Does the Availability of DPP-4 Inhibitors Affect the Glycemic Control in Patients with Type 2 Diabetes Mellitus?

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Abstract

Background: To investigate whether the availability of DPP-4 inhibitors (DPP-4I) affect the glycemic control in patients with T2DM.
Methods: A total of 667 patients with T2DM were enrolled in this cross-sectional study. The patients were divided into two groups according to their medical insurance plans; the University (290 patients) and the Ministry (377 patients) groups. Both groups had comparable access to anti-diabetic medications except for DPP-4I which were available only to the University group. Accordingly, the University group was divided into two subgroups depending on their use of DPP-4I; DPP-4I users and non-users. Glycemic control, as assessed by HbA_1C and rates of hypoglycemia, DKA and non-ketotic hyperosmolar state (NKHS), were compared in the three groups. Odds ratios were calculated to establish a correlation.
Results: The rate of inadequate glycemic control (HbA1c ≥ 7%) was 72.3% in the University DPP-4I users, 51.5% in the University DPP-4I non-users and 59.9% in the Ministry group (p=0.003). After adjusting for various factors that influence glycemic control, the multivariate analysis showed that the University DPP-4I users were more likely to have inadequate glycemic control compared to those in the Ministry group (p=0.002, OR= 2.4). No significant difference was observed in the rate of hypoglycemia, DKA and NKHS in the three groups.
Conclusion: Our results suggested that, in the studied population, the availability of DPP-4I did not improve glycemic control nor reduce the rate of acute complications of DM. On the contrary, inadequate glycemic control in the DPP-4I users was significantly higher compared to the non-users.

Keywords: DPP4 Inhibitors, glycemic control, medical insurance.

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Background

Glycosylated hemoglobin (HbA1c) has been routinely used as a measure of the adequacy of chronic glycemic control in patients with diabetes mellitus (DM). A HbA1c less than 7% is indicative of optimal glycemic control according to the American Diabetes Association guidelines [1]. However, studies across multiple populations frequently report that the percentage of patients with an

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HbA1c below 7% is less than desired [2] and only 6.9% of DM patients achieve glycemic, lipid and blood pressure targets [3].

In the majority of patients' multiple factors contribute to the failure to achieve optimal glycemic control. Such factors include patient related factors; namely noncompliance with dietary advice and/or drug therapy regimens, or physician related factors including delayed initiation of appropriate antidiabetic drug regimen changes or insulin therapy initiation [4].

In the last two decades, several new classes of anti-diabetic medications have been made available for patients with type 2 DM (T2DM) including glucagon like peptide-1 (GLP1) agonists, and dipeptidyl peptidase-4 inhibitors (DPP-4I) DPP-4I improve glycemic control by inhibiting the DPP-4 enzyme, which enzymatically degrades GLP1. GLP1 is a peptide hormone produced in the small intestine in response to a meal/glycemic load [5]. Thus, the higher GLP1 levels, resulting from DPP-4I therapy, increases the glucose-dependent insulin release from the pancreatic beta cells [6] and inhibits the inappropriately elevated post-meal glucagon levels in patients with T2DM [5]. At Jordan University Hospital (JUH), a tertiary teaching hospital in Jordan, DPP-4I were available to diabetic patients under the University insurance plan, however, were not available under the Ministry insurance plan.

This study aimed to investigate whether the availability of DPP-4I affects the glycemic control in patients with T2DM. This was achieved by comparing the glycemic control of patients with T2DM under the University insurance plan with patients with T2DM under the Ministry insurance plan in the same hospital.

We hypothesized that DPP-4I users would have higher rates of optimal glycemic control because of DPP-4I's unique glucose-dependent insulinotropic and glucagoneostatic effects. In addition, we expected reduced complications of DM as DPP-4I are characterized by lower risk for hypoglycemia compared to sulfonylureas [7-10]

Methods

This cross-sectional study was conducted at JUH between October 2013 and March 2014, following approval from the institutional review board. The target population of our study was all patients attending the outpatient endocrine clinic at JUH who met the following criteria; T2DM, aged 18 years or more, able to provide a written consent and on stable antidiabetic medications for at least three months. Exclusion criteria included pregnancy, breastfeeding, patients who received steroid therapy within 3 months before the onset of the study, patients with T1DM and inability to provide a written consent.

