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Treatment with liraglutide, a glucagon-like peptide-1 analogue, improves effectively the skin lesions of psoriasis patients with type 2 diabetes: A prospective cohort study

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ABSTRACT

Background: It has been reported that GLP-1 analogue can improve the skin lesions of psoriasis. However further research is needed to confirm that finding.

Objective: The study can provide further data regarding the efficacy and safety of GLP-1 analogue liraglutide in the treatment of psoriasis patients with type 2 diabetes.

Methods: We recruit 7 psoriasis patients with type 2 diabetes, and use hypodermic injection with liraglutide 1.8 mg. In 12 weeks of treatment, we estimate the difference of before and after respectively, like BMI, waist circumference, fasting blood glucose, fasting C-peptide, HbA1c, blood lipid levels, CRP, PASI, DLQI, skin tissue and pathological analysis of psoriasis.

Results: After 12 weeks of treatment, the mean value of PASI decreased from 15.7 ± 11.8 to 2.2 ± 3.0 ($P = 0.03$), while the DLQI decreased from 21.8 ± 6 to 4.1 ± 3.9 ($P = 0.001$). HbA1c was significantly improved after 12 weeks of treatment, decreased to $6.4 \pm 0.8\%$ ($P = 0.04$), the BMI decreased to $21 \pm 3 \text{ kg m}^{-2}$ ($P < 0.01$), and the waist circumference was also significantly improved to $83 \pm 1 \text{ cm}$ ($P < 0.05$). And 12 weeks after, the fasting C-peptide levels increased to $1.9 \pm 0.5 \text{ ng/ml}$ ($P = 0.006$), HOMA - IR fell to 1.6 ± 0.6 ($P = 0.03$). Histological analysis showed a reduction in epidermal thickness after treatment. The mean PASI decreased from 15.7 (1.5–31.3) to 2.0 (0.3–8.7) ($P = 0.03$), the DLQI decreased from 22 (8–27) to 4 (0–10) ($P = 0.001$).

Conclusion: GLP-1 analogue liraglutide can improve the skin lesions of psoriasis patients with type 2 diabetes effectively, especially for extremely severe psoriasis patients. Its therapeutic effect may be related to anti-inflammatory, hypoglycemic and reducing weight.

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1. Introduction

Psoriasis is a chronic immune-mediated inflammatory skin disease, which is characterized by flaking, erythema, pruritus and plaque formation to varying degrees. The skin changes of

psoriasis have its unique characteristics, and the diagnosis of psoriasis is often confirmed by skin pathological biopsy. There are three main layers of normal skin structure. The first layer is the epidermis, which mainly composed of keratinocytes. The second layer is the dermis, mainly composed

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of collagen, which contains fibroblasts and a rich neurovascular network. The third is the subcutaneous adipose tissue layer, which has supporting interstitial cells. In the pathogenesis of psoriasis, abnormal accumulation of cuticle cells causes the formation of scales, reduction of epidermal granule layer, and extension of dermal network with vasodilatation. The number of white blood cells, such as the proportion of neutrophils, increased significantly. It was related to the activation of immune-related pathways.

Currently, the treatment of psoriasis is faced with great challenges, including high prevalence rate, high disability rate and common comorbid diseases such as diabetes [1]. The association between psoriasis and type 2 diabetes has been studied extensively [2–4], like the psoriasis patients have increased incidence to get type 2 diabetes, and the symptoms of desquamation and erythema increased significantly in psoriasis patients with poor glycemic control. GLP-1 receptor agonist (GLP-1 analogue) is a kind of multifunctional peptide hormone, it is a commonly used hypoglycemic drug in recent years. Some studies have been reported [5–8] that GLP-1 analogue can improve the skin lesions of psoriasis. However further research is needed to confirm that finding. We therefore hypothesized that GLP-1 analogue therapy can improve the skin lesions of psoriasis patients with type 2 diabetes.

In this study, we established a prospective cohort study to observe the therapeutic effect and safety of GLP-1 analogue liraglutide on a group of psoriasis patients with type 2 diabetes.

