Al-Kindy College Medical Journal (KCMJ)

Research Article

Assessing the Effect of Apremilast on Serum Leptin levels in Obese Patients with Psoriasis

Haitham M. Saad[1]*, Adil A. Noaimi[2], Halla G. Mahmood[3]

[1] Al-Anbar Health Directorate, Ministry of Health, Anbar, Iraq
[2] Dermatology and Venereology, College of Medicine, University of Baghdad, Baghdad, Iraq
[3] Clinical Biochemistry Department, College of Medicine, University of Baghdad, Baghdad, Iraq

* Corresponding author's email: hms.stariraq@gmail.com

Article history:
Received 27 August 2024
Accepted 7 December 2024
Available online 1 December 2024

https://doi.org/10.47723/9crsx315

Keywords: Apremilast; psoriasis; Leptin; Iraq

ABSTRACT

Background: Psoriasis is a common inflammatory condition worldwide, with an average prevalence ranging from 2% to 3%. However, the incidence of psoriasis varies among different ethnic groups and regions. Elevated leptin levels have been associated with increased cellular proliferation, including T-cells. Additionally, high leptin levels may stimulate the synthesis of proinflammatory cytokines such as IL-6 and TNF-α.
Objectives: To evaluate the effect of Apremilast on Leptin in obese psoriatic patients.
Subjects and Methods: Thirty patients with psoriasis were included in This prospective cohort study to measure the levels of serum Leptin by using the ELISA technique, before and after receiving Apremilast.
Result: The present work found the concentration of Leptin before receiving Apremilast was 2.365 ng/ml, and after six months from baseline, it was reduced to 1.933 ng/ml, which was statistically significant ($P<0.05$).
Conclusion: This prospective cohort study provides evidence that Apremilast can decrease elevated Leptin levels in individuals diagnosed with psoriasis. The study observed a 0.42 ng/ml reduction in Leptin levels after 6 months of Apremilast treatment.

Introduction

Psoriasis is a prevalent inflammatory illness, with a worldwide incidence ranging from 2% to 3%. The prevalence of this condition is variable with variation based on different ethnic groups and geographical locations (1). Psoriasis is characterized by the presence of keratinocyte hyper-proliferation and abnormal cell differentiation, leading to epidermal hyperplasia(2). Psoriasis is infiltrated with inflammatory cells, leading to scaling of the skin, as the cells of the skin come to the surface quickly before their complete maturation (3).

Leptin plays a crucial role in the regulation of various physiological processes, including food intake, body mass control, proinflammatory immunological responses, angiogenesis, and lipolysis (4). Leptin, a hormone synthesized by adipose tissue, exhibits proinflammatory properties and serves as a regulator in the T-helper cell response(5). While there is growing evidence to suggest the association between psoriasis and obesity as well as cardiovascular disease, the relationship between psoriasis and leptin remains a topic of debate in the academic literature (6). Individuals diagnosed with psoriasis have a heightened prevalence and incidence

of obesity in comparison to the broader community. Moreover, individuals with severe psoriasis demonstrate an increased risk of obesity when contrasted with those with mild psoriasis (7).

Further research is needed to examine the effectiveness and potential metabolic adverse effects of recently developed biologic medicines through additional prospective studies. It is important to note that Apremilast, a phosphodiesterase 4 inhibitor, has demonstrated the ability to decrease body weight, promote lipolysis, improve insulin sensitivity, and reduce the buildup of adipose tissue in the liver, particularly in those with elevated levels of glycated hemoglobin (8). The administration of Apremilast resulted in a significant decrease in plasma concentrations of crucial cytokines implicated in the development of psoriasis. However, there were no significant changes observed in the levels of IL-23, leptin, adiponectin, apolipoproteins, Th17 cells, or regulatory T-cell populations (9).

