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Acne and Diet: Facts and Controversies

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SUMMARY Acne is a common skin disorder characterized by follicular hyperkeratinization and obstruction of the pilosebaceous follicles, androgen stimulated sebum production, colonization of the follicles by *Propionibacterium acne*, and inflammation. A large number of epidemiological studies have shown a low incidence of acne in non-Western societies, suggesting that diet might be an important factor in acne pathogenesis, particularly in mediating inflammation, oxidative stress and androgen stimulation in the acne process. Consequently, it has been hypothesized that diet might have a preventive or therapeutic effect in this skin disorder. Since the majority of recent data have not been consistent, the aim of this article is to present current knowledge and scientific assumptions on the relationship between diet and acne.

KEY WORDS: acne vulgaris, diet, hyperinsulinism, insulin-like growth factor 1, fatty acids

INTRODUCTION

Acne is common skin disorder affecting 80% of young people between 12 and 18 years of age. It is a chronic and self-limiting skin disease that causes physical and psychological morbidity in up to 90% of adolescents and young adults (1).

An association between diet and acne has long been postulated. Numerous ecological and migration studies have shown that there is astonishing difference in the acne incidence and prevalence rates between non-westernized and fully modernized societies, pointing to a conclusion that environmental factors such as nutrition, besides genetic and ethnic factors, play an important role in acne pathogenesis (2,3). There is suggestive evidence that in non-industrialized societies, the incidence of acne is lower than in westernized populations (2). It has been noted that acne remains rare in rural societies, e.g., among the Inuit, Okinawan Islanders, Ache hunter-gatherers and Kitavan Islanders (2,4). Additionally, recent studies have shown that, as these populations made their transition to modern life, either through relocation or a local cultural change, adopting Western diet, the prevalence of acne increased and became similar to that in Western societies (5).

A wide variety of food items have been identified to be associated with acne including milk and other dairy products, chocolate, cereals, bread, nuts, eggs and pork (2,3). However, the results of case reports and studies have not consistently supported any dietary factor (6). Considering that recent randomized controlled trials have shown an improvement in acne after glycemic index and glycemic load were reduced, some researches believed that variables such as glycemic index and glycemic load were more important than specific nutrients such as carbohydrates or fats (7). In contrast, a different conclusion was reached by

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Kaymak *et al*., who did not find that dietary glycemic index or glycemic load and insulin level had a role in the pathogenesis of acne in young patients (8).

Given the conflicting evidence, the role of diet in the development of acne remains controversial.

HIGH-GLYCEMIC-INDEX FOODS, HYPERINSULINEMIA AND ACNE

One of the recent studies has shown that diet-induced acute or chronic hyperinsulinemia initiates a hormonal cascade that promotes unregulated tissue growth by simultaneously elevating the levels of free insulin-like growth factor 1 (IGF-1) and reducing the levels of insulin-like growth factor binding protein 3 (IGFBP-3) (9,10). In a hyperinsulinemic state, increased levels of IGF-1 and decreased levels of IGFBP-3 lead to an imbalance that culminates in the hyperproliferation of keratinocytes (11,12). These data support the idea that insulin-triggered elevation in free IGF-1 levels may promote acne *via* skin hyperkeratinization.

IGF-1 is a potent mitogen which is required for keratinocyte proliferation and has a potential of stimulating growth in tissues, including the follicle. A study conducted in transgenic mice showed that overexpression of IGF-1 resulted in hyperkeratosis and epidermal hyperplasia (13).

Furthermore, insulin and IGF-1 stimulate the synthesis of androgens in ovarian and testicular tissues, and inhibit the hepatic synthesis of sex hormone binding globulin (SHBG) (14-16). Moreover, IGF-1 stimulates androgen receptor signaling by increasing adrenal and gonadal androgen synthesis as well as androgen receptor transactivation (17-20). IGF-1 is also a strong stimulator of sebaceous lipogenesis and acne pathogenesis through stimulation of the follicle and sebocyte growth (21).

In contrast, low-glycemic diet induces normal insulinemic response and seems to have beneficial effect on acne formation. Two large cross-sectional studies conducted in Papua New Guinea (n=1200) and Paraguay (n=115) found that the rural populations' low-fat and low-glycemic-index diets could be the reason for the absence of acne in these groups (22).

The association between insulin levels and acne has been supported by the high prevalence of acne in women with polycystic ovary syndrome (PCOS), a condition associated with insulin resistance, hyperinsulinemia, hyperandrogenism, elevated IGF-1 and low SHBG levels (23,24). Also, it is interesting how individuals with Laron syndrome who carry mutations in the growth hormone receptor (GHR) gene that leads to severe congenital IGF-1 deficiency with decreased insulin/IGF-1 signaling (IIS) exhibit reduced prevalence rates of acne, diabetes and cancer (21).