2. Materials and methods

2.1. Participants

Participants were recruited from the diabetology and dermatology outpatient clinics at the 900 Hospital of the Joint Logistics Team between December 2017 to June 2018. Inclusion criteria were: (i) 18–75 years old, male or female, (ii) diagnosed type 2 diabetes patients according to WHO standards (1999), with psoriasis confirmed by clinical and histopathological examination, (iii) in the past 2 months, no vitamin A acid, steroid hormones, immuno suppressants and psoriasis medications that were not applied topically before the screening. Exclusion criteria were patients with severe adverse reactions, type 1 diabetes, pregnancy and lactation, history of malignant tumor, serious heart, lung, kidney and liver diseases, previous history of pancreatitis. All participants sign relevant informed consent to all participants signed a form indicating their informed consent to study participation.

2.2. Intervention

The clinical characteristics of participants (including age, gender, height, body weight, duration of disease, presence of familial history of psoriasis, and psoriatic arthritis) were collected. Following the guidance of the doctor, participants had subcutaneous injection of liraglutide 0.6 mg every day before bedtime, after 1 week increased the dosage to 1.2 mg per day, and finally increased to the maximum dosage 1.8 mg

2.3. Assessments

We give separate assessments of before and after 4,8,12 weeks treatment, including body mass index (BMI), waist circumference, fasting blood glucose, fasting C-peptide, fasting insulin, glycosylated hemoglobin (HbA1c), blood lipid levels, C-reactive protein (CRP), the Psoriasis Area and Severity Index (PASI), the Dermatology Life Quality Index (DLQI), skin tissue and pathological analysis of psoriasis. The PASI has been used to quantify disease severity of erythema, infiltration or thickness, scaling and the extent of lesions in patients with widespread disease [9]. Each patient's BMI was Body weight (kg) divided by the square of their height (m^2). To estimate insulin resistance, HOMA-IR (fasting insulin mU/mL 3[fasting glucose (mmol/L)/22.5]) was calculated. The changes of psoriasis skin lesions were recorded by a Nikon camera (Japan, D750), and PASI was used to assess the severity of psoriasis before and after treatment, which evaluated the efficacy of liraglutide. Took the damaged skin and the adjacent uninjured skin from the patient, both the diameters were 5 mm, and produced paraffin section. Though hematoxylin staining, we observed pathological changes of psoriatic skin under optical microscope.

2.4. Statistical analysis

All data are expressed as means standard deviation (SD). Data were analyzed by using the SPSS 19.0 software (SPSS Inc. Chicago, USA). The significance of differences between means was assessed by paired Student's *t*-test. Values of $P < 0.05$ were considered statistically significant.

3. Results

3.1. Clinical data

A total of 7 participants with psoriasis patients with type 2 diabetes were selected in this study, including 6 males (86%) and 1 female (14%), the mean age was 60 ± 8 years. The PASI was 15.7 ± 11.9 , the highest was 31.3, reaching the standard of severe psoriasis, and none of them had psoriatic arthritis. The mean duration of psoriasis in all participants was 6 ± 2 years, and 10 ± 5 years for type 2 diabetes. Before using liraglutide, the patients' hypoglycemic therapies were as follows: 1 patient did not use any hypoglycemic drugs before, 2 participants have used metformin combined with alpha-glucosidase inhibitor, 2 participants have used metformin combined with sulfonylureas, and last 2 participants have used insulin. None of 7 participants have taken retinoic acid, steroid hormone, immunosuppressant and other drugs before. During the treatment period, liraglutide was well tolerated, and 4 patients (57%) presented different degrees of nausea and vomiting at the initial stage of treatment. There is no adverse reactions with the continued treatment of gastrointestinal, and no severe adverse events such as hypoglycemia and serious complications occurred in all patients.

As shown in Table 1, the mean baseline of BMI was $23 \pm 4 \text{ kg m}^{-2}$, and the waist circumference was $87 \pm 9 \text{ cm}$ before using liraglutide. After 12 weeks, the BMI decreased

Table 1 – Changes in BMI, waist circumference, fasting blood glucose, HbA1c, fasting C-peptide, Low-density Lipoprotein (LDL), CRP, PASI and DLQI after the use of liraglutide.

