

An evidence-based review on the treatment of psoriasis and comorbid conditions with glucagon-like peptide-1 receptor agonists

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1. Introduction

- Psoriasis is commonly associated with metabolic syndrome (MetS), cardiovascular disease, obesity and diabetes [1].
- Moderate to severe psoriasis may increase the risk for developing metabolic and cardiovascular diseases [1, 2].
- Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are being explored as possible treatment options for patients with both psoriasis and metabolic diseases

2. Methods

01

A systematic literature search in the PubMed and ScienceDirect databases was conducted in July of 2024.

02

Combinations of the search terms 'psoriasis', 'GLP-1 receptor agonist', 'metabolic syndrome', 'obesity', 'diabetes', 'hyperlipidemia', 'etiology', 'treatment', 'cardiovascular disease', and 'antidiabetic drugs' were used to identify all relevant articles.

03

We present the current understanding of psoriasis and comorbid conditions, the use of GLP-1 RAs in the treatment of psoriasis, and studies that explore the efficacy and safety of GLP-1 RAs in the treatment of psoriasis

04

Supporting articles were included to provide fundamental information on the relationship between psoriasis and metabolic syndrome, cardiovascular disease, obesity and diabetes mellitus (DM)

3. Psoriasis and Comorbid Conditions

- There is a higher prevalence of abdominal obesity, hypertension, elevated triglycerides, and elevated fasting plasma glucose level in patients with psoriasis [3, 4].
- Patients with psoriasis had an increased odds of MetS compared to the general population [1].
- Patients with psoriasis had an increased relative risk of having a myocardial infarction [2].
 - The risk was greatest in younger patients with severe psoriasis [2].
 - Results persisted despite controlling for major cardiovascular risk factors (diabetes, hyperlipidemia, hypertension, smoking) [2].
- The imbalance in production of pro and anti-inflammatory adipokines in obesity contributes to psoriasis.
 - A cohort study conducted on patients with morbid obesity and psoriasis showed improvement of psoriasis six months after bariatric surgery in all but one patient [5].
- The exact mechanism linking diabetes mellitus (DM) to psoriasis remains unclear.
 - Evidence suggests that DM and psoriasis are related through genetic / epigenetic mechanisms.

Table 1. Summary of Case Reports

Authors	Source	GLP-1 RA administration	Initial patient presentation	Outcome
Hogan, A. E., Tobin, A. M., Ahern, T., Corrigan, M. A., Gaostwae, G., Jackson, R., O'Reilly, V., Lynch, L., Doherty, D. G., Moy-nagh, P. N., Kirby, B., O'Connell, J., O'Shea, D. (2011)	Case report	exenatide for 2 months, followed by liraglutide for 9 months.	60-year-old female patient with type 2 diabetes, BMI of 37, PASI greater than 15 since childhood.	Following 2 weeks of treatment with exenatide, PASI was 10.5. After discontinuing exenatide due to nausea, PASI was 15.3 by the end of 2 weeks. Following treatment with liraglutide for 9 months, PASI was 10.5.
Brusschaert, M., Tenst-edt, D., Preumont, V. (2012)	Case Report	exenatide 0.005 mg two times a day for 49 weeks with a 7 month period of discontinuation during study period.*	61-year-old male with type 2 diabetes, PASI 11, HbA1c 7.6, weight 81.0 kg.	PASI 3.1, HbA1c of 8.2, weight 78.0 kg.
Reid, C. T., Tobin, A. M., Ahern, T., O'Shea, D., Kirby, B. (2013)	Case report	liraglutide with acitretin 50 mg daily for one year.	54-year-old male with a PASI of 14.2, DLQI of 25, melanoma (Breslow thickness of 5 mm) and BMI of 42.1.	PASI 7.6, DLQI 12, 10 kg weight loss.
Faurschou, A., Knop, F. K., Thyssen, J. P., Zachariae, C., Skov, L., Vilsbøll, T. (2014)	Case report	liraglutide 0.6 mg once daily, increased to 1.2 mg once daily after 1 week, followed by an increased to 1.8 mg once daily after 5 weeks. Total observed treatment period of 12 weeks.*	59 year-old male with type 2 diabetes, hypertension, hypercholesterolemia, acute MI with stent placement, PGA 3, HbA1c 8.9, weight 91.8 kg.	PGA 1, HbA1c 5.9, weight 84.0 kg.

*patients were on other antidiabetic medications

4. Discussion

- There is a higher prevalence of metabolic disease and myocardial infarction in psoriatic patients when compared to the general population.
 - This may be due to psoriatic-induced hypercoagulability, systemic inflammation, and endocrine dysfunction.
- There was improvement of psoriasis seen in patients who achieved weight loss after bariatric surgery [5].
- There was no improvement of psoriasis seen in patients who achieved weight loss with GLP-1RAs [6].
 - GLP-1 RAs may only provide benefit to psoriatic patients with diabetes.
- GLP-1 RAs have pleiotropic effects that may mitigate the morbidity and mortality risks in psoriatic patients.
- The anticancer effects of GLP-1 RAs are particularly appealing.
 - Psoriatic patients are at an increased risk for cancer compared to the general population [7].
- The case reports mentioned in this review provide merit for further studies to explore the use of GLP-1 RAs for the treatment of psoriasis.
- It is difficult to attribute the improvement in psoriatic symptoms and measured anti-inflammatory response to the use of GLP-1 RAs alone.
 - Many of the studies lacked randomization and comparison to a control group.
 - Many of the studies did not discontinue the simultaneous use of other antidiabetic and psoriatic medications during the study period.

