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Effect of Sitagliptin on glycemic profiles and their correlation with PASI score in patients with plaque psoriasis

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Abstract

Psoriatic patients with plaque psoriasis particularly those with high body mass index have increasing risk of developing a diabetes mellitus type 2 (DM). Since both conditions are associated with dysregulation in DPP-IV, DPP-IV inhibitors have been suggested as therapeutic drugs for both diseases. The role of enzyme in the diabetes pathogenesis is well-known; however information on psoriatic patients is conflicting. The objective of this study is to determine the effect of Sitagliptin on glycemic profiles and their correlation with PASI score in psoriatic patients with DM. The study was conducted on 50 diabetic patients with moderate to severe plaque psoriasis who were divided into two groups: Placebo group (n =25) Patients were administered placebo 100mg once daily plus dietary control and exercise for 3 months ; Sitagliptin group (n =25) Patients were administered Sitagliptin tablet 100mg once a day plus dietary control and exercise for 3 month. PASI score for all patients was assessed before and after 12 weeks of treatment. The blood samples were obtained from the patients in both groups at baseline and after 12 week of therapy were used to measure the concentration of serum fasting blood sugar and HbA1c. Compared with baseline in Sitagliptin group and control group after 12 week, the level of fasting blood sugar, HbA1c, were significantly reduced and correlated with PASI score after 12 week of sitagliptin treatment ($P < 0.05$). The current results reveal that sitagliptin improves psoriasis possibly via a reduction in glycemic profiles which were significantly correlated with PASI score.

Keywords: Psoriasis; Diabetes; Sitagliptin; PASI score; Correlation

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Introduction

Psoriasis represents a complex chronic systemic cell immune- mediated inflammatory disease characterized by erythematous, scaly plaques of skin and joints [1]. It is now well known that psoriatic patients are at risk for developing metabolic syndrome [2]. It is interesting that psoriasis and obesity

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share the same inflammatory mediators involved in chronic inflammatory process such as IL-6 and TNF-α [3]. A tough correlation between increased body weight, abdominal fat, and psoriasis has been shown and proved by many researchers [4, 5]. TNF-α and IL-6 may exacerbate an inflammatory process of psoriasis and a chronic inflammation in islet cell of pancreases lead to insulin resistance and diabetes [6].

Methotrexate and TNF-α antagonists therapeutic effect in psoriasis is further proved by their ability to reduce insulin resistance and serum level of above mentioned cytokines and increase in HDL level [7, 8]. Gliptins are a novel class of oral anti-diabetic agents that enhance and prolong the physiological actions of incretin hormones by competitively antagonizing the enzyme that metabolize or degrade these hormones called dipeptidyl peptidase-4 (DPP-IV) [9]. Seventeen years old female psoriatic patients with type 2 diabetes discontinued systemic treatment with cyclosporine and topical steroid ointment given for treatment of psoriasis because of lacking satisfaction with the efficacy of these drugs. Administration of sitagliptin for control of diabetes is associated with gradual improvement in psoriatic lesions during three months of therapy without any reported adverse effects or improvement in HbA1c [10].

A study done by Ansorge S. et al [11] proposed that DPP-IV inhibitors could be an alternative drugs for the treatment of psoriasis when it is accompanied by diabetes mellitus. Exenatide and liraglutide have an incretin like effect similar to Sitagliptin given for control of diabetes result in improvement of PASI score in diabetic patients with plaque psoriasis [12]. In contrast Mas-Vidal A et. al [13] showed that psoriasiform rash was induced in 59-year-old woman after administration of six doses of sitagliptin for control of her diabetes.

The aim of study to assess the clinical efficacy of Sitagliptin on patients with moderate to severe plaque psoriasis by estimation of PASI score and to evaluate effect of drug on glycemic profiles, and their correlation with severity of plaque psoriasis (PASI score) after 12 week of treatment.

Material and methods

Patients and study design

The study was conducted over a period of 12 month from February 2015 until February 2016. Samples were collected from the out patients clinic of dermatology in Al-Sader Teaching Hospital in Najaf City/Iraq. The laboratory work was performed at the department of pharmacology in College of Medicine / University of kufa. Fifty diabetic patients with plaque psoriasis were enrolled in this study and divided into two groups:

Control group: Twenty five patients were administered placebo 100mg cap. once daily plus dietary control and exercise for 12 week.

