In line with the recommendations of these two guidelines, the patients' data included in the study were evaluated by classifying their HbA1c as ≤6.5%, 6.6-7.5%, 7.6-8.0%, and ≥8.1% (8).

Statistical Analysis

IBM SPSS 21.00 packaged software was used for data analysis. Descriptive statistics were used to evaluate the data. Categorized data are presented as frequency-percentage ratios, and quantitative data are presented as mean and standard deviation and compared using Student's t-test.

RESULTS

Between 2010 and 2017, the files of 7087 patients who were followed up in our center diagnosed with type 2 diabetes were scanned, and 250 people (138 women and 112 men) aged 65 years and over who had at least three follow-up visits between these dates were included in the study.

The mean age at the first application was 72.0±6.6 (65-89) years, the duration of diabetes was 13.8±7.9 (2-40) years, and the weight was 82.5±14.8 (40-128) kg (Table 1).

Hypertension was observed in 78.8% of patients, dyslipidemia in 58.4%, coronary artery disease in 32%, chronic renal failure in 10%, cerebrovascular disease in 7.2%, and cancer in 14.4%. It was determined that 10.8% had thyroid dysfunction, 3.6% had chronic obstructive pulmonary disease, and 2.8% had peripheral artery disease.

The malignancies seen were breast (32.4%), colon (11.8%), rectum (8.8%), thyroid papillary capillaries (5.8%), Hodgkin lymphoma (5.8%), chronic lymphocytic leukemia (5.8%), skin cancer (5.8%), lung (2.94%), endometrium (2.94%), and gastrointestinal (2.94%) cancers, as well as melanoma (2.94%), adrenal adenoma (2.94%), bladder (2.94%), prostate (2.94%), and vulva (2.94%) tumors.

Diabetic neuropathy was associated in 26% of the patients, nephropathy in 22.8%, and retinopathy in 20.8%. It was observed that there were diabetic feet in seven cases, and amputation was applied to 4 of them.

Of the patients, 48% complied with medical nutrition therapy, 25.6% regularly exercised, and 58.9% regularly measured their blood glucose at home.

Insulin use increased from 21.6% at the first visit to 49.2% at the last visit. Of the 232 patients whose hypoglycemia frequency was questioned, 83.6% reported that they were not, 4% were nocturnal, 2% during the day, and 3.2% reported hypoglycemia at any time of the day. In addition to hypoglycemia, no patient was admitted to the hospital with hyperosmolar non-ketotic coma or lactic acidosis, which can often be seen, especially in older adults.

The mean HbA1c of all patients at the first admission was 8.1±2.0% (4.8-14.8%), while 7.5±1.5% (4.3-14.0%) at the last visit ($p<0.001$) was found as. The biochemical characteristics of the patients at their first admission are presented in Table 2.

The number of patients at the first and last visit within the determined HbA1c ranges were 30.8% (n=77) and 29.2% (n=73) for HbA1c ≤6.5%, respectively; 18.8% (n=47) and 30.8% (n=77) for HbA1c 6.6%-7.5%; 3.6% (n=9) and 11.2% (n=28) for HbA1c 7.6-8.0%; and 46.8% (n=117) and 28.8% (n=72) for ≥8.1%. The number of patients using antidiabetic drugs that have the risk of causing hypoglycemia in the first application and last treatments and those who had hypoglycemia according to the HbA1c ranges is summarized in Table 3.