Body mass index (BMI) is another possible factor that may have impact on acne pathogenesis (25). A study conducted in 2006 suggested connection between higher BMI and acne in schoolchildren, due to the fact that obesity is frequently accompanied by peripheral hyperandrogenism. The researchers concluded that children with a BMI <18.5 seem to be less predisposed to acne formation, while BMI-for-age ≥95% may be a significant risk factor for acne in schoolchildren (25).

FATTY ACID INTAKE

Fat and fatty acid intake also influences the development of acne and the severity of the condition. Omega-6 fatty acids have proinflammatory ability and their mediators have been associated with acne, while omega-3 fatty acids have anti-inflammatory properties and may be associated with a decreased risk of acne by decreasing IGF-1 levels and follicle inflammation (26-28). Derivatives of α-linoleic acid (omega-3 fatty acids) can modulate the immune response of the epidermis by influencing T lymphocytes, acting on Toll-like receptors (TLRs) and activating cascades that influence many inflammatory dermatoses, including acne vulgaris, psoriasis, atopic dermatitis, systemic lupus erythematosus, and skin cancer (29).

Presumption that omega-3 fatty acids might positively influence acne originates from older epidemiological studies which found that communities that maintained a traditional diet high in omega-3 fatty acids, consuming the greatest amounts of fish and seafood, had low rates of acne (30-32). Western diets have a low ratio of omega-3 to omega-6 fatty acids, as compared with diets observed in non-industrialized nations. The intake of omega-6 fats is approximately 10 times greater than omega-3 fats in traditional Western diet, while large amounts of omega-3 fats are lost or oxidized during food processing and cooking (29).

Researches suggest that increased intake of green leafy vegetables, nuts, seeds, and cold-water fish over time can improve the concentration of omega-3 fatty acids in cellular membranes (29).

CHOCOLATE

An early investigation conducted in 1930 suggested that impaired glucose tolerance occurred in acne patients and consequently acne was considered to be a skin condition caused by disturbed and imbalanced carbohydrate metabolism (33). Consequently,

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the majority of acne patients were advised to avoid eating excessive amounts of carbohydrates and high-sugar foods (34,35).

A clinical study conducted in 1969 found no exacerbation of acne lesions in the group that consumed a chocolate bar compared with the group that ingested a placebo bar (36). Although this has been the most widely cited reference that dissociated diet and acne, a large number of authors have criticized this study because of the flaws in the study design (37-39).

So far, there have been no studies assessing the effects of pure chocolate (made of 100% cocoa) on acne (40). The majority of studies suggesting that diet and acne are not related looked at acne outbreaks after the consumption of chocolate which contained added ingredients such as milk, sugar, and nuts, so it has not been set out what effect pure chocolate has on acne exacerbation (40). A recent study conducted on 10 healthy male subjects between 18 and 35 years of age with a history of facial acne vulgaris found a statistically strong correlation between the amount of chocolate that was consumed and the amount of acneiform lesions that developed (40). This study was limited to males because the researchers wanted to exclude hormonal influence that women have regarding their menstrual cycle.

MILK AND OTHER DAIRY PRODUCTS

Several studies have shown an association between the intake of milk and other dairy products with acne (41). Hormonal content of milk may be responsible for the association of milk intake and acne. Milk contains estrogens, progesterone, androgen precursors including androstenedione and dehydroepiandrosterone-sulfate, and 5α-reduced steroids like 5α-androstanedione, 5α-pregnanedione, and dihydrotestosterone, some of which have been implicated in comedogenesis (42,43).

Apart from hormones, milk also contains bioactive molecules that act on the pilosebaceous unit, such as glucocorticoids, IGF-1, transforming growth factor-β (TGF-β), neutral thyrotropin-releasing hormone-like peptides, and opiate-like compounds, some of which survive processing, but their detailed biochemistry, transport, and metabolism are not known (16,43,44). Hormonal influence has also been postulated regarding cheese consumption, because fermentation results in the production of more testosterone from its precursors in milk (41).

Milk intake has been associated with increased plasma IGF-1 levels and may be related to acne through this pathway (41,45-47). IGF-1 may mediate some of the effects of comedogenic factors, like androgens, growth hormone, and glucocorticoids (48). Several recent studies have shown that high serum IGF-1 and androgen levels have been noted in patients with adult acne. As a result of high IGF-1 levels, sebum production increases.

The addition of proteins like α-lactalbumin to low-fat and skim milk, in order to simulate the consistency of whole milk, might also play a role in comedogenesis, either directly or as carriers of bioactive molecules (41).

CONCLUSION

Acne remains a significant cause of morbidity among adolescents and young adults. Although in the 1970s researchers suggested that there was no connection between diet and acne, recently this connection has been re-evaluated, due to greater understanding of how diet may affect endocrine factors involved in acne pathogenesis.