Sitagliptin group: Twenty five patients were administered sitagliptin tablet 100mg (Januvia) once a day plus dietary control and exercise for 12 week.

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Inclusion criteria

1. Male patients with moderate to severe plaque psoriasis (PASI score more than 10).
2. Age 20-60.
3. Diabetic patients.
4. BMI > 30.

Exclusion criteria

The psoriatic patients who received topical therapy within 4 weeks, or systemic drug therapy and photo chemotherapy within 3 month

History and PASI score

A complete history was taken from all patients with careful attention to age, sex, and duration of disease, past topical or systemic treatment or concurrent chronic diseases as mentioned before. Patients were graded according to psoriasis area and severity index (PASI) score and patients with moderate to severe type were included in the study. PASI score for all patients was assessed before and after 12 weeks of treatment.

Blood sampling

Venous blood samples were drawn from psoriatic and control patients by using disposable syringes in the sitting position. Five ml of blood were obtained from each patient by vein pierce and pressed slowly into plain disposable tubes. Blood was allowable to coagulate at 37˚C for 10-15 minutes and then centrifuged at 3000 rpm for about 10-15 minutes, then the serum was obtained and stored at -20˚C until laboratory analysis for lipid profiles would be done.

Statistical analysis

The data were coded and entered the statistical analysis using the program statistical package for social sciences (SPSS) version 16 under windows version AMD. Our results were expressed as Mean ± SE. Student's t-test was used to clarify the effect of sitagliptin on PASI score and glycemic profiles. The linear regression analysis was applied to verify the relationships between different glycemic profiles level in psoriatic patients in relevance to PASI score after 12 weeks of sitagliptin treatment. Statistical variation was considered as significant when the P value was < 0.05.

Results

General characteristics of placebo and sitagliptin group of psoriatic patients

Table 1.
Mean and standard error mean of age, BMI, PASI score and FBS in placebo and sitagliptin groups

Parameter	Placebo group	Sitagliptin group	P-value
Age (year)	38.24±2.75	35.32±2.36	> 0.05
BMI (kg/m^2)	32.34± 2.25	31.84± 2.92	>0.05
PASI score	17.56±3.73	19.48±3.94	>0.05
FBS (mg/dl)	170.32±2.61	173.54±2.62	>0.05

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Numbers of psoriasis patients according to severity of disease

Table 2.
Numbers of psoriasis patients according to their PASI score

No. of patients	Placebo group	Sitagliptin group
Moderate PASI score	11	14
Severe PASI	12	13

Effect of sitagliptin on PASI score

The baseline of PASI score in sitagliptin group as well as in placebo group were statistically not significant. PASI score after 12week was significantly (*P*< 0.05**)** lower than that of baseline in sitagliptin group. The PASI score of sitagliptin treated group was significantly (*P*< 0.05**)** lower than that of placebo group after 12 week of treatment as shown in figure 1. Sitagliptin treatment resulted in marked improvement in patients with plaque psoriasis regarding scale, in duration and erythema but without complete clearance of lesion as shown in figure 2.

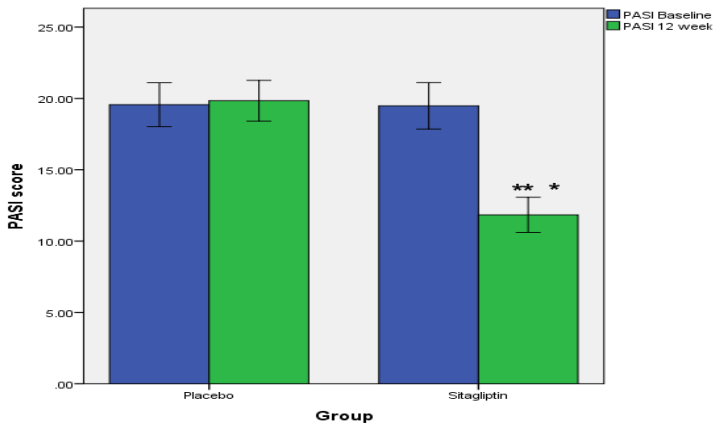

Figure 1.
Changes of psoriatic patients PASI score of the placebo and sitagliptin groups. Data expressed as Mean ±SEM (N=25 in each group) using paired T- test.**P*< 0.05 means significant changes in the sitagliptin group.** *P*< 0.05 means significant changes in comparison with placebo group.

