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Nutrition and psoriasis

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Abstract Nutritional supplementation may provide a viable treatment alternative in patients with psoriasis. Randomized, controlled trials have shown the effectiveness of topical vitamin A and D derivatives, intravenous ω-3 fatty acids, oral inositol, and various combined therapies. Dual therapies of ultraviolet B phototherapy and fish oil, retinoids and thiazolidinediones, and cyclosporine and a low-calorie diet were effective in the treatment of psoriasis in randomized, controlled trials. This contribution also reviews the potential negative effect of alcohol and the potential positive effects of vitamin B_{12}, selenium, retinoic acid metabolism-blocking agents, and a gluten-free diet in the treatment of psoriasis.
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Introduction

The role of nutrition in the treatment of psoriasis has been studied for many years. Most recently, the observation of comorbid conditions associated with psoriasis has stimulated renewed interest in nutrition as a way to improve comorbid conditions in addition to underlying skin disease.

The efficacy of vitamin A and vitamin D derivatives has been well established. Topical corticosteroids and topical vitamin D analogues are effective for chronic plaque psoriasis. Vitamin A derivatives applied topically may also potentially confer benefit.[1] The ω-3 polyunsaturated fatty acids (eicosapentaenoic acid [EPA] or docosahexanoic acid [DHA], or both) administered topically, orally, and intravenously all have reported benefits in psoriasis if taken in high enough doses and may be useful as adjuvant therapy. Similarly, changes in dietary behaviors may help to augment the effect of well-established treatments. Limitation of alcohol use, adoption of a low-calorie or gluten-free diet, or treatment of comorbid conditions, when applicable to a particular patient, may hasten clearing of psoriatic lesions in patients undergoing phototherapy or receiving topical or systemic medications. Vitamin B_{12} and select antioxidants may also provide some benefit. Although many dermatologists often overlook the role of nutrition in the treatment of psoriasis, consideration of nutritional alternatives in select patients may help to enhance care.

Fish oil and psoriasis

The mechanism of action of fish oil in the treatment of psoriasis is based widely on the alteration of serum and epidermal and blood cell membrane lipid composition. Arachidonic acid (AA) is found in high levels in psoriatic skin lesions, and its metabolite, leukotriene B4, is thought to be a mediator of inflammation in psoriasis.[2] When the ω-3 polyunsaturated fatty acid EPA is metabolized by cyclooxygenase or lipoxygenase, or both, in place of AA in cell membranes, it may help to mitigate inflammation. The metabolites of EPA, including leukotriene B5, are far less potent inflammatory mediators than the degradation products of AA. The addition of fish oil to the diet of psoriasis patients led to an increase in the plasma and platelet EPA-to-AA ratios and, by in vitro studies, to a significant decrease in leukotriene B4 synthesis by neutrophils. This change corresponds with clinical improvement.[3]

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Several of the initial open studies with oral fish oil supplementation showed that between 3.6 and 14 grams of EPA daily for a range of 6 weeks to 6 months resulted in some clinical improvement with minimal side effects.[3-6] Clinical response in some studies was associated with uptake of EPA and DHA into the serum, neutrophils, and epidermis[4]; inhibition of leukotriene B4 synthesis by peripheral blood polymorphonuclear leukocytes in vitro[3]; increases in the peripheral blood neutrophil LTB5/LTB4 ratios[5]; reversal of abnormalities in erythrocyte membrane lipid patterns; and decreases in platelet malondialdehyde production.[7] All of these findings showed that clinical improvement may have been associated with increased EPA metabolism. Lower doses taken for a shorter time period, however, resulted in poorer clinical outcomes. Supplementation with EPA (3.2 g/d) along with DHA (2.2 g/d) for only 6 to 8 weeks in patients with plaque psoriasis did not result in any clinically significant improvement.[8]

