International Journal of Advances in Medicine
Avci D et al. Int J Adv Med. 2019 Apr;6(2):264-270
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: http://dx.doi.org/10.18203/2349-3933.ijam20190540

Original Research Article

Are dipeptidyl peptidase-4 inhibitors effective and safe in long term when added to ongoing therapies of diabetics? a real-life study in tertiary referral center

Deniz Avci*, Ali Çetinkaya

Department of Internal Medicine, Kayseri Training and Research Hospital, Kayseri, Turkey

Received: 14 December 2018
Accepted: 29 January 2019

***Correspondence:**
Dr. Deniz A. V. C. I.,
E-mail: denav38@gmail.com

ABSTRACT

Background: The aim of this study was to determine how HbA1c, lipid, renal functions and such parameters were affected in the long term by adding dipeptidyl peptidase-4 inhibitors to the ongoing treatment regimens of patients with Type 2 diabetes mellitus.
Methods: The study was conducted in diabetes mellitus outpatient clinic of Kayseri Training and Research Hospital between February 2012 and May 2017, with patients who did not achieve the sufficient success in diabetes their controls at the time of admission. From these patients, those who added (dipeptidyl peptidase-4 inhibitors) to their treatments were selected. Patients were followed up as long as they continued to these new treatments and the parameters at the baseline were compared with final values.
Results: A total of 80 diabetic patients were followed in the study. The median age of the patients was 56.08±9.71 years. During this follow-up, an average decrease of 1.03% was noted when patients were compared with 9.53±1.87% of the initial hemoglobin A1c, and 8.50±1.48% of the Hemoglobin A1c values at the end of follow-up. This decrease was statistically significant ($p < 0.001$). However, differences in the initial and final values of the lipid parameters of the patients were not statistically significant.
Conclusions: Addition of dipeptidyl peptidase-4 inhibitors to patients' treatments causes significant decreases in Hemoglobin A1c mean values. This decline is long lasting. However, there are no positive or negative effects on biochemical parameters such as lipids, kidney and liver functions.

Keywords: Diabetes mellitus, Dipeptidyl peptidase-4 inhibitors, Incretin, Sitagliptin, Vildagliptin

INTRODUCTION

Diabetes mellitus is a global concern that can cause to serious consequences. The prevalence of diabetes mellitus is steadily increasing. The World Health Organization predicts that in 2030 there will be around 439 million diabetic individuals in the world.[1] According to NHANES 2015-2016 data, only half of diabetic patients can achieve the HbA1c target of <7%.[2]

In 1906, Moore identified a chemical substance as a stimulant for the pancreas, and in 1930 Labarre used the term of "incretin" for the first time. McIntyre and colleagues were the first to define the “incretin effect” in 1964.[3] In 1987, Kreyman and colleagues demonstrated that GLP-1 leads to insulin secretion in the human body.[4] In 2006, FDA approved the first DPP-4 inhibitor sitagliptin as an option in the treatment of diabetes mellitus. Because of the advantage of oral use and the

low side-effect profile, DPP-4 inhibitors inhibiting GLP-1 degradation seem to be more practical in use.

Studies investigating the efficacy and safety of combinations of DPP-4 (dipeptidyl peptidase-4) inhibitors with other oral anti-diabetic agents have been conducted since DPP-4 inhibitors were introduced into marked. Nishimura and colleagues found that the combination of sitagliptin with repaglinide was effective at 24 weeks.[5] Ji L et al, demonstrated the efficacy of co-administration of metformin sitagliptin in multicentre studies at 24 weeks.[6] In another study, insulin glargine and metformin combination were compared with sitagliptin metformin combination in obese DM patients with HbA1c >9.5%. The study resulted in favor of sitagliptin metformin group (body weight, HbA1c site, etc.).[7]

The main purpose of this research was to learn the long-term effects of DPP-4 inhibitors (sitagliptin and vildagliptin) when added to any type of ongoing therapy.

METHODS

The study was conducted on patients, who failed to achieve successful control in diabetes at time of admission in diabetes mellitus outpatient clinic of Health Sciences University, Kayseri Training and Research Hospital between February 2012 and June 2017. Of these patients, those who were been prescribed DPP-4 inhibitors in addition to their ongoing treatments were selected. At the time of research onset, only sitagliptin and vildagliptin were available in Turkey as DPP-4 inhibitors. Thus, these two drugs were used in the study. Regardless of treatment types received, patients who had DPP-4 inhibitors added were followed as long as they continued to these new treatment regimens without a modification in their therapies these times were recorded as the follow-up periods.