The evidence of the association between smoking and the development of PsA among psoriasis patients is unclear and controversial. Some studies detected an inverse association whereas others found a positive association or no effect between smoking and the development of PsA(10). There aren't many studies on how Apremilast affects Leptin and its effects as a treatment for psoriasis sufferers. For that reason, the purpose of this study was to find out how the Apremilast medication affected the Leptin levels in obese psoriatic patients.

Subjects and Methods

This prospective cohort study was conducted at the Dermatology Center, Medical City in Baghdad, Iraq at trial registration no. 133 in 23/1/2022, between November 2021 and December 2022. After a full explanation for each patient about the nature of the disease, course prognosis, treatment and complications by a Dermatologist, in addition to the target of this study, formal consent was obtained from each patient before starting the study. Ethical approval was obtained from the Development Department of the Medical City Directorate in Baghdad, Iraq.

The study included a sample of thirty participants who were registered at the outpatient clinic. The patients were provided Apremilast (Aprezo)®, daily after meals, with a time interval of roughly 12 hours, for a duration of six months. Out of the total number of patients included in the trial, a subset of 6 individuals did not successfully finish their participation in the study due to various causes. All patient is assessed the status of obesity by the body mass index (BMI), [BMI= weight (kg) / height (m)²]. According to the international standard measurement of body mass (BMI). Baseline body weight, height and BMI were measured and monitored monthly.

Prior to administering Apremilast, blood samples were collected from all patients at the baseline in order to evaluate Leptin levels. The practical component of the study was conducted at Baghdad Hospital-Medical City Directorate and the International Centre for Research and Development (ICRD). The Human Leptin hormone kit used in this study was obtained from ELK Biotechnology-China. The Statistical Analysis System- SAS (2018) program was used to detect the effect of difference between the two groups in study parameters. T-test was used to significant compare between means. Chi-square test was used to significant compare between percentage (0.05 and 0.01 probability).

Results

Sex, Smoking and Age group:

In the present work, sex group was found that nineteen (63.3%) of the participants were males and eleven (36.7%) were females. Moreover, in this work, cigarette smokers only four (13.3%) of the participants were smokers, while twenty-six (86.7%) were non-smokers. In addition, the average age of the group was 38 years. The most common age group was 30-40 years, about 60%, followed by >40 years which was about 26.6%, as illustrated in Table 1.

Table 1: General characteristics of the study sample

	No	Percentage (%)
Sex		
Male	19	63.33
Female	11	36.67
Total	30	100%
P-value	---	0.074 NS
Smoking		
Yes	4	13.33
No	26	86.67
Total	30	100%
P-value	---	0.0001 **
** (P≤ 0.01)		
Age group (year)		
<30 yr.	4	13.33
30-40 yr.	18	60.00
>40 yr.	8	26.67
Total	30	100%
P-value	---	0.0052 **

** (P≤ 0.01), NS: Non-Significant

Table 2: Comparison of Leptin levels and BMI before and after receiving Apremilast

Group	**Mean ± SE**
Leptin (ng/ml)	
Patients: Before treatment	2.365±0.134
Patients: After treatment	1.933±0.075
P-value	0.0114 (P≤0.05)
BMI (kg/m2)	
Patients: Before treatment	32.97 ±1.07
Patients: After treatment	30.48 ±1.14
P-value	0.349

Leptin levels and BMI:

In this study, the concentration of Leptin before receiving Apremilast was found to be 2.365 ng/ml. After six months from

baseline, the concentration was reduced to 1.933 ng/ml, which was a statistically significant difference (P<0.05) as illustrated in Table 2.

The international standard measurement of body mass index was used as an indicator to measure the body mass index of all cases. There was no significant difference (P>0.05) in BMI before and after receiving Apremilast, but after six months of treatment with Apremilast the BMI was reduced by 2.5 Kg/m^2 as shown in Table 2.

Discussion

Psoriasis is the most prevalent chronic inflammatory dermatological condition. This research study represents an important in examining the impact of Apremilast on Leptin levels in individuals diagnosed with psoriasis in Iraq. The findings of this study revealed a significant decrease in serum Leptin levels after a six-month treatment period with Apremilast.