Despite promising results from early open studies, double-blinded controlled trials of oral fish oil yielded conflicting results. For example, among 30 patients with stable psoriasis who completed the trial, 14 received oral olive oil supplementation, and 13 in the experimental group received fish oil, containing approximately 1.8 grams of EPA, daily for 8 weeks.[9] Although there was a significant increase in the ω-3 fatty acid content in the serum phospholipids in the treatment group and no significant change in the serum phospholipid fatty acid composition in the control group, no clinically significant changes were documented in the measured clinical parameters of erythema, infiltration, desquamation, and body surface area (BSA) involvement between the two groups.[9]

In another study, 28 patients with stable, chronic psoriasis were investigated after their diet was supplemented with fish oil capsules containing 1.8 grams of EPA or olive oil capsules with negligible amounts of ω-3 fatty acids for 12 weeks.[10] A statistically significant greater improvement in erythema ($P < .05$) was noted in the fish oil group. Improvements in other measured clinical parameters, including scaling, pruritus, and BSA involvement, were not statistically significantly greater with fish oil compared with olive oil.[10]

In another trial, 145 patients with moderate to severe psoriasis were supplemented with 6 grams of fish oil per day, containing 5 grams of EPA and DHA, or corn oil.[11] Neither the Psoriasis Area Severity Index (PASI) nor the patient-reported subjective score changed significantly. Oral fish oil perhaps showed the greatest benefit as an adjuvant therapy with suberythemal doses of ultraviolet (UV) B[2] and with oral etretinate.[12] The addition of fish oil resulted in a greater improvement in psoriasis in both studies. The addition of dietary ω-3 fatty acids, however, was unable to augment the beneficial effects of topical betamethasone dipropionate.[13]

Randomized, controlled studies of topically applied fish oil have also yielded conflicting results. Twenty-five patients applied topical fish oil (containing 15.8% EPA and 10.1% DHA) or liquid paraffin under an occlusive dressing daily for 4 weeks.[14] A statistically significantly greater improvement in plaque scaling and induration was noted with fish oil. No difference between treatment groups with respect to erythema was appreciated.[14] By contrast, a multicenter trial of 52 patients with moderate plaque psoriasis given topical ω-3 polyunsaturated fatty acid (1% or 10%) therapy or placebo showed no statistically significant difference between the treatment groups and placebo groups for local PASI, BSA involvement, erythema, desquamation, induration, or pruritus after 8 weeks.[15]

Intravenous ω-3 fatty acid lipid infusions produced a significant improvement over the shortest time course as shown in randomized, controlled trials. Twenty patients admitted to the hospital with acute guttate psoriasis with at least 10% BSA involvement were given infusions of 2.1 grams EPA and 21 grams of DHA or an n-6 lipid emulsion with negligible amounts of EPA and DHA for 10 days.[16] Although both groups experienced improvement, the EPA/DHA treatment group had significantly greater improvement across all clinical scores for erythema, infiltration, desquamation, and a patient-based subjective score. Eighty-three patients with chronic plaque psoriasis noted to have a minimum PASI score of 15 received an ω-3 fatty acid-based lipid emulsion with EPA and DHA or a conventional ω-6 fatty acid-based lipid emulsion for 14 days.[17] A significantly greater decrease in total PASI score was achieved in the ω-3 group. The ω-3 group PASI score decreased by 11.2, which was a significantly greater decrease compared with the 7.5 decrease in the ω-6 group ($P = .048$). A higher percentage of patients in the ω-3 emulsion group also achieved a decrease in PASI by at least 50%.[17]

The beneficial effects of fish oil on retinoid-induced hyperlipidemia have also been evaluated in open studies. Fish oil produced a dramatic reduction in isotretinoin, etretinate,[18] and acitretin-induced hypertriglyceridemia.[19] Similarly, several researchers have suggested that fish oil may be beneficial in cyclosporine-induced nephrotoxicity.[20] A pilot study showed some positive results with fish oil in patients with psoriasis taking cyclosporine.[21] Fish oil supplementation in renal transplant patients treated with cyclosporine, however, showed no effect on cyclosporine-mediated hyperlipidemia.[22] The effect of fish oil supplementation on medication-induced hyperlipidemias in patients with psoriasis receiving treatment with cyclosporine deserves evaluation.