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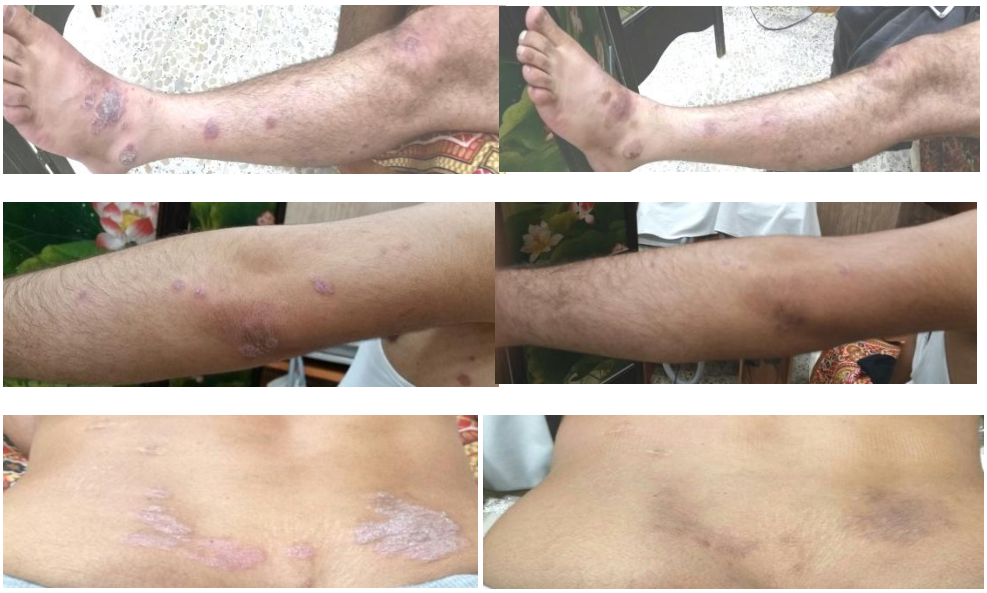

(A) (B)

Figure 1.
Marked systemic antipsoriatic effect of sitagliptin in patient with plaque psoriasis without complete absence of lesions. Typical untreated skin lesions at leg/foot, elbow and trunk (back) are shown before (A) and after 12 week of therapy (B)

Effect of sitagliptin on fasting blood glucose and HbA1c %

The baseline levels of FBS and HbA1c were not different between both groups. There were a statistically significant decrement ($P< 0.01$) in FBS and HbA1c levels after 12 week in comparison to baseline in sitagliptin treated group. The FBS and HbA1c levels of sitagliptin treated group were significantly ($P< 0.01$) lower than that of placebo treated group after 12 week as shown in figure 3 and figure 4 respectively.

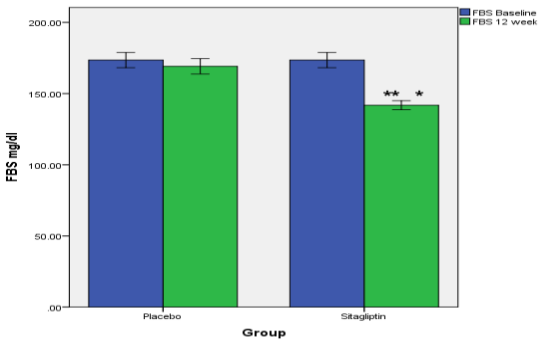

Figure 3.
Change of psoriatic patients FBS (mg/dl) of the placebo and Sitagliptin groups.
Data expressed as Mean±SEM (n=25 in each group) using paired T- test. $^{*}P< 0.05$ means significant changes in the sitagliptin group. $^{**}P<0.05$ means significant changes in comparison with placebo group after 12 week.