Table 1. Demographic characteristics of patients

Age (mean ± SD)	**72.06±5.55**	**Marital status (n%)**	
Gender		Married	159 (95.8)
Woman (n)	138 (55.2%)	Single	6 (3.6)
Man (n)	112 (44.8%)	Widow	1 (0.6)
Weight (kg)		**Smoking (n%)**	
Initial	82.57±14.86	Non-smoke	161 (67.1)
Final	81.63±14.86	Smoke	27 (11.3)
BMI (kg/m²)		Smober	52 (21.7)
Educational status (n%)		**Alcohol use (n%)**	
Illiterate	6 (2.9)	User	222 (92.5)
Primary school	105 (51.2)	Non-user	7 (2.9)
Secondary school	20 (9.8)	Quit	11 (4.6)
High school	38 (18.5)	**Diabetes duration (year)**	13.81±7.99
University	36 (17.6)	**Diabetes onset (n%)**	
Employment status (n%)		Acute hyperglycemia	8 (4.1)
Employee	21 (10.2)	DKA	1 (0.5)
Retired	117 (56.8)	3P	47 (24)
Housewife	68 (33.0)	OGTT	7 (3.6)
		Random	133 (67.9)

BMI: Body mass index, DKA: Diabetic ketoacidosis, 3P: Polyphagia, polyuria, polydipsia, OGTT: Oral glucose tolerance test, SD: Standard deviation

Table 2. Biochemical characteristics of the patients

HbA1c (%)			
Initial	8.17±2.04	Lipase (U/L)	41.64±25.71
Final	7.57±1.47	hsCRP (mg/L)	19.18±40.75
Glucose (mg/dL)	150.14±55.32	Total cholesterol (mg/dL)	193.63±43.47
Urea (mg/dL)	42.73±25.97	HDL (mg/dL)	47.33±15.74
Creatinine (mg/dL)	1.12±1.13	LDL (mg/dL)	114.36±34.74
Uric acid (mg/dL)	8.13±12.85	TSH (mIU/L)	3.90±12.29
AST (U/L)	20.76±9.98	Vitamin D (ng/mL)	27.72±25.79
ALT (U/L)	21.81±12.08	PTH (pg/dL)	67.44±47.31
GGT (U/L)	32.33±37.91	Calcium (mg/mL)	10.00±6.55
ALP (U/L)	74.40±27.32	Phosphorus (mg/dL)	3.48±0.57
Amylase (U/L)	77.88±36.20	Albumin (g/dL)	4.40±0.37

HbA1c: Glycated hemoglobin, AST: Aspartate transaminase, ALT: Alanine aminotransferase, GGT: Gamma-glutamyl transferase, ALP: Alkaline phosphatase, hsCRP: High-sensitivity C-reactive protein, HDL: High-density lipoprotein cholesterol, LDL: Low-density lipoprotein cholesterol, TSH: Thyroid stimulating hormone, PTH: Parathyroid hormone

Table 3. Summary of the treatment changes of people using antidiabetic drugs at risk of hypoglycemia according to different HbA1c levels at the first application and the number of people with hypoglycemia

