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The use of oral vitamin A in acne management: a review

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Abstract

Background: Changes to the iPLEDGE platform on December 13, 2021 made isotretinoin virtually inaccessible for many patients. Prior to the FDA approval of isotretinoin, a derivative of vitamin A, in 1982, vitamin A was used for severe acne.

Objective: To review the efficacy, safety, affordability, and practicality of vitamin A as a substitute for isotretinoin when the latter is inaccessible.

Methods: A literature review of PubMed was conducted using the key words: oral vitamin A, retinol, isotretinoin, Accutane, acne, iPLEDGE, hypervitaminosis A, and side effects.

Results: We identified 9 studies (8 clinical trials and one case report); acne improved in 8 studies. Dosages ranged from 36,000IU daily to 500,000IU with 100,000IU as the most common. Mean duration until clinical improvement was 7 weeks to four months after initiation of therapy. Mucocutaneous side effects were most common, along with headaches, which resolved with either continued treatment or cessation.

Conclusion: Oral vitamin A is efficacious for the treatment of acne vulgaris, although the available studies have limited controls and outcomes. Side effects are qualitatively similar to those of isotretinoin and avoiding pregnancy for at least three months after stopping treatment is critical; like isotretinoin, vitamin A is a teratogen.

Keywords: acne, iPLEDGE, isotretinoin, retinol, vitamin A

Introduction

Isotretinoin (13-cis-retinoic acid) is a vitamin A derivative that was approved by the Food and Drug

Administration (FDA) for the treatment of moderate to severe acne in 1982 and has been widely used ever since due to its high rates of efficacy. Isotretinoin use is strictly regulated due to teratogenicity [1]. In 2005, the program iPLEDGE was established to regulate the potential fetal exposure of isotretinoin by requiring all female patients of reproductive age to undergo monthly pregnancy tests and use two forms of birth control, one month before, during, and one month after treatment with isotretinoin [2].

In October 2021, the FDA announced that new changes to the iPLEDGE system, which included new gender neutral options for patient risk categories and changes to the pharmacy system, would be implemented on December 13, 2021 [3]. The process of changing systems has left some providers without the ability to prescribe isotretinoin for any of their patients [4, 5]. Emergency meetings were held on December 16, 2021 and December 21, 2021 between the American Academy of Dermatology and the US Food and Drug Administration to discuss the issues with the new system [6, 7]. The half-life of isotretinoin is 24-29 hours, allowing patients to miss 4-5 days of treatment without much consequence. However, it was unknown when patients' next dose would become available [8]. A temporary substitute for isotretinoin may be helpful to minimize treatment relapse in patients during times where the drug is not available.

Vitamin A (retinol) consists of a polar end group, a cyclic end group, and a polyene side chain. Isotretinoin was developed from vitamin A by altering the polar end group (**Figure 1**), [9]. Vitamin A is a fat-soluble vitamin that is important for vision, cellular differentiation, epithelial barrier strength,

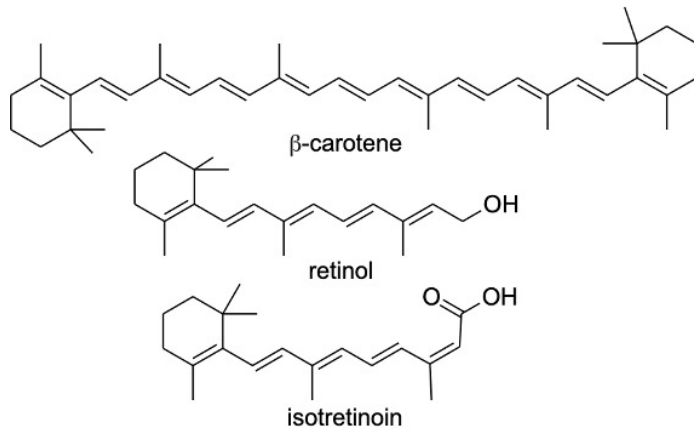


Figure 1. Vitamin A is pre-formed (retinol) and obtained in the diet from meat and dairy products; pro-vitamin A (beta-carotene) is obtained in the diet from fruits and vegetables. Both forms are eventually converted to retinal and retinoic acid [34,35]. Isotretinoin is a derivative of vitamin A with a carboxyl group present in place of the terminal alcohol group.