Exclusion criteria

- Patients who had new agents added to their treatments,
- Those who had modifications in their treatments,
- Patients without available tests results at the end of the follow-up period and
- Patients with other hypo-glycemic agents started simultaneously with the DPP-4 inhibitors

After these exclusions, a total of 80 patients were remained. Of these patients, 40 were treated with vildagliptin and 40 were treated with sitagliptin. The serum glucose, creatinine, aspartate aminotransferase (AST), Alanine aminotransferase, total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides and HbA1c were recorded at baseline and end of follow-up. In addition, the initial waist circumferences, body mass indexes and diabetes durations were recorded in all patients.

Informed consent statement

The permissions for the use of patient data were taken from the local ethics committee (Kayseri training and research hospital). The research was conducted in accordance with the Helsinki Declaration.

Statistical analysis

The continuous data were presented as means and standard deviations or medians and percentiles. Student's t test was used to compare continuous variables between groups. Mann-Whitney U test was used to compare medians of continuous variables with skewed distribution. Chi-square test was used to compare categorical variables. Pearson correlation analysis was used to assess relationship between patient and control groups. The pretest-posttest measurements were performed by using paired sample T and Kruskal-Wallis tests where appropriate. A p value <0.05 was considered as statistically significant. All statistical analyses were performed by using SPSS version 21.0 (Statistical Package for Social Sciences; SPSS Inc., Chicago, Illinois).

RESULTS

Overall, results at baseline and end of follow-up were compared in 80 diabetic patients. The median age of whole group was 56.08±9.71 years. Of the patients, 39.5% were male whereas 60.5% were female. The median follow-up duration of DPP-4 inhibitor was 18 (2-64) months.

Table 1: Demographic characteristics, physical measurements of patients and group comparisons of these parameters.

Variables	T Total group (n=80)	Subgroups		p
		Vildagliptin (n=40)	Sitagliptin (n=40)	
Age (years)*	56.08 ±9.71	55.88 ±11.1	56.28 ±8.2	p=0.855
Waist (cm)	104.36 ±13.0	104.4 ±13.1	104.3 ±13.1	p=0.979
BMI (kg/m^2)	30.2 ±6.2	33.5 ±6.6	33.2 ±5.8	p=0.297
DM duration (years)	5 (0-25)	4(0-25)	7 (0-23)	p=0.594
DPP-4 inhibitor duration (months)	18 (2-64)	25(3-64)	10 (2-58)	p=0.725

[#]P values represent comparisons of vildagliptin and sitagliptin groups with each other. DPP-4 inhibitor duration: DPP-4 inhibitor follow-up (months), BMI: Body Mass Index

The patients were receiving 4 types of treatment. Forty-six percent of the patients (n=37) were using a

sulfonylurea plus metformin. Twenty-two percent of patients (n=18) were using metformin in addition to insulin. The proportion of patients using solely metformin was 28.8% (n=23). Only 2.5% (n=2) of the patients were on insulin therapy alone. During the follow-up period, the HBA1C level was decreased from 9.53±1.87% at baseline to 8.50±1.48% at the end of follow-up, corresponding a significant decrease by 1.03% in average (p <0.001).

Table 2: Laboratory values of patients and group comparisons of these parameters.

Variables	Total group (n=80)	Subgroups		P
		Vildagliptin (n=40)	Sitagliptin (n=40)	
Glucose (mg/dl)	217.06±72.14	215.55±78.43	218.0±66.21	p=0.853
BUN (mg/dl)	14.49±4.67	14.18±4.52	14.80±4.85	p=0.553
Cr (mg/dl)	0.72±0.17	0.72±0.16	0.72±0.49	p=0.995
AST (U/L)	19 (11-77)	19.5 (14-70)	19 (11-49)	p=0.783
ALT (U/L)	21(6-80)	20.5 (6-80)	21.5 (9-79)	p=0.668
T. Chol. (mg/dl)	200.25±43.93	207.38±46.02	193.13±41.08	p=0.148
LDL (mg/dl)	113.67±37.53	118.81±37.14	108.53±37.67	p=0.223
HDL (mg/dl)	47.39±10.17	47.48±10.84	47.30±9.60	p=0.939
Triglycerides (mg/dl)	179 (46-771)	188 (58-771)	173 (46-725)	p=0.513
A1c initial (%)	9.53±1.87	9.60±2.29	9.46±1.35	p=0.736
A1c final (%)	8.50±1.48	8.60±1.57	8.40±1.40	p=0.554

[#]P values represent comparisons of vildagliptin and sitagliptin groups with each other. BUN: Blood urea nitrogen, Cr: Creatinine, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, T.chol: Total cholesterol, LDL: Low density lipoprotein, HDL: High density lipoprotein, A1c initial: A1c before DPP-4 inhibitor initiation, A1c final: A1c after the follow up period.

