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Original Research Article

Efficacy and Safety of Sitagliptin in Type 2 Diabetic Libyan patients

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Abstract: Sitagliptin is a drug used in treatment of type 2 diabetes mellitus. Incretin hormones, including glucagon-like peptide-1 analogue and dipeptidyl peptidase-4 inhibitor have recently been found to regulate glucose metabolism. Thus, the aim of this study was to evaluate the effect of sitagliptin on glycemic control and it is associated side effects in Libyan patients with type 2 diabetes, who had inadequate response to existing anti-diabetic drugs. Hundred patients with a known history of type 2 diabetes were recruited in this study during the period of 2019 and 2020. Sitagliptin (100 mg daily) was added on to the pre-existing therapy for type 2 diabetes and the main outcome measures were a change from the base line in glycated hemoglobin and fasting plasma sugar as well as the incidence of symptomatic hypoglycemia. All patients were engaged from outpatient clinic of National Diabetes and Endocrinology Center at Tripoli, Libya. The findings show that the actions of dipeptidyl peptidase-4 inhibitors improve glycaemic control in the patients, and glycated hemoglobin as well as fasting plasma sugar. Thus, sitagliptin is a profound drug for a comprehensive treatment of patients with type 2 diabetes with a low incidence of hypoglycemia.

Keywords: Diabetes, blood sugar, patients, sitagliptin, Libya.

INTRODUCTION

Type 2 diabetes (T2DM) is a chronic metabolic disease that caused by pancreas β-cell dysfunction, deficiency in insulin secretion, insulin resistance and/or increased hepatic glucose production. Individuals with T2DM are at high risk for microvascular and macrovascular complication [1]. Modern treatments are often inefficient at sustaining glycemic control and may cause undesirable side effects, such as weight gain and episodes of hypoglycemia. Therefore, new and more effective drugs have been developed with di-peptidyl peptidase-4 (DPP-4) inhibitors playing a significant role [2]. Inhibition of DPP-4 leads to increase in the active levels of incretins such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) which are involved in glucoregulation [3, 4]. Several studies have demonstrated the superior efficacy and safety of DPP-4 inhibitors [5, 6] among which Sitagliptin was the first DPP-4 inhibitor used for treatment of T2DM [7].

Sitagliptin can be used as mono-therapy in patients who are inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindication or intolerance or when a sulphonylurea, diet and exercise plus maximal tolerated dose of sulphonylurea alone do not provide adequate glycemic control [6]. Sitagliptin has many advantage in comparison to other anti-diabetic drugs as it is well tolerated, weight neutral and does not cause hypoglycemia [8]. The efficacy and safety of DPP-4 inhibitors has been established by studies that were carried out in several parts of the world. However, reports about sitagliptin use and its side effects in Libyan population are lacking. Therefore, this study was carried out to address this problem by evaluating the effects of sitagliptin on glycemic control and it is most common side effects in patients with T2DM who had a poorly or an inadequate responsive to, existing anti-diabetic drugs.

MATERIALS AND METHODS

A retrospective study that contains Libyan patients (n = 100) with a history of T2DM and follow up in Diabetes and Endocrinology Center (DEC) was adapted at Tripoli, Libya. Patients were evaluated for both efficacy and safety of sitagliptin therapy during the period of 2019 and 2020. All the patients were initially on treatment with anti-diabetic drugs as mono-therapy or in combinations with sulfonylurea, biguanide and insulin therapy but had inadequate response as determined by fasting blood sugar (FBS) and glycated hemoglobin (HbA1c). Those patients were continue their existing anti-diabetic drugs with addition of sitagliptin (100 mg per day) and the main outcome measures were change from base line in glycated hemoglobin (HbA1c) and fasting plasma sugar (FBS) and the incidence of symptomatic hypoglycemia. The study was approved by the medical ethics committee of University Teaching Hospital and University of Tripoli (approval number 2019010011). Data was collected from medical records and relevant information before and after the addition of sitagliptin. Data was extracted and recorded in a prepared data collection form. Other information analyzed included demographic data of patients, medical condition, medication and other clinical data before and after administration of sitagliptin and reported side effects or hypoglycaemia episodes. All the patient were provided with disease and treatment information, details about diet recommendation and lifestyle modification during each follow up visit. Data were analyzed using descriptive statistical measures such as frequency distribution, percentage, mean and standard deviation.

