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Compliance to treatment and reaching of metabolic goals are better in OAD-treated diabetics than insulin-treated diabetics in the Turkish population

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Aim: We assessed the success rates of reaching glycated haemoglobin (HbA1c) goals in different treatment groups.

Materials and methods: This was a single-centre, retrospective study including 2995 patients. The proportion of patients reaching their HbA1c goals, according to the International Diabetes Federation (IDF), American Association of Clinical Endocrinologists (AACE), and American Diabetes Association (ADA), were determined.

Results: There were 4 different treatment groups: 1) diet group (n = 140), 2) oral antidiabetic drug (OAD) group (n = 1238), 3) insulin group (n = 765), and 4) insulin + OAD group (n = 812). According to the IDF and AACE criteria, the proportion of patients reaching HbA1c levels of $\leq 6.5\%$ was 92% in group 1, and 1 year later it was 100%. In the OAD group the proportions were 61% and 69%, respectively. In the insulin group, the rate was 15% and 1 year later 33% of patients had reached their goals. In the insulin + OAD group, the rates were 10% and 21%, respectively ($P < 0.05$ for all). According to the ADA criteria, the rate of patients reaching HbA1c levels of $\leq 7\%$ was 40% in the total group and, at the end of 1 year, 59%. In the diet group, the rates were 95% and 100%, respectively. In the OAD group, the rates were 75% and 83%, respectively. In the insulin group, the rates were 23% and 52%, respectively. In the insulin + OAD group, the rates were 16% and 32%, respectively.

Conclusion: A large number of patients seemed to reach their HbA1c goals. The success rate was especially higher in the OAD group than in the insulin group.

Key words: HbA1c goals, oral antidiabetic drugs, insulin

1. Introduction

The amount of glycated haemoglobin (HbA1c) correlates well with fasting and postprandial blood glucose levels (1,2). In the Cost of Diabetes in Europe – Type 2 (CODE-2) study, only 31% of individuals achieved good glycaemic control (HbA1c = 6.5%) according to current European guidelines (3). In the US National Health and Nutrition Examination Survey (NHANES) of 1999–2000, only 37.0% of participants achieved the target goal of HbA1c levels less than 7.0%, and 37.2% of participants were above the recommended “take action” HbA1c level of greater than 8.0% (4).

Despite evidence that good glycaemic control has significant health and economic benefits, most patients with diabetes do not achieve the recommended treatment goals. According to studies conducted in the United State, Europe, and Asia-Pacific, most patients have poor glycaemic control (HbA1c > 8%); less than one-third, and substantially less in some countries, achieve the

recommended target levels for HbA1c (3,5,6). For example, in the DiabCare Asia Study (6), the mean HbA1c level was 8.6%, with only 21%, 13%, or 7% of patients achieving recommended HbA1c goals according to the criteria of the American Diabetes Association (ADA; <7%), the European Diabetes Policy Group ($\leq 6.5\%$), or the Asia Pacific Type 2 Diabetes Policy Group 1999 (APDPG; <6.2%; note that the APDPG 2002 guidelines recommend a goal of $\leq 6.5\%$). These data are supported by numerous other studies. For instance, in the UK Asian Diabetes Study, a community-based study conducted in Birmingham and Coventry in the United Kingdom, 66% of patients had HbA1c levels of >7% (7).

A very recent nationwide observational study from Sweden reported that the proportion of patients reaching HbA1c levels of $\leq 7\%$ varied between 70.1% (metformin) and 25.0% (premixed insulin + sulphonylureas) in patients with pharmacological treatment, and that 84.8% of the patients with nonpharmacological treatment reached their

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targets. Compared to patients on metformin, patients on other pharmacological treatments had a lower likelihood (with reported hazard ratios ranging from 0.58; 95% confidence interval of 0.54–0.63 to 0.97; 0.94–0.99) of having HbA1c levels of $\leq 7\%$, adjusted for covariates. Patients on insulin-based treatments had the lowest likelihood, while nonpharmacological treatment was associated with an increased likelihood, of having HbA1c levels of $\leq 7\%$ (8).

There are no available data on patients' diabetes regulation rates in the Turkish population. The aim of this study was to assess the success rates of reaching HbA1c goals in different treatment groups in a Turkish population.