No significant difference was found between initial and final values of the lipid parameters of the patients. At baseline, mean total cholesterol, LDL, HDL and triglyceride values were 200.25±43.93mg/dL, 113.377±37.53mg/dL, 47.39±10.17mg/dL and 179 (46-771) mg/dL, respectively (p=0.904, 0.195, 0.782, and 0.549, respectively) were changed to 200.6±42.5mg/dL, 119.4±7.3mg/dL, 48.2±15.2mg/dL and 174 (49-636) mg/dL respectively.

Demographic characteristics, physical measurements and laboratory values of patients and group comparisons of these parameters are summarized in Tables 1 and 2.

Correlation analysis

There was no significant correlation between age and the change of HbA1c with the DPP-4 inhibitor therapy (p=0.072). There was no significant correlation between waist circumference of patients and HbA1c changes (p=0.336). There was no significant correlation between body mass index (BMI) and HbA1c changes of patients (p=0.905). There was no significant correlation between diabetic mellitus duration and HbA1c exchange (p=0.144). There was no significant correlation between the duration of DPP-4 inhibitor use and decrease in HbA1c (p=0.668). There was no significant correlation between lipid levels of patients (total cholesterol, LDL, HDL, Triglyceride) and HbA1c reduction. P values for total cholesterol, LDL, HDL and triglyceride were 0.136, 0.239, 0.272 and 0.557, respectively. There was no significant correlation between micro-protein/creatinine ratio of patients and decrease in HbA1c (p=0.348).

Comparison of sitagliptin and vildagliptin

The two DPP-4 inhibitors vildagliptin and sitagliptin also were compared in the patients. The comparisons made are shown in table 2. The remarkable point was that there was no statistically significant difference in the decrease in the group of sitagliptin (1.06%) compared to decrease in the vildagliptin group (1.06%) (p=0.263).

Comparisons of patients with follow-up duration ≥12 months

Of 80 patients, 50 patients with at least 12 months follow-up with DPP-4 inhibitors were evaluated separately. There was a significant difference between median in HbA1c values at baseline (9%) and end of follow-up (8.5%), indicating statistical significance (p=0.005).

Sitagliptin and vildagliptin showed no statistically significant difference in HbA1c decline and other parameters, when compared with patients who were followed for at least 12 months. Other parameters are summarized in Table 3 and Table 4.

The differences in the lipid parameters of the patients indicate no statistical significance when the initial and final values were compared. At baseline, mean values of

total cholesterol, LDL, HDL and triglyceride were 195.2±40.9mg/dL, 105.1±34.8mg/dL, 46.1±10.0mg/dL and 191.5 58-771mg/dL. These values were 196.1±42.8 mg/dL, 113.8±38.4 mg/dL, 47.9±17.7mg/dL and 188 (59-636) mg/dL at the end of follow-up, respectively (p=0.961, 0.170, 0.572 and 0.727, respectively).

Table 3: Demographic characteristics and physical measurements of patients (DPP-4 inhibitor duration >12 months) and group comparison.

Variables	Total group (n=50)	Subgroups		p
		Vildagliptin	Sitagliptin	
Age (years)*	55.70±9.43 (n=50)	55.84±11.02(n=31)	55.47±6.3 (n=19)	p=0.149
Waist (cm)	104.8±11.8 (n=35)	104.2±12.4 (n=22)	105.8±11.0 (n=13)	p=0.688
BMI (kg/m^2)	33.4±6.1 (n=37)	33.3±6.6 (n=24)	33.5±5.3 (n=13)	p=0.947
DM duration (years)	4(0-25) (n=45)	5 (0-25) (n=28)	4 (0-20) (n=17)	p=0.730
DPP-4 inhibitor duration (months)	36.5 (12-64) (n=50)	30 (12-64) (n=31)	44 (13-58) (n=19)	p=0.174

#P values represent comparisons of vildagliptin and sitagliptin groups with each other. DPP-4 inhibitor duration: DPP-4 inhibitor follow-up (months), BMI: Body Mass Index.