RESULTS

In Table 1, a total of one hundred patients were enrolled in this study. The socio-demographic characteristics of the patients are shown in Table 1. Fifty eight patients were males (58%) and 42 patients were females (42%). The peak age group was old adult group (> 50 years old) representing about 60% of the patients followed by middle age group (30 - 50 years) representing about 40%. The smallest group consists of those patients with young adult group (less than 30 years old) and representing a very small percentage (3%) of the whole study population. Furthermore, the education level were found to be about 40% for secondary level, about 40% for university level, whereas, 20% was for primary level. With regards to the geographical distribution of the diabetic patients, out of the total patients (n = 100), 83% were of a local inhabitants at a Tripoli city, 17% of the patients came from outside the major city (rural areas). Moreover, of the 100 patients, the largest group of the patients were government work (51%) and 17% self-employed while 32% had no work (unemployed). Of the total patients, only 9% of the patients were smokers.

Regarding treatment of T2DM in this study, all the patients were initially on treatment with anti-diabetic drugs as mono-therapy or combinations (sulfonylurea, biguanide, insulin) therapy as shown in Table 2. The smallest percentage which is only 3% representing patient who take sulfonylurea and the largest number is 29% represents patients who use biguanide and insulin. Thus, sitagliptin (100 mg per day) was add to the pre-existing therapy. Table 2 shows that the highest group (36%) of our patients were using sitagliptin for 3 - 6 months and lowest group (5%) for more than 6 months (Table 2).

Table-1: Socio-demographic characteristic of patients

Study variables	**Number and percentage, n (%)**
Gender	
Male	58 (58)
Female	42 (42)
Age group	
Young adult patients (< 30)	3 (3)
Middle age patients (30-50)	39 (39)
Old adult patients (> 50)	58 (58)
Educational status	
University	39 (39)
Secondary school	40 (40)
Primary	)21 (21
Geographic distribution	
Tripoli city	83 (83)
Out Tripoli city	17 (17)
Occupation	
Government servant	51 (51)
Self-employed	17 (17)
Exposure the patients to the cigarettes	
Yes	9 (9)
No	91 (91)

Table-2: Drugs taken by the patients during study

Study variables	Number and percentage of patient, n (%)
Anti-diabetic drugs taken by the patients	
Sulfonylurea	3 (3)0
Biguanide	27 (27)
Insulin	4 (4)0
Biguanide and Insulin	29 (29)
Biguanide and Sulfonylurea	24 (24)
Biguanide, Sulfonylurea, and Insulin	13 (13)
Total	100 (100)
Duration period of Sitagliptin intake	
< 1 months	13 (13)
3-6 months	36 (36)
> 6 months	05 (5)
> 1 year	13 (13)
1-2 years	16 (16)
> 2 year	17 (17)
Total	100

In Table 3, the effectiveness of sitagliptin was analyzed and the main outcome measures in FBS and HbA1c were compared with the baseline. Prior to the administration of sitagliptin, three patients with blood glucose level less than 150 mg/dl (3%), 59 patients with blood glucose level 150 - 300 mg/dl (59%) and 38 patient with blood glucose level more than 300 mg/dl (38%). After sitagliptin was administration, the number of patients who achieved blood glucose level less than 150 mg/dl were increased to 38% whereas the number of patients who achieved blood glucose level more than 300 mg/dl were decreased to 5% **(**Figure 1**)**. Regarding HbA1c, prior to the administration of sitagliptin, the HbA1c was less than 7% for six patients, 7 - 9% for 28 patients and 33 patients were more than 9% of HbA1c. After sitagliptin was administration, the number of patients who achieved HbA1c below 7% increased from six patients at base line to 21%, the number of patients with HbA1c 7 - 9% were increased from 28% at baseline to 51%. Whereas, the number of patients with HbA1c more than 9% were decreased from 33% at baseline to 26% (Figure 2). Moreover, in current study, out of 100 patients 43% have other comorbidities and receiving different therapy and 57% never suffer from other diseases (data not shown).