Alcohol and psoriasis

Do patients with psoriasis have poor dietary and alcohol abuse habits that may increase their risk of developing psoriasis and adversely affect their disease course and overall prognosis? Do the dietary and alcohol habits of psoriatic patients influence their development of comorbid conditions? The directionality of these associations is not yet clear.

Alcohol consumption may predispose individuals, especially men with a family history of psoriasis, to developing psoriasis.[23,24] This association is especially concerning given that psoriatic men and women both exhibit higher alcohol consumption than healthy controls.[25] Several studies have also shown an association between alcohol intake and poor prognosis in psoriatic patients. Alcohol consumption in women may be positively correlated with clinical severity, particularly with increased BSA involvement.[26] Alcohol intake in men may be associated with resistance to treatment.[27] A nationwide study in Finland of the causes of death of 3132 male and 2555 female inpatients admitted for psoriasis and followed-up for 22 years from 1973 to 1995 suggested that alcohol consumption was associated with increased mortality rates in patients with moderate to severe psoriasis.[28] Whether modification of alcohol intake in patients with psoriasis affects the disease course needs further study.

Low-calorie diet and psoriasis

Many studies have evaluated the effect of calorie restriction in psoriasis; however, none has provided consistent evidence for a benefit of calorie restriction over an extended period of time.[29,30] Calorie restriction as adjuvant therapy with cyclosporine in obese patients with psoriasis was evaluated. A randomized, controlled, investigator-blinded clinical trial was conducted on 61 obese patients (body mass index >30 kg/m^2) with moderate to severe chronic plaque psoriasis given low dose cyclosporine (2.5 mg/kg/d).[31] The patients were restricted to a low-calorie diet to reduce body weight by 5% to 10%. A control group was given cyclosporine without any dietary caloric restrictions. The experimental group accomplished a significant reduction in body weight ($P < .001$), averaging 7 kg. A significantly greater percentage of the experimental group (66.7%) reached a PASI of 75 ($P < .001$).[31] Caloric restriction with a corresponding decrease in body weight in obese patients may have a role in cyclosporine augmentation.

Metabolic syndrome and psoriasis

Metabolic syndrome has been defined as the presence of dyslipidemia, glucose intolerance, obesity, and hypertension.[32] Several studies have suggested an increased prevalence of each of the components of metabolic syndrome in patients with psoriasis[33-36] as well as an increased prevalence of atherosclerosis.[37] Other investigators have found a higher presence of dyslipidemias in active and inactive psoriasis vs healthy controls.[38] A prospective evaluation of women nurses between 1991 and 2005 showed that women with psoriasis were at increased risk of developing diabetes (adjusted relative risk [RR], 1.63), and hypertension (adjusted RR, 1.17). This risk seemed to be independent, because confounding factors were taken into consideration.[39]

Does the treatment of the underlying comorbidities result in improvement in the psoriasis? Some authors suggest this might be the case. A case report of a patient with psoriasis and metabolic syndrome suggested that a treatment program created by nutritionists and endocrinologists that resulted in dietary modification and treatment of comorbidities caused an improvement in blood glucose, blood cholesterol, and BMI and also a clinical improvement in psoriasis.[32]

What is the effect of insulin-sensitizing agents in the treatment of psoriasis? Thiazolidinediones stimulate the γ-subtype of the peroxisome proliferator-activated receptor (PPAR), which functions as transcription factor and regulates inflammation, blood glucose levels, and blood lipids. In psoriasis, thiazolidinediones, by modulating both retinoic acid and PPAR-γ receptor activity, may be of benefit. PPAR-γ receptor activation can result in decreased proliferation of keratinocytes in vitro.[40] A pilot study of oral pioglitazone in moderate plaque psoriasis showed that thiazolidinediones may be beneficial.[40] A randomized, double-blind, placebo-controlled study involving 70 patients with at least moderate psoriasis treated with pioglitazone revealed a significant decrease in the average PASI score of patients in the treatment group.[41] Another randomized, double-blind, placebo-controlled trial evaluating monotherapy with acitretin or combination therapy with both pioglitazone and acitretin also found a significantly greater improvement in PASI score in the combination therapy group.[42] Studies of the efficacy of rosiglitazone as monotherapy vs placebo were not as promising.[43]