Anti-diabetic medication	**HbA1c ≤6.5% (n=77)**		**HbA1c 6.6-7.5% (n=47)**		**HbA1c 7.6-8.0% (n=9)**		**HbA1c ≥8.1% (n=117)**	
	Initial treatment	**Final treatment**	**Initial treatment**	**Final treatment**	**Initial treatment**	**Final treatment**	**Initial treatment**	**Final treatment**
Gliclazide (n, %)	12 (15.58)	34 (44.15)	5 (10.63)	6 (12.76)	2 (22.22)	1 (11.11)	17 (14.52)	17 (14.52)
Glimepride (n, %)	2 (2.59)	2 (2.59)	2 (4.25)	0 (0.00)	0 (0.00)	1 (11.11)	7 (5.98)	2 (1.70)
Repaglinide (n, %)	2 (2.59)	15 (19.48)	2 (4.25)	9 (19.14)	0 (0.00)	4 (44.44)	2 (1.70)	34 (29.05)
Nateglinide (n, %)	2 (2.59)	1 (1.29)	0 (0.00)	2 (4.25)	0 (0.00)	0 (0.00)	2 (1.70)	2 (1.70)
Basal insulin (n, %)								
Glargine	9 (11.68)	20 (25.97)	6 (12.76)	9 (19.14)	4 (44.44)	5 (55.55)	21 (17.94)	62 (52.99)
Detemir	0 (0.00)	4 (5.19)	1 (2.12)	5 (1.06)	0 (0.00)	2 (22.22)	1 (0.85)	7 (5.98)
NPH	0 (0.00)	2 (2.59)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (0.85)	2 (1.70)
Regular insulin (n, %)	3 (3.89)	7 (9.09)	2 (4.25)	3 (6.38)	3 (33.33)	2 (22.22)	7 (5.98)	22 (18.80)
Analog insulin (n, %)	1 (1.29)	4 (5.19)	1 (2.12)	1 (2.12)	1 (11.11)	0 (0.00)	6 (5.12)	6 (5.12)
Mixt insulin (n, %)	3 (3.89)	3 (3.89)	2 (4.25)	1 (2.12)	1 (11.11)	0 (0.00)	7 (5.98)	2 (1.70)
Hypoglycaemia (n, %)	**Initial**	**Final**	**Initial**	**Final**	**Initial**	**Final**	**Initial**	**Final**
Night	2 (2.70)	3 (4.60)	1 (2.40)	2 (2.70)	0 (0.00)	1 (3.70)	7 (6.50)	4 (5.90)
Daytime	1 (1.41)	1 (1.40)	1 (2.40)	1 (1.40)	0 (0.00)	0 (0.00)	3 (2.80)	1 (1.50)
Uncertain time	1 (1.41)	1 (1.40)	0 (0.00)	1 (1.40)	0 (0.00)	1 (3.70)	7 (6.50)	3 (4.40)
None	68 (94.52)	60 (92.30)	40 (95.20)	69 (94.50)	9 (100.0)	25 (92.60)	91 (84.30)	60 (88.20)

HbA1c: Glycated hemoglobin, NPH: Neutral protamine hormone

The general treatment distributions in the first and last visits of the patients and patients who received treatment according to the targeted HbA1c intervals are summarized in Figure 1 and Table 4.

While all patients with coronary artery and cerebrovascular disease used acetylsalicylic acid, only 24% of those with dyslipidemia used lipid-lowering medication. The HbA1c value of patients using oral antidiabetic (OAD) was found

to be 7.7±2.0% at the beginning and 7.1±1.2% at the last control. The distribution of the OADs used is shown in Figure 2. The most significant of the treatment changes was the addition of basal insulin to patients' treatment using OAD alone (n=23), an additional decrease of 0.9% in HbA1c, and a 1.2% additional decrease in basal-bolus insulin (n=10). HbA1c of 57 patients with nephropathy, whose mean age was 73.3±6.0, increased from 8.9±2.1% to 8.2±1.2% (p=0.033), weight 83.3±13, from 9 kg to 82.9±14.2 kg (p=0.570); HbA1c of 52 patients with retinopathy with a mean age of 72.7±5.8 years from 8.8±1.3% to 8.3±1.5% (p=0.136), and weight 85.1±15.1 kg to 84.3±15.4 kg (p=0.425); HbA1c of 65 patients with neuropathy with a mean age of 72.4±5.4 years from 8.2±1.8% to 7.8±1.4% (p=0.005), weight 83.3±15.9 kg

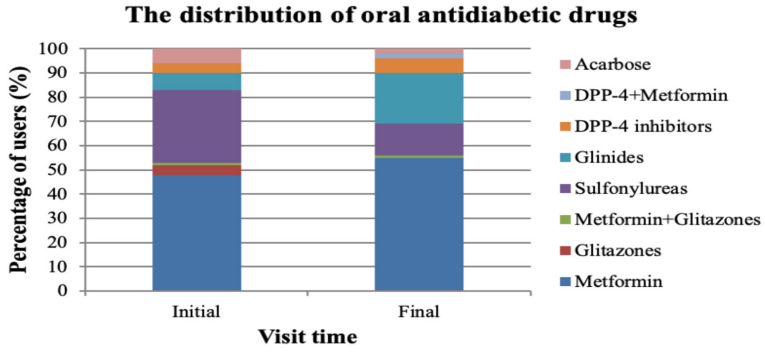

Figure 1. Treatment distribution in the first and last visits of the patients

Table 4. Summary of antidiabetic drug use and treatment changes according to different HbA1c levels at first admission