Table-3: The clinical characteristic of patients (laboratory test results)

Patients clinical characteristics	Number and percentage of patient, n (%)
Fasting blood glucose (mg/dl) prior administration sitagliptin (Baseline)	
< 150	3 (3)0
150 - 300	59 (59)
> 300	38 (38)
Total	100 (100)
Fasting blood glucose (mg/dl) after administration sitagliptin	
< 150	38 (38)
150 - 300	57 (57)
> 300	5 (5)0
Total	100 (100)
Cumulative blood sugar level (HbA1c (%) prior administration sitagliptin (Baseline)	
< 7	06 (6)
7 - 9	28 (28)
> 9	33 (33)
Unknown	33 (33)
Total	100 (100)
Cumulative blood sugar level (HbA1c (%) after administration sitagliptin	
< 7	21 (21)
7 - 9	51 (51)
> 9	26 (26)
Unknown	2 (2)0
Total	100 (100)

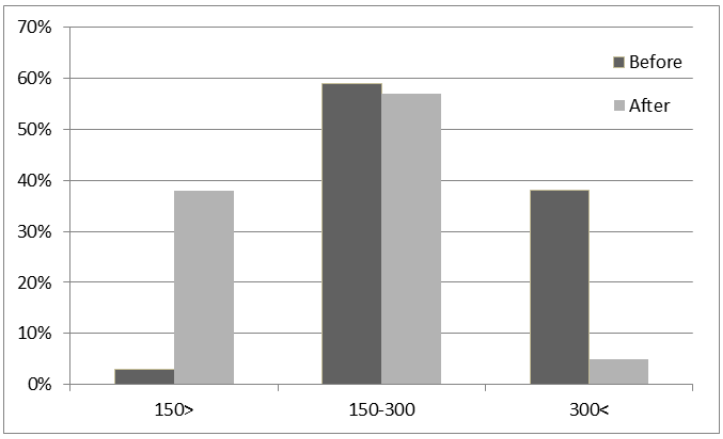

Fig-1: Fasting blood glucose (mg/dl) before and after administration sitagliptin

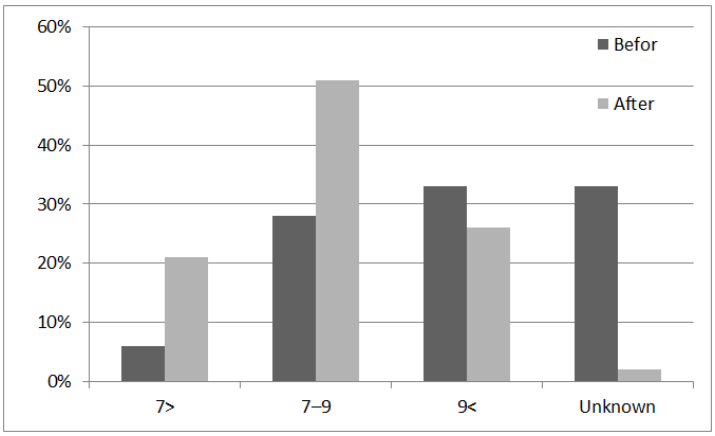

Fig-2: Cumulative blood sugar level (HbA1c, %) before and after administration sitagliptin.

Safety of sitagliptin was also assessed by adverse event and hypoglycemic episodes as well as other symptom during the study period as shown in Table 4. Prior to the administration of sitagliptin, 69% of the patients had never exposure to hypoglycemia and 31% of the patients had exposed to hypoglycemia. After sitagliptin was administration, the number of patients who were exposure to hypoglycemia was slightly reduced by 7% of the patients. Moreover, hypoglycemic coma has not been occurred at all our study population.

With regards to body weight changes, out of 100 patients with T2DM, 58% were shown a change in the body weight. Of these patients, 47 of the patients were lost some weight (81.1%) and only 11 patients were gained some weight (18.9%). Out of 47 patients, 37 patients have lost less than 10 kilograms (78.72%), nine patients (19.2%) lost 10 - 20 kg, while only one patient has lost more than 20 kg (2.1%).

Table 5 shows side effects of sitagliptin were assessed by presence of other symptom including: immune system, nervous system, respiratory system, gastrointestinal, skin and subcutaneous tissue, musculoskeletal and connective tissue disorder as well as renal and urinary disorders. It is found that sitagliptin was associated with back pain (17%), arthralgia (16%), dizziness (15%), constipation (15%), myalgia (14%), impaired renal function (14%) and headache (13%). Other adverse events were uncommon during sitagliptin treatment. No acute pancreatitis or pancreatic cancer was detected in our studied patients (Table 5).