Table 4: Laboratory values of patients (DPP-4 inhibitor duration >12 months) and group comparisons.

Variables	Total group (n=50)	Subgroups		p#
		Vildagliptin (n=31)	Sitagliptin (n=19)	
Glucose (mg/dl)	211.1±79.0	204.3±78.5	222.2±80.6	p=0.443
BUN (mg/dl)	14.2±3.9	14.2±3.9	14.4±4.0	p=0.836
Cr (mg/dl)	0.72±0.16	0.72±0.16	0.72±0.17	p=0.997
AST (U/L)	19.5 (11-49)	19 (14-48)	26 (11-49)	p=0.051
ALT (U/L)	21 (6-79)	20 (6-69)	24 (9-79)	p=0.308
T. Chol. (mg/dl)	195.2±40.9	201.3±40.1	185.2±41.4	p=0.180
LDL (mg/dl)	105.1±34.8	110.3±32.0	96.7±38.3	p=0.182
HDL (mg/dl)	46.1±10.0	46.3±9.3	45.8±11.2	p=0.874
Triglycerides (mg/dl)	191.5 (58-771)	192 (58-771)	186 (88-480)	p=0.484
A1c initial (%)	9.44±2.02	9.37±2.34	9.54±1.40	p=0.774
A1c final (%)	8.43±1.23	8.46±1.43	8.39±1.04	p=0.868

#P values represent comparisons of vildagliptin and sitagliptin groups with each other. BUN: Blood urea nitrogen, Cr: Creatinine, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, T. chol: Total cholesterol, LDL: Low density lipoprotein, HDL: High density lipoprotein, A1c initial: A1c before DPP-4 inhibitor initiation, A1c final: A1c after the follow up period.

Table 5: Demographic characteristics, physical measurements of patients (DPP-4 inhibitor duration <12 months) and group comparisons.

Variables	Total group (n=33)	Subgroups		p
		Vildagliptin (n=12)	Sitagliptin (n=21)	
Age (years)*	56.2±10.0	54.8±10.6	57.0±9.8	p=0.557
Waist (cm)	103.7±14.9	105.8±15.0	105.0±15.3	p=0.688
BMI (kg/m^2)	33.2±6.4	33.9±6.4	32.3±6.6	p=0.732
DM duration (years)	5 (0-23)	4 (1.5-12)	7.5 (0-23)	p=0.199
DPP-4 inhibitor duration (months)	5 (2-12)	5.5 (3-12)	5 (2-10)	p=0.326

#P values represent comparisons of vildagliptin and sitagliptin groups with each other. DPP-4 inhibitor duration: DPP-4 inhibitor follow-up (months), BMI: Body Mass Index

Comparisons of patients with follow-up duration ≤12 months

When patients with follow-up duration of 12 months or less were selected, a subgroup of 33 patients was identified. Of these 33 patients, 12 were in vildagliptin group, while the remaining 21 were in sitagliptin group. The mean HbA1c value at baseline was 9.49±1.65 whereas 8.60±1.69% at the end of follow-up (p=0.002). The comparisons are summarized in Tables 5 and 6.

The differences in the lipid parameters of the patients indicated no statistical significance when the initial and final values were compared. At baseline, mean cholesterol, LDL, HDL and triglyceride median values were 209.2±46.2mg/dL, 128.1±37.3mg/dL, 48.8±10.2mg/dL and 158 (46-725) mg/dL. These values were changed to 211.2±43.2 mg/dL, 128.5±35.0mg/dL, 48.3±10.6mg/dL and 161 (49-429) mg/dL respectively after the follow-up (p=0.947, 0.584, 0.729 and 0.518, respectively).

Table 6: Laboratory values of patients (DPP-4 inhibitor duration <12 months) and group comparisons.

Variables	Total group (n=33)	Subgroups		P#
		Vildagliptin (n=12)	Sitagliptin (n=21)	
Glucose (mg/dl)	225.7±58.1	243.8±66.2	215.3±51.8	p=0.179
BUN (mg/dl)	14.73±5.6	13.9±5.9	15.2±5.6	p=0.540
Cr (mg/dl)	0.72±0.18	0.72±0.16	0.71±0.19	p=0.971
AST (U/L)	18 (12-77)	24 (14-77)	18 (12-42)	p=0.200
ALT (U/L)	22 (10-80)	38 (11-80)	20 (10-55)	p=0.024
T. Chol. (mg/dl)	209.2±46.2	224.9±53.2	200.3±40.4	p=0.143
LDL(mg/dl)	128.1±37.3	143.5±38.4	119.2±34.6	p=0.072
HDL(mg/dl)	48.8±10.2	45.0±13.9	48.7±7.9	p=0.930
Triglycerides (mg/dl)	158 (46-725)	155.5 (64-278)	170 (46-725)	p=0.782
A1c initial (%)	9.49±1.65	9.65±2.15	9.38±1.33	p=0.611
A1c final (%)	8.60±1.69	8.92±1.74	8.41±1.68	p=0.413