Anti-diabetic medication	HbA1c ≤%6.5 (n=77)		HbA1c 6.6-7.5% (n=47)		HbA1c 7.6-8.0% (n=9)		HbA1c ≥8.1% (n=117)	
	Initial treatment	Final treatment	Initial treatment	Final treatment	Initial treatment	Final treatment	Initial treatment	Final treatment
MNT (n, %)	35 (45.53)	10 (13.00)	16 (34.00)	4 (8.50)	2 (22.22)	0 (0.00)	44 (37.61)	8 (6.81)
OAD (n, %)	30 (39.0)	39 (50.61)	22 (46.81)	28 (59.61)	2 (22.22)	2 (22.22)	45 (38.52)	36 (30.82)
OAD + basal insulin (n, %)	4 (5.21)	14 (18.21)	2 (4.35)	7 (14.90)	0 (0.00)	5 (55.63)	4 (3.43)	39 (33.33)
Basal insulin (n, %)	2 (2.64)	2 (2.64)	1 (2.12)	3 (6.42)	0 (0.00)	0 (0.00)	5 (4.32)	4 (3.43)
Basal + bolus insulin (n%)	3 (3.92)	10 (13.00)	3 (6.42)	4 (8.53)	4 (44.44)	2 (22.22)	14 (12.00)	28 (23.91)
Mixt insulin (n, %)	1 (1.30)	0 (0.00)	0 (0.00)	0 (0.00)	1 (11.11)	0 (0.00)	4 (3.43)	0 (0.00)
OAD + mixt insulin (n, %)	2 (2.64)	2 (2.64)	2 (4.35)	1 (2.12)	0 (0.00)	0 (0.00)	1 (0.90)	2 (1.73)
Basal + bolus + mixt insulin (n, %)	0 (0.00)	0 (0.00)	1 (2.12)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)

HbA1c: Glycated hemoglobin, OAD: Oral antidiabetic, MNT: Medical nutrition therapy

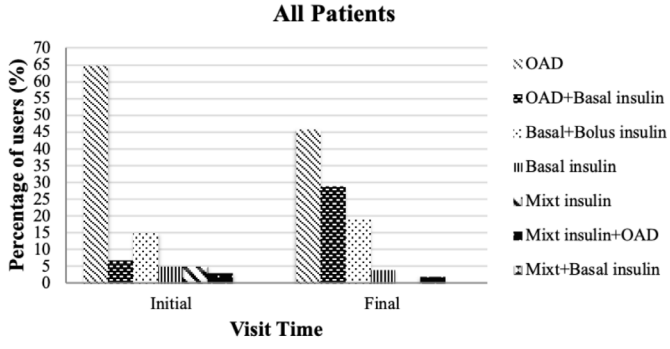

Figure 2. Summary of the distribution of oral anti-diabetics used in first application and final control
OAD: Oral antidiabetic

from 83.7±15.3 kg (p=0.604). The distribution of patients with microvascular complications according to the targeted HbA1c ranges is summarized in Table 5, and the distribution of preferred treatments is summarized in Figure 3.

