

The influence of insulin-like growth factor IGF-1 on the course of acne vulgaris

Wpływ insulinopodobnego czynnika wzrostu IGF-1 na występowanie trądziku pospolitego

ABSTRACT

Finding the cause of acne is a key aspect to improve skin appearance and eliminating the problem completely. Due to the multitude of origins and their coexistence, acne treatment is in most cases long-lasting and cannot be limited to one action. Increasing importance in the occurrence and course of acne vulgaris is paid to the high glycemic index of consumed food and insulin-like growth factor (IGF-1). IGF-1 receptors are located on keratinocytes and in acne patients their elevated expression in the epidermis and sebaceous glands is noticed. High levels of IGF-1 are observed in adolescents, as well as in adult women struggling with late acne affecting people over 30 (*Acne tarda*). It is suspected that it is not androgens, but IGF-1, that is the key element in the appearance and course of *Acne vulgaris*.

Keywords: acne vulgaris, acne tarda, IGF-1, insulin-like growth factor, high glycemic index

STRESZCZENIE

Znalezienie przyczyny rozwoju trądziku jest kluczowym aspektem do poprawy wyglądu skóry i całkowitego wyleczenia choroby. Ze względu na mnogość przyczyn i ich współwystępowanie, leczenie trądziku jest w większości przypadków długotrwałe i nie może się ograniczać do jednokierunkowej terapii.

Celem pracy było przedstawienie, na podstawie dostępnych źródeł, oddziaływania wysokiego indeksu glikemicznego spożywanej żywności oraz insulinopodobnego czynnika wzrostu (IGF-1) na występowanie oraz przebieg trądziku pospolitego.

Receptory dla IGF-1 zlokalizowane są na keratynocytach, a u osób z trądzikiem zauważana jest ich wzmożona ekspresja w naskórku i gruczołach łojowych. Obserwuje się wysokie stężenie IGF-1 u nastolatków z objawami trądziku pospolitego oraz u dorosłych kobiet z objawami trądziku późnego (*Acne tarda*). Podejrzewa się, iż to nie androgeny, a insulinopodobny czynnik wzrostu, jest kluczowym elementem w pojawianiu się i przebiegu *Acne vulgaris*.

Słowa kluczowe: trądzik pospolity, trądzik późny, IGF-1, insulinopodobny czynnik wzrostu, wysoki indeks glikemiczny

INTRODUCTION

Acne (*Acne vulgaris*) belongs to the group of civilization diseases, which also include type II diabetes, obesity, insulin resistance, metabolic syndrome, and neoplastic diseases [1]. Its occurrence is estimated at 85-90% among adolescents and

almost 50% in adulthood, with an increasing tendency [2]. The first symptoms of the disease appear in various age groups, most often at the age of 14-17 in girls and 16-19 in boys [3]. Acne vulgaris is not only a medical problem but also a social and psychological one.

AIM OF THE WORK

The study aimed to present, based on available sources, the influence of the high glycemic index of consumed food and insulin-like growth factor (IGF-1) on the occurrence and course of acne vulgaris.

ACNE ETHOLOGY

Finding the cause of acne is a key aspect to improve the skin appearance and to completely cure the disease. The etiology of acne vulgaris unfolds on several planes and consists of both endogenous and exogenous factors. Due to the multitude of causes and their coexistence, acne treatment is in most cases long-lasting and cannot be limited to only one aspect [3].

Acne is associated with excessive growth of sebocytes and increased production of sebum. Its location coincides with the places of greater accumulation of sebaceous glands [4]. Other reasons of the disease are keratosis disorders within the hair follicles resulting in hyperkeratinization and comedogenesis. The hyperkeratosis of the follicle leads to the formation of primary non-inflammatory changes, such as micro-blackheads, followed by the appearance of open and closed comedones. In the further course of the disease, inflammatory changes in the form of pustules and papules appear. The obstructed hair follicle does not fulfil its secretory function, which creates conditions for the growth of *Cutibacterium acnes* (*C. acnes*) bacteria. *C. acnes* bacteria secrete lipases, hyaluronidases, and proteases [4].

Bacterial lipases lead to the hydrolysis of triglycerides and a change in the composition of sebum. More free fatty acids are produced that stimulate inflammation. The number of ceramides and the tightness of the epidermal hydrolipid barrier are reduced.