The majority of participants in this study were male, which is in agreement with the findings of *Hägg et al* (11). The observed distribution of psoriasis across males and females shows inconsistency across several studies. Several studies have reported a higher prevalence of psoriasis in males compared to females. However, contrasting findings have also been documented, suggesting comparable incidence rates between the two sexes (12). One study posits that women may exhibit less severe manifestations of psoriasis compared to men. Hence, drawing a definitive conclusion regarding the distribution of psoriasis between males and females is challenging (13).

There is a strong correlation between smoking and the occurrence and severity of psoriasis. Research indicates that individuals who smoke cigarettes long-term are about twice as likely to develop psoriasis compared to those who have never smoked (14). Existing research also shows that current and former smokers have a higher risk of developing psoriasis compared to those who have never smoked (15). Numerous research findings demonstrate a correlation between cigarette smoking, alcohol consumption, and psoriasis severity. Several studies have shown an association between smoking cigarettes and drinking alcohol and increased severity in individuals with psoriasis (16). Furthermore, heavy smokers have over double the likelihood of developing psoriasis compared to non-smokers (17).

Leptin affects appetite and is one of the major adipokines associated with obesity. Leptin also affects immune cells, including dendritic cells (DC), neutrophils, natural killer (NK) cells, and T and B cells, through leptin receptors located on the surface of immune cells, and regulates the production of various cytokines. These signaling patterns induce a wide range of physiological effects by altering immune and inflammatory responses(18). The research conducted by *Yan et al* (19). observed a notable reduction in leptin levels following a 12-week course of Apremilast medication among a cohort of 20 individuals diagnosed with moderate to severe plaque psoriasis. The observed decline exhibited a strong correlation with a decrease in the severity of the condition. Previous research has indicated that the administration of Apremilast could potentially lead to a decrease in leptin levels in individuals with psoriasis, possibly attributable to its anti-inflammatory properties(8). Furthermore, a study by *Gisondi et al* (20). observed a reduction in leptin levels among 18 patients following a 16-week treatment with Apremilast. This decrease in leptin levels was found to be associated with the clinical improvement of psoriatic lesions.

Recent studies suggested that circulating adipokine concentrations are altered in psoriatic patients and are suggested to represent the pathophysiologic link between psoriatic lesions and metabolic alterations. Both leptin and resistin are known to promote the production of pro-inflammatory mediators involved in the pathogenesis of psoriasis, such as TNFα(21). Noteworthy, the phosphodiesterase 4 inhibitor Apremilast has been shown to reduce body weight, enhance lipolysis, increase insulin sensitivity, and reduce the accumulation of adipose tissue in the liver, especially in patients with high glycated hemoglobin(22).

Conclusion

The efficacy of Apremilast as a monotherapy has been demonstrated in reducing Leptin levels, hence conferring advantageous outcomes for individuals suffering with psoriasis. This study provides evidence that supporting the efficacy of Apremilast in reducing Leptin levels among persons who have been diagnosed with psoriasis. The present study showed a decrease in Leptin concentrations during a six-month period of Apremilast treatment, in comparison to the initial values recorded before to the initiation of therapy. The findings suggest that the therapeutic effectiveness of Apremilast in the treatment of psoriasis can be attributable to its capacity to modulate various inflammatory pathways.

Funding

This research did not receive any specific fund.

Conflict of Interest

Authors declare no conflict of interest.

Data availability

Data are available upon reasonable request

ORCID

Haitham Saad 0009-0003-3135-0281
Adil Noaimi 0000-0002-2436-7988
Halla Mahmood 0000-0002-7248-4409

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To cite this article: Saad HM, Noaimi AA, Mahmood HG. Assessing the Effect of Apremilast on Serum Leptin levels in Obese Patients with Psoriasis. Al-Kindy Col. Med. J. 2024;20(3):250-253. https://doi.org/10.47723/9crsx315