Patient	Sex	Age(years)	BMI (kg m ⁻²)		waist circumference (cm)		fasting blood glucose (mmol/L)		HbA1c (%)		fasting C-peptide (ng/ml)		LDL (mmol/L)		CRP (mg/L)		PASI		DLQI	
			Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
1	M	51	20.9	19.4	88	76	9.5	4.6	13.3	6.8	0.81	1.96	2.9	2.9	16.6	3.8	11.6	3.2	23	6
2	M	54	27.2	24.3	94	83	5.9	5.3	6.5	4.8	1.94	2.17	2.98	2.98	120	6.6	31.3	0.4	27	0
3	M	64	23.2	22.2	91	90	6.9	6.5	7.7	7.0	1.34	1.93	2.9	2.9	3.2	0.9	1.5	1.2	18	8
4	M	69	24.5	22.8	93	89	5.6	6	7.1	6.5	1.9	2.21	2.85	2.85	2.4	6.3	19	8.7	26	10
5	M	55	28.4	27.7	97	97	5.7	6	6.5	6.3	1.21	1.68	1.72	1.72	1.7	0.2	2.4	0.3	8	0
6	F	55	19.3	18.5	74	72	5.7	6.1	7.9	7.2	2.43	2.65	2.53	2.53	10.6	2.5	15	1.4	24	3
7	M	70	19.5	16.8	75	71	4.4	4.3	7.8	6.2	0.12	0.9	2.32	2.32	42.7	3.3	29.4	0.3	27	2
Mean ± SD		60 ± 8	23 ± 4	21 ± 3**	87 ± 9	83 ± 1*	6.2 ± 1.6	5.5 ± 0.8	8.1 ± 2.3	6.4 ± 0.8*	1.4 ± 0.7	1.9 ± 0.5**	2.6 ± 0.5	2.3 ± 0.3	28 ± 43	3.3 ± 2.4	15.7 ± 11	2.2 ± 3.0*	21.8 ± 7	4.1 ± 3.9**

M, male; F, female; Before, before treatment; After, 12 week after of treatment.

* P < 0.05 vs. Before.

** P < 0.01 vs. Before

to $21 \pm 3 \text{ kg m}^{-2}$ ($P < 0.01$), and the waist circumference was also significantly improved to $83 \pm 1 \text{ cm}$ ($P < 0.05$). In terms of glucose metabolism, fasting blood glucose concentration decreased from 6.2 mmol/L ($4.4\text{--}9.5 \text{ mmol/L}$) to 5.5 mmol/L ($4.3\text{--}6.5 \text{ mmol/L}$, $P = 0.3$), which did not reach statistical significance. However, HbA1c was significantly improved after 12 weeks of treatment, decreased from $8.1 \pm 2.3\%$ to $6.4 \pm 0.8\%$ ($P = 0.04$) (Fig. 1A). For improving the function of the pancreas, compared with that before treatment, after 4 weeks of treatment with liraglutide, the fasting C-peptide levels, HOMA - IR (insulin resistance index) get improved significantly, and 12 weeks after, the fasting C-peptide levels increased from $1.4 \pm 0.7 \text{ ng/ml}$ to $1.9 \pm 0.5 \text{ ng/ml}$ ($P = 0.006$) (Fig. 1B), HOMA - IR fell from 2.8 ± 0.8 to 1.6 ± 0.6 ($P = 0.03$) (Fig. 1C), both have obvious statistical significance. The values of LDL and CRP decreased from 2.6 ± 0.5 to $2.3 \pm 0.3 \text{ mmol/L}$ ($P = 0.14$) and decreased from 28 ± 43 to $3.3 \pm 2.4 \text{ mg/L}$ ($P = 0.16$) respectively.

3.2. PASI and DLQI

Liraglutide has improvement on skin lesions of psoriasis, the mean PASI decreased from 15.7 ($1.5\text{--}31.3$) to 2.0 ($0.3\text{--}8.7$) ($P = 0.03$) (Fig. 1D), among 6 participants (86%) decreased by more than 50%, even 5 participants (71%) dropped by more than 75%. Alike, the DLQI decreased from 22 ($8\text{--}27$) to 4 ($0\text{--}10$) ($P = 0.001$) (Table 1). And one of them has PASI of 31.3 (Fig. 2A₁₋₃), erythema, papules and nodules of different sizes can be seen in the extremities, accompanied by itching, belong to extremely severe psoriasis patients. There were large patches of yellow scales all over his body, it accorded

with standard for severe pustular psoriasis. After 4 weeks of treatment with liraglutide, the PASI dropped to 13.5 (decreased $> 50\%$) (Fig. 2B₁₋₃), with the silver crumbs plaques, narrow, itching symptoms improved significantly, 12 weeks after treatment, the body did not show the plaques, scales, PASI dropped to 0.4 (compared with before treatment, decreased $> 98\%$) (Fig. 2C₁₋₃).