The eligible patients were recruited consecutively. A total of 667 patients were enrolled in the study. All patients enrolled in the study signed a written consent and were not compensated for their participation. They were divided into two major groups according to their medical insurance plans; the University insurance and the Ministry insurance plans. Both groups had similar access to antidiabetic medications except for DPP-4I which were available only to the University group. Thus, the University group was divided into two subgroups depending on their use of DPP-4 Inhibitors; the users and the non-users of DPP-4I. Glycemic control, as assessed by HBA1c and rates of hypoglycemia, DKA and NKHS, were the

primary endpoints of the study. Blood pressure control and lipid profile were also compared in the three groups (University DPP-4I users, University DPP-4I non-users, Ministry non-DPP-4I users) and were considered secondary outcomes of this study.

All patients, regardless of Insurance plan, were eligible for metformin, sulfonylureas, pioglitazone and all types of insulins, as available in the hospital; premixed insulin 70/30, regular, glargine, aspart and premixed aspart 70/30. However, GLP-1 agonists, glucose transporter inhibitors, meglitinides, and alpha-glucosidase inhibitors were not available to all groups.

Fasting blood samples were drawn by trained nurses and immediately sent to the JUH laboratory for fasting lipid and HbA1c analysis. Serum HbA1c was measured by ion exchange high-performance liquid chromatography (D-10 Dual Program; Bio-Rad, Hercules, CA). Patients with HbA1C levels below 7% were considered to be optimally controlled [1].

All patients had their seated blood pressure measured by experienced clinic nurses from the patient's right arm after five minutes of rest. Weight (kg) and height (cm) were also measured by trained nurses. The body mass index (BMI) was defined by using the equation of BMI = weight (Kg) / height (m^2).

BMI values between 18.5 and 24.9 were defined as normal, values between 25 and 29.9 were defined as overweight, whereas values of 30 and higher were defined as obese [11, 12]. Hypoglycemia was defined as a serum glucose less than 70mg/dl with symptoms [13] or a serum glucose of 60 mg/dl or less regardless of symptoms [14]. Severe hypoglycemia was defined as a hypoglycemic episode requiring assistance from another person [13]. All participants were asked to record the frequency, details and symptoms of hypoglycemic episodes, in addition to precipitating factors and details of any hospitalization that ensued.

Data were analyzed using SPSS IBM version 20. Data were described by using means and percentages. The differences in the means of continuous variables were compared using one-way ANOVA. The Chi-square test was used to analyze the difference between proportions. The association between sub-optimal glycemic control and insurance/DPP4-I use status was tested by multivariate analysis using binary logistic regression. A p-value of less than 0.05 was considered statistically significant.

Results

This study included 377 patients with Ministry Insurance, 196 University DPP-4I non-users and 94 University DPP-4I users. Table 1 displays each patient group's demographic, clinical and other relevant characteristics. The mean age of Ministry, University DPP4-I non-users and University DPP-4I users was 59.6±11.5 (yrs), 57.8±11.9 and 57.8±8.9 respectively. There was no significant difference in age between the three groups. Insulin and metformin use was significantly less common, and sulfonylurea use more common, in the University DPP-4I users compared to the other patient groups. Other baseline patient characteristics were not significantly different between the three patient groups.

Table 1. Patient group demographic, clinical, and relevant characteristics (page 7)