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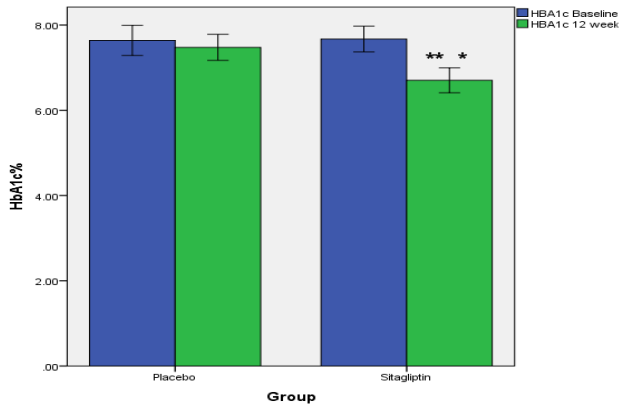

Figure 4.
Change of psoriatic patients HbA1c (%) of the placebo and Sitagliptin groups.
Data expressed as Mean±SEM (N=25 in each group) using paired T- test. *P< 0.05 means significant changes in the sitagliptin group. ** P< 0.05 means significant changes in comparison with placebo *group after 12 week.*

Correlation between PASI score with glycemic profiles after 12 week of Sitagliptin treatment

Figure 5 and figure 6 showed a significant (P < 0.05) positive correlation between PASI score and glycemic profiles (FBS, HbA1c) respectively.

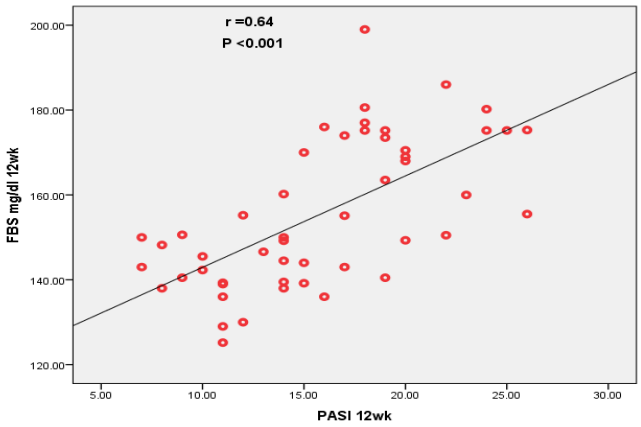

Figure 5.
Linear regression of FBS in sera of psoriatic patients with PASI score after 12 week of sitagliptin treatment

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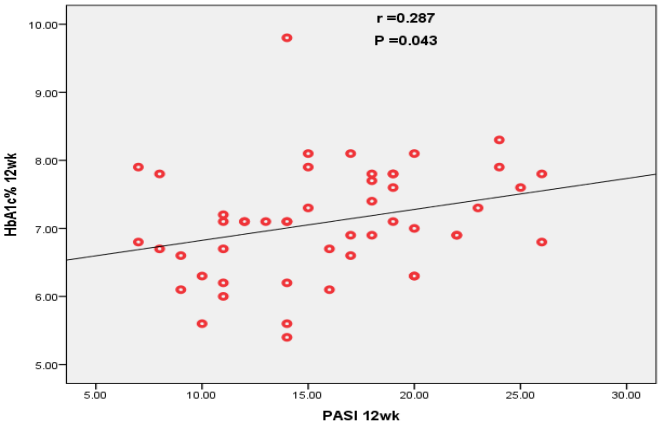

Figure 6.
Linear regression of HbA1c in sera of psoriatic patients with PASI score after 12 week of sitagliptin treatment

Discussion

Sitagliptin showed a significant decrease in PASI score after 12 week of treatment in comparison to baseline PASI score in sitagliptin- treated group and in comparison to placebo- treated group after 12 week. Our results are in agreement with those obtained by Atsuya Nishioka T. et al [10] who reported an improvement of psoriatic lesions after 12 weeks of sitagliptin treatment for diabetic female patient with psoriasis. Maeve Lynch et al [14] reported an improvement in psoriasis severity in patients with plaque psoriasis treated by sitagliptin NB-UVB for 24 week.