Gluten-free diet and psoriasis and celiac disease

The mechanism by which celiac disease might be related to psoriasis is currently unclear. Both conditions involve Th1 cytokines in the pathogenesis of the disease process. Interleukins (IL)-1 and IL-8 released from rapidly dividing keratinocytes are thought to activate the Th1 inflammatory cascade.[44] Although a clear association between celiac disease and psoriasis has not yet been established, several researchers suggest an increased association,[44-46] whereas others deny any association.[47,48] Whether patients with psoriasis have an increased prevalence of antibodies associated with celiac disease is also controversial. An evaluation of serum immunoglobulin (Ig) G and IgA antigliadin antibody (AGA) levels in 100 patients with psoriasis alone, 100 patients with both psoriasis and psoriatic arthritis, and 100 healthy patients found no difference in the percentage of patients with elevated AGAs compared with controls.[49] Other studies detected increased levels of antibodies found in celiac disease in patients with psoriasis or psoriatic arthritis.[50-53] Patients with elevated AGAs or antitissue transglutaminase antibodies were more likely to

have had treatment with immunosuppressive medications than were patients with antibody levels within normal reference ranges.[52]

A series of investigations in patients with psoriasis and elevated AGAs revealed that 16% had elevated serum IgA AGAs. There was no significant difference in the mean IgG AGA level.[50] A follow-up study showed that in these patients with elevated IgA AGA or IgG AGA, higher serum IgA AGA levels were associated with abnormal scores on duodenal biopsy specimens.[54] The same authors subsequently treated these same 33 AGA-positive and 6 AGA-negative patients with psoriasis with 3 months of a gluten-free diet (GFD), followed by a resumption of the normal diet for the same time period. After 3 months of the GFD, there was a statistically significant reduction in the mean PASI score. Patients without an elevated AGA level did not respond to the GFD.[55] Similarly, a case report of a patient with both severe psoriasis and celiac disease showed that treatment with a GFD resulted in improvement in psoriatic skin lesions.[56]

Prospective trials are needed to determine the true incidence of celiac disease and the true percentage of patients with increased levels of antigliadin, antiendomysial, and antitissue transglutaminase antibodies in psoriasis. Randomized, controlled studies on the use of GFD in the treatment of psoriasis are also warranted.

Vitamin B_{12} and psoriasis

When levels of vitamin B_{12} in psoriatic plaques were low, researchers examined the potential use of vitamin B_{12} in the treatment of psoriasis. Studies have shown efficacy with intramuscular and systemic vitamin B_{12}.[57,58] The benefit in topical vitamin B_{12} was also demonstrated recently. A randomized, prospective clinical trial evaluated the effects of topical calcipotriol cream vs vitamin B_{12} cream (700 mg/kg methyl glycoside stearate) containing avocado oil (containing 82.9 mg/kg vitamin E, α-tocopherol) applied twice daily for 12 weeks in 13 patients with chronic plaque psoriasis.[59] Use of both creams resulted in a statistically significant improvement in the PASI score. The calcipotriol group average PASI dropped from 9.2 to 4.39, while the vitamin B_{12} cream group average PASI score dropped from 9.1 to 5.58 ($P < .0001$ for both groups). The beneficial effects in the vitamin B_{12} group were slower to develop, but by week 12 no difference in PASI scores between the two groups was noted.