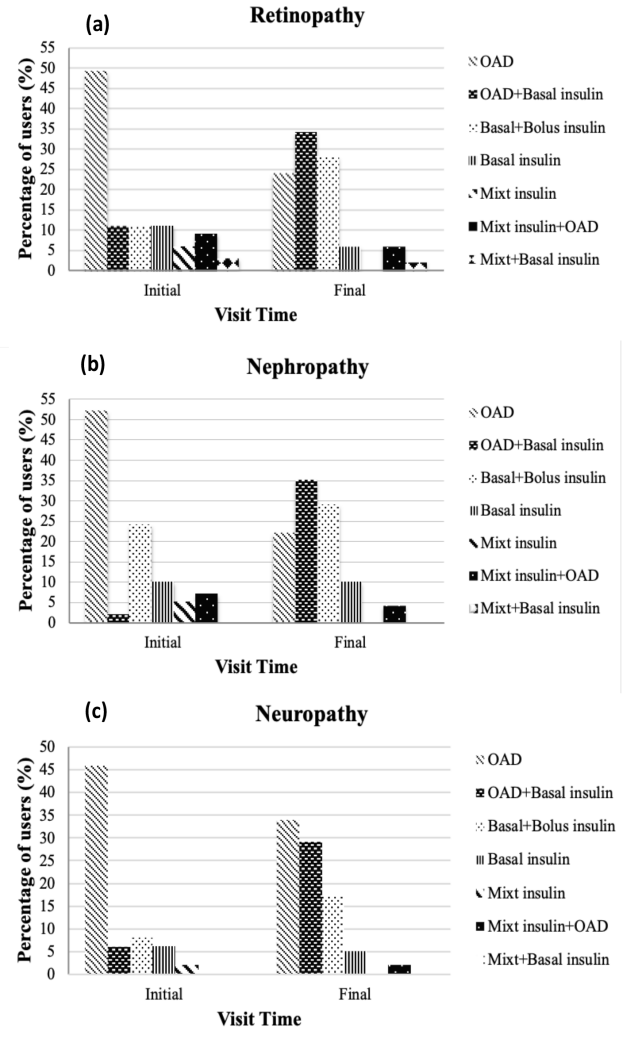

Figure 3. Distribution of selected treatments according to microvascular complications: (a) Retinopathy, (b) nephropathy, and (c) neuropathy
OAD: Oral antidiabetic

DISCUSSION

As the human lifespan increases, the prevalence of developing type 2 diabetes increases accordingly. Individuals with diabetes over the age of 65 years are at a similar risk to younger diabetes patients in terms of the risk of developing microvascular complications. However, their late detection of the disease also reduces their absolute risk. However, their absolute risk of macrovascular complications is significantly higher than that for young diabetics (2).

Our study revealed the necessity of re-evaluating and closely monitoring the treatment of all diabetic patients aged 65 years, especially those with comorbidities. In this way, both glycemic targets can be achieved, control of additional diseases can be achieved, and patients' quality of life can be increased (9).

Few data exist to make specific recommendations for the treatment of type 2 diabetes in older adults (10). However, patients over the age of 65 years have been included in many diabetes drug trials, including studies evaluating cardiovascular endpoints. Therefore, the approach to choosing initial, alternative, and combination therapies is similar in older and younger adults. All types of oral hypoglycemic drugs and insulin are effective in older patients, but each has some limitations. Most importantly, oral and injectable agents with a low risk of hypoglycemia should be used.

Increased risk of hypoglycemia and weight gain in the use of sulfonylureas (SU), which have an essential place in intensive treatment protocols in reducing the risk of microvascular complications, are two important problems to be considered (5) and may lead to severe consequences for the older adult population (11). Therefore, the American Geriatrics Association does not recommend the use of some drugs in the SU group, especially glibenclamide, in older adults (12). Our clinical approach in this regard was mostly the use of short-acting secretagogues, and the drugs of approximately 30% of the patients who used SU at their first application were replaced with repaglinide or

Table 5. Number of patients with different HbA1c levels and average age of patients with microvascular complications at first admission