The results of present study are supported by Drucker DJ and Rosen CF [15] who demonstrated that exenatide and liraglutide which have an incretin like effect similar to sitagliptin given for control of diabetes result in improvement of PASI score in diabetic patients with plaque psoriasis. Our results disagree with Masvidal A. et al [16] who found that sitagliptin treatment for old diabetic woman produce un expected psoriasiform eruption on her trunk and both limbs after receiving six doses of drug, this can be explained as rare reaction to the drug and only one case study. Other randomized placebo-controlled trial, showed no significant change in psoriasis severity after 8 week of treatment with GLP-agonist liraglutide. Those patients included in this study had no diabetes, in comparison to our study that include only diabetic patients [17].

The improvement of PASI score could be immunological due to their additional anti-inflammatory effect, as treatment with sitagliptin resulted in a reduction in the number of natural killer cells in psoriatic plaques and an increase in their number in circulation [18].

Atsuya Nishioka and his colleagues [10] observed an improvement of

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psoriasis lesions in diabetic patient treated with a DPP-4 inhibitor, which may be attributed to an increase in GLP-1 levels and impairment in function of immune T cells by sitagliptin, probably due to the down regulation of DDP-4 on the surface of keratinocytes and multiple immune cell subtypes [19].

Sitagliptin showed a significant decrease in fasting blood glucose and HbA1c to baseline in sitagliptin- treated group and placebo- treated group after 12 week. The current results are in agreement with that reported by Buysschaert M. et al [20] who studied the effect of exenatide on diabetic patients with psoriasis and they showed that PASI score improved immediately after 1 month of treatment and hyperglycemia and HbA1c improved significantly after 3 months.

These results are in disagreement with that reported by Atsuya Nishioka T. et al [10] who showed improvement in psoriasis, despite lack of control of FBS and HbA1c (this one case study in comparison to 25 patients in our research). our results are disagreed with result of Faurschou et al [21] who demonstrated that PASI score reduced after 3 months of treatment, despite uncontrolled diabetes by therapy, improvement of psoriasis can be explained by a direct anti-inflammatory effect of liraglutide [22]. Improvement in hyperglycemia may be attributed to a reduction in TNF-α level by sitagliptin treatment (since TNF-α may interfere with insulin signaling and responsiveness in many cells such a s hepatic cells, fatty cells or skeletal muscles [23, 24]. A decrease in IL-6 and TNF-α concentration by sitagliptin treatment may lead to upregulation of adiponectin which is regarded as important sensitizer for insulin secretion and cardio protective factors for atherogenesis and inflammatory process [25, 26].

In present study there is a positive correlation between PASI score and fasting blood sugar and HbA1c after 12 week of sitagliptin treatment, and these results are agreed with those reported by Lynch M. et al [19] and Lamharzi N1. et al [27] who found that a decrease in hyperglycemia lead to decrease in macrophage proliferation and accumulation in psoriatic lesions which could be attributed to a reduction in oxidation of LDL which might play a role in induction of macrophage recruitment to psoriatic plaques. Gyldenløve M1. et al [28] and Derosa G. et al [29] demonstrated that patients with psoriasis are more insulin resistant compared with healthy control subjects and they showed that sitagliptin is effective in improving the sign of hyperglycemia together with a reduction of insulin resistance. Anti-inflammatory effect of sitagliptin on cytokines and natural killer cells in psoriatic lesion might lead to diminution in insulin resistance and hyperglycemia which could be a contributing factor of epidermal cells dysfunction and formation of psoriatic plaques [30].

Adequate control of hyperglycemia by 12 week sitagliptin treatment, in the absence of weight gain, leads to a reduction in lipid profile including cholesterol and triglyceride and an increase in HDL, improvement of

hyperlipidemia with high HDL result in a decrement in IL-6 which is one of important cytokine in pathogenesis of psoriasis [31].

In conclusion, the current results reveal that sitagliptin improves psoriasis possibly via a reduction in glycemic profiles which were significantly correlated with PASI score.

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