Increased inflammation is observed within the skin lesions in the course of acne vulgaris. Langerhans cells, T lymphocytes and CD4 + helper lymphocytes are stimulated. Cytokines and chemokines trigger cell migration to the site of inflammation. There is an increased amount of B lymphocytes, neutrophils, tumor necrosis factor (TNF), interleukins IL8 and IL1a [5].

Disorders of the skin microbiome also contribute to the activation of inflammation. In people with acne lesions, an increase in the level of *Cutibacterium acnes* bacteria is observed, as well as *Staphylococcus aureus*, *Propionibacterium granulosum*, *Propionibacterium avidum*, *Staphylococcus epidermidis*, and fungi - *Plasmodium ovale* [5].

The hormonal balance plays an important role in the etio-pathogenesis of the disease. During sexual maturation, the secretion of androgens increases. In the sebaceous glands, dehydroepiandrosterone sulphate (DHEA-S) is converted into testosterone, which under the influence of the 5-alpha-reductase enzyme is converted to dihydrotestosterone (DHT). Dihydrotestosterone affects the enlargement and hypertrophy of the sebaceous glands, the proliferation of se-

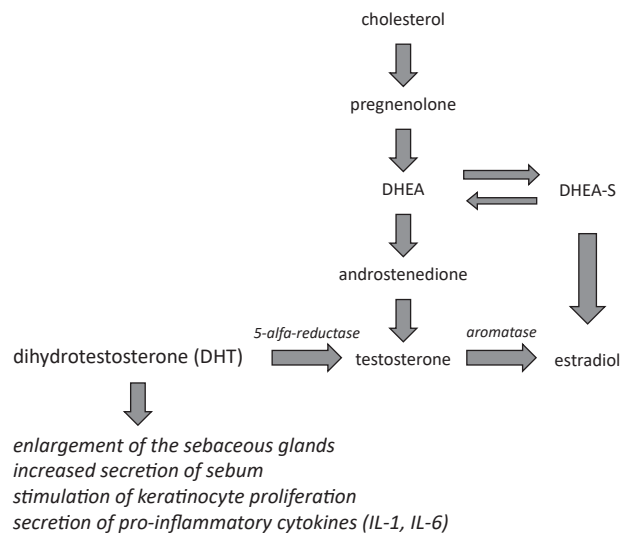


Fig. 1 Transformation of androgens
Source: Own study

bocytes, and the occurrence of acne lesions. Importantly, in most acne cases the serum androgen level remains normal [6]. The importance of androgen transformations in the aspect of acne vulgaris is presented in Fig. 1.

Other causes of Acne vulgaris development include linoleic acid deficiency, which exhibits anti-inflammatory properties, improper care, use of comedogenic substances, stress and genetic factors. The genetic background of acne is a very complex issue. Multiple studies showed that the chance of developing severe acne is almost 3 times higher in people whose closest relatives have suffered from the disease. Gene stimulation leads to hypersensitivity of the 5-alpha-reductase enzyme and increased sensitivity of the sebaceous glands to the secretion of excessive amounts of sebum [7].

IGF-1 - INSULIN-LIKE GROWTH FACTOR

Insulin-like growth factor (IGF) influences the growth of cells, their proliferation and causes nuclear effects. There are two types of IGF: IGF-1 and IGF-2, six proteins that bind to them (IGFBP), and two receptors: IGF-1R and IGF-2R. IGF activates receptors located on the cell membrane, while IGF-1R is also involved in the regulation of gene expression. It modifies the activity of chromatin proteins, creates transcriptional complexes. Some of the IGFBP binding proteins have a nuclear localization signal, and in the nucleus, they regulate the DNA repair process [8].

IGF-1 AND ACNE

Increasing importance in the occurrence and course of acne vulgaris is attributed to the high glycemic index of consumed food and IGF-1. IGF-1 receptors are located on keratinocytes, and in acne patients their increased expression in the epidermis and sebaceous glands is noticed. High levels of IGF-1 are

observed in adolescents with symptoms of acne vulgaris and in adult women with symptoms of late acne (*Acne tarda*). It is suspected that it is not androgens, but IGF-1, which is the key element in the appearance and course of acne vulgaris [9].

There are more and more pieces of evidence for the important role of IGF-1 in the course of acne. The key fact is that people suffering from Laron's dwarfism characterized by IGF-1 deficiency do not suffer from a civilization disease such as acne [9]. The studies conducted by Vor et al. [11] showed a linear relationship between the level of IGF-1 and the secretion of sebum in patients. Other studies have linked the relationship between the deterioration of the skin condition in the course of acne with an increase in the level of IGF-1 (level 543.9 ng / ml in people who noticed a deterioration of the skin condition after eating certain foods, to a level of 391.3 ng / ml in people without visible skin deterioration) [12].