and immune response. Vitamin A also reduces sebum production and has anti-keratinization properties, explaining its role in the management of acne in which hyperplasia and hyperkeratinization of the pilosebaceous unit are driving factors in pathogenesis [9, 10]. In the decades leading up to the FDA approval of isotretinoin, studies were published on the use of vitamin A in acne treatment, with the first successful trial published in 1943 [11].

This review will focus on the potential of oral vitamin A to serve as a substitute for isotretinoin in the management of acne during times where the latter drug is unavailable or unaffordable.

Methods

A review of the literature was conducted using PubMed and Google Scholar repositories for relevant literature published between 1934-2021 utilizing the keywords: oral vitamin A, retinol, isotretinoin, Accutane, acne, iPLEDGE, hypervitaminosis A, side effects, and regulation. The search was expanded to discover relevant literature on the side effects associated with the use of vitamin A in other diseases using the following keywords: retinol, side effects, vitamin A. Articles were prescreened by reviewing the abstracts and relevant sections. Review articles and clinical trials relevant to vitamin A and its derivatives, isotretinoin's iPLEDGE process,

isotretinoin efficacy and safety, and vitamin A efficacy and safety were selected. A Google News search was also conducted using the terms "isotretinoin" and "iPLEDGE" to identify articles discussing the current events surrounding the change in the iPLEDGE process.

Results

Nine studies (eight clinical trials and one case report) on the efficacy, safety, and dosing of oral vitamin A use in patients with acne were included.

1943

In a prospective clinical trial, one-hundred patients with acne were treated with 100,000 International Units (IU) daily of vitamin A mixed in oil solution for months duration [11]. Of the 100 patients, 79 had improvement in their acne following treatment. Skin irritation increased in patients during the beginning of treatment but no other side effects were mentioned. The improvement in acne usually occurred after three months of treatment and often did not occur until after nine months [11].

1947

In a prospective clinical trial, 52 university students (majority women) with acne of various severity were administered 100,000IU oral vitamin A. One-third of patients had failed previous treatments from other physicians [12]. Patients were given no other treatments and were instructed to follow-up every 3-4 weeks. Of the 52 patients who began treatment, 45 patients continued treatment for 4-5 months. Of those, 7 discontinued treatment after 6-8 weeks due to lack of considerable improvement; 73% had improvement in their acne, with 46% considered good and 27% considered slightly improved. One patient was completely clear at the end of treatment. Females appeared to improve more than males but this did not reach statistical significance. Five patients who had improved relapsed after treatment was finished but improved with reinstatement of treatment. No side effects were discussed [12].

1948

In a double-blinded, prospective, randomized controlled trial, 65 students at University of California

with acne (severity not noted) were treated with either 100,000IU oral vitamin A daily or placebo. Patients were treated for a range of 1-7 months, with 5-6 months being most common. In this trial, 22 subjects dropped out within the first month due to dissatisfaction with their lack of improvement [13]. Of the remaining patients, 35 were given vitamin A and 8 were given placebo (according to the study's methods section, there was a shortage of placebo pills related to the war). Patients were examined at monthly intervals. Twenty of 35 (57%) patients given vitamin A had improvement in their acne compared to 4/8 (50%) of those in placebo group. Improvement was rarely seen in less than two months. No side effects were mentioned [13].