P values represent comparisons of vildagliptin and sitagliptin groups with each other. BUN: Blood urea nitrogen, Cr: Creatinine, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, T.chol: Total cholesterol, LDL: Low density lipoprotein, HDL: High density lipoprotein, A1c initial: A1c before DPP-4 inhibitor initiation, A1c final: A1c after the follow up period

Table 7: Demographic characteristics, physical measurements of patients (due to HbA1c situation) and group comparisons.

Variables	Total group (n=33)	Subgroups		P
		↓ (n=55)	○/↑ (n=25)	
Age (years)*	56.08±9.71	53.44±10.8	57.27±9.0	p=0.855
Waist (cm)	104.36±13.0	98.0±13.6	106.5±12.2	p=0.979
BMI (kg/m^2)	30.2±6.2	30.9±5.5	34.1±6.3	p=0.861
DM duration (years)	5(0-25)	7 (0-23)	4.5 (0-25)	p=0.759
DPP-4 inhibitor duration (months)	18(2-64)	25 (3-64)	16 (2-58)	p=0.107

#P values represent comparisons of vildagliptin and sitagliptin groups with each other. DPP-4 inhibitor duration: DPP-4 inhibitor follow-up (months), BMI: Body Mass Index.

Table 8: Laboratory values of patients (due to A1c situation) and group comparisons.

Variables	Total group (n=80)	A1c Subgroups					
		A1c ○/↑ Initial (n=25)	A1c ○/↑ Final (n=25)	P2	A1c ↓initial (n=55)	A1c ↓ final (n=55)	P3
Glucose(mg/dl)	217.06±72.14	182.9±69.6	230.3±79.4	p=0.005	232.6±68.4	174.5±65.4	p<0.001
BUN (mg/dl)	14.49±4.67	14.4±5.7	13.9±4.6	p=0.358	14.5±4.2	14.5±5.2	p=0.998
Cr (mg/dl)	0.72±0.17	0.73±0.18	0.75±0.18	p=0.345	0.71±0.16	1.02±0.76	p=0.270
AST (U/L)	19 (11-77)	19 (11-60)	19 (11-62)	p=0.741	19 (12-77)	21 (12-38)	p=0.134
ALT (U/L)	21(6-80)	22 (6-69)	20.5 (6-100)	p=0.948	21 (10-80)	22.5 (9-123)	p=0.440
Chol. (mg/dl)	200.25±43.93	198.5±37.0	211.9±	p=0.184	201.1±47.1	195.5±43.6	p=0.285
LDL (mg/dl)	113.67±37.53	113.5±31.3	124.3±32.3	p=0.150	113.8±40.3	117.0±39.6	p=0.516
HDL (mg/dl)	47.39±10.17	47.7±10.0	46.5±21.4	p=0.492	47.3±10.4	46.8±11.5	p=0.553
TG (mg/dl)	179 (46-771)	159 (88-385)	211.5 (140-304)	p=0.216	188 (46-771)	171 (49-636)	p=0.076
A1c initial (%)	9.53±1.87	8.71±1.18	9.71±1.51	p<0.001	9.90±2.01	7.96±1.10	p<0.001

A1c ○/↑: A1c remains the same or increased, A1c ↓: A1c decreased; BUN: Blood urea nitrogen, Cr: Creatinine, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, Chol: Total cholesterol, LDL: Low density lipoprotein, HDL: High density lipoprotein, TG: Triglycerides, A1c initial: A1c before DPP-4 inhibitor initiation, A1c final: A1c after the follow up period

Comparisons between patients with unchanged /increased HbA1c and decreased hba1c after addition of dpp-4 inhibitors

Overall 80 patients were classified according to whether their mean HbA1c level decreased or not after DPP-4 the usage of DPP-4 inhibitors. According to this, 68.8% (n=55) of the patients had a decrease in HbA1c while 31.2% had increased or unchanged HbA1c. There was no statistically significant difference in terms of age, waist circumference, duration of diabetes, duration of DPP-4 inhibitor use, and parameters shown in Table 7 and Table 8 when the groups were compared.