2. Materials and methods

2.1. Study design

This was a single-centre, retrospective study. All patients with documented files who were screened during the period of January 2005 to January 2006 were chosen in succession and enrolled for the study. Patients were divided into 4 different groups according to the treatment they were started on, or were using, at the beginning of the study: 1) diet group, 2) oral antidiabetic drug (OAD) group, 3) insulin group, and 4) insulin + OAD group. Patients who had to change treatments because of inadequate glucose control during the 1-year follow-up period were excluded from the study. Patients who only needed dose adjustments or additional agents and remained in the same treatment group were not excluded. Having complications was not an exclusion criterion.

2.2. Subjects

A total number of 3354 patients were admitted to our diabetes outpatient clinic as a primary care unit in the year 2005. All data were obtained from the patients' files, which were archived in our outpatient clinic. Age, sex, body mass index (BMI), duration of disease, type of diabetes, number of visits in 1 year, HbA1c levels (for 3-month intervals in 1 year), and type of treatment were evaluated. BMI was calculated by dividing weight in kilograms by height in square metres. HbA1c levels were measured by the high performance liquid chromatography method. All parameters were also evaluated at a follow-up at the end of 1 year. HbA1c levels were compared at the beginning and the end of the study. The rate of patients reaching the HbA1c goals according to the criteria of the International Diabetes Federation (IDF), American Association of Clinical Endocrinologists (AACE), and ADA were determined. All parameters were compared between different treatment groups. HbA1c levels were also compared between patients with diabetes duration of ≥ 5 years or < 5 years and ≥ 10 years or < 10 years.

2.3. Statistical analysis

Statistical analyses were performed with SPSS. Results are expressed as the mean \pm standard deviation of the mean (SD). The Student t-test, repeated measurement variant analyses, and Tukey and Wilcoxon methods were used to compare parameters. A P value of less than 0.05 was considered significant.

3. Results

A total of 3354 files were screened and 354 patients were excluded because of a change in treatment groups during the 1-year follow-up. Due to missing data in their files, 5 patients were dropped from the study. Thus, 2995 diabetic patients were recruited for the study; 3.1% of the patients had type 1 diabetes mellitus and 96.9% had type 2 diabetes mellitus. There were 58.2% females and 41.8% males.

There were 4 different treatment groups: 1) diet group (n = 140), 2) OAD group (n = 1238), 3) insulin group (n = 765), and 4) insulin + OAD group (n = 812). At the beginning, the mean HbA1c levels of the 4 groups were $5.65 \pm 1.09\%$, $6.96 \pm 1.71\%$, $9.28 \pm 2.57\%$, and $9.30 \pm 2.15\%$, respectively. No significant difference was observed between groups 3 and 4, while all other groups were significantly different. At the end of the study, the mean HbA1c levels of the 4 groups were $5.20 \pm 0.57\%$, $6.36 \pm 0.99\%$, $7.39 \pm 1.38\%$, and $7.70 \pm 1.49\%$, respectively. No significant difference was determined between groups 1 and 2 or between groups 3 and 4. Other group comparisons were statistically significant. The percentage reductions of HbA1c of the 4 groups were 0.45 ± 0.52 , 0.30 ± 0.72 , 1.89 ± 1.19 , and 1.60 ± 0.66 , respectively, after treatment. The biggest reduction was observed in group 3. The percentage reduction of HbA1c was greater in groups 3 and 4 compared to groups 1 and 2. However, no significant difference was determined between groups 1 and 2 or between groups 3 and 4. According to IDF and AACE criteria, the percentage of patients reaching HbA1c levels of $\leq 6.5\%$ was 32% in the total group. At the end of 1 year, it was 45%. In the diet group, 92% of patients, and 1 year later, 100% of patients, had reached the goals. In the OAD group, the rate was 61%, and the next year it was 69%. In the insulin group, 15% of patients, and 1 year later, 33% of patients, reached the target HbA1c levels. In the insulin + OAD group, the rates were 10% and 21%, respectively. All these changes were statistically significant (P < 0.05; Table 1).

According to the ADA criteria, patients reaching HbA1c levels of $\leq 7\%$ were 40% in the total group and, at the end of 1 year, 59%. In the diet group, 95% of patients, and 1 year later, 100% of patients, had reached the goals. In the OAD group, the rate was 75%, and the next year it was 83%. In the insulin group, 23% of patients, and 1 year later, 52% of patients, had reached the target HbA1c levels. In the insulin + OAD group, the rates were 16% and 32%, respectively. All these changes were statistically significant (P < 0.05; Table 2).

Table 1. Proportion of patients reaching HbA1c of $\leq 6.5\%$ according to IDF and AACE criteria.