1949

In a prospective clinical trial, 30 patients (males and females) ages 14-26 with primarily moderate to severe acne were administered 36,000-40,000IU of vitamin A in aqueous dispersion (4 cubic centimeter) daily for 2-5 months. Aqueous dispersion was used because authors felt that adherence to the aqueous form was better than oil dispersion as used in a previous trial [14]. Twenty out of 30 patients received therapy for over two months. Criteria for improvement were fewer acne outbreaks and involution of old lesions. At 2-4 weeks of treatment, all but two patients had improvement. Most patients continued to improve with moderate to complete clearing of lesions at the end of the treatment. Overall, 7/30 (23.3%) were almost clear after 2.5-4 months; 9/30 (30%) were moderately improved after 2-5 months; 2/30 (6.7%) were completely clear at the end of treatment. Only 2/30 patients (6.7%) had no improvement after 2-2.5 months of treatment, although (at least) one of these patients was taking the medication irregularly. Of the 20 patients who received treatment for over two months, five patients had temporary mild worsening of their acne, with four occurring during the first month. One patient with epilepsy noted her epilepsy worsened while on the treatment and improved following cessation of the treatment. Two patients had to stop treatment after 1-2 weeks, one related to abdominal pain, and the other as a result of diarrhea. At four months after discontinuation of therapy, 8/9 patients had a recurrence of their acne, ranging from mild to severe [14].

1951

In a prospective, placebo controlled clinical trial, 30 adolescents (males and females) with mild to severe acne were administered 100,000IU vitamin A intramuscularly (intragluteal), vitamin A in oil solution three times a week, or placebo for 2-5 months. All patients were photographed two days before starting treatment and one week after cessation of treatment [15]. Patients were categorized as better, worse, or the same, as assessed by photographs by the authors and two additional physicians. Of these, 2/9 (22.2%) patients in the vitamin A oil solution group improved after treatment, 1/10 (10%) of patients in the vitamin A intragluteal group improved after treatment, and 2/11 (18.2%) of patients in the control group improved after treatment. Side effects included injection site reactions such as pain, discomfort, and swelling. No side effects were noted in the group receiving oil vitamin A [15].

1956

In a prospective clinical trial, 229 patients with various skin diseases including acne vulgaris, rosacea, psoriasis, lichen planus, neurodermatitis, keratoma senile, ichthyosis vulgaris, and other disorders of hyper-keratinization were treated with synthetic vitamin A (palmitate) in either an aqueous or oily solution [16]. Of those patients, 45 patients with acne of ranging severity were treated with 100,000-300,000IU vitamin A palmitate daily for at least four months. Patients were subsequently placed on a maintenance regimen of 25,000 to 50,000IU vitamin A daily and 42 (93%) patients had improvement in their acne independent of initiation dose level. In acne patients, the mean duration until clinical improvement was 7 weeks. Some relapses were seen upon lowering of the maintenance dose to 25,000IU or when treatment was stopped completely. Resumption of therapy was followed by a favorable response in most cases. No side effects were discussed for this group of patients [16].

1963

In a double-blinded, prospective, randomized controlled trial, 80 acne patients between 14-21 years old were given either 150,000IU of vitamin A daily or placebo for 12 weeks. During the 12 weeks of

treatment, patients followed up monthly with their family doctor and response was recorded on a clinical scorecard [17]. An additional method of assessment was the use of photography at baseline and at the end of treatment. Images were assessed by a panel of two general practitioners and one dermatologist who were blinded to which picture was taken before or after treatment. Panelists judged improvement in acne as improved, no change, or worsened. Because of default, 19 patients were excluded from the trial, 11 for faulty photographs, 5 for over-age, and one for sunbathing. Of the 30 patients in the treatment arm, 10 were considered improved by panelists. Of the 31 patients in the placebo group, 11 were considered to be improved by panelists. Worsening of acne as rated by panelists occurred more frequently in the placebo group (11/31 subjects) compared to the vitamin A group (2/30). Outcomes were unrelated to age or sex. Family doctors rated 24/30 vitamin A patients improved based on clinical impression, while finding that 22/31 placebo patients were also improved [17].