Microvascular complication	HbA1c ≤6.5% (n=77)		HbA1c 6.6-7.5 (n=47)		HbA1c 7.6-8.0% (n=9)		HbA1c ≥8.1% (n=117)	
	Yes	No	Yes	No	Yes	No	Yes	No
Age (mean ± SD)	72.36±5.33		71.93±6.03		73.25±4.06		71.85±5.61	
Retinopathy (n, %)	7 (9.10)	70 (90.90)	6 (12.80)	41 (87.20)	2 (22.22)	7 (77.80)	37 (31.60)	80 (68.40)
Nephropathy (n, %)	10 (13.00)	67 (87.00)	7 (14.90)	40 (85.10)	3 (33.30)	6 (66.70)	37 (31.60)	80 (68.40)
Neuropathy (n, %)	19 (24.70)	58 (75.30)	10 (21.30)	37 (78.70)	2 (22.20)	7 (77.80)	34 (29.10)	83 (70.90)

HbA1c: Glycated hemoglobin, SD: Standard deviation

nateglinide. Short-acting secretagogues provide significant advantages in older adult patients because of the low risk of hypoglycemia and the fact that the dose can be easily changed according to the patient's number and amount of meals.

Metformin is the first-line diabetes therapy for all ages; it is effective and safe, inexpensive, and may reduce the risk of cardiovascular events and death. Metformin, recommended by the American Geriatrics Society and increased the usage rate from 48% to 55% in our outpatient clinic, improves the treatment results when added to the treatment of diabetics over 65 years of age who have no contraindications for use (12). Recent studies have shown that metformin can be safely used in patients with an estimated glomerular filtration rate of 30 mL/min/1.73 m^2. However, its use in patients with severe renal insufficiency is contraindicated. It should also be used cautiously in patients with hepatic dysfunction or congestive heart failure because of the increased risk of lactic acidosis. However, it is associated with weight loss, frailty, and lactic acidosis in older adults.

Metformin can also have both gastrointestinal side effects and decreased appetite, which can be problematic for some older people. Metformin reduction or discontinuation may be necessary for patients experiencing persistent gastrointestinal side effects (10). Weight loss is a common trigger factor for frailty and sarcopenia, with a high risk of being overlooked. Vitamin B12 deficiency is another nutritional deficiency often observed in patients receiving metformin treatment. Older adults are more prone to vitamin B12 deficiency because of various factors. In this context, clinicians should know when to cease metformin treatment in patients with malnutrition and/or frailty (13).

Insulin use is closely associated with hypoglycemia risk. While the patients' insulin use followed up in our study increased approximately twice, 83.6% of them stated that they did not experience any hypoglycemia, contrary to what was expected (11). The time of hypoglycemia was stated as 4% at night, 2% during the day, and 3.2% at any time of the day. In our study, the lower frequency of hypoglycemia than expected may be related to the inability to notice hypoglycemia due to advanced diabetes age and accompanying autonomic neuropathy. At this point, it is essential to educate patients about hypoglycemia and for physicians to ask patients about the frequency of hypoglycemia during visits.

Although the goals in managing hyperglycemia and diabetes complications in older people are similar to those of young people with diabetes, they should be determined by considering the presence of severe comorbidity, the state of their cognitive functions and functionality, the patient's life expectancy, and the risks of complications (10).

Glycemic control targets of older adult patients with normal functional and cognitive capacity and life expectancy (e.g. >10 years) long enough to allow for the use of treatment benefits should be as in young diabetes patients: A1c 7-7.5%, fasting and preprandial plasma glucose (PG) 80-130 mg/dL, night PG 90-150 mg/dL. Survival is shortened in older adult patients with multiple chronic diseases and mild to moderate cognitive dysfunction. In this group of patients, targets should be A1c 7.5-8%, fasting and preprandial PG 90-150 mg/dL, night PG 100-180 mg/dL. Glycemic and metabolic targets should be more flexible in older adult patients with advanced complications, accompanying major cardiac problems, short life expectancy, and fragile and limited functional or cognitive capacity. In these patients, recommendations are as follows: A1c 8-8.5%, fasting or preprandial PG 100-180 mg/dL, night-time PG 110-200 mg/dL (14).

