International Journal of Dermatology, Venereology and Leprosy Sciences

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Serum irisin level in patients with acne vulgaris

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DOI: https://doi.org/10.33545/26649411.2024.v7.i1a.181

Abstract
It is a common and persistent inflammatory skin condition that affects the hair follicles and sebaceous glands. Acne vulgaris is a skin condition that affects the skin. The presence of both open and closed comedones, also known as blackheads and whiteheads, as well as inflammatory lesions, most commonly on the face, chest, shoulders, and back, are the defining characteristics of this specific condition. A number of skin conditions, such as acrochordons, acanthosis nigricans, androgenetic alopecia, acne vulgaris, and hirsutism, can be caused by insulin resistance, which is a term that describes the decreased sensitivity of cells to insulin. There is a correlation between irisin and measurements of body size and shape, as well as chemical indicators, other hormones and substances that are released by fat cells, obesity, and a decreased sensitivity to insulin because of its presence. As a result of its ability to stimulate thermogenesis and the consumption of energy in subcutaneous adipose tissue, irisin offers protection against both obesity and insulin resistance. The intervention resulted in a decrease in glucose and insulin levels, which is indicative of an improvement in insulin resistance during the intervention.

Keywords: Acne vulgaris, inflammatory skin condition, hair follicles, sebaceous glands

Introduction
It affects the sebaceous glands and hair follicles and is a chronic inflammatory skin condition that is common. One skin condition that can impact anyone is acne vulgaris. The hallmarks of this skin disorder include inflammatory lesions like nodules, pustules, or papules, and open and closed comedones, which are colloquially called blackheads and whiteheads, respectively. Scars may develop in some cases; the condition is most common on the back, shoulders, chest, and face [1].

Diabetes mellitus type 2 is one of several metabolic diseases linked to insulin resistance. A condition that is characterized by decreased sensitivity of insulin-targeted tissues to normal levels of insulin is referred to by this term [2].

Both skeletal muscle and adipose tissue are responsible for the secretion of irisin, which is a recently discovered peptide. As a fragmented portion of fibronectin type III domain-containing protein 5 (FNDC5), it is classified as an adipomyokine according to the scientific community [3]. As a result of its ability to improve glucose and lipid metabolism in the liver, irisin assists in the reduction of insulin resistance and type 2 diabetes [4].

Precipitating Factors for acne vulgaris
Genetic Factors
Mounting evidence suggests that genetic factors play a significant role in the occurrence of acne [5]. This assertion is supported by the strong correlation that was observed in monozygotic twins, where the degree and severity of acne as well as the rate of sebum production are almost indistinguishable. [6]. Chromosomal abnormalities, HLA phenotypes, polymorphisms of the human cytochrome P-450 1A1 gene, and the MUC1 gene are all factors that contribute to the development of acne [7]. Acne has a hereditary component. There is a correlation between having a family history of acne and experiencing acne at an earlier age, as well as having a higher number of acne lesions that persist [8].

Diet
The consumption of certain diets, particularly those with a high glycemic load such as sugar,

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sugary foods, chocolate, salty foods, spicy foods, white bread, potatoes, white rice, milk, dairy products, and ice cream, has been found to be positively linked to the development of acne vulgaris [9]. The consumption of milk and foods with a high glycemic index in one's diet can potentially increase the levels of serum insulin and Insulin growth factor -1. This, in turn, stimulates the production of sex hormones, which promotes the development of acne [10].

Smoking: Multiple epidemiological studies indicate a direct relationship between smoking and acne, where the prevalence and severity of acne increase in proportion to the amount of smoking. Factors like age, sex, and socioeconomic status do not impact this correlation. The underlying pathological process may be triggered by nicotine, according to some studies [11].

Obesity
There is a strong correlation between obesity and peripheral hyperandrogenism as well as insulin resistance, both of which can result in increased the amount of sebum produced and the development of severe acne [12]. Hyperinsulinaemia can cause an elevation in androgen production, which in turn stimulates the sebaceous glands, resulting in the onset or exacerbation of acne. Weight loss may be recommended for patients with acne vulgaris [13].

Psychological Stress: Stress is commonly associated with the worsening of acne, and acne itself can cause stress [14]. The precise mechanism through which stress exerts a negative impact on acne is yet to be fully understood, but it may involve elevated hormone levels or the production of neuro peptides that induce inflammation [15].