Group (n)	Beginning proportion (%)	1 year later (%)	P
Diet group (140)	92	100	0.01
OAD group (1238)	61	69	0.01
Insulin group (765)	15	33	0.01
OAD + insulin group (812)	10	21	0.01
Total group	32	45	0.01

3.1. Age

Group 3 was younger compared to group 2 and group 4 ($P = 0.004$ and $P = 0.001$, respectively; Table 3).

3.2. BMI

Group 3 had lower BMI values compared to groups 1, 2, and 4 ($P = 0.001$ for all). Group 2 had the highest BMI values (Table 3).

3.3. Diabetes duration

Group 3 had the longest diabetes duration, and it was significantly different from those of groups 1 and 2 ($P = 0.001$ for both), but not statistically different from group 4. Group 4 also had a longer diabetes duration compared to groups 1 and 2 ($P = 0.001$ for both; Table 3).

When patients with a diabetes duration of ≥ 5 years or < 5 years were compared at the beginning and 1 year later, HbA1c levels were found to be higher in the ≥ 5 -year group ($P = 0.001$ and $P = 0.004$ respectively).

The same results were found when patients with diabetes duration of ≥ 10 years or < 10 years were compared ($P = 0.001$; Table 4).

3.4. Number of visits

Group 4 had a higher number of visits compared to group 2 ($P = 0.024$; Table 3). In the OAD group, the number of visits were decreasing while HbA1c levels were increasing ($R = -0.2$, $P = 0.001$). In the insulin group a similar correlation was observed between the number of visits and HbA1c levels ($R = -0.2$, $P = 0.005$).

4. Discussion

A large number of patients with diabetes mellitus seem to reach their HbA1c goals in different treatment groups in the Turkish population.

Table 2. Proportion of patients reaching HbA1c of $\leq 7\%$ according to ADA criteria.

Group (n)	Beginning proportion (%)	1 year later (%)	P
Diet group (140)	95	100	0.01
OAD group (1238)	75	83	0.01
Insulin group (765)	23	52	0.01
OAD + insulin group (812)	16	32	0.01
Total group	40	59	0.01

Table 3. Comparison of different parameters in different treatment groups.

	Group 1	Group 2	Group 3	Group 4	P
Age (years)	54.84 \pm 12.62	55.48 \pm 10.94	53.55 \pm 15.56	56.34 \pm 10.46	0.001
BMI initial (kg/m ²)	29.64 \pm 5.56	31.67 \pm 5.57	27.20 \pm 5.60	30.93 \pm 5.27	0.001
Diabetes duration (years)	2.95 \pm 3.99	4.16 \pm 4.88	8.36 \pm 7.73	8.22 \pm 6.43	0.001
Number of visits/year	2.13 \pm 1.20	2.21 \pm 1.26	2.23 \pm 1.46	2.38 \pm 1.42	0.024

The percentage of patients reaching the HbA1c target levels according to the IDF and the AACE was 45%, and it was 59% according to the ADA criteria, in the overall group in our study. The results were much better compared to findings of CODE-2 and NHANES 1999–2000, which were 31% and 37%, respectively (3,4).

The American College of Endocrinology and the AACE adopted a target HbA1c of <6.5% at their diabetes treatment consensus conference in 2001. They created a series of detailed “Roadmaps to Achieve Glycemic Control in Type 2 Diabetes Mellitus” for health care providers; these roadmaps recommend detailed individualised treatment regimens and advancement of therapy every 3 months until the target HbA1c is achieved.

Based on these studies, the recommendations of the ADA position statement of 2008 included lowering HbA1c to an average of 7%, which has clearly been shown to reduce microvascular and neuropathic complications of diabetes and, possibly, macrovascular disease. Therefore, the HbA1c goal for nonpregnant adults in general is <7%. Epidemiologic studies have suggested a small incremental benefit to lowering HbA1c from 7% into the normal range. Therefore, the HbA1c goal for selected individual patients is as close to normal (<6%) as possible, without significant hypoglycaemia. Less stringent HbA1c goals may be appropriate for patients with a history of severe hypoglycaemia, patients with limited life expectancies, children, individuals with comorbid conditions, and those with longstanding diabetes and minimal or stable microvascular complications (1).

In 2006, the ADA and European Association for the Study of Diabetes first published a consensus statement, in which they provided an algorithm for the management of hyperglycaemia in type 2 diabetes mellitus (9). A revision of the consensus statement was published in early 2009 (10). The glycaemic management goal recommended in the algorithm is the attainment and maintenance of an HbA1c level of <7.0%. Some organisations, such as the AACE, have set more aggressive goals (11).