Oral vitamin D and psoriasis

Although the role of topical vitamin D in the treatment of psoriasis has been well established, the mechanism of action has yet to be fully elucidated. Calcitriol (1,25 dihydroxyvitamin D_3 [1,25(OH)2-D_3]), the biologically active form of vitamin D, and its analogues act through binding the vitamin D receptor (VDR), a member of the steroid/thyroid hormone nuclear receptor superfamily. VDR is a ligand-dependent transcription factor that forms heterodimers with other nuclear receptors, including the retinoid X receptor. The complex of the ligand, retinoid X receptor, and VDR, translocates to the nucleus and binds to the promoter regions of responsive genes, ultimately resulting in the initiation of transcription, cell differentiation and proliferation, immunomodulation and mineral homeostasis.[60] In vitro studies show that extraphysiologic doses of 1,25(OH)2-D_3 inhibits proliferation of keratinocytes.[61] The downregulation of keratinocyte proliferation and the induction of differentiation are important vitamin D_3-mediated mechanisms in the treatment of psoriasis.[62]

The effect of oral 1,25-(OH)2-D_3 in the treatment of psoriasis has known beneficial effects but is associated with the potential side effects of hypercalcemia, hypercalciuria, and kidney stones. Early case reports showed a potential benefit for oral vitamin D_3 in the treatment of psoriasis.[63,64] A small prospective study was conducted of 17 patients with moderate to severe psoriasis who were given orally or topically administered 1,25-(OH)2-D_3, starting with 0.25 μg once or twice daily. The dose was increased during follow-up visits as long as urinary calcium levels remained within normal reference ranges. The authors found that giving a single dose at bedtime, rather than twice daily, helped to minimize the hypercalciuria. Ten of the 14 patients had "significant clearing," whereas 4 patients had no benefit or only mild clinical improvement.[65]

Another pilot study of oral 1,25-(OH)2-D_3 in the treatment of psoriatic arthritis found that 2 μg for 6 months resulted in at least moderate improvement in joint tenderness for 7 of 10 patients. Four of nine patients evaluated for their skin lesions had "marked" improvement, whereas two patients experienced worsening of the psoriatic plaques.[66] Similarly, another trial showed that oral 1,25-(OH)2-D_3 dosed at 0.5 to 2 μg/d for 6 months produced at least a moderate improvement in skin lesions in two of eight enrolled patients.[67]

The most well-designed study, a randomized, placebo-controlled, double-blind trial of 1 μg daily of 1-α-hydroxyl vitamin D_3 for 12 weeks in 41 patients with moderate to severe psoriasis, showed no difference in PASI score improvement between the two groups.[68]

Why do only some psoriasis patients respond to oral vitamin D_3 supplementation? Proposed theories include possible variations in messenger RNA levels for the VDR and probable allelic variations in individual VDR genes.[69] Indeed, an increased association of the A allele for the VDR was found in patients with psoriasis.[70]

The prevalence of vitamin D deficiency and insufficiency is high in the United States of America and in Europe.[71] More studies on the vitamin D status in patients with psoriasis are needed. Although extraphysiologic doses of oral vitamin D

may have deleterious effects, supplementation of vitamin D in patients with insufficiency may have a role in psoriasis.

Selenium and psoriasis

Selenium in high and low doses has an inhibitory effect on DNA synthesis and a stimulatory effect on and cellular proliferation. Selenium is also known for its UVA and UVB protective, antioxidant, and anti-inflammatory effects.[72] As an antioxidant, selenium provides for some glutathione peroxidase activity in vivo. One study examined the effect of selenium and vitamin E on patients with depressed glutathione peroxidase levels. Levels of glutathione peroxidase increased after 6 to 8 weeks of supplementation. Eight patients with psoriasis and low glutathione peroxidase levels were included in the study, but the effect on skin lesions was indeterminate.[73]

The relationship between selenium status and psoriasis has been evaluated in many pilot studies and open trials. Selenium levels may be depressed in patients with psoriasis.[74-78] In particular, selenium levels were statistically significantly lower in patients with a history of psoriasis for more than 3 years compared with healthy volunteers (38.69 vs 48.41, $P < .05$).[78] Selenium supplementation alone has not been found to improve psoriasis. A small prospective study of seven patients with psoriasis with normal baseline selenium levels failed to show that 6 weeks of selenium (400 μg/d) had any effect on the clinical manifestations of psoriasis. There was no effect, the authors concluded, even though the number of dermal CD4+ cells had increased significantly.[79]

