

Acne related to dietary supplements

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Abstract

Multiple prescription medications may cause or aggravate acne. A number of dietary supplements have also been linked to acne, including those containing vitamins B6/B12, iodine, and whey, as well as “muscle building supplements” that may be contaminated with anabolic-androgenic steroids (AAS). Acne linked to dietary supplements generally resolves following supplement discontinuation. Lesions associated with high-dose vitamin B6 and B12 supplements have been described as monomorphic and although pathogenesis is unknown, a number of hypotheses have been proposed. Iodine-related acne may be related to the use of kelp supplements and has been reported as monomorphic, inflammatory pustules on the face and upper trunk. Whey protein supplements, derived from milk and used for bodybuilding, are associated with papulonodular acne involving the trunk and sometimes the face. Finally, AAS-induced acne has been described as acne fulminans, acne conglobata, and acne papulopustulosa. With studies indicating that about half of US adults report using dietary supplements, it is important that dermatologists directly ask acne patients about their supplement use and educate them on the potential risks of even seemingly innocuous dietary supplements.

Keywords: supplements, dietary supplements, acne, vitamin B6, vitamin B12, iodine, whey, anabolic steroids

Introduction

Acne may be caused by a number of prescription medications and for clinicians treating acne it is important to obtain an accurate medication history.

Drugs that may induce acne include corticosteroids, anabolic-androgenic steroids, hormonal drugs, lithium, antituberculosis medications, and drugs that contain halogens, specifically iodides and bromides [1-7]. There are also reports of acne potentially induced by cancer therapies, immunosuppressants, and autoimmune disease medications [7].

Multiple dietary supplements have also been linked to acne. A number of case reports and series have described the onset of acne with certain dietary supplements, with resolution following discontinuation of supplement use. These include vitamins and dietary ingredients that may seem innocuous from the standpoint of the consumer or physician. In some cases, supplements have ingredients in common with the aforementioned acne-inducing drugs, such as iodine-containing vitamin and kelp supplements [7,8]. Vitamin B6, vitamin B12, and whey protein supplements have also been linked to acne [7,9]. In addition, the FDA has reported many cases of adulteration of supplements with steroids or steroid like-substances [10].

The mechanism of action of drug-induced acne appears to be specific to the causative drug and in many cases remains unclear. Clinically, the skin findings in cases of drug-induced acne resemble acne, although some describe a monomorphous appearance or a more widespread distribution. The medical history is typically notable for sudden onset, along with a medical history of drug intake, and resolution following medication withdrawal [11]. Reports of drug-induced acne date back to the 1920s, with reports of acne-like lesions related to iodides and chlorinated hydrocarbons [7].

Although a number of pathogenic mechanisms have been proposed, the exact pathogenesis of drug-induced acne is not clear. Different mechanisms have been described with different medications. In the case of medications such as testosterone and anabolic-androgenic steroids (AAS), skin biopsy specimens have demonstrated hypertrophy of the sebaceous glands. Studies have also indicated an increase in skin surface lipids and cutaneous *Propionibacterium acnes* [12]. In the case of lithium, the pathogenesis has been related in part to direct effects on the follicular epithelium, leading to follicular plugging [5].

In this review, we describe the clinical findings reported in supplement-induced acne. We also describe the specific mechanisms of action, when known or hypothesized, reported for each supplement. As this review indicates, the link between acne and dietary supplements is well described. It is therefore important for physicians to directly ask acne patients about the use of any dietary supplements. Dietary supplements are widely used, with reports indicating that approximately half of U.S. adults report using dietary supplements [13-16]. Unfortunately, many patients do not include this information on medical intake forms. A Mayo Clinic study found that only 30.5% of patients reported taking dietary supplements on a written questionnaire. This number rose to 61.0% when patients were interviewed and asked about their use of dietary supplements [17]. It is therefore vital that physicians directly ask about supplement use and educate patients on the potential risks of even seemingly innocuous dietary supplements.

Discussion

Vitamin B6/B12

Supplementation with high doses of vitamins B6 and B12 have been reported to worsen existing acne, with more reports in females than males [18-20]. Supplementation with high-dose vitamin B12 (more than 5-10mg per week) or use for long periods has been described as contributing to acne outbreaks [19,21]. Eruptions resulting from the combination of vitamin B12 with vitamins B1, B2, or B6 in particular, have also been described [19-21].

Clinically, acne that develops after intramuscular injection or oral vitamin B supplementation tends to appear as monomorphic facial papulopustules, mainly on the chin and forehead, or as widespread papules [18-20]. Acne can also be found on the neck, shoulders, arms, chest, and back [18-21].