1981

In a prospective clinical trial, 136 patients ranging from adolescent to young adult, with severe, recalcitrant acne were recruited from the authors' private practices and treated with 300,000IU vitamin A in water dispersion for a minimum of 3-4 months. Patients were permitted to use 5% benzoyl peroxide once daily to increase compliance of treatment by suppressing patients' urge to use another therapy to strengthen their current regimen [10]. The use of oral contraceptives was not permitted to minimize confounding bias; however, proper counseling was provided. Patients were clinically evaluated for efficacy every two weeks during the first month, and every three weeks thereafter. Treatment responses were categorized as excellent (75% or greater improvement), good (about 50% improved), fair (about 25% improved), and poor (no change or worse). Assessment of lesion counts was not considered feasible in this clinical setting. At the end of study 50.7% had an excellent response and 41.2% of patients had a good response [10].

The second aspect of the study was assessing toxicology. Thirty male patients with acne were paid

to participate, and 20 were randomized to 300,000IU vitamin A daily for 12 weeks, 10 were randomized to 300,000IU for week 1, 400,000IU for week 2, and 500,000IU for the remaining 10 weeks. Laboratory monitoring with serum vitamin A and comprehensive metabolic panels (CMP) were obtained at baseline and at weeks 2, 4, 6, 8, and 12. Patients also followed up weekly with a physician to monitor for any side effects. Of the 20 patients who were treated with 300,000IU daily for 12 weeks, 4/20 (20%) had an excellent response and 14/20 (70%) had a good response. Of the 10 patients that had their dose escalated to 500,000IU, 5/10 (50%) had an excellent response and 5/10 (50%) had a good response with no patients categorized as fair or poor [10].

The authors noted that those who were destined to experience near complete clearance displayed some improvement starting at one month. Truncal lesions were more resistant than facial lesions. Results were also better with pustules and papules than larger nodules, which often needed 3-4 months to involute [10].

For the group of 136 patients treated with 300,000IU daily, side effects were considered infrequent and of little consequence. Only 2/136 patients left the study, both due to headaches. Another three patients had headaches and were advised to continue treatment with the addition of aspirin as needed. The headaches disappeared 2-3 weeks later. The most common side effects included cheilitis, which occurred in the majority of patients. Approximately 75% had xerosis, which was remediated with petrolatum ointment. Only 5% of patients had minor epistaxis. Nail and hair changes were not observed. Other side effects included tiredness, nausea, and difficulty concentrating in a few patients. Side effects were similar for the group of men receiving 300,000IU for 12 weeks. In the 500,000IU group, 5/10 had minor epistaxis, 6/10 had headaches although they were controlled by aspirin, and almost all had cheilitis and xerosis, which was more severe at this higher dosage. Notably, the authors state that the studies were carried out in the wintertime which could aggravate mucocutaneous side effects [10].

The 300,000 and 500,000IU regimens did not appear to have different laboratory profiles. Minor aspartate transaminase (AST) and alanine transaminase (ALT) elevations were seen infrequently and elevations in triglycerides were seen in all patients, returning to normal within 2-3 weeks of stopping vitamin A treatment. Serum vitamin A levels were not correlated with therapeutic response or adverse effects [10].

2019

A 14-year-old with recalcitrant nodulocystic acne of three years duration over his entire face, presented to the clinic [18]. He had failed a variety of over-the-counter medications and several courses of antibiotics using doxycycline and erythromycin prior to presentation. He was prescribed a 4-month course of daily vitamin A supplementation, starting at a daily dose of 100,000IU for the first, before increasing to 200,000IU daily. Photos were taken at baseline and after treatment. At four months he was completely clear. The patient had weekly follow ups to monitor for progression and side effects. Side effects included dry, chapped lips, which were well controlled with lip balm, redness near the cheeks and nose, and dry, peeling skin in that area. These side effects self-resolved at two months without the use of moisturizer or any other topicals. Improvement was observed as early as one month. At two months, the author described melanin deposits, consistent with post-inflammatory hyperpigmentation, that developed in the locations of previous areas of acne. At three months, the condition had largely improved, but treatment was continued for one more month to decrease chance of relapse. The patient was followed for 6 more months after treatment resolution, and he remained completely clear [18].