A diet rich in ingredients with a high glycemic index leads to an increase in blood insulin levels and the secretion of growth hormone, which in turn stimulates the overproduction of IGF-1. The phosphoinositide-3 (PI3) / Akt kinase is activated and the level of the nuclear transcription factor FoxO1 is reduced. FoxO1 deficiency is associated with the transactivation of the androgenic receptor, stimulation of lipogenesis, the growth of sebocytes, and comedogenesis [13].

IGF-1 is a potential factor that stimulates the synthesis of dehydroepiandrosterone, as well as its conversion to testosterone and dihydrotestosterone [13].

CAUSES OF IGF-1 INCREASE

The importance of diet in the course of acne is widely discussed, while the latest reports indicate that it may be a key element of acne therapy. A Western diet, rich in dairy products, processed foods, and products with a high glycemic index correlates with the prevalence of acne vulgaris. There are several studies supporting the above statement. Otto Schaefer followed the Inuit population for 30 years. The problem of acne was not observed in the indigenous peoples eating traditionally, but with the adoption of Western eating habits, the incidence of acne was very similar to the one in developed countries [14]. The population of Papua New Guinea was also studied. Among 1,200 people living in this place and eating mainly fruit, fish and coconuts, no acne lesions were observed [15].

Dairy products are a large group of food products that increase the level of IGF-1. Milk is a non-heterogeneous substance containing a wide variety of ingredients. The key factors are whey protein and lactalbumin. They are the main element of protein supplements and are also added to skim milk. It is also worth noting that the sold milk is most often obtained from pregnant cows. It contains significant amounts of androgen precursors and growth factors increasing the level of IGF-1 [16].

Cody Z. Watling et al. proved a positive correlation between the consumption of protein from milk and yoghurt with a higher IGF-1 level and a negative correlation with the consumption of protein from cheese. This may be due to the higher content of whey protein in milk and yoghurts. Studies also showed significantly lower levels of IGF-1 in people on vegan diet. The correlation between the consumption of fibre from whole grain foods and the increase in IGF-1 concentration was proved. It is assumed that this may be influenced by the anaerobic intestinal microbiota, which by fermenting fiber produces short-chain fatty acids, resulting in an increase in the concentration of IGF-1 [17]. Examples of products with high and low glycemic indexes are presented in Table 1.

Table 1. Examples of food products with high and low glycemic index

Products with a high glycemic index	Products with a low glycemic index
- watermelon	- raspberry
- boiled potatoes	- apple
- wheat bread	- pomelo
- cornflakes	- carrot
- white rice	- tomato
- semolina	- broccoli
- candy	- Brown rice
- ice-cream	- bulgur groats
- fatty milk	- mozzarella cheese
- honey	- 0% natural yogurt
- chips	- milk 1.5%
- Pizza	- eggs
- sweetened drinks	- almonds
	- pumpkin seeds
	- sesame
	- peanuts

Source: Own study

IGF-1 AND SKIN AGING

Aging is a natural, biological and inevitable process. There are many theories about the degenerative changes that occur during the life of organisms. One of these concerns the influence of the IGF-1 signalling pathway. In many species, a reduced level of IGF-1 is associated with an increase in life expectancy, while in humans this case is more complicated. The low level of IGF-1 increases the risk of cardiovascular diseases, diabetes and osteoporosis. On other hand, too high level of IGF-1 was associated with the occurrence of cancer. It is assumed that to prolong life it is recommended to keep IGF-1 levels low in adolescence but higher levels later in life. This mechanism is certainly very complex and requires further research [18, 19].

SUMMARY

The skin is an organ related to the functioning of other body systems. Disturbances in their functioning very often manifest themselves on the surface of the epidermis and sho-

uld be an alarm signal for further diagnosis. In the daily work of a cosmetologist, the influence of the diet on the condition of the skin cannot be ignored. Both the shortage or excess of some ingredients may have an impact on the external appearance. With the help of a properly selected diet, the course of many diseases can be modulated, including acne vulgaris. It is a long-term disease of very complex etiopathogenesis, which makes treatment and care difficult. An interdisciplinary look at the skin as a part of the body, correlated with many organs, allows creation of effective treatment protocols as well as recommendations regarding diet and lifestyle.

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