DISCUSSION

The main purpose of this research was to investigate the long-term outcomes of DPP-4 inhibitors when added to any type of therapy. After a median follow-up, it can be said that DPP-4 inhibitors (sitagliptin and vildagliptin) are effective in long term and they do not worsen the biochemical parameters.

When used as monotherapy, vildagliptin, and sitagliptin, have been shown to be more effective in reducing HbA1c than placebo.[8,9] In addition to ongoing metformin treatment, sitagliptin as well as vildagliptin were found to be effective.[10,11] Vildagliptin, when added to the sulfonylureas, provided statistically significant reductions in HbA1c, and similarly in the past years significant reductions was shown in HbA1c with sitagliptin.[12-14] Also, there are studies showing the activity of sitagliptin and vildagliptin added to ongoing insulin treatment.[15,16]

In the literature, we found a single study in which the addition of DPP-4 inhibitors to metformin and insulin-using patients.[17] In this study, sitagliptin was added and a statistically significant decrease in HbA1c was recorded.

The majority of these studies were designed and conducted as studies where patients were followed for weeks (4-52 weeks). We did not specify a specific upper limit for the follow-up time of the patients in this study. The follow-up time after addition of the DPP-4 inhibitor varied from 2 months (8 weeks) to 64 months (256 weeks). The length of the follow-up period determined the follow-up processes of the patients. That is, the patients used in the study were not imprisoned for a particular study design and consisted of patients who were monitored according to real life and treatment conditions. The median follow-up was thus 18 months (72 weeks).

In this study, which included 80 patients, a mean improvement in HbA1c of 1.03% was observed in patients who received DPP-4 inhibitors in addition to their current treatment. This is a statistically significant difference. While this significant difference was found in the total group, this improvement in HbA1c was observed as 1.0% in vildagliptin subgroup and 1.06 in sitagliptin subgroup. The reductions in HbA1c in the two subgroups were also significant, but the two subgroups were not statistically significant in their comparison to each other.

There was no positive or negative contribution of DPP-4 inhibitors to the lipid parameters in the total group (Table 2).

Patients with at least 12 months (48 weeks) of follow-up were analyzed. Median follow-up time was 36.5 (12-64) months (146 weeks). Overall, 50 patients had a mean reduction of 1.03% in HbA1c. This decrease was statistically significant, but the vildagliptin and sitagliptin subgroups had no advantage over the other. The lipid parameters of the patients who were followed for at least 12 months also did not change significantly when they were taken as initial and follow-up results.

When we examined the effects of adding DPP-4 inhibitors in the first year, we also found significant differences between starting and ending HbA1c. Patients had a median improvement of 0.89% over 5 months (2-12) or 20 (8-48) weeks. Patients in the vildagliptin subgroup and patients in the sitagliptin subgroup were not statistically different in terms of HbA1c reduction or lipid parameters compared to each other.

When patients with a decrease in mean HbA1c value were considered as a subgroup, they did not make any significant difference in terms of lipid and biochemical changes seen in Table 8 with other patients in the group.

It may be possible to derive these results from all these;

Addition of DPP-4 inhibitors to patients' treatments leads significant decreases in HbA1c mean values. This decline is long lasting. However, there are no positive or negative effects on biochemical parameters such as lipids, kidney and liver functions. This finding is consistent with the literature.[18] Furthermore, a study published in 2017 showed that sitagliptin is not superior to placebo in patients with nonalcoholic hepatosteatosis.[19]

Patients' ages or duration of diabetes are not predictive of their benefit from DPP-4 inhibitors. The literature is rich in studies with shorter follow-up. The distinguishing feature of our study is the long follow-up period. Even considering the long follow-up times, these two types of DPP-4 inhibitors can be said to be safe in the context of the above mentioned parameters. The same design can be repeated with higher number of patients.

CONCLUSION

The purpose of this research was to investigate the long-term outcomes of DPP-4 inhibitors when added to any type of therapy. After a median follow-up, it can be said that DPP-4 inhibitors (sitagliptin and vildagliptin) are effective in long term and they do not worsen the biochemical parameters.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Avci D, Çetinkaya A. Are dipeptidyl peptidase-4 inhibitors effective and safe in long term when added to ongoing therapies of diabetics? a real-life study in tertiary referral center. Int J Adv Med 2019;6:264-70.