Discussion

Efficacy and dosage

Improvement in patients' acne was observed in eight of the nine vitamin A studies included in the review. On average, 82.6% of patients had improvement in their acne. In comparison, isotretinoin has a complete clearance rate of around 85%; in a

systematic review of eleven clinical trials, all patients had clinically relevant improvement (>10% reduction in lesion counts) with isotretinoin use [19,20]. Although improvement in acne was an outcome measure in all of the studies reviewed, complete clearance was mentioned only in two of the studies [11,14]. Three trials compared vitamin A to placebo and of those, two had improvements in patients' acne compared to placebo. However, in the trial with equivocal results, there was less worsening of acne compared to placebo (6.7% versus 35%, respectively) [17]. The length of treatment in this trial was only 12 weeks, which may not have been a sufficient length of time to cause remission, as discussed by the authors. The remaining eight studies had treatment lengths ranging from 1 to 7 months. Clinical improvement was not present until 7 weeks to four months after the initiation of therapy. Thus, patience may be needed with patients who do not immediately improve on this treatment.

Relapse was assessed in 3/9 (33.3%) of the studies reviewed. Observation periods following treatment varied among the trials and some studies did not mention relapse rates. In one study, patients had partial relapse within 4-6 weeks after completion of therapy with vitamin A [10]. However, relapse rates varied across studies. In the case report, no relapse was noted for 6 months after treatment completion [18]. Another study reported relapse in 27% of patients within four months of treatment completion. However, the treatment dose used in this trial was 36,000IU-40,000IU, which was less than half the dose used in the other trials [14]. Overall, the relapse rates for vitamin A are comparable to the relapse rates for isotretinoin, which range from 20-40% [21]. In the studies, it was noted vitamin A was more efficacious for the treatment of facial lesions compared to truncal lesions, although truncal lesions improved, albeit more slowly. Vitamin A also appeared more efficacious in the treatment of papules, pustules, and milder forms of acne, than acne consisting of deeper, cystic nodules, but many of the study populations consisted of severe acne patients who also improved with vitamin A [10-17].

There is no standardized dose of oral vitamin A for the treatment of acne. Based on the clinical trials and

case report included in this review, a range between 36,000IU- 500,000IU oral vitamin A daily improved patients' acne. Five of the 9 studies included administered a dose of 100,000IU daily, with four of them improving patients' acne at that dose. One trial included an additional maintenance dose of 25,000-50,000IU oral vitamin A daily following completion of treatment to reduce relapse rates in patients [16]. Maintenance dose following treatment completion has been recommended to prevent relapse but no dose was determined (and maintenance treatment may be problematic in women of child bearing potential), [10]. The studies using a higher dose of 300,000IU daily had a response considered excellent or good in 90% of patients (>50% reduction in acne). In another trial with dosages ranging from 100,000-300,000IU, 93.3% of patients reported improvement in their acne. A 14-year-old patient achieved complete clearance of acne after four months of treatment in which they received 100,000IU daily for one week before escalating to 200,000IU daily for the remainder of treatment. Overall, rates of improvement in the studies were higher with 300,000IU doses compared with 100,000IU doses. However, marked improvement still occurred in those receiving 100,000IU daily [10-14].