Recently concluded studies reveal that targeting HbA1c levels below 7.0% may not be a viable option anymore. Furthermore, achieving tight blood glucose control is easier said than done due to the risks of hypoglycaemia and treatment-induced weight gain (11,12).

Another study, “The Action to Control Cardiovascular Risk in Diabetes (ACCORD)”, conducted in middle-aged or older type 2 diabetics and patients with high cardiovascular risk, compared the benefits of intensive treatment (an HbA1c target of <6.0%) with standard treatment (HbA1c target of 7.0%–7.9%). After an average treatment period of 4 years, the intensive therapy arm of the study was abandoned due to increased mortality in comparison to the standard treatment group. The reasons for the increased mortality are as of yet undetermined;

however, it is clearly seen that intensive treatment was not beneficial to the high-risk patients. However, in other studies, such as Action in Diabetes and Vascular Disease: Preterax and Diamicon Modified Release Controlled Evaluation (ADVANCE), the findings were not in agreement with those of ACCORD (13,14).

The incidence of clinical complications of diabetes is strongly associated with glycaemia. Each 1% reduction in updated mean HbA1c is associated with a risk reduction of 21% for diabetes-related complications, 21% for diabetes-related deaths, 14% for myocardial infarction, and 37% for microvascular complications (15–18).

In our study, nearly half of all patients reached their HbA1c targets. In the OAD group, targets of $\leq 6.5\%$ and $\leq 7\%$ were reached at rates of 69% and 83%, respectively. In the insulin group, these rates were 33% and 52%. All groups showed significant positive changes compared to initial HbA1c levels after 1 year. The percentage reduction of HbA1c was greater in the insulin and insulin + OAD groups compared to the diet and OAD groups. This could be explained by the fact that groups 3 and 4 had higher levels of HbA1c at the beginning. Although a higher reduction was observed in HbA1c percentages in groups 3 and 4, larger numbers of patients in the OAD and diet groups reached their target levels.

Group 2 had the highest initial BMI levels compared to the other groups. The lowest BMI was observed in group 3. These results suggest the presence of insulin resistance in group 2 and decreased beta cell function in group 3.

Groups 3 and 4 had longer diabetes durations compared to the other 2 groups. They were older diabetics and received insulin therapy. Both OAD and insulin users showed a negative correlation between the number of visits and HbA1c levels, suggesting that more visits are necessary for better glycaemic control.

When patients with diabetes duration of ≥ 5 years or <5 years or with diabetes duration of ≥ 10 years or <10 years were compared, it was found that patients with a longer diabetes duration had higher HbA1c levels.

From a clinician’s point of view, all of these studies and guidelines fail to point out a clear target in HbA1c, mainly due to the varying results of 3 recently concluded major studies (ADVANCE, ACCORD, and the Veterans Affairs Diabetes Trial). On one hand, a curvilinear correlation in the reduction of HbA1c and the prevention of diabetic complications suggests a lower target of HbA1c for patients, but on the other hand, risks of severe hypoglycaemic episodes, weight gain, and increased risk of cardiovascular events raise some points of concern.

Regardless of clinicians’ perspectives on whether to target a level of <7% or <6.5%, in our study we showed that more than 60% of our patients using OADs reached their HbA1c target. This may be explained due to a shorter duration of disease in patients using OADs and better

compliance to their therapy regimens. On the contrary, just 21%–33% of patients using insulin reached the target of <6.5%. However, these results were better than the quoted results in major studies. Although the percentage reductions in HbA1c were greater in insulin-treated groups, more patients in the OAD-treated group reached the targets, which might be due to lower starting levels of HbA1c in this group. The facts that a competent nurse was present to educate our patients and that the patients made more frequent visits to our clinic possibly contributed to our better results. Highlighted in our study is the fact that there is a negative correlation between the frequency of visits and HbA1c levels.

We can frankly admit to the fact that neither the frequency of hypoglycaemic episodes nor the weight gain of patients was evaluated in our study, which may be considered a weakness. However, our primary focus was the evaluation of our patients' success in reaching the HbA1c targets.

In conclusion, the success rates of Turkish diabetic patients in reaching their target HbA1c levels are considerably better than in other studies. The rate was especially greater in the OAD group than in the insulin group. This might be due to the fact that patients under OAD treatment have a shorter duration of diabetes and better compliance to their therapy regimen.

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