Combination antioxidant therapy may be helpful in patients were severe erythrodermic or arthropathic psoriasis. Supplementation with selenium, coenzyme Q10 (ubiquinone acetate, 50 mg/d), and vitamin E (natural α-tocopherol, 50 mg/d) was associated with more rapid clinical improvement in patients with severe erythrodermic and arthropathic psoriasis in a randomized, controlled trial. There were statistically significant improvements in measured clinical parameters in the arthropathic and erythrodermic psoriasis groups that received the antioxidants compared with the corresponding groups that received the soy lecithin placebo.[80]

Combined antioxidant supplementation in patients with moderate to severe chronic plaque psoriasis was less effective. A double-blind, placebo-controlled study of the effects of selenium and vitamin E in the treatment of selenium-deficient patients with moderate and severe chronic plaque psoriasis for 12 weeks showed that selenium, platelet glutathione peroxidase activity, and vitamin E levels increased significantly with treatment, but the patients did not improve clinically. The authors suggest that the treatment was ineffective because skin selenium content did not change throughout the trial.[74]

As adjuvant therapy with phototherapy or topical therapies, selenium has no known benefit. Selenium supplementation in patients with psoriasis receiving treatment with narrowband UV[81] or topical 5% salicylic acid and 0.1% to 0.3% dithranol ointment[82] had no positive effect.

The role of selenium in balneotherapy for psoriasis has been noted. A statistically significant reduction in the mean PSAI was noted in 92 selenium-deficient patients with moderate to severe psoriasis who were treated with a high-pressure shower regimen and selenium-rich spa water daily for 3 weeks. Mean plasma selenium levels increased significantly after the therapy.[83]

Topical and systemic vitamin A and psoriasis

Various topical and systemic vitamin A derivatives are highly effective in the treatment of psoriasis. There are two families of retinoid receptors: retinoic acid receptors and retinoid X receptors, and each family has α, β, and γ subtypes.[60] Through these receptors, retinoids may act to inhibit the growth of hyperproliferative keratinocytes and induce their terminal differentiation.[61]

There are conflicting reports regarding the serum vitamin A level in patients with psoriasis. Serum vitamin A levels were reported to be decreased in patients with "common psoriasis,"[84] severe erythrodermic, and pustular psoriasis,[85] and in patients with both active and inactive psoriasis.[38] Other researchers found no difference in levels of vitamin A in patients with and without psoriasis.[86,87] Other abnormalities in vitamin A metabolism have been found in psoriatic skin, including increased retinoic acid synthesis and elevated levels of cellular retinoic acid binding protein 2, which functions as an all-trans-retinoic acid binding protein.[88]

The effectiveness of topical and systemic vitamin A analogues in psoriasis is well known, but the potential adverse side effects remain a large barrier to their widespread use, and include hair loss, hypertriglyceridemia, hyperostosis, tissue calcification, xerosis, and teratogenicity.[61] Researchers are studying a relatively new class of medicines, the retinoic acid metabolism-blocking agents, in the treatment of psoriasis, hoping to minimize the deleterious effects of other retinoid analogues. Liarozole inhibits cytochrome P450-dependent all-trans-retinoic acid-4 hydroxylase enzymes, allowing for decreased destruction of natural all-trans-retinoic acid[60] and has a demonstrated benefit in psoriasis.[89] A phase IIa open label clinical trial of oral rambazole, 1 mg daily for 8 weeks, resulted in significant improvement in plaque severity and epidermal proliferation and differentiation.[90]

Inositol and zinc in psoriasis

A randomized, placebo-controlled, double-blind trial demonstrated a significant improvement in the PASI score in lithium-treated patients taking inositol (6 g/d) vs a lactose placebo for 10 weeks.[91] Zinc supplementation, however, did