Safety and laboratory monitoring

Six of the nine studies on oral vitamin A included in this review reported side effects during treatment. Side effects included cheilitis, xerosis, epistaxis, headaches, and abdominal pain, with benign elevations in triglycerides and liver enzymes [10,11,14-16,18]. The most frequent side effects reported were mucocutaneous in nature. The relationship between severity of side effects and dosage varied amongst the studies. Side effects were considered "few and slight" in those receiving 300,000IU oral vitamin A for 6 months [16]. Mucocutaneous side effects severity was greater for those receiving 500,000IU oral vitamin A daily compared to those receiving 300,000IU daily. However, no serious side effects were noted in either group [10]. In one clinical trial, a patient with epilepsy noted their epilepsy worsened while receiving 40,000IU daily, but resolved with discontinuation of treatment [14]. Side effects, specifically headaches, decreased in severity as treatment progressed, often

resolving within 4-6 weeks. When comparing vitamin A and isotretinoin, similar mucocutaneous side effects, such as cheilitis and xerosis, are reported with isotretinoin use [14,16,20,22-25]. In the vitamin A studies, benign elevations in triglycerides and liver enzymes were noted, although they returned to baseline within 2-3 weeks after stopping treatment [10]. This is similar to isotretinoin [20,22,23,25].

Historically, vitamin A has also been utilized at doses of 100,000-200,000IU for the treatment of measles and Ebola; doses of 300,000-500,000IU daily have been used to improve immune response in COVID-19 patients [26-28]. Vitamin A has also been utilized at even higher doses for longer durations in cancer patients as an adjuvant therapy. In a randomized controlled trial, 307 patients with stage I lung cancer were treated with 300,000IU oral vitamin A daily for 12 months. Side effects included mucocutaneous effects (61%), pruritus (23%), transient liver enlargement (14%), epistaxis (9%), headache (7%), and alopecia (3%). Most symptoms subsided during treatment or disappeared following treatment. Triglycerides increased constantly as treatment progressed but returned to baseline levels following treatment completion [29]. Oral vitamin A has been used in the treatment of psoriasis. Past studies have utilized dosages ranging from 400,000IU daily to 2,000,000IU daily. At doses of 400,000-600,000IU daily for one month, patients had no side effects [30]. However, when doses peaked above 1,000,000IU daily, signs of acute toxicity were present [31].

A concern of chronic vitamin A treatment is hypervitaminosis A syndrome. Symptoms include hepatosplenomegaly, edema, lymphadenopathy, fatigue, emotional lability, bone pain, muscle pain, and headaches. Whereas studies noted headaches to be a side effect from treatment, patients' headaches have abated with aspirin use [10]. Although many of the headaches experienced by patients in the studies were not severe, subsided with either treatment progression or cessation, and lacked concurrent symptoms of diplopia or papilledema, the progression of these symptoms should be monitored. A case of pseudotumor cerebri was noted in a female patient taking 150,000IU daily for four consecutive years [32]. Thus, taking high doses for very long periods of time may increase the risk for

toxicity. For the management of acne, a shorter duration of treatment is typical.

Baseline with follow-up liver function tests and lipid panels in addition to baseline and monthly urine or serum pregnancy tests in females are required for patients initiating treatment with isotretinoin [33]. Although there is no set recommendation for laboratory monitoring in patients taking oral vitamin A, based on the similar elevations in liver function tests and triglycerides seen with oral vitamin A therapy that are seen with isotretinoin therapy, it may be prudent to perform similar laboratory monitoring. These include liver function tests and lipids at baseline and 2-4 weeks following initiation of therapy or an increase in dosage for any patient taking oral vitamin A [10].

Baseline and monthly pregnancy tests are also required as vitamin A is, like isotretinoin, teratogenic [34,35]. The half-life of isotretinoin is 24-29 hours and female patients are recommended to wait at least one month and one full menstrual cycle after stopping therapy before conceiving a child [8]. The half-life of vitamin A is considerably longer, around 12 days [36]. Therefore, it may be prudent to recommend being off vitamin A treatment for at least three months before considering pregnancy. A similar period off drug may be appropriate before blood donation as well.