Recent work has demonstrated the association of high glycemic load and glycemic index with acne. The mechanism that is responsible for this effect is through the introduction of increased amounts of testosterone by elevated insulin and IGF-1. Researchers have postulated that this mechanism may be a significant contributor to the high prevalence of acne seen in westernized societies because the typical Western diet consists of numerous dairy sources and foods with high glycemic index that produce hyperglycemia, reactive hyperinsulinemia and increased formation of IGF-1. Also, some nutrients such as milk can influence comedogenesis and androgenesis because they contain androgens like 5α-reduced steroids and other nonsteroidal growth factors that affect keratinization and sebaceous growth.

Based on the endocrine effects of diet, it could be hypothesized that low-glycemic-load diet may have preventive and therapeutic effect on acne. However, the authors' experience suggests that avoiding particular before mentioned foods affects acne differently among individuals. These observations confirm the importance of the influence of other pathogenetic factors in the development of acne. It can be concluded that, despite recent evidence regarding the influence of diet on acne, this relationship should be additionally evaluated.

References

1. White GM. Recent findings in the epidemiologic evidence, classification, and subtypes of acne vulgaris. J Am Acad Dermatol 1998;39 Suppl:S34-S37.

2. Cordain L, Lindeberg S, Hurtado M, Hill K, Eaton SB, Brand-Miller J. Acne vulgaris: a disease of Western civilization. Arch Dermatol 2002;138:1584-90.
3. Robinson HM. The acne problem. South Med J 1949;42:1050-60.
4. Schaefer O. When the Eskimo comes to town. Nutr Today 1971;6:8-16.
5. Ferdowsian HR, Levin S. Does diet really affect acne? Skin Therapy Lett 2010;15:1-25.
6. Kilkenny M, Merlin K, Plunkett A, Marks R. The prevalence of common skin conditions in Australian school students. III: Acne vulgaris. Br J Dermatol 1998;139:840-5.
7. Smith RN, Mann NJ, Braue A, Mächeläinen H, Varigos JA. A low-glycemic-load diet improves symptoms in acne vulgaris patients: a randomized controlled trial. Am J Clin Nutr 2007;86:107-15.
8. Kaymak Y, Adisen E, Ilter N, Bideci A, Gurler D, Celik B. Dietary glycemic index and glucose, insulin-like growth factor-1, insulin-like growth factor binding protein 3, and leptin levels in patients with acne. J Am Acad Dermatol 2007;57:819-23.
9. Danby FW. Nutrition and acne. Clinics in Dermatology 2010;28:598-604.
10. Holly JMP. The physiological role of IGFBP-1. Acta Endocrinol 1991;124:55-62.
11. Ludwig DS. The glycemic index: physiological mechanism relating to obesity, diabetes, and cardiovascular disease. JAMA 2002;8:2414-23.
12. Toyoda M, Morohashi M. Pathogenesis of acne. Med Electron Microsc 2001;34:29-40.
13. Rudman SM, Philpott MP, Thomas GA, Kealey T. The role of IGF-I in human skin and its appendages: morphogen as well as mitogen? J Invest Dermatol 1997;109:770-7.
14. Cara JF. Insulin-like growth factors, insulin-like growth factor binding proteins and ovarian androgen production. Horm Res 1994;42:49-54.
15. Bebakar WM, Honour JW, Foster D, Liu YL, Jacobs HS. Regulation of testicular function by insulin and transforming growth factor-beta. Steroids 1990;55:266-70.
16. Costa A, Lage D, Moisés TA. Acne and diet: truth or myth? An Bras Dermatol 2010;85:346-53.
17. Smith TM, Gilliland K, Clawson GA, Thiboutot D. IGF-1 induces SREBP-1 expression and lipogenesis in SEB-1 sebocytes *via* activation of the phosphoinositide 3-kinase/Akt pathway. J Invest Dermatol 2008;128:1286-93.
18. Ma Q, Fu W, Li P, Nicosia SV, Jenster G, Zhang X *et al*. FoxO1 mediates PTEN suppression of androgen receptor N- and C-terminal interactions and coactivator recruitment. Mol Endocrinol 2009;23:213-25.
19. Rosenfield R. Polycystic ovary syndrome and insulin resistant hyperinsulinemia. J Am Acad Dermatol 2001;45:S95-S104.
20. Rosenfield RL. Ovarian and adrenal function in polycystic ovary syndrome. Endocrinol Metab Clin North Am 1999;28:265-93.
21. Melnik BC, John SM, Schmitz G. Over-stimulation of insulin/IGF-1 signaling by western diet may promote diseases of civilization: lessons learnt from Laron syndrome. Nutr Metab (Lond) 2011;8:41.
22. Smith RN, Mann NJ, Braue A, Mächeläinen H, Varigos JA. A low-glycemic-load diet improves symptoms in acne vulgaris patients: a randomized controlled trial. Am J Clin Nutr 2007;86:107-15.
23. Dunaif A, Segal K, Shelley D, Green G, Dorbrjansky A. Profound peripheral insulin resistance, independent of obesity in polycystic ovary syndrome. Diabetes 1989;38:1165-74.
24. Franks S. When should an insulin sensitizing agent be used in the treatment of polycystic ovary syndrome? Clin Endocrinol (Oxf) 2011;74:148-51.
25. Tsai MC, Chen W, Cheng YW, Wang CY, Chen GY, Hsu TJ. Higher body mass index is a significant risk factor for acne formation in schoolchildren. Eur J Dermatol 2006;16:251-3.
26. James MJ, Gibson RA, Cleland LG. Dietary polyunsaturated fatty acids and inflammatory mediator production. Am J Clin Nutr 2000;71(1 Suppl):343S-8S.
27. Kaaks R, Bellati C, Venturelli E, Rinaldi S, Secreto G, Biessy C, *et al*. Effects of dietary intervention on IGF-I and IGF-binding proteins, and related alterations in sex steroid metabolism: the Diet and Androgens (DIANA) Randomised Trial. Eur J Clin Nutr 2003;57:1079-88.
28. Simopoulos AP. Essential fatty acids in health and chronic disease. Am J Clin Nutr 1999;70(3 Suppl):560S-9S.
29. McCusker MM, Grant-Kels JM. Healing fats of the skin: the structural and immunologic roles of the omega-6 and omega-3 fatty acids. Clin Dermatol 2010;28:440-51.
30. Logan AC. Linoleic and linolenic acids and acne vulgaris. Br J Dermatol 2008;158:201-2.
31. Hitch JM, Greenburg BG. Adolescent acne and dietary iodine. Arch Dermatol 1961;84:898-911.