3.3. Psoriasis skin tissue and pathological changes

Histopathological analysis was performed on the skin of the participants for HE staining. Although there was not pathological change, the pathological results of the normal skin showed that the skin layer of the participants was thicker than that of healthy people (Fig. 3A). Before the treatment with liraglutide, skin pathology in psoriasis shows extensive keratosis accompanied by edema exudation, hypertrophy of the spine layer, decreased epidermal granule layer, vasodilatation of the dermis, neutrophil infiltration with Munro micro-ulcer formation (Fig. 3B). After 12 weeks injection of liraglutide, shearing and comparing the same parts of the skin, which shows no typical psoriasis skin changes under naked eye, and seen to normal skin view (Fig. 2C₁₋₃). The pathological results indicated that the thickness of epidermis layer has reduced, Munro microulcer and neutrophils have disappeared (Fig. 3C).

4. Discussion

The results of that liraglutide can significantly improve psoriasis related symptoms and skin thickness of skin lesions.

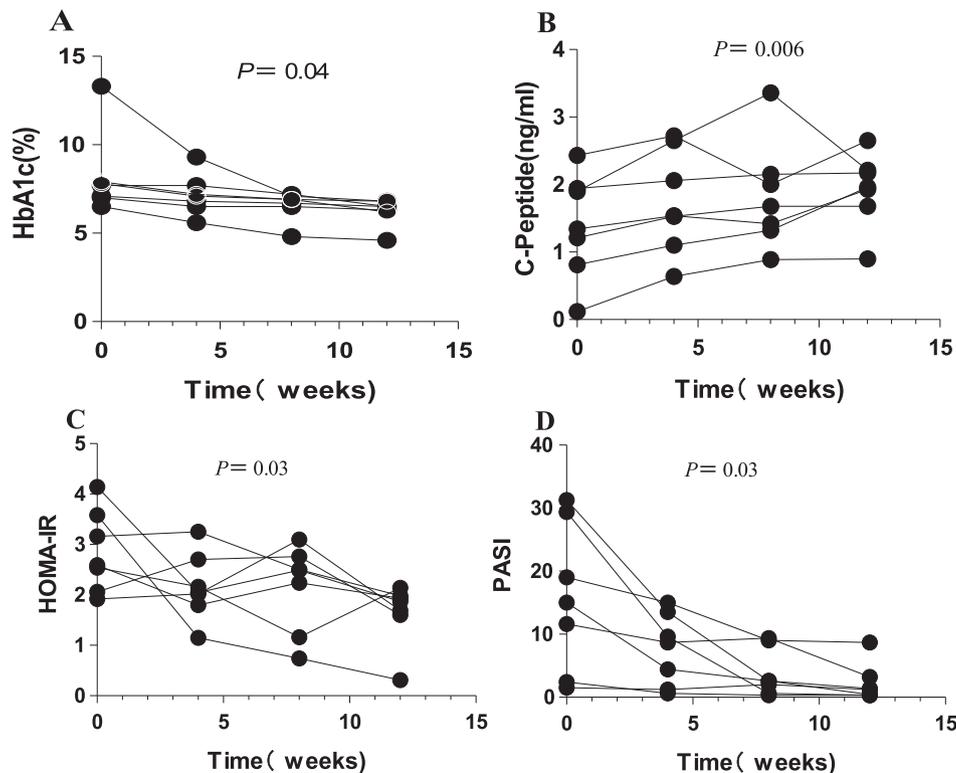


Fig. 1 – Improvement of some indicators in psoriasis patients with type 2 diabetes after 12 weeks of treatment with liraglutide (A) HbA1c. (B) Fasting C-peptide. (C) HOMA-IR. (D) PASI.



Fig. 2 – One of the most serious cases of type 2 diabetes mellitus with psoriasis lesion changes in head and neck, chest, forearm and back before treatment (A₁₋₃), 4 weeks after treatment (B₁₋₃), 12 weeks after treatment (C₁₋₃).

There were 2 participants from a state of severe psoriasis by using the liraglutide after 12 weeks treatment, who got clinical cure nearly while the body did not see erythema and desquamation. Such an observation was previously mentioned in case reports of patients or several small clinical studies who were treated for shorter periods [5–8,15].