Cost

Vitamin A is readily accessible and is available over the counter in various drug and grocery stores. One-hundred capsules of 25,000IU of vitamin A can be purchased for under \$10 [37]. At a dose of 100,000IU vitamin A daily, a one month supply of medication would cost approximately ten dollars, compared to approximately \$89 monthly with a GoodRx discount for isotretinoin [38]. However, the cost of these treatments goes beyond the price of the medication, as monthly laboratory monitoring and doctor visits are required for isotretinoin therapy and would be recommended for oral vitamin A treatment as well. Despite the initial greater cost of treatment, the overall long-term cost benefit can be greater with isotretinoin, and potentially vitamin A, than with other conventional acne treatments due to lower relapse rates and greater long-term efficacy [39]. Oral

vitamin A could potentially be a cost-effective option for patients in the management of their acne.

Limitations

Limitations to this review pertain to the overall quality of the studies included. According to the National Institutes of Health, all eight of the trials included can be defined as a clinical trial [40]. However, many of the trials were published over 50 years prior and lack the standardized components of trials today such as randomization, placebo groups, blinding, validated measures of acne severity, and statistical analysis. Baseline acne severity in patients varied in the studies and no standardized grading system was used. Some studies defined severity based on the type of lesions present (pustules, papules, cystic lesions), whereas others stated severity levels without defined criteria. There was also variability in baseline patient severity amongst studies. When assessing improvement in patients' acne, some studies did not state specific outcome measures, whereas others used subjective measurements such as photographs and clinical scorecards. Only three of the studies had a placebo group for comparison. Additionally, only four of the studies mentioned follow-up periods to assess relapse rates in patients; of those, each had variable observation lengths. Three of 9 studies failed to discuss side effects; for those studies we cannot determine if side effects were not present or were not reported. Only two studies explicitly stated inclusion and exclusion criteria. Some studies included vulnerable patient populations, such as prisoners and persons with intellectual disabilities, which likely violates the ethical principles of autonomy and beneficence; these, patients may not have had a choice to participate in the studies and side effects or adverse events may have been underreported.

Conclusion

Based on the available literature, starting acne patients on 100,000IU daily and increasing to a maximum dose of 300,000IU daily as needed in patients that do not respond to the initial dose may be appropriate. Although doses of 500,000IU vitamin

A daily did not have many reported side effects, responses to treatment were effective at lower doses. Treatment lengths of at least 5-6 months appear to mitigate rates of relapse while maximizing efficacy. Laboratory monitoring should be similar to that for isotretinoin, including baseline and monthly liver function tests and lipid panels. Counseling patients about teratogenicity, along with baseline and monthly pregnancy tests for childbearing females, should be mandatory.

Studies on the use of oral vitamin A for acne treatment have diminished since the FDA approval of isotretinoin. Although the discovery of isotretinoin was influenced by the desire to find a treatment more efficacious and safe than oral vitamin A, there are currently no head-to-head clinical trials comparing the two [9]. The risk of hypervitaminosis A from the doses effective in treating acne may be exaggerated [10,18]. Within the limitations of the

available data, the use of oral vitamin A may serve as a possible substitute for isotretinoin.

Potential conflicts of interest

Dr. Steven Feldman has received research, speaking and/or consulting support from a variety of companies including Galderma, GSK/Stiefel, Almirall, Leo Pharma, Baxter, Boeringer Ingelheim, Mylan, Celgene, Pfizer, Valeant, Taro, Abbvie, Cosmederm, Anacor, Astellas, Janssen, Lilly, Merck, Merz, Novartis, Regeneron, Sanofi, Novan, Parion, Quriat, National Biological Corporation, Caremark, Advance Medical, Sun Pharma, Suncare Research, Informa, UpToDate and National Psoriasis Foundation. He is founder and majority owner of www.DrScore.com and founder and part owner of Causa Research, a company dedicated to enhancing patients' adherence to treatment. Madison K. Cook and Patrick O. Perche have no conflicts of interest to report.

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