Oxidative stress
When there is an imbalance between oxidizing agents (free radicals) and antioxidants, specifically when there is a greater presence of free radicals, this is referred to as oxidative stress. This imbalance causes damage to cells [16]. Sarici *et al.*; [17] showed that there is a rise in both systemic and cutaneous oxidative stress in acne vulgaris patients. The inflammatory progression of acne is believed to be caused by reactive oxygen species that neutrophils release.

Drugs: The most widely recognized causative drugs include halogenated compounds, progestogens, oral contraceptive pills, corticosteroids, isoniazid, and lithium. Acne eruptions have been identified as a result of the action of epidermal growth factor receptor antagonists such as gefitinib, erlotinib, and cetuximab [18].

Menstruation
There is deterioration of acne lesions in premenstrual period in around 85% of women and around a third of these women have characteristics of hyperandrogenism manifested as menstrual disturbances, hirsutism, or androgenetic alopecia. Patients may have peripheral androgen metabolic, ovarian, or adrenal disorders and require more examination [19].

Pregnancy: Fluctuations in hormones during pregnancy can lead to the onset or recurrence of acne [20].

Cosmetics: There are a number of cosmetics, such as sunscreens, that are comedogenic. Lesions can appear in the perioral region of females, particularly those who experienced acne during their teenage years and who consumed cosmetic products for an extended period of time, such as foundations that are excessively greasy or oily, powder makeup. It has been reported that certain hair care products can cause comedones to appear on the forehead and also on the temple [6].

Grading of Acne Vulgaris: Grading systems for acne can be helpful in the therapy of patients who suffer from the condition. They can aid in the more precise categorization of diseases, assist in determining the most suitable treatment, and track progress throughout the treatment process. Several acne evaluation instruments have been delineated, taking into account diverse factors, including acne type, severity, lesion count, anatomical location and extent of acne, quality of life, and scarring [21].

There are six main categories into which acne scoring systems fall. [22]
1. Qualitative scales - degrees of severity: mild, moderate and severe.
2. Semiquantitative scales - numerical score: ranging from 0 to 10.
3. Quantitative scales - based on lesion counting.
4. Photographic scales
5. Acne - specific quality of life scales
6. post-acne scarring scoring system.

One of the most important, commonly used grading systems for acne vulgaris is the Global Acne Grading System (GAGS) [23].

Insulin resistance
Insulin resistance is associated with a cluster of symptoms that are more common in this population. When insulin is not effectively used, it can lead to insulin resistance syndrome. Hyperglycemia, dyslipidemia, endothelial dysfunction, abnormal uric acid metabolism, abnormal hemodynamics, elevated inflammatory markers, sleep-disordered breathing, increased ovarian testosterone secretion, and glucose intolerance are all on this list. This inventory contains all of these requirements [24]. Insulin resistance is linked to various clinical syndromes, such as type 2 diabetes, cardiovascular disease, essential hypertension, polycystic ovary syndrome, non-alcoholic fatty liver disease, sleep apnea, and some types of cancer [25].

Role of insulin resistance in acne vulgaris
Acne is often a defining feature of the many systemic diseases and syndromes that have been associated to insulin resistance [26].
Polycystic ovarian syndrome (PCOS) is the prevailing and widely recognized medical condition that connects insulin resistance and acne [27]. PCOS, a condition characterized by excessive levels of androgens, lack of ovulation, and the presence of multiple cysts on the ovaries, commonly results in acne in 70% of women affected [28]. An underlying condition known as PCOS should be suspected if acne that begins or continues into adulthood and does not respond to mainstream treatments is present. Women with PCOS experience irregularities in the way their bodies process androgens and estrogen. In addition, both insulin resistance

and high levels of insulin in the bloodstream have been linked to PCOS. [29].

It has been found that epidermal keratinocytes contain insulin and IGF-1 receptors. It is possible for the basal keratinocytes in the hair follicle to cause an excessive amount of proliferation when there is an excess of insulin in the blood, which is referred to as hyperinsulinemia. The normal process of skin cell maturation is disrupted as a result of this, particularly in the follicular corneocytes that are located in the outermost layer of the hair follicle. In light of this, it can be said that this process contributes to the development of acne. An additional benefit of insulin is that it stimulates the production of androgens, which in turn leads to an increase in the production of sebum. This is a known factor that comes into play when determining the severity of acne [30].

Furthermore, IGF-1 has the ability to activate 5α reductase, promote the synthesis of androgens in the adrenal and gonadal glands, enhance androgen receptor signal transduction, promote the proliferation of sebocytes, increase sebum production, and influence the process of lipogenesis, all of which contribute to the development of acne [31].