Table 1 A. Fish oil in the treatment of psoriasis

Study, year	Type of study	Pts	Type of psoriasis	Therapy	Duration	Results
Oral fish oil alone						
Soyland,[11] 1993	DB, MC	145	Moderate-severe psoriasis	Oral fish oil (5 g EPA + DHA) vs corn oil	4 mon	No significant change in PASI
Bittiner,[10] 1988	DB, R, PC	28	Stable, chronic psoriasis	Oral fish oil (1.8 g EPA) qd vs olive oil	8 wks	Significantly better improvement in erythema ($P < .05$) in fish oil group. Nonsignificant improvements in pruritus, scaling, & BSA involvement in fish oil group
Bjorneboe,[9] 1988	R, DB, PC	30	Stable psoriasis	Oral fish oil (1.8 g EPA) qd vs olive oil	8 wks	No significant difference in erythema, desquamation, infiltration, BSA involvement
Danno,[12] 1998		40		Etretinate + EPA vs etretinate 20 mg/d monotherapy		Significant improvements in erythema, thickness, and scale in EPA group
Oral fish oil + UVB						
Gupta,[2] 1989	DB, PC	18	Stable, plaque psoriasis	UVB + oral fish oil (5.4 g EPA + 3.6 g DHA) qd vs olive oil	Fish oil 15 wks; UVB from wk 3 to 11	Significantly greater total decrease in total BSA and greater clinical improvement vs olive oil group
Oral fish oil + topical betamethasone dipropionate						
Gupta,[13] 1990	R, DB, PC	25	Stable, plaque psoriasis	Fish oil (5.4 g EPA + 3.6 g DHA) vs olive oil + topical betamethasone dipropionate	9 wks	No significance difference between fish oil and placebo
Intravenous fish oil						
Mayser,[17] 1998	DB, R, PC, MC	83	Chronic, plaque psoriasis (PASI $\geq$ 15)	ω-3 EPA + DHA lipid emulsion vs ω-6 lipid emulsion	14 days	Significantly greater decrease in PASI by 11.2 ± 9.8 in ω-3 group vs by 7.5 ± 8.8 in the ω-6 group ($P = .048$)
Grimminger,[16] 1993	DB, PC	20	Acute guttate psoriasis ($\geq$10% BSA)	ω-3 vs ω-6 intravenous emulsion	10 days	Moderate clinical improvement ($P < .05$)
Topical fish oil						
Escobar,[14] 1992	R, PC, SB	25	Plaque psoriasis	Topical fish oil (15.8% EPA + 10.1% DHA) vs liquid paraffin	4 wks	Significantly improved erythema and scaling w/ fish oil and liquid paraffin; significant decrease in lesion induration with fish oil only
Henneicke-von Zepelin,[15] 1993	DB, PC, MC	52	Moderate, plaque psoriasis	Topical ω-3 PUFAs (1% or 10%) vs placebo	8 wks	No statistically significant difference between ω-3 vs placebo group

Fish oil, retinoid-induced hyperlipidemia						
Marsden,[18] 1987	Open + placebo	19	Severe acne	Isotretinoin 1 mg/kg/d + fish oil (2.6 g EPA + 2.5 g DHA) qd or corn/olive oil	Isotretinoin for 12 wks; fish oil or corn/olive oil ×2 wks	Statistically significant reduction in TG and cholesterol with fish oil
		9	Severe psoriasis	Etretinate + oral fish oil	Fish oil ×4 wks	Statistically significant reduction in TG
Ashley,[19] 1988	Pilot	25	Psoriasis >20% BSA or disabling form	Etretinate or acitretin + oral fish oil (1.8 g EPA + 1.2 g DHA)		Statistically significant reduction in TG level
Fish oil, cyclosporine-induced nephrotoxicity						
Stoof,[21] 1989	Pilot	20	Psoriasis	CyA vs CyA + fish oil (6 g EPA + DHA)	3 mon	A statistically significant greater decrease in GFR in the CyA alone group vs CyA + fish oil