32. Labadarios D, Cilliers J, Visser L, van Stuijvenberg ME, Shephard GS, Wium D, *et al*. Vitamin A in acne vulgaris. Clin Exp Dermatol 1987;12:432-6.
33. Campbell G. The relation of sugar intolerance to certain disease of the skin. Br J Dermatol Syph 1931;43:297-304.
34. Belsario J. Acne vulgaris: its aetiology and treatment. Aust J Dermatol 1951;1:85-111.
35. Sulzberger M, Baer R. Acne vulgaris and its management. Year book of dermatology and syphilology. Chicago, IL: The Year Book Publishers, 1948:9-39.
36. Fulton J, Plewig G, Kligman A. Effect of chocolate on acne vulgaris. JAMA 1969;210:2071-4.
37. Mackie B, Mackie L. Chocolate and acne. Aust J Dermatol 1974;15:103-9.
38. Rasmussen J. Diet and acne. Int J Dermatol 1977;16:488-91.
39. Cordain L. Implications for the role of diet in acne. Semin Cutan Med Surg 2005;24:84-91.
40. Lowry F. Chocolate May Exacerbate Acne in Men, American Academy of Dermatology (AAD) 69th Annual Meeting: Abstract 305. 2011 February 6.
41. Adebamowo CA, Spiegelman D, Berkey CS, Danby FW, Rockett HH, Colditz GA, *et al*. Milk consumption and acne in teenaged boys. Dermatol Online J 2006;12:1.
42. Darling JA, Laing AH, Harkness RA. A survey of the steroids in cows' milk. J Endocrinol 1974;62:291-7.
43. Donnet-Hughes A, Duc N, Serrant P, Vidal K, Schiffrin EJ. Bioactive molecules in milk and their role in health and disease: the role of transforming growth factor-beta. Immunol Cell Biol 2000;78:74-9.
44. Hartmann S, Lacorn M, Steinhart H. Natural occurrence of steroid hormones in food. Food Chem 1998;62:7-20.
45. Holmes MD, Pollak MN, Willett WC, Hankinson SE. Dietary correlates of plasma insulin-like growth factor I and insulin-like growth factor binding protein 3 concentrations. Cancer Epidemiol Biomarkers Prev 2002;11:852-61.
46. Heaney RP, McCarron DA, Dawson-Hughes B, Oparil S, Berga SL, Stern JS, *et al*. Dietary changes favorably affect bone remodeling in older adults. J Am Diet Assoc 1999;99:1228-33.
47. Giovannucci E, Pollak M, Liu Y, Platz EA, Majeed N, Rimm EB, Willett WC. Nutritional predictors of insulin-like growth factor I and their relationships to cancer in men. Cancer Epidemiol Biomarkers Prev 2003;12:84-9.
48. Deplewski D, Rosenfield RL. Role of hormones in pilosebaceous unit development. Endocr Rev 2000;21:363-92.