Psoriasis is a common skin disease, the age of onset was mainly 16–22 and 57–60 years old, there was no gender differences [10]. Qureshi et al [3] found that the relative risk of diabetes with psoriasis in 1 813 patients was 1.63 (95% CI,

1.25–2.12) during a 14 years follow-up period, independent of age, BMI and other risk factors, and the risk was positively correlated with the severity of psoriasis. It suggests that patients with psoriasis have a higher risk of type 2 diabetes. Similarly, a prospective cohort study of 8124 patients with psoriasis and 76,599 healthy people was conducted in the United States, and similar conclusions were reached after 4 years of follow-up [11]. Genetic studies also show that is a common pathogenic mechanism between psoriasis and diabetes [12]. A recent genetic study for psoriasis patients

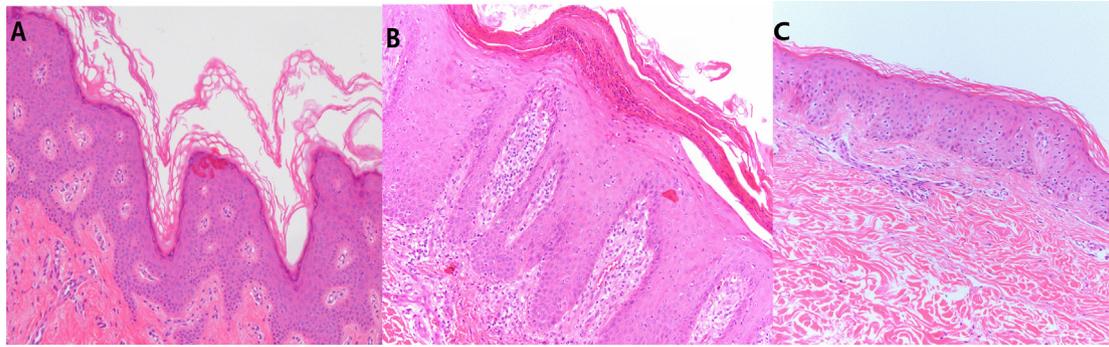


Fig. 3 – Histopathological analysis of HE staining. (A) healthy skin in patients with psoriasis; (B) skin lesions in patients with psoriasis before treatment; (C) skin lesions in patients with psoriasis after 12 weeks treatment ($\times 200$).

with type 2 diabetes prompt that [4], there are 3 susceptible genes exist in psoriasis and T2DM patients simultaneously, PTPN22, ST6GAL1 and JAZF1. The PTPN22 gene can affect the t-cell-mediated inflammatory signaling pathway, there may be common inflammatory pathways in the pathogenesis of these two diseases. At present, the main method of clinical treatment for psoriasis patients with type 2 diabetes is to treat them separately, which has aggravated the physical, psychological and economic burden of patients. Therefore, the development of drugs that can simultaneously treat psoriasis patients with type 2 diabetes is the future development trend of this field.

GLP-1 is a multifunctional peptide hormone, which mainly secreted by ileum and colon L cells. GLP-1 analogue has a similar function of GLP-1 [13]. GLP-1 receptors are widely expressed in many cells and organs such as skin, kidney, lung, heart, hypothalamus, endothelial cells and pancreatic cells, it suggests that GLP-1 analogue may have other functions besides hypoglycemic action. GLP-1 analogue has been reported to exert anti-inflammatory effects on skin, liver, vascular system, brain and kidney by reducing the production of inflammatory cytokines and immune cells in tissues [14]. Therefore GLP-1 analogue may be used to treat psoriasis.

Currently, small sample clinical cases have observed that GLP-1 analogue can improve the skin lesion of psoriasis. In a clinical study involving 7 participants with psoriasis patients with type 2 diabetes [8], the severity of psoriasis in most patients with type 2 diabetes was significantly improved after 20 weeks of GLP-1 analogue treatment. Also, the number of NK cells in psoriatic skin lesions was significantly higher than that in non-psoriatic skin lesions, which suggested that the therapeutic effect may be related to reducing the inflammatory response. Hogan et al. [5] confirmed that the effective therapeutic effect of GLP-1 analogue on psoriasis through regulation of human invariant natural killer T cells. Ahern et al. [15] observed 7 psoriasis patients with type 2 diabetes, and found that PASI and DLQI were significantly improved after GLP-1 analogue treatment. Meanwhile, the study found a 53% decrease in the number of circulating monocytes that produced TNF- α in response to a LPS challenge. A similar result was reported for the observation of patients with psoriasis patients with type 2 diabetes treated with liraglutide [6]. In this study, we observed the changes of CRP in patients with psoriasis before and after treatment for 12 weeks, compared with