	Insurance Type						
	University DPP-4I users		University DPP-4I nonusers		Ministry		
	Mean	SD	Mean	SD	Mean	SD	P-value
Gender, n (%)							.014
Female	46	48.9	94	48.0	224	59.4	
Male	48	51.1	102	52.0	153	40.6	
Age (yrs)	57.8	8.9	57.8	11.9	59.6	11.5	.119
Duration of diabetes in years	7.1	4.1	8.5	8.0	8.9	7.8	.118
SBP (mm Hg)	133.9	14.9	128.7	19.4	133.1	20.3	.021
DBP (mm Hg)	75.0	9.7	73.5	10.4	73.4	10.0	.369
TC (mmol/L)	169.0	40.7	165.9	35.4	171.7	47.0	.357
LDL (mmol/L)	98.0	33.1	96.3	29.9	99.4	37.9	.603
HDL (mmol/L)	44.5	23.3	43.5	12.3	42.7	12.2	.675
TG (mmol/L)	164.1	79.4	153.4	90.8	161.0	101.7	.678
Drug use, n (%)							
Insulin	23	24.5	76	38.8	171	46.0	.001
Biguanides	68	72.3	172	87.8	310	83.3	.005
Sulfonylureas	49	52.1	48	24.5	126	33.9	.000
Statins	90	96.8	169	87.1	311	83.8	.004
Body mass index (BMI)							.153
Normal	10.0	10.8	25.0	12.8	28.0	7.6	
Overweight	36.0	38.7	74.0	37.8	126.0	34.1	
Obesity	47.0	50.5	97.0	49.5	216.0	58.4	
HbA1c							0.003
Controlled (<7%)	26	27.7	95	48.5	149	40.1	
Not controlled≥7%	68	72.3	101	51.5	223	59.9	

DBP, diastolic blood pressure; DPP4I, dipeptidyl peptidase 4 inhibitors; HDL, high density lipoprotein; Ministry, LDL-C, low density lipoprotein cholesterol; Ministry of Health; SBP, systolic blood pressure; TG, triglycerides.

The rate of sub-optimal glycemic control (HbA1c level ≥7%) was 72.3% in the University DPP-4I users, 51.5% in the University DPP-4I non-users and 59.9% in the Ministry group (P value = 0.003).

In the multivariate analysis, after adjusting for relevant factors (Table 2), the University DPP-4I users were significantly more likely to have sub-optimal glycemic control compared to patients in the Ministry group (OR = 2.4 [1.4-4.1]; p=0.002). No significant difference in glycemic control was observed between patients in the Ministry group (all DPP-4I non-users) and the University DPP-4I non-users.

Table 2. Adjusted association between insurance and poor glycemic control

	OR	95% confidence interval		p-value
Duration of DM	1.01	1.01	1.1	.005
Insulin use	3.6	2.3	5.6	.000
Sulfonylureas	2.9	2.0	4.4	.000
Insurance				
University DPP-4I users	2.4	1.4	4.1	.002
University DPP-4I non-users	0.9	0.6	1.3	.571
Ministry	1.0			
Body mass index				
Normal				
Overweight	1.7	1.1	3.2	.046
Obesity	1.3	0.7	2.4	.344

DM, Diabetes Mellitus; DPP-4I, dipeptidyl peptidase 4 inhibitors; OR, odds ratio.

In order to delineate whether the difference in glycemic control was the DPP-4I use status or purely an effect of different insurance-schemes the same analysis was applied to two reallocated patient groups; the DPP-4I group (N=97) and the No DPP-4I group which was a combination of University and Ministry Insurance patients (N=570). The baseline demographic and clinical characteristics for these groups are shown in Table 3 and Table 4. Again the rate of sub-optimal glycemic control is significantly higher in the DPP4-I group (Table 4).

Table 3. DPP-4I Group Statistics

	DPP4I	N	Mean	Std. Deviation	Std. Error Mean	P value
HbA1c (%)	No	570	7.6570	1.62795	.06789	.126
	Yes	97	7.9311	1.18915	.12535	
Age (years)	No	570	59.3865	11.10765	.46242	.230
	Yes	97	57.9111	8.92874	.94117	
BMI (kg/m^2)	No	570	31.3042	5.67926	.23643	.206
	Yes	97	30.4991	5.13203	.54096	
DM duration (yrs)	No	570	8.7766	7.82851	.32591	.072
	Yes	97	7.2556	4.21157	.44394	
SBP (mmHg)	No	570	131.3258	20.07628	.83579	.235
	Yes	97	133.9556	15.59308	1.64365	
DBP (mmHg)	No	570	73.3137	10.05439	.41857	.175
	Yes	97	74.8556	9.77794	1.03069	
LDL (mg/dl)	No	570	98.7730	35.10098	1.46127	.865
	Yes	97	99.4444	33.66561	3.54867	