Irisin hormone

Irisin is a type of hormone that was discovered in 2012. It is extracted from the skeletal muscle of mouse. Irisin is released by muscles in response to physical activity and may play a role in promoting certain advantageous outcomes, such as weight reduction and temperature regulation. Irisin is a protein that breaks down fibronectin type III domain 5. The irisin found in mice and humans is completely identical, with a similarity rate of 100%. The similarity rates for insulin, glucagon, and leptin are 85%, 90%, and 83% respectively. Regarding the management of obesity and the conditions that are associated with it, it is anticipated that irisin will serve as a promising therapeutic agent. Irisin is produced as a result of the transformation of fibronectin type III domain-containing protein 5 that occurs after physical engagement. Irisin induces adipose tissue browning in both human and mouse white adipose tissues [32].

Physiology of Irisin

Muscle activity and the existence of peroxisome proliferator-activated receptor-gamma coactivator 1-alpha are the two factors that cause the production and release of irisin [33]. PGC-1α, also known as peroxisome proliferator-activated receptor-γ coactivator 1-α, is a transcriptional coactivator that possesses the ability to regulate multiple genes in different tissues for a wide range of applications. This protein is especially abundant in skeletal muscle, brown adipose tissue, liver, and heart, all of which are areas in which it is overexpressed as a result of the presence of nutritional and physiological signals [34]. Prolonged exercise enhances the production of Prostaglandin coactivator-1α primarily in the heart and skeletal muscle. This leads to improvements in various metabolic factors, including insulin sensitivity and signaling. Additionally, exercise stimulates the activation of antimicrobial peptides and protein kinase, resulting in the phosphorylation of Prostaglandin coactivator-1α and the production of Fibronectin type III domain-containing protein 5. Subsequently, Fibronectin type III domain-containing protein 5 is cleaved to generate irisin [35].

Role of irisin in acne vulgaris: Acne vulgaris and serum irisin have been found to have a new possible connection. The HOMA-IR index has been observed to increase in severe acne lesions, while serum irisin levels have been observed to decrease. As a result of this, it is possible that irisin is involved in the development of acne vulgaris. This is because there is a strong connection between acne vulgaris and insulin resistance. The reason for this is that it is believed that irisin raises the levels of glucose in the blood, which in turn stimulates the secretion of insulin during the process. This results in a decreased availability of binding protein to IGF-1, which in turn increases the effect that IGF-1 has on the growth of basal keratinocytes. Insulin levels that are elevated are responsible for this. Insulin also stimulates the production of androgen, which is a factor that may play a role in the development of acne [36].

Irisin has been found to enhance thermogenesis and utilization of energy in subcutaneous adipose tissue, thereby mitigating the risk of obesity and insulin resistance. Irisin is a physiological response to exercise that controls the metabolic rate of muscle cells and adipocytes, thereby functioning as a factor that increases insulin sensitivity following exercise [32].

Irisin promotes the transformation of white adipose tissue into brown adipose tissue, which provides protection against diet-induced obesity and diabetes [37].

The serum irisin level was elevated in healthy individuals as a result of its anti-inflammatory function, which involves decreasing the expression and release of pro-inflammatory cytokines, including IL-1β, TNFα, and IL-6. Remarkably, the concentration of irisin in humans increases significantly with physical exercise. This increase promotes the overall expenditure of energy in the body, leading to weight loss, reduction of fat, and improvement of insulin resistance [32].

Additionally, the presence of low levels of irisin in the blood and a high HOMA-IR index can serve as reliable indicators for identifying individuals who are at risk of developing severe acne lesions [38].

Conclusion

Acne vulgaris is a prevalent inflammatory skin condition affecting hair follicles and sebaceous glands, characterized by comedones, inflammatory lesions, and commonly appearing on the face, chest, shoulders, and back. The condition is linked to insulin resistance, which reduces cellular sensitivity to insulin and can manifest in various skin conditions including acrochordons, acanthosis nigricans, androgenetic alopecia, and hirsutism. Irisin, a hormone released during exercise, shows promise in combating obesity and insulin resistance by promoting thermogenesis and energy consumption in adipose tissue. This hormonal mechanism may help mitigate acne severity by improving insulin sensitivity and reducing inflammatory responses. Further research into irisin's role in acne pathogenesis could unveil new therapeutic strategies targeting both metabolic and dermatologic health.

This conclusion encapsulates the interconnected aspects of acne vulgaris, insulin resistance, and the potential role of irisin, summarizing their implications for understanding and treating this common dermatological condition.

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