before treatment, 7 participants of CRP were decreased, but did not reach statistical significance ($P = 0.16$). The histopathological analysis of psoriasis skin lesions was further performed, and the treatment was performed after 12 weeks with liraglutide, significantly reduce the epidermis thickness, with Munro ulcer, neutrophils disappeared. It may suggests that liraglutide for psoriasis skin chronic inflammatory status have certain effect, and anti-inflammatory effect is obvious, but the specific mechanism remains to be further explored.

In addition, long-term hyperglycemia increases inflammatory mediators in the body, which can lead to the occurrence and development of inflammation [16]. The psoriasis patients with type 2 diabetes are in a state of high glucose toxicity for a long time, which is bound to aggravate psoriasis related inflammatory response. Clinical studies have shown that [15], GLP-1 analogue can alleviate psoriasis related symptoms by assisting in hypoglycemia. Ogoshi [17] reported a case of psoriasis in a patient with type 2 diabetes in whom psoriatic lesions improved rapidly in association with the lowering of glucose by insulin treatment and consider that glycemic control may be vital in the treatment of certain patients with psoriasis accompanied by diabetes. However, some researchers believe that the therapeutic effect of liraglutide is not related to glycemic control [5,18], outside of GLP-1 analogue, no glucose-lowering medication has been shown to decrease PASI. In this study, it was found that after 12 weeks of treatment with liraglutide, the PASI score of the patients decreased with good blood glucose control, but the therapeutic effect whether or not be related to glycemic control is need further confirmation.

Obesity is due to the accumulation of adipocytes, resulting in reduced adiponectin secretion, inflammatory signaling pathways are activated, thus inducing high expression of inflammatory mediators, so that the body is in a chronic inflammatory state. A meta-analysis of a prospective study which involving 695,471 patients with psoriasis suggested [19] that as BMI increased, the risk of psoriasis increased and the relative risk RR was 1.19 (95% CI: 1.10–1.28, $I^2 = 83.1\%$, $P < 0.0001$), which can help to explain the causes of psoriasis in obese patients, and why they were generally more difficult to treat [20–21]. A series of small randomized controlled trials showed that [5,7,8], GLP-1 analogue may be used to treat psoriasis by weight reduction. After observing the bariatric surgery of 33 patients with psoriasis combined

with obesity, Romero-Talamás et al. [22] found that almost 40% patients improved several months after bariatric surgery, and the improvement is directly related to the degree of post-operative weight loss. In this study, we observed that 12 weeks after the treatment with liraglutide, the BMI and waist circumference of all patients were significantly improved, and the improvement effect occurred before the decline of PASI. It may suggest that the weight reduction effect of liraglutide has an important significance in the treatment of psoriasis.

Of course, the limitations of this study are the lack of randomized controlled trials in the placebo group, too few participants ($n = 7$), insufficient follow-up time (12 weeks), and inability to assess the long-term efficacy of the treatment, so the conclusion is not perfect enough. However, this study further confirmed the effective therapeutic effect of GLP-1 analogue liraglutide on skin lesions of psoriasis, and the experimental subjects included patients with mild to extremely severe psoriasis. We evaluated the therapeutic effect of liraglutide in patients with different degrees of psoriasis, and found that liraglutide had significant therapeutic effect on extremely severe psoriasis. In addition, no serious adverse events such as hypoglycemia and severe complications occurred in all patients, so its security is good. This study may provide directions for further research.

In conclusion, GLP-1 analogue liraglutide can improve the treatment of psoriasis patients with type 2 diabetes effectively, the therapeutic effect may be related to the synergistic effect of anti - inflammation, hypoglycemic and reducing weight. In the future, we still need to confirm the feasibility of GLP-1 analogue and improve its mechanism of action by more cases, longer follow-up, and increased clinical trials in a randomized control group.

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Conflict of interest

All authors declare that there is no conflict of interest to report.

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.diabres.2019.03.002>.