Table 4. Use of different antidiabetic drug therapy by DPP-4I therapy group

			DPP-4I users	DPP-4I nonusers	Total	
Insulin	No	N	73	314	387	
		%	75.3%	55.1%	58.0%	
	Yes	N	24	256	280	
		%	24.7%	44.9%	42.0%	
Metformin	No	N	25	94	119	
		%	25.8%	16.6%	17.9%	
	Yes	N	72	476	548	
		%	74.2%	83.4%	82.1%	
SU	No	N	47	401	448	
		%	48.5%	70.4%	67.2%	
	Yes	N	50	169	219	
		%	51.5%	29.6%	32.8%	
Statins	No	N	13	106	119	
		%	13.4%	18.6%	17.8%	
	Yes	N	84	464	548	
		%	86.6%	81.4%	82.2%	
HbA1C	<7%	Count	27	224	251	0.000
		% within DPP4I	27.8%	39.3%	37.6%	
	7%+	Count	70	346	416	0.000
		% within DPP4I	72.2%	60.7%	62.4%	

BMI, Body mass index; DBP, diastolic blood pressure; DM, Diabetes Mellitus; DPP4I, dipeptidyl peptidase 4 inhibitors; HbA1c, Glycosylated haemoglobin; LDL, low density lipoprotein; N, number; SBP, systolic blood pressure.

DPP4I, dipeptidyl peptidase 4 inhibitors; HbA1c, Glycosylated haemoglobin; N, number; SU, sulfonylureas.

The total number of hypoglycemic episodes in DPP-4I users and non-users were 2 and 13 respectively, this difference being not significant (P value = 0.625). Of those episodes, 2 were severe hypoglycemic episodes in the DPP-4I non-users, whereas DPP-4I users reported no severe hypoglycemic episodes (P value = 0.730). In the whole study sample, there were no episodes of NKHS. One episode of DKA was reported in the DPP-4I non-users.

The mean systolic blood pressure (SBP) was significantly lower in the University non-DPP4-I users (Table 1).

Discussion

The discovery of the DPP-4 enzyme in 1966 led to the development of the first DPP-4I in 2006 [15,16]. Since then at least 11 DPP-4I have been approved for medical use. Incretin-based therapies, which include DPP-4I and GLP1 agonists, have been attractive to both clinicians and patients because of their unique glucose-dependent insulinotropic and glucagoneostatic effects [17, 18, 19]. As such, incretin-based therapies have consistently demonstrated beneficial effects on glycemic

control as well as on β-cell function, gastric emptying and appetite [17]. Furthermore, in comparison sulfonylureas, DPP-4I have been characterized by reduced hypoglycemic episodes and a neutral effect on weight [20]. However, DPP-4I are more expensive, which make them less available to many patients [21].

To our knowledge, no previous data in the English literature has examined the impact of DPP-4I availability on T2DM glycemic control in the clinical setting. Due to the high cost of this class of antidiabetic medication, our study results may assist local health authorities in deciding whether to adopt such medications into their available drug lists. This is especially true of countries with limited economic resources.

Our data demonstrated that there was no benefit to glycemic control in DPP-4I users compared to DPP-4I non-users. To the contrary, there was worse glycemic control in DPP4-I users as indicated by the lower percentage of patients who achieved optimal glycemic control (HbA1c < 7%) (P 0.003). Furthermore, there was a trend toward inferior glycemic control in DPP-4I users, as indicated by the elevation in mean HbA1c level in these patients, however the mean HbA1c difference between DPP-4I users and non-users was not statistically significant (P 0.254).

The cause for these unexpected negative trends is not readily apparent. The mean age of each patient group was comparable. Furthermore, it is unlikely that obesity caused this trend as the mean BMI scores were significantly higher in patients in the Ministry group who were not using DPP4I, which should presumably worsen glycemic control, not improve it. In addition the issue of DPP-I drug noncompliance is a potential cause for these results, this issue was addressed by direct questioning of the study subjects regarding compliance with their medications, and by reviewing pharmacy records for drug refills.

Lastly, patients early in their diabetes course tend to have better glycemic control; however the mean duration of diabetes in each patient group was statistically comparable.