Table-4: Safety of sitagliptin

Patients characteristics	Number and percentage of patient, n (%)
hypoglycemia symptom prior administration of sitagliptin	
Yes	31 (31)
Never	69 (69)
Total	100 (100)
hypoglycemia symptom after administration of sitagliptin	
Yes	24 (24)
Never	76 (76)
Total	100 (100)

Hypoglycemic-coma	
Yes	00 (0)
Never	100 (100)
Body weight changes after administration sitagliptin	
Yes	58 (58)
No	42 (42)
Weight lost (Kg)	
< 10 Kg	37 (78.7)
10 - 20 Kg	9 (19.2)
> 20 Kg	01 (2.1)
Total	47 (100)
Weight gained (Kg)	
< 10 Kg	05 (45.5)
10 - 20 Kg	06 (54.5)
> 20 Kg	00
Total	11 (100)

Table-5: Other symptoms of adverse reaction

Patients characteristics	**Number and percentage of patient, n (%)**
Other symptoms of adverse reaction	
Disorders of immune system	
Hypersensitivity reaction (anaphylactic response)	03 (3)
Disorders of nervous system	
Headache	13 (13)
Dizziness	15 (15)
Respiratory system disorders	
Interstitial lung disease	00 (0)
Disorders of gastrointestinal system	
Constipation	15 (15)
Vomiting symptom	05 (5)
Acute pancreatitis	00 (0)
Fetal and non-fetal hemorrhagic and necrotizing pancreatitis	00 (0)
Disorders of skin and subcutaneous tissue	
Angioedema	00 (0)
Rash	02 (2)
Urticaria	00 (0)
Cutaneous vasculitis	00 (0)
Musculoskeletal and connective tissue disorder	
Arthralgia	16 (16)
Myalgia	14 (14)
Back pain	17 (17)
Renal and urinary disorder	
Impaired renal function	14 (14)
Acute renal failure	00 (0)

DISCUSSION

In this study, the efficacy and safety of the DPP-4 inhibitor (sitagliptin) added to the existing anti-diabetic drugs were assessed in patients with T2DM who had inadequate glycemic control. Thus, all the patients were initially on treatment with anti-diabetic drugs as mono-therapy or combinations (sulfonylurea, biguanide, insulin) therapy but had inadequate response as determined by the levels of FBS and HbA1c. Those patients were continue their existing anti-diabetic drugs with addition of sitagliptin (100 mg per day) and the main outcome measures where changes from baseline in HbA1c and FBS. Previous studies reported that sitagliptin improves HbA1c and FBS levels both as a single-drug therapy [9, 10] and as a combination therapy [11]. Our present study showed that HbA1c and FBS levels in patients who had taken sitagliptin concomitantly with other existing anti-diabetic drugs is reduced in uncontrolled patients. Prior to the administration of sitagliptin, only three patients with blood glucose level less than 150 mg/dl but 38% of the patients with blood glucose level more than 300 mg/dl. After sitagliptin was taken, the number of patients who achieved blood glucose level less than 150 mg/dl was increased to 38%. Whereas, the number of patients who achieved blood glucose level more than 300 mg/dl were decreased to 5%. Also, it was noticed that on administration of sitagliptin, the number of patients

who achieved HbA1c below 7% increased from 6% at base line to 21%, the number of patients with HbA1c 7 - 9% were increased to 51%, whereas, the number of patients with HbA1c more than 9% were decreased to 26%.

Treatment with sitagliptin led to a better HbA1c and FBG control compared with treatment with existing anti-diabetic drugs. One retrospective study which also assessed the effectiveness of sitagliptin in clinical practice reported a similar increase the proportion of patients achieving glycemic control after using sitagliptin [10, 12, 13]. Safety of sitagliptin was assessed by adverse events and hypoglycemic episodes as well as other symptoms including following disorders: immune system, nervous system, respiratory system, gastrointestinal, skin and subcutaneous tissue, musculoskeletal and connective tissue and renal and urinary. Thus, it has previously been reported that sitagliptin does not induce excessive hypoglycemia [9], however, in the present study; about 25% patients had hypoglycemia. DPP-4 inhibitors also do not induce body weight increases [14]. In our study, about 80% of the patients had lost some weight which indicated that sitagliptin does not cause an increase in the body weight. Sitagliptin is generally well tolerated with minimal adverse effects [15]. In this study, treatment with sitagliptin 100 mg once daily added to the existing therapy was well tolerated. Thus, low incidence of clinical adverse experiences have been reported by the patients such as low back pain, arthralgia, dizziness, constipation, myalgia, impaired renal function and headache. However, no other adverse events were reported or seen during sitagliptin treatment.

In conclusion, this study suggests that sitagliptin improves glycaemic control in Libyan patients with a low incidence of hypoglycemia.

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