REFERENCES

- [1] Boehncke WH, Schon MP. Psoriasis *Lancet* 2015;386:983–94.
- [2] Gelfand JM. Psoriasis, diabetes, and obesity: weighing the evidence. *JAMA Dermatol* 2016;152(7):753.
- [3] Qureshi AA, Choi HK, Setty AR, et al. Psoriasis and the risk of diabetes and hypertension: a prospective study of US female nurses. *Arch Dermatol* 2009;145(4):379–82.
- [4] Wang H, Wang Z, Rani PL, et al. Identification of PTPN22, ST6GAL1 and JAZF1 as psoriasis risk genes demonstrates shared pathogenesis between psoriasis and diabetes. *Exp Dermatol* 2017;26(11).
- [5] Hogan AE, Tobin AM, Ahern T, et al. Glucagon-like peptide-1 (GLP-1) and the regulation of human invariant natural killer T cells: lessons from obesity, diabetes and psoriasis. *Diabetologia* 2011;54(11):2745–54.
- [6] Faurischou A, Knop FK, Thyssen JP, et al. Improvement in psoriasis after treatment with the glucagon-like peptide-1 receptor agonist liraglutide. *Acta Diabetol* 2014;51(1):147–50.
- [7] Reid CT, Tobin AM, Ahern T, et al. Liraglutide in combination with acitretin for severe recalcitrant psoriasis. *Br J Dermatol* 2013;169(1):230.
- [8] Buysschaert M, Tennstedt D, Preumont V. Improvement of psoriasis during exenatide treatment in a patient with diabetes. *Diabetes Metabol* 2012;38(1):86–8.
- [9] Schmitt J, Wozel G. The psoriasis area and severity index is the adequate criterion to define severity in chronic plaque-type psoriasis. *Dermatology* 2005;210:194–9.
- [10] Kim WB, Jerome D, Yeung J. Diagnosis and management of psoriasis. *Can Fam Physician* 2017;63(4):278–85.
- [11] Wan MT, Shin DB, Hubbard RA, et al. Psoriasis and the risk of diabetes: a prospective population-based cohort study. *J Am Acad Dermatol* 2017;78(2).
- [12] Azfar RS, Gelfand JM. Psoriasis and metabolic disease: epidemiology and pathophysiology. *Curr Opin Rheumatol* 2008;20(4):416–22.
- [13] Hare KJ, Knop FK. Incretin-based therapy and type 2 diabetes. *Vitam Horm* 2010;84:389–413.
- [14] Wang XC, Gusdon AM, Liu H, et al. Effects of glucagon-like peptide-1 receptor agonists on non-alcoholic fatty liver disease and inflammation. *World J Gastroenterol* 2014;20(40):14821–30.
- [15] Ahern T, Tobin AM, Corrigan M, et al. Glucagon-like peptide-1 analogue therapy for psoriasis patients with obesity and type 2 diabetes: a prospective cohort study. *J Eur Acad Dermatol Venereol* 2013;27(11):1440–3.
- [16] Esposito K, Nappo F, Marfella R, et al. Inflammatory cytokine concentrations are acutely increased by hyperglycemia in humans: role of oxidative stress. *Circulation* 2002;106(16):2067–72.
- [17] Ogoshi M, Horikawa T. Rapid improvement of psoriasis in diabetes subsequent to glucose lowering. *Int J Dermatol* 2014;53(2):e106–7.
- [18] Buysschaert M, Baeck M, Preumont V, et al. Improvement of psoriasis during glucagon-like peptide-1 analogue therapy in type 2 diabetes is associated with decreasing dermal $\gamma\delta$ T-cell number: a prospective case-series study. *Br J Dermatol* 2014;171(1):155–61.
- [19] Aune Dagfinn et al. Body mass index, abdominal fatness, weight gain and the risk of psoriasis: a systematic review and dose-response meta-analysis of prospective studies. *Eur J Epidemiol* 2018;27(11):1440.
- [20] Faurischou A, Zachariae C, Skov L, et al. Gastric bypass surgery: improving psoriasis through a GLP-1-dependent mechanism? *Med Hypotheses* 2011;77(6):1098–101.
- [21] Torres T, Selores M. Does treatment of metabolic syndrome components improve psoriasis? Report of three cases. *Eur J Dermatol* 2012;22(2):270–2.
- [22] Romero-Talamás H, Aminian A, Corcelles R, et al. Psoriasis improvement after bariatric surgery. *Surg Obes Related Dis* 2014;10(6):1155–9.