Some studies have demonstrated that diabetic women reach their targets of glycemic control (HbA1c), blood pressure and LDL-cholesterol less often than their male counterparts, although the cause for this is unclear [22]. In our population there were significantly more women in the Ministry group compared to the University groups, however the proportion of women in the University DPP-4I users and non-users was comparable. Hence it is unlikely that female sex caused the observed difference in our population's glycemic control results, as the Ministry group achieved a higher rate of optimal glycemic control despite having significantly more women in the group.

Our data shows that patients on DPP-4I were prescribed sulfonylureas much more commonly, and insulin less commonly, when compared to DPP-4I non-users (Table 3). This difference suggests that the cause for the DPP-4I users having inferior glycemic control is a physician-factor, namely that there may be a delay in the initiation of insulin therapy if DPP-4I are available to the patient. This factor may be further exacerbated by patients' hesitation to start insulin therapy [23].

In regard to other glycemic outcomes of this study, several studies have reported reduced rates of hypoglycemic episodes associated with DPP-4I use compared to sulfonylureas [6,7,8,9] However, our data did not show a significant difference in the rate of

hypoglycemic episodes between DPP-4I users and non-users. This may be attributed to the effect of the concomitant use of other anti-diabetic medications in the studied groups. However it may also be due to under powering to detect a significant difference in hypoglycemic episodes (relatively rare events). Similarly, there was no significant difference among the studied groups in the rate of DKA and NKHS, and similar causes of this non-significance may apply.

Our analysis also revealed a significant SBP disparity between the studied groups, with SBP being significantly lower in the University DPP-4I non-users (p-value=0.021) compared to the University DPP-4I users and Ministry groups. The cause for this SBP difference is not readily apparent as patient characteristics, such as age and length of diabetes, was comparable between the three groups. The effect of DPP-4I on blood pressure has not yet been clearly defined [24,25] though DPP-4I use is unlikely to explain the SBP difference between the two groups as the reduced SBP was in University DPP4-I non-users. In this study, we did not specifically analyze the anti-hypertensive regimens of patients across all groups as this was not within the primary aim of the study.

To the best of our knowledge, we believe that this is the first study which addresses the effect of the availability of DPP-4I on glycemic control and the rate of acute complications of T2DM including hypoglycemia, DKA and NKHS. However, limitations include the small number of DPP-4I users and the non-randomised nature of this study.

Conclusion

In the studied population we were unable to detect a significant beneficial effect for glycemic control based on the availability of DPP-4I. On the contrary the DPP-4I users had worse glycemic control outcomes compared to non-users. There were no significant differences in the rates of hypoglycemia, DKA or NKHS between the DPP-4I users and non-users.

Future studies with a larger population size, specifically with more DPP4-I users, may be needed to clarify this negative correlation between glycemic control and unavailability of DPP-4I. The SBP difference between DPP-4I and insurance groups also requires a detailed examination. These differences may be due to different antihypertensive medication availability from different insurance providers or it may be due to other unidentified factors in the studied population.

Abbreviations

BMI Body Mass Index
DKA Diabetic Ketoacidosis
DM Diabetes Mellitus
DPP-4 Dipeptidyl Peptidase-4
DPP-4I Dipeptidyl Peptidase-4 Inhibitor
GLP1 Glucagon Like Peptide-1
HbA1C Glycosylated Hemoglobin
JUH Jordan University Hospital
LDL Low-Density Lipoprotein
NKHS Nonketotic Hyperosmolar Syndrome
SBP Systolic Blood Pressure
T1DM Type 1 Diabetes Mellitus
T2DM Type 2 Diabetes Mellitus.

Declarations

The study was conducted after approval from Jordan University Hospital institutional review board, and a written consent form was signed by all subjects enrolled in the study.

Competing interests

The author declares that he has no competing interests.

References

1. American Diabetes Association. Standards of medical care in diabetes—2016. Diabetes Care 2016. Available at http://care.diabetesjournals.org/content/suppl/2015/12/21/39.Supplement_1.DC2/2016-Standards-of-Care.pdf Accessed May 31, 2017
2. Hoerger T, Segel J, Gregg E, Saaddine J. Is Glycemic Control Improving in U.S. Adults?. Diabetes Care. 2007;31(1):81-86.
3. Menon A, Ahluwalia A. The ABC of diabetes. How many patients are able to achieve the goal laid down by American Diabetes Association? Medical Journal Armed Forces India. 2015;71(2):132-134.
4. Bartels D. Adherence to Oral Therapy for Type 2 Diabetes: Opportunities for Enhancing Glycemic Control. Journal of the American Academy of Nurse Practitioners. 2004;16(1):9-17.
5. Koliaki C, Doupis J. Incretin-based therapy: a powerful and promising weapon in the treatment of type 2 diabetes mellitus. Diabetes Therapy. 2011;2(2):101-121.
6. Lee Y, Jun H. Anti-diabetic actions of glucagon-like peptide-1 on pancreatic beta-cells. Metabolism. 2014;63(1):9-19.
7. Nauck M, Meininger G, Sheng D, Terranella L, Stein P. Efficacy and safety of the dipeptidyl peptidase-4 inhibitor, sitagliptin, compared with the sulfonylurea, glipizide, in patients with type 2 diabetes inadequately controlled on metformin alone: a randomized, double-blind, non-inferiority trial. Diabetes, Obesity and Metabolism. 2007;9(2):194-205.
8. Gautier J, Monguillon P, Verier-Mine O, et al. Which oral antidiabetic drug to combine with metformin to minimize the risk of hypoglycemia when initiating basal insulin? Diabetes Research and Clinical Practice. 2016;116:26-28.
9. Gitt A, Bramlage P, Binz C, Krekler M, Deeg E, Tschöpe D. Prognostic implications of DPP-4 inhibitor vs. sulfonylurea use on top of metformin in a real world setting - results of the 1 year follow-up of the prospective DiaRegis registry. International Journal of Clinical Practice. 2013;67(10):1005-1014.
10. Deacon C, Lebovitz H. Comparative review of dipeptidyl peptidase-4 inhibitors and sulphonylureas. Diabetes, Obesity and Metabolism. 2016;18(4):333-347.
11. Executive Summary of the Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. Journal of the American Dietetic Association. 1998;98(10):1178-1191.
12. Ulijaszek S. Obesity: Preventing and Managing the Global Epidemic. Report of a WHO Consultation. WHO Technical Report Series 894. Pp. 252. (World Health Organization, Geneva, 2000.) SFr 56.00, ISBN 92-4-120894-5, paperback. Journal of Biosocial Science. 2003;35(4):624-625.
13. Defining and Reporting Hypoglycemia in Diabetes: A report from the American Diabetes Association Workgroup on Hypoglycemia. Diabetes Care. 2005;28(5):1245-1249.
14. Boon NA, ed., Colledge NR, ed., Walker BR, ed. Davidson's principles & practice of medicine. 20th ed. Edinburgh: Elsevier/Churchill Livingstone, 2008.
15. Deacon C, Nauck M, Toft-Nielsen M, Pridal L, Willms B, Holst J. Both Subcutaneously and Intravenously Administered Glucagon-Like Peptide I Are Rapidly Degraded From the NH2-Terminus in Type II Diabetic Patients and in Healthy Subjects. Diabetes. 1995;44(9):1126-1131.
16. Hopsu-Havu V, Glenner G. A new dipeptide naphthylamidase hydrolyzing glycyl-prolyl-?-

naphthylamide. Histochemie. 1966;7(3):197-201.