B. Other therapies in the treatment of psoriasis

Study, year	Type	Pts	Type of psoriasis	Therapy	Duration	Results
Vitamin B_{12}						
Stücker,[59] 2001	R, prospective; right/left-side comparison	13	Chronic plaque psoriasis	Topical calcipotriol on one arm, and topical vitamin B12 with avocado cream to the opposite arm	12 wks	At 12 weeks, vitamin B_{12} significantly improved PASI score ($P < .05$); was as effective as calcipotriol
Thiazolidinediones						
Mittal, 2009	R, DB, PC	41 pts	Moderate to severe chronic, plaque-type psoriasis	Acitretin (25 mg) + placebo versus acitretin (25 mg) + pioglitazone (15 mg)	12 wks	Significantly greater reduction in PASI score in pioglitazone group ($P = .04$)
Ellis,[43] 2007	2 large scale, R, DB, PC	1563 + 1032 pts	Moderate to severe chronic plaque psoriasis	Rosiglitazone 2, 4 or 8 mg/d	26 wks	No difference in rosiglitazone-treated patients vs placebo-treated patients
Robertshaw,[40] 2005	Small, open pilot	5	Chronic plaque psoriasis	Pioglitazone. 30 mg/d	6 mon	Clinical improvements in 4 pts noted
Shafiq,[41] 2005				Pioglitazone monotherapy		
Oral vitamin D						
Siddiqu,[68] 1990	R, DB, PC	50 (41 completed the trial)	Moderate to severe psoriasis	Oral 1-α-hydroxylvitamin D_3 1 μg/d	12 wks	Nonsignificant improvement in PASI between vitamin D3 vs placebo; (45% vs 38.2% had <33% reduction in PASI).
Inositol						
Allan,[91] 2004	R, PC, DB	15 taking lithium	Psoriasis	Lithium 300-1200 mg/d + inositol 6g/d or lactose placebo	10 wks	Significantly lower (better) PASI score in pts taking inositol vs placebo (P = .015).

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Table 1 (*continued*)

Study, year	Type of study	Pts	Type of psoriasis	Therapy	Duration	Results
Zinc						
Burrows,[92] 1994	R, DB, PC	27	Psoriasis	Zinc sulfate (45 mg/d elemental zinc) or placebo + betamethasone valerate 0.0025% ointment.	12 wks of zinc sulfate	No significant improvement in zinc-treated patients
Selenium						
Kharaeva,[80] 2009	R, PC	58	Severe erythrodermic psoriasis & severe psoriatic arthritis	Selenium (aspartate salt 48 μg/d) + coenzyme Q (ubiquinone acetate, 50 mg/d) + vitamin E (α-tocopherol, 50 mg/d) vs placeboy	30-35 days	Significant improvement (vs placebo) in clinical skin scores in erythrodermic & psoriatic arthritis variants
Serwin,[82] 2003	DB, PC, parallel group	22	Active plaque psoriasis	Topical 5% salicylic acid + 0.1% to 0.3% dithranol ointment + 200 μg /d selenomethionine or placebo	4 weeks	No effect of Se supplements on improvement in clinical psoriasis
Serwin,[81] 2006	DB, R, parallel group	37	Active psoriasis	Selenomethionine 100 μg/d or placebo + NBUVB 5× wk	4 weeks	No significant difference in reduction of PASI score between groups
Fairris,[75] 1989	PC, DB	69	Psoriasis	600 μg Se-enriched yeast or 600 μg Se-enriched yeast + 600 IU vitamin E or placebo	12 weeks	No clinical improvement with any of the regimens
Harvima,[79] 1993	Pilot	7	Mild to severe plaque psoriasis	Selenomethionine-yeast tablets (total 400 μg/d Se)	6 wks	No clinical improvement noted
RAMBAs						
Bovenschen,[90] 2007	Small prospective	6	Psoriasis	Rambazole, 1 mg/d	8 wks	Significant decrease from baseline in plaque severity scores ($P < .05$)

C. Alcohol intake, gluten-free diet, and low-calorie diet in psoriasis

Study, year	Study type	Pts, No.	Type of psoriasis	Therapy	Duration	Results
Poikolainen,[28] 1999	Retrospective cohort	3132 M, 2555 W	Psoriasis	N/A	N/A	M and W with psoriasis have higher SMRs, 1.62 and 1.54, respectively; SMRs for causes of death directly attributable to alcohol were high for M (4.46) and W (5.60)

Gupta	Prospective study	48 M, 46 W	Psoