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Re-Training of Type 2 Diabetic Patients for Better Adherence to Diabetes Care Plan in Oral Anti-Diabetics and Plus Insulin Treatment Groups

Oral Antidiyabetik ve Artı İnsülin Alan Gruplarda, Diyabet Bakım Planına Daha İyi Uyum İçin Tip 2 Diyabetik Hastalarının Eğitimi

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Abstract

Purpose: This prospective observational single-centre study was designed to evaluate the effect of patient re-training for better adherence to regular self-monitoring of blood glucose (SMBG), standard diabetic diet and exercise program in ambulatory patients with type 2 diabetes mellitus (T2DM) receiving oral anti-diabetic (OAD) and OAD plus insulin treatments.
Material and Method: In this study, we enrolled a total of 61 patients with T2DM in whom ongoing therapy with OAD (n=34) and OAD+insulin (n=27) failed to achieve adequate glycemic control. The patients were educated for lifestyle behavior, adherence to diet and exercise therapy, close monitoring with SMBG without change in their ongoing drugs and dosing. Changes in glycemic parameters, serum lipids and anthropometrics at the end of 3rd month were compared between the treatment groups.
Results: During the course of the study, a significant decrease in the body weight and fat were observed in OAD (p<0.001 and p=0.002) and OAD+insulin groups (p=0.044 and p=0.008, respectively). A significant decrease in the HbA1c % (6.1%; 8.2% to 7.6%) was observed in the overall population (p<0.001) as well as in OAD (p=0.011) and OAD+insulin (p=0.001) groups. A significant decrease was noted in the post-prandial capillary blood glucose levels in only OAD+insulin group.
Discussion: Re-training approach with close follow-up and frequent SMBG seems to be important factors for the maintenance of achieved glycemic control. In our study, the effect of diabetes education on postprandial capillary blood glucose levels was more pronounced in OAD+insulin group. *Turk Jem 2015; 19: 49-54*
Key words: Diabetes education, oral anti-diabetics, insulin, glycemic control

Conflicts of Interest: The authors reported no conflict of interest related to this article.

Özet

Amaç: Bu prospektif gözlemsel tek merkezli çalışma, ayaktan takip edilen tip 2 diyabet hastalarında, oral anti-diyabetik (OAD) ve OAD+insülin kullanan gruplarda, hastanın evde kendi kendine kan şeker takibi, standart diyabetik diyet ve egzersiz programına uyumunu arttırmak için tekrar eğitim verilmesinin etkilerini değerlendirmek üzere tasarlanmıştır.
Gereç ve Yöntem: Devam eden tedavileri ile yeterli glisemik kontrol sağlanamayan toplam 61 diyabetik hasta OAD (n=34) ve OAD+insulin (n=27) gruplarında çalışmaya dahil edilmiştir. Hastalar mevcut devam edilen ilaçları ve dozları değiştirilmeden, yaşam tarzı davranışı, diyet ve egzersiz uyumu, evde kendi kendine kan şeker ölçümleri ile yakın takip için tekrar eğitilmiştir. Üçüncü ayın sonunda glisemik parametreler, serum lipid değerleri ve antropometrik ölçümlere ait değişiklikler tedavi grupları arasında değerlendirilmiştir.
Bulgular: Çalışma süresince OAD ve OAD+insülin gruplarında, vücut ağırlığı ve yağ oranlarında anlamlı bir düşme gözlenmiştir (OAD: p<0,001 ve p=0,002), (OAD+insulin: p=0,044 ve p=0,008). HbA1c düzeyinde tüm hastalarda olduğu gibi (%6,1, p<0,001), her iki OAD (p=0,011) ve OAD+insulin (p=0,001) gruplarında anlamlı bir düşme gözlenmiştir. Post-prandiyal kapiller glukoz değerlerinde ise sadece OAD+insülin grubunda anlamlı düşme tesbit edilmiştir.
Tartışma: Yakın takip ve kendi kendine sık düzenli kan şeker ölçümleri ile birlikte yeniden eğitim yaklaşımı hedeflenen glisemik kontrolün sağlanması için önemli faktörler olarak görülmektedir. Çalışmamızda, diyabet eğitiminin postprandiyal kapiller kan glukoz düzeyleri üzerine etkisi OAD+insülin kullananlarda daha belirgin bulunmuştur. *Turk Jem 2015; 19: 49-54*
Anahtar kelimeler: Diyabet eğitimi, oral anti-diyabetik, insülin, glisemik control

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Introduction

Despite improvements in treatment and management of diabetes, adequate glycemic control in many patients is not achieved yet (1). Long-term positive effects of adequate glycemic control on reduction of serious complications associated with diabetes are known with very good evidence (2,3), however, achievement of strict glycemic control without healthier lifestyle and adherence of patients has not been considered effective for the appropriate management of the disease and better control of glycemic parameters (4,5).

This prospective observational single-centre study was designed to evaluate the effects of patient reinforcement for better adherence to regular self-monitoring of blood glucose (SMBG), standard diabetic diet and exercise program in oral anti-diabetic (OAD) and OAD plus insulin treatment groups among ambulatory T2DM patients.

Materials and Methods

Study Population

A total of 61 ambulatory patients with T2DM in whom ongoing therapy failed to achieve adequate glycemic control (HbA1c >7.5) were included in this 3-month prospective observational single-centre study conducted between 2012 and 2013 at a tertiary care hospital located in Bursa, Turkey. OAD and OAD+insulin groups consisted of 34 and 27 patients (mean (SD) age: 53.0 (9.7) and 54.3 (6.0) years, respectively, 73.5% were females in the OAD and 66.7% in the OAD+insulin groups). Patient inclusion criteria were duration of diabetes of 1-20 years, age between 35 and 65 years, and HbA1c levels of 7.5-10% during screening. Written informed consent was obtained from each subject following a detailed explanation of the objectives and protocol of the study which was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and approved by the institutional ethics committee.

Study Design and Parameters

Data on patient demographics, anthropometrics (height, weight, waist circumference, hip cir-cumference), duration of diabetes mellitus, type of ongoing anti-diabetic treatment (OAD and OAD plus insulin use), body fat percentage, blood biochemistry (creatinine, uric acid and serum lipids) and glycemic parameters (HbA1c, 8-point self-monitoring of capillary blood glucose) were collected in each patient at the baseline visit performed during study enrolment. No change was made to patient's ongoing anti-diabetic drugs. As a part of routine practice carried out for diabetic patients with poor compliance to treatment in our clinic, each patient had diabetes-related education aiming to increase patient's knowledge level as well as adher-ence to diabetes care plan including regular SMBG, standard diabetic diet and isometric/isokinetic exercise consisted of 30-45-minute training sessions with one-to-one instruction according to the disease status and needs of the patient by a training team composed of an endocrinology specialist, a diabetes nurse and a sports physician who were qualified certified diabetes educators.

The patients were trained in the use of glucose meter and to perform an eight-point glucose profile within four consecutive days including morning fasting/postprandial levels on day 1, noon fasting/postprandial levels on day 2, evening fasting/postprandial levels on day 3 and night-time 23:00 and 02:00 hrs levels on day 4, per week and return their recordings during the follow-up visit. All patients were re-evaluated after 3 months of the initial training visit for the change in each study parameter with respect to type of the ongoing anti-diabetic treatment.

Statistical Analysis

Statistical analysis was made using computer software SPSS version 21.0 (SPSS Inc. Chicago, IL, USA). Chi-square (χ^2) test was used for the comparison of categorical data, while the Mann-Whitney U and Wilcoxon tests were used for numerical data. Comparison of treatment groups in terms of change in study parameters in time was made using general linear models (GLM). Data were expressed as mean (standard deviation-SD), minimum-maximum values and percent (%) where appropriate. A p value of less than 0.05 was considered statistically significant.

Results

Patient Characteristics with Respect to Treatment Groups

The mean (SD) duration of diabetes mellitus was 9.1 (±7.1) years in the overall population. Patients receiving OADs composed 55.7% of the study population, while 44.3% of patients were on OAD+insulin combination therapy. Patients in the OAD and OAD+insulin groups were homogenous in terms of demographics and anthropometric measurements, whereas the duration of T2DM was significantly longer in the OAD+insulin group compared with OAD group (12.3 (±7.5) vs. 6.6 (±5.8) years, p=0.001) (Table 1).

Change in Anthropometrics and Blood Biochemistry During the Course of the Study

From baseline to the end of follow-up at the third month, a significant decrease in the body weight and fat % was observed in OAD (p<0.001 and p=0.002) and OAD+insulin (p=0.044 and p=0.008) groups. No difference in creatinine levels was detected during the course of the study, while a significant increase in uric

Table 1. Patient characteristics with respect to treatment groups

	OAD group (n=34)	OAD+insulin group (n=27)	p value OAD vs. OAD+insulin
Age (years)	53.0 (9.7)	54.3 (6.0)	0.416[1]
Male n (%)	9 (26.5)	9 (33.3)	0.559[2]
Female n (%)	25 (73.5)	18 (66.7)	
Duration of T2DM (years)	6.6 (5.8)	12.3 (7.5)	**0.001**[1]
BMI (kg/m^2)	32.4 (5.8)	33.6 (4.7)	0.273[1]
Weight (kg)	84.1 (12.3)	88.3 (13.0)	0.140
Waist circumference (cm)	98.3 (8.7)	102.0 (10.7)	0.156[1]
Hip circumference (cm)	109.4 (10.8)	112.6 (10.0)	0.107[1]