17. Deacon C. Therapeutic Strategies Based on Glucagon-Like Peptide 1. Diabetes. 2004;53(9):2181-2189.
18. Deacon CF, Holst JJ. Pharmacology of GLP-1-based therapies. Review of Endocrinology 2008*(January):* 17–22.
19. Holst JJ, Deacon CF. Inhibition of the activity of dipeptidyl-peptidase IV as a treatment for type 2 diabetes. Diabetes 1998*;* 47*:* 1663–1670
20. Gooßen K, Gräber S. Longer term safety of dipeptidyl peptidase-4 inhibitors in patients with type 2 diabetes mellitus: systematic review and meta-analysis. Diabetes, Obesity and Metabolism. 2012;14(12):1061-1072.
21. Chamberlain J, Herman W, Leal S, Rhinehart A, Shubrook J, Skolnik N et al. Pharmacologic Therapy for Type 2 Diabetes: Synopsis of the 2017 American Diabetes Association Standards of Medical Care in Diabetes. Annals of Internal Medicine. 2017;166(8):572.
22. Kautzky-Willer A., Weitgasser R, Fasching P, Hoppichler F, Lechleitner M. [Sex- and gender-aspects in regard to clinical practice recommendations for pre-diabetes and diabetes]. Wien Klin Wochenschr. 2012 Dec;124 Suppl 2:91-6.
23. Ng C, Lai P, Lee Y, Azmi S, Teo C. Barriers and facilitators to starting insulin in patients with type 2 diabetes: a systematic review. International Journal of Clinical Practice. 2015;69(10):1050-1070.
24. Scheen A. A review of gliptins for 2014. Expert Opinion on Pharmacotherapy. 2014;16(1):43-62.
25. Jackson E, Mi Z, Tofovic S, Gillespie D. Effect of Dipeptidyl Peptidase 4 Inhibition on Arterial Blood Pressure Is Context DependentNovelty and Significance. Hypertension. 2014;65(1):238-249.

هل يؤثر توافر عقاقير DPP-4I على معدلات ضبط السكري عند مرضى السكري من النوع الثاني

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الملخص

الخلفية: التحقق من أن توافر عقاقير DPP-4 I يوثر على ضبط معدلات السكر عند المرضى المصابين بالنوع الثاني من مرض السكري

الطرق: تم إدراج ما مجموعه 667 من المرضى المصابين بالنوع الثاني من مرض السكري في هده الدراسة المستعرضة. تم تقسيم المرضى إلى مجموعتين حسب نوع التأمين الطبي: تأمين الجامعة (290 مريض) و الوزارة (377 مريض). كلتا المجموعتين كان لديها فرصة الحصول على كافة العلاجات المتوفرة باستثناء عقاقير DPP4-I والتي كانت متوافرة فقط لمجموعة تأمين الجامعة. ثم تم تقسيم مجموعه تأمين الجامعة إلى مجموعتين فرعيتين حسب استخدام هذه العقاقير. قورنت معدلات ضبط السكري باستخدام خضاب الدم السكري، كما تم مقارنة معدلات هبوط مستوى السكر في الدم وارتفاعات السكر الحادة في الدم والمترافقه مع حموضة الدم أو الفرط الاسمولي (DKA or hyperosmolar state)

النتائج: معدلات ضبط السكري غير الكافية (خضاب الدم السكري أكثر من أو يساوي 7%) كانت 72.3 % في مجموعة تأمين الجامعة الذين يستخدمون عقاقير DPP4-I، و 51,5% في مجموعة تأمين الجامعة الذين لا يستخدمون هذه العقاقير. وكانت النسبة 59,9% في مجموعة تأمين الوزارة .(p=0.003). بعد الأخذ بعين الاعتبار عوامل مختلفة قد تؤثر على ضبط السكري فإن التحليل الإحصائي أظهر أن مجموعة تأمين الجامعة الذين يستخدمون عقاقير DPP4-I هم أكثر احتمالية للتعرض لمعدلات ضبط السكري غير الكافية مقارنة بمجموعة مرضى الوزارة .(p=0.002, OR= 2.4)

لم يلاحظ وجود أي اختلافات مهمة احصائيا في معدلات هبوط مستوى السكر في الدم أو ارتفاعات السكر الحادة في الدم والمترافقة مع حموضة الدم أو الفرط الاسمولي

الخلاصة: تقترح النتائج من العينة المدروسة أن توافر عقاقير DPP4-I لم يؤد إلى تحسين ضبط معدلات السكري في الدم و لم يؤد إلى تخفيض معدلات المضاعفات الحادة لمرض السكري. بل تشير النتائج إلى أن معدلات ضبط السكر كانت اسوأ في المجموعة التي استخدمت هذه العقاقير مقارنة بالمجموعات الأخرى.

الكلمات الدّالّة: عقاقير مثبطات DPP4، ضبط السكر ،التأمين الطبي.