Table 2. Summary of Studies

Authors	Source	GLP-1 RA administration	Initial patient presentation	Outcome
Hogan, A. E., Tobin, A. M., Ahern, T., Corrigan, M. A., Gaostwae, G., Jackson, R., O'Reilly, V., Lynch, L., Doherty, D. G., Moy-nagh, P. N., Kirby, B., O'Connell, J., O'Shea, D. (2011)	Clinical study	liraglutide for 6 weeks.	Participant 1: 48-year-old male with diabetes, hypertension, BMI 48, HbA1c 8.7%, PASI 15.2. INKT cells in skin 2.16%. INKT cells in blood 0.12%. Participant 2: 49 year-old male with diabetes, hypertension, dyslipidemia, BMI 43, HbA1c 5.9%, PASI 4.8, INKT cells in skin 0.22%, INKT cells in blood 0.16%.	Participant 1: BMI 46.3, HbA1c 5.9%, PASI 10.8, INKT cells in skin 0.07%, INKT cells in blood 0.05%. Participant 2: BMI 41.1, HbA1c 5.8%, PASI 3.8, INKT cells in skin 0.00%, INKT cells in blood 0.07%.
Ahern, T., Tobin, A. M., Corrigan, M. A., Hogan, A., Sweeney, C., Kirby, B., O'Shea, D. (2013)	Cohort study	liraglutide 0.6 mg once daily for 2 weeks, titrated to 1.2 mg once daily for 10 weeks.	7 patients with chronic plaque psoriasis, mean BMI 50, mean PASI 8.7, mean DLQI 6.9.	mean weight loss in 6 patients, mean PASI of 5.0, mean DLQI 3.8, decrease in TNF α percentage by a median of 53, increase in circulating INKT cells by a median of 27.9%.
Brusschaert, M., Back, M., Pronunt, V., Marol, L., Hendricks, J., Van Belle, A., Dumontier, L. (2014)	Case-series	exenatide 0.005 mg twice daily in one patient, liraglutide 0.6 mg once a day for 1 week, increased to 1.2 mg once daily followed by an increase to 1.8 mg once daily if glycemic control was not sufficient in 5 patients for mean of 18 +/- 2 weeks.	7 patients with type 2 diabetes, chronic plaque psoriasis, mean PASI 12.0 +/- 5.9, mean BMI 29.0 +/- 10.1, mean HbA1c 7.5 +/- 1.2%, % T cell 5.9 +/- 4.6%.	mean PASI 9.2 +/- 6.4, mean BMI 30.6 +/- 9.1, mean HbA1c 6.5 +/- 0.8%, mean % T cell 2.9 +/- 3.5%.
Faurschou, A., Gylendow, M., Rohde, U., Thomsen, J., Zachariae, C., Skov, L., Kirup, F. K., Vilsbøll, T. (2015)	randomized-controlled trial	liraglutide 0.6 mg once daily for one controlled week, 1.2 mg once daily for the following week, 1.8 mg once daily for the remaining week, to total study period of 8 weeks.	placebo group: Mean PASI 11.6, mean DLQI 7.9, mean BMI 25, mean HbA1c 5.7%. liraglutide group: mean PASI 14.5, mean DLQI 8.7, mean BMI 37, mean HbA1c 5.4%.	liraglutide group: mean weight loss of 4.7 +/- 2.5, no change in PASI between treatment and placebo group seen at 8 weeks.
Xu, X., Lin, L., Chen, P., Yu, Y., Chen, S., Chen, X., Shao, Z. (2019)	cohort study	liraglutide 0.6 mg once daily for 1 week, increased to 1.2 mg once daily followed by an increase to 1.8 mg for 12 weeks.	mean BMI 23 +/- 4, mean HbA1c 8.1 +/- 2.5%, mean PASI 15.7 +/- 11, mean DLQI 23 +/- 7.	mean BMI 21 +/- 3, mean HbA1c 6.4 +/- 0.8%, mean PASI 2.2 +/- 3.0, mean DLQI 4.1 +/- 3.9.
Lin, L., Xu, Y., Ye, H., He, X., Chen, S., Chen, X., Shao, Z., Chen, P. (2020)	randomized-controlled study	liraglutide for 12 weeks.	placebo group: mean PASI 13.2 +/- 5.0, mean BMI 18.23 +/- 5.17, mean HbA1c 7.3 +/- 3.10, mean HbA1c 7.30 +/- 1.88 %. liraglutide group: mean PASI 14.02 +/- 10.67, mean DLQI 22.00 +/- 5.85, mean BMI 23.65 +/- 3.09, mean HbA1c 7.80 +/- 2.65 %.	decrease in PASI, DLQI, BMI, IL-23, IL-17 in the treatment group compared to the placebo group. No statistically significant difference in TNF α in the treatment group compared to placebo group.

Subjects in the studies may have been on other antidiabetic medications and psoriatic treatments

5. Conclusion

- It is recommended that psoriatic patients undergo preventative measures, frequent screenings, and lifestyle modifications to mitigate the high prevalence of systemic comorbidities associated with psoriasis.
- This review focuses on the potential use of GLP-1 RAs in the treatment of psoriatic patients with diabetes, obesity, and MetS.
- There is a need for longitudinal studies to focus on three areas for a better understanding of the true impact of GLP-1 RAs as a potential treatment option for psoriasis:
 - There is a need to clarify the patient profile of psoriatic patients that would most benefit from the use of GLP-1 RAs.
 - There is a need to investigate the role of GLP-1 RAs as either monotherapy or adjuvant therapy.
 - There is a need to study the long-term efficacy and safety profile of GLP-1 RAs as a treatment option for psoriasis.

6. References

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