OAD: oral antidiabetic agents, BMI: Body mass index,
[1]Mann-Whitney U test, [2]χ^2 test

acid levels occurred in the overall population (p=0.002) as well as in OAD (p=0.021) and OAD+insulin (p=0.037) groups. Change in uric acid levels over time was markedly greater in OAD+insulin than in OAD groups (p=0.016) (Table 2). Most commonly used OAD agent was metformin when all of the patients were given (80.3%).

Table 2. Using ratio of different treatment agents and modalities in patients (%)

	OAD group (n=34)	OAD+insulin group (n=27)	Total (n=61)
Metformin	94.1	63.0	80.3
Sulfonylurea	76.5	18.5	50.8
Pre-mixed insulin		48.1	21.3
DPP4 inhibitor	26.5	3.7	16.4
Pioglitazone	20.6	0	11.5
Basal insulin		25.9	11.5
Intesive insulin regimen		25.9	11.5
Glinide	11.8	0	6.6
Acarbose	5.9	3.7	**4.9**

Half of the patients were on the basal insulin and intensive insulin regimens with same percentages and the other half were on the pre-mixed insulin regimens in the OAD+insulin group (Table 3).

No difference in total cholesterol and triglyceride levels was detected during the course of the study, while a slight decrease in HDL-cholesterol levels occurred only among patients receiving OAD+insulin treatment (p=0.037) (Table 3).

Change in Glycemic Parameters During the Course of the Study

From baseline to the end of follow-up at the third month, a significant decrease in the HbA1c % was observed in OAD (p=0.011) and OAD+insulin (p=0.001) groups. Treatment groups did not differ with respect to amount of change occurred in HbA1c levels over time (Table 3).

From baseline to the end of follow-up at the third month, a significant decrease in the post-prandial capillary blood glucose levels measured in the morning (p=0.021), noon (p=0.023) and evening (p=0.019) along with fasting capillary blood glucose levels measured in the evening (p=0.005) and nighttime (02:00) capillary blood glucose levels (p=0.016) only in the OAD+insulin group (Table 4).

Nighttime (23:00) capillary blood glucose levels decreased from baseline to the third month both in the overall population and in the OAD+insulin group (p=0.003 for each).

Table 3. Change in anthropometrics and blood biochemistry during the course of the study with respect to treatment groups

	OAD group			OAD+insulin group			p² OAD vs. OAD+insulin
Body weight	**N**	**Mean (SD)**	**p¹**	**N**	**Mean(SD)**	**p¹**	
Baseline	34	84.1 (12.3)	**<0.001**	27	88.3 (13.0)	**0.044**	0.142
3rd month	33	81.9 (12.9)		27	87.0 (12.2)		
Fat %							
Baseline	34	37.7 (9.7)	**0.002**	27	39.3 (7.3)	**0.008**	0.559
3rd month	33	36.1 (9.7)		26	36.9 (8.2)		
Blood biochemistry							
Creatinine (mg/dL)							
Baseline	24	0.74 (0.14)	1.000	20	0.76 (0.22)	0.856	0.652
3rd month	25	0.74 (0.14)		19	0.76 (0.15)		
Uric acid (mg/dL)							
Baseline	20	4.1 (1.1)	**0.021**	16	4.6 (1.8)	**0.037**	**0.016**
3rd month	26	4.4 (1.2)		15	5.5 (1.3)		
Cholesterol (mg/dL)							
Baseline	29	217.4 (42.4)	0.820	19	213.5 (45.9)	0.099	0.773
3rd month	26	218.6 (36.2)		20	224.9 (46.5)		
HDL (mg/dL)							
Baseline	26	48.8 (8.8)	0.666	20	52.1 (17.9)	**0.034**	0.556
3rd month	29	46.9 (8.5)		19	47.1 (10.4)		
Triglyceride (mg/dL)							
Baseline	26	175.8 (63.8)	0.853	20	196.9 (104.2)	0.825	0.776
3rd month	29	204.7 (185.0)		19	193.9 (114.1)		

OAD: Oral antidiabetic agents, ¹Wilcoxon test, ²General linear models

Table 4. Change in glycemic parameters during the course of the study with respect to treatment groups

	OAD group			OAD+insulin grouprd			p² OAD vs. AD+insulin
	N	Mean (SD)	p [1]	N	Mean (SD)	p [1]	
HbA1c %							
Baseline	34	8.0 (0.8)	**0.011**	27	8.4 (0.9)	**0.021**	0.212
3rd month	30	7.6 (1.1)		23	7.8 (1.2)		
Morning-fasting							
Baseline	30	156.1 (32.0)	0.973	26	152.7 (50.5)	0.484	0.417
3rd month	30	153.5 (32.3)		25	140.3 (29.6)		
Morning-PP							
Baseline	28	205.3 (49.9)	0.600	24	216.3 (77.0)	**0.021**	0.329
3rd month	28	213.2 (58.9)		24	168.3 (55.9)		
Noon-fasting							
Baseline	28	152.4 (56.8)	0.670	23	156.5 (43.6)	0.421	0.393
3rd month	26	140.7 (37.8)		23	144.2 (55.7)		
Noon- PP							
Baseline	30	198.9 (64.0)	0.647	25	229.0 (51.1)	**0.023**	**0.042**
3rd month	26	188.5 (41.8)		21	187.9 (44.0)		
Evening-fasting							
Baseline	27	155.7 (65.6)	0.412	24	198.9 (62.3)	**0.005**	**0.007**
3rd month	29	151.0 (35.9)		23	159.9 (39.9)		
Evening-PP							
Baseline	29	205.4 (63.0)	0.665	26	213.1 (47.3)	**0.019**	0.910
3rd month	30	207.4 (55.5)		22	186.0 (54.7)		
Nighttime-2300							
Baseline	23	184.7 (58.4)	0.193	23	203.4 (44.7)	**0.003**	0.219
3rd month	24	158.1 (46.5)		19	159.6 (43.3)		
Nighttime-0200							
Baseline	20	153.0 (44.8)	0.196	20	189.3 (52.3)	**0.016**	**0.010**
3rd month	23	154.3 (37.0)		12	149.0 (32.4)		

OAD: Oral antidiabetic agents; PP: Post-prandial; [1]Wilcoxon test, [2]General linear models

The amount of change over time was significantly higher in OAD+insulin than in OAD group for noon-postprandial (p=0.042), evening-fasting (p=0.007) and nighttime (02:00, p=0.010) capillary blood glucose levels (Table 4).

There was no difference or relationship between change in glycemic parameters and different antidiabetic agents or regimens. Also, there was no correlation between A1c or changes in eight-point glucose levels and other characteristics, such as age, disease duration, body mass index (BMI), lipid parameters or uric acid levels.

Discussion

The present prospective single-centre study investigated the effect of patient reinforcement for better adherence to regular SMBG, standard diabetic diet and exercise program on the change in anthropometric, lipidemic and glycemic parameters within 3 months of follow-up among ambulatory T2DM patients who failed to achieve adequate glycemic control under OAD or OAD+insulin treatment.

Our findings revealed that with no change in ongoing treatment regimen during the follow-up, while a significantly longer duration of T2DM noted in OAD+insulin than OAD group; a significant decrease in body weight, fat % and HbA1c levels was noted in T2DM patients at the end of 3-month follow-up, similarly in both treatment groups. A significant decrease in capillary blood glucose levels was noted only among patients receiving OAD+insulin treatment who were also determined to have markedly greater change in noon-postprandial, evening-fasting and nighttime capillary blood glucose levels as well as uric acid levels over time compared with patients under OAD treatment. Longer duration of diabetes indicated lesser percentage of body fat, while none

of the other factors investigated were determined to be effective in predicting the end of the follow-up levels of anthropometric, lipidemic and glycemic parameters, except for the baseline level of each parameter which predicted its own level at the end of follow-up.

Similarly, in a past study concerning the effect of a diabetes care plan with reinforcement of glycemic control in diabetic patients, HbA1c levels were reported to significantly decrease in 3 months and were maintained at approximately constant levels at intervals for up to 1 year in all patients, whereas HbA1c decrement was significantly greater among diabetic patients who completed four education courses compared to control group who missed at least half of the diabetes education sessions (6). Although our findings are limited to 3-month follow-up with no data available on whether the improvement obtained in glycemic control would be maintained in longer term, it should be noted that the majority of the HbA1c decrement was reported to be achieved during the first 3 months of an integrated care plan, which contributed 95.6% of the total HbA1c decrement over the year (6). Hence, our findings are in agreement with the studies which indicated that the effect of diabetes care on the improvement of glycemic control was most pronounced during the initial phase of the intervention program, during which the diabetes education was delivered (7,8).

Owing to the central role of consistently managing HbA1c levels in patients with diabetes, clinical guidelines recommend the range of 6.5-7.0% to motivate health professionals and patients to constantly manage blood glucose levels (6,9,10). More frequent SMBG was associated with clinically and statistically better glycemic control regardless of diabetes type or therapy (11).

Patients who failed to achieve optimal glycemic control under OAD+insulin treatment in our study population had similar demographic and baseline anthropometric characteristics with patients under OAD treatment, except for the significantly longer duration of disease. Receiving education about better adherence to diabetes care plan was associated with significant improvement in HbA1c levels in both OAD and OAD+insulin groups with no superiority of one regimen to the other. This seems consistent with the statement that a lifestyle change program was as effective as other treatments, such as drugs with demonstration of lifestyle changes to be almost twice as effective as metformin therapy in those with impaired glucose tolerance (12) and to be as effective as insulin treatment in improving glycemic index in patients with poorly controlled T2DM (13).

Notably, possibly in relation to longer duration of diabetes along with insulin-related changes in immediate and short-term glucose levels in the OAD+insulin group, although improvement in anthropometrics and HbA1c levels were similar between treatment groups at the end of 3rd month, capillary blood glucose measurements revealed significant decrease only in the OAD+insulin treatment group in our study population.

Indeed, global satisfaction with current diabetes treatment has been reported to be closely associated with improved glycemic control in T2DM patients, while improvement in patient convenience was indicated to provide better compliance with therapeutic regimen and greater patient satisfaction, which consequently leads to better glycemic control (1). In this regard, emphasizing the role of inclusion of better adherence of patients to SMBG within the education plan; achievement of significant reductions in SMBG levels among our T2DM patients under OAD+insulin therapy is worth noting, despite the longer of duration of diabetes in this group and the consistently reported association between treatment with OAD+insulin combination and poor glycemic control (14).

Significant decrease in self-monitored capillary blood glucose levels among patients receiving OAD+insulin treatment but not in OAD-treated patients in the present study is in agreement with the well-recognized benefits of SMBG in improving glycemic control in patients with type 1 diabetes and those with T2DM who are being treated with insulin (15). While the inconsistency considering the potential role of SMBG in patients with T2DM not treated with insulin has been considered likely to lead to underutilization of SMBG in this population (15), studies have also shown a high correlation of HbA1c and mean glucose as measured by SMBG, and the positive effect of diabetes education on SMBG activities of T2DM patients (16). Nevertheless, it should be noted that regular use of SMBG has not been shown to be superior to irregular/never use of SMBG on glycemic control in a recent study conducted on Turkish T2DM patients, while it was considered to be a good intervention for the prevention of diabetic nephropathy (17).

It should be noted that maintaining the beneficial effect of diabetes education on glycemic control has been considered to be a real debate (6) and data from meta-analysis of the results of several randomized control trials (RCTs) revealed modest and gradually declining effect of patient education on the glycemic control of diabetic patients (18,19,20), unless self-management was enhanced by reinforcement of the education plan (21).

Due to influence of several confounding variables, such as the demographic and physiological characteristics of patients, teaching methods used, types of anti-diabetic medication as well as the presence of complications in clarification of whether an integrated care plan, including diabetes education does have benefits in terms of the outcomes of glycemic control (6), conduction of future RCTs, as the most reliable study design to address this issue (22), has been recommended to be designed by specialists from multiple disciplines and that incorporate the dedication of patients, healthcare providers and institution facilities (6).

Serum uric acid levels were found to be slightly elevated at the end of the study period. In the literature, to our knowledge, there is no evidence or data that the improvement of glycemic control worsening to uric acid levels. In addition, a recently published study has showed that serum uric acid levels were not different in diabetic and non-diabetic groups in 3280 patients who underwent coronary angiography, and it is stated that age, renal function, hypertension, smoking, use of diuretics, and dyslipidemia were independent predictors for higher serum uric acid levels while there were no association between uric acid levels and glycemic control parameters (23). These findings may be coincidental in our study, but may be related to volume reduction due to increased exercise activity, changes in diet or weight loss.

In conclusion, our findings seem to emphasize the likelihood of achievement of improved glycemic control in short term with implementation of diabetes care plan including patient education and active participation, while reinforcement approach with close follow-up and frequent SMBG seems to be important factors for the maintenance of achieved glycemic control. There was no difference in HbA1c change between OAD and OAD+insulin treatment groups, and this improvement was not affected by the duration of diabetes. The effect of diabetes education on postprandial capillary blood glucose levels was more pronounced in OAD+insulin group when compared with those receiving only OAD.

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