In general, the average HbA1c values of our patients when they first came to the outpatient clinic were 8.17%, which was taken into the target range by decreasing 0.6% until the last control. The most appropriate treatments have been predominantly determined for patients with comorbidities, and their treatments have been customized. All patients were given medical nutrition therapy, medication use patterns, correct injection techniques for insulin users, and training on blood glucose measurement at home, and they were frequently called for follow-up visits. In older adult patients, a single daily dose of long-acting basal insulin may be preferred to maintain fasting blood glucose levels within the desired range. In cases where fasting glucose is close to normal limits and the HbA1c value is high, short-acting insulin can be added to the treatment. However, this multi-injection treatment, defined as basal + bolus, should not be used in patients with vision problems and dementia symptoms and who tend to miss or delay meals. Multiple insulin therapy can be a difficult option for older adults. In older adult patients with limited mobility and adjustment disorders. It can also cause hypoglycemia (9).

In this study, we found that the addition of basal insulin to OADs, which can be safer to achieve the glycemic target, is preferred, especially in patients with microvascular complications, neuropathy, nephropathy, and retinopathy. This intervention resulted in a significant decrease in HbA1c levels (from 8.7% to 8.0%, p=0.012), while providing nearly 3 kg of weight loss compared with the initial values. In contrast, basal + bolus therapy was the preferred treatment primarily in patients with microvascular complications,

especially retinopathy, in our outpatient clinic. While the patients' weight using basal + bolus increased by 1.5 kg, as expected, HbA1c values decreased by 0.4%.

Our study has both strengths and limitations. A few studies in the literature reveal both the current diabetes treatment of patients with type 2 diabetes aged 65 years and over and the results of reorganization in line with the recommendations and accompanying comorbidities. Our study fills a significant gap in this regard. On the other hand, our study's most significant limitation is that patients who applied before 2017 were included in the study, and their number was low. Therefore, the results of patients who used drugs with both weight-neutral and cardiovascular effects, such as SGLT-2 inhibitors introduced after this date, and those with a low risk of hypoglycemia, such as U-300 insulin, could not be included in the study. In addition, because the data of patients followed in a single center were evaluated in our study, it is not generalizable considering the living conditions in Türkiye. Finally, lifestyle changes, which have a significant place for treating diabetes, should also be considered when interpreting the results. From this point on, new studies are planned in our department, including more patients and evaluations, including today's applications.

CONCLUSION

Our study has shown that continuing the use of metformin in older adults with diabetes with preserved renal functions and adding insulin to their existing treatments when needed, despite all the reservations, provides an effective treatment by decreasing the HbA1c value. However, the lower than expected hypoglycemia frequency in our study may be due to the progressive age of diabetes and hypoglycemia unawareness due to accompanying autonomic neuropathy. Education of patients gains importance in this regard.

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ETHICS

Ethics Committee Approval: This study was approved by the Ethics Committee of İstanbul University, İstanbul Faculty of Medicine (decision no: 08, date: 02.04.2021) and was conducted in accordance with the Declaration of Helsinki Principles.

Informed Consent: Written informed consent was obtained from each participant.

Authorship Contributions

Surgical and Medical Practices: F.Ç., H.H., R.Ç., A.K.Ü., Ö.S.S., N.G., K.K., M.T.Y., N.D., İ.S., Concept: A.K.Ü., Ö.S.S., N.G., K.K., M.T.Y., N.D., İ.S., Design: A.K.Ü., Ö.S.S., N.G., K.K., M.T.Y., N.D., İ.S., Data Collection or Processing: F.Ç., D.G., H.H., R.Ç., Analysis or Interpretation: F.Ç., D.G., A.K.Ü., İ.S., Literature Search: F.Ç., A.K.Ü., İ.S., Writing: F.Ç., A.K.Ü., İ.S.

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