In one case, a female patient presented with edema on the cheeks, central facial erythema, and inflamed pustules and papules, without comedones. It was discovered that the patient was taking vitamin supplements, including 100mg of vitamin B6 and 100µg of vitamin B12, which equated to 5,000% and 1,666% of the daily recommended allowance (RDA), respectively. The acne improved three weeks after halting supplement use, and flared once the patient took the supplement again [19]. Similar cases report the onset of acne following initiation of vitamin B supplementation, most of which resolved within two to three weeks after therapy was discontinued [18,19,21,22]. In another case, a female patient developed a papulopustular eruption on the face, the back, and the chest, without cysts or comedones. The outbreak started 12 hours after the patient received vitamin B12 intramuscular injections [18]. In a series of five female patients, acneiform eruptions developed after use of vitamin B12. Most patients developed pustules and papules on the face, whereas three patients also developed lesions on the back, shoulders, chest, and neck [21]. Another case described papules and pustules on the face and neck of a 44-year-old woman undergoing intramuscular vitamin B12 administration [22]. Finally, in a unique case, a 5-year-old boy with unexplained severe, monomorphic, itchy papulopustules and nodules on the neck and back had taken a multivitamin supplement and showed elevated serum B12. The supplement's dose had been doubled two weeks before the skin eruption and acne resolved once the supplement was stopped [23].

The pathogenesis of vitamins B6- and B12-induced acne is uncertain [19,24]. In one interesting study comparing post-adolescent acne patients with healthy controls, vitamin B12 deficiency was significantly higher in control subjects [25]. Another study compared levels of vitamin B12 before and after four months of treatment with isotretinoin.

Following treatment, patients had decreased serum levels of vitamin B12, as well as a decrease in a transport system involved in vitamin B12 absorption [26,27]. Numerous hypotheses explaining this connection between vitamin B and acne have been proposed [7,19–21,24,25,28,29]. Acne related to vitamin B6 and B12 could be similar to isoniazid acne, which results from slow inactivation of the drug [19,20,30]. It has been shown that anaerobe metabolism of *Propionibacterium acnes* depends on B12, and that supplementing *P. acnes* cultures with B12 increases porphyrin synthesis, which causes inflammation in acne [21,28]. Another theory is that iodine or sorbitol found in B12 ampoules, play a role in B12-induced acne [7,21]. More generally, continuous B12 excretion could irritate follicular epithelium, resulting in inflammation [24,25].

Literature describing an association between vitamins B6 and B12 and acne is mostly limited to case reports [18,19,21]. Research on vitamin B6 and acne is especially lacking as its influence is uncertain and its dose-acne relationship is unknown [7,19,20]. Still, B12 is widely used [23] and US adults report taking vitamins B6 and B12 for general health and to enhance energy [13]. Healthcare practitioners should therefore question inflammatory acne patients about nutritional supplement use and vitamins B6 and B12 specifically [19,23].

Iodine

The link between iodine and acne is widely reported [31,32]. Iodine can produce acneiform eruptions and exacerbate existing acne [8,31,33]. Acne induced by iodine sometimes resembles acne triggered by steroids and may present initially as pustules, most commonly on the upper trunk and face [31,34,35]. In patch tests, potassium iodide has been associated with inflammatory follicular pustules [34,36]. It has even been hypothesized that the potential link between acne and dairy consumption in some patients may be related to the iodine content of milk, which comes from iodine-containing animal feed and milking sanitizing solutions [33,37].

In addition to its common use in vitamin and mineral supplements, iodine is found in kelp seaweed supplements [31]. In a 1976 case report, two teenagers broke out in inflammatory pustules on the

back, shoulders, neck, and face following use of kelp vitamins and tablets [38]. Another report described two cases with acne development or aggravation in connection with the use of kelp tablets. Of note, in one patient kelp and vitamin B6 tablets were taken together [32]. Acne resolved in all cases once kelp supplementation was discontinued.

Whey protein

The use of whey protein supplements for bodybuilding has grown in popularity, especially among adolescents [9,39,40]. Whey originates from milk, consists of globular proteins, and is produced during cheese manufacturing [9,40]. Whey is believed to support muscle growth because it is rich in branched chain amino acids, which provide substrates for protein synthesis [40].

Recent reports associate whey protein supplements with acne [9,39,41,42]. In one study, 30 gym-frequenters and dermatology clinic patients were examined before, after 30 days, and after 60 days of protein-calorie supplement use. Whey protein was the most common supplement (taken by 22 of the 30 subjects), though acne lesion count was not affected by the type of protein supplement. The authors reported a strongly positive correlation of acne and protein-calorie supplements, with only 56.7% of subjects presenting with acne at the start, compared to 100% of subjects after two months [39]. Results showed a statistically significant increase in the number of acne pustules, papules, and comedones among protein-supplement users over the study period [39]. When the Leeds Acne Grading System revised by Cunliffe was applied, 93% of participants exhibited none or mild acne at the beginning of the study, compared to only 26.7% at the end of the study [39].

In another case series, six men between the ages of 16 and 18 developed acne on the trunk after taking whey protein bodybuilding supplements. The authors attribute acne improvement in these cases primarily to cessation of the protein supplements [9]. Another series reported five adult male bodybuilders who experienced acne eruptions after ingesting whey protein supplements [9,41]. Finally, another case series described five teenagers who developed acne following whey protein supplementation for

weight gain and muscle building. Four of these patients' skin cleared after stopping supplementation and one developed acne again after restarting supplementation [42].

Although the pathogenesis is not known, theories have focused on hormonal effects related to dairy, as the concentrated supplements commonly used by bodybuilders have the same whey content as 6 to 12 liters of milk [9,39,43]. Milk increases levels of insulin-like growth hormone-1 (IGF-1), which has been associated with keratinocyte proliferation, estrogen synthesis, androgen production, and androgen receptor signal transduction [9,43–46]. IGF-1 also enhances cutaneous cell division and growth and luteinizing hormone efficacy [39,43,47]. As such, IGF-1 could promote comedogenic factors [39] and this is reflected by elevated IGF-1 levels in adults with acne [43].

Anabolic-androgenic steroids

Acne is a common effect of AAS use by bodybuilders [2]. Unfortunately, even if bodybuilders are not abusing steroids directly, steroids may be present in certain dietary supplements they take to build muscle [10]. In a study of 776 dietary supplements from the US Food and Drug Administration (FDA) Tainted Supplements database, it was found that 89.1% of “muscle building supplements” were adulterated with steroid-like ingredients or synthetic steroids [10].

Clinically, AAS-induced acne can appear as papulopustular acne, acne fulminans, or acne conglobata. [1,3]. It may exacerbate existing acne vulgaris and may also be accompanied by hirsutism and male pattern hair loss [2,3]. Of note, administration of vitamins B2, B6, and B12 can make AAS-induced acne worse [3,20].

Anabolic-androgenic steroids are believed to promote acne by increasing skin surface lipids, the free fatty acid and cholesterol content of these lipids, and the density of *P. acnes* on the skin. Histopathology shows hypertrophy of the sebaceous glands [7,12]. Dermatologists treating acne should therefore ask about the use of any muscle building supplements, not only AAS use.

Conclusion

Overall, a number of dietary supplements have been associated with acne, including those containing vitamins B6 and B12, iodine, whey protein, and “muscle building supplements” that may potentially be contaminated with AAS. A summary of these links is provided in **Table 1**. When patients present with acne, healthcare professionals must therefore ask not only about their use of prescription medications, but also their use of dietary supplements.

It is also important that physicians not rely on a written medication history, but instead verbally elicit

Table 1. Summary of Acne Associated with Dietary Supplements.

Supplement	Clinical Findings Described	Notable Features
Vitamin B6/B12	Monomorphic lesions, facial papulopustules, and widespread papules found on neck, shoulders, arms, chest, and/or back [18-21]	Reported with high-dose B12 supplements and from combination of B12 with B1, B2, or B6 [19-21]
Iodine	Monomorphic, inflammatory pustules, facial and upper trunk involvement, and can resemble acne triggered by steroids [31, 32, 34, 35, 39]	May be found in vitamin and mineral supplements as well as kelp seaweed supplements [31]
Whey Protein	Papulonodular acne on the trunk. Some reports included facial acne, others did not [9, 43]	Concentrated whey supplements used by bodybuilders have the same whey content as 6 to 12 liters of milk [9]
Anabolic-Androgenic Steroids (muscle building supplements)	Acne fulminans, acne conglobata, or acne papulopustulosa with male pattern hair loss and/or hirsutism [1, 3]	89.1% of adulterated “muscle building supplements” tainted with steroid-like ingredients or synthetic steroids, per the FDA Tainted Supplements database [10]

this information, given that written questionnaires often do not adequately address full nutritional supplement use [17]. Finally, as most of these recommendations are based on case reports or case series only, further research is warranted.

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Potential conflicts of interest

RK serves on the Advisory Board for Vichy Laboratories and is the author of a book for the general public on dermatology. DHZ and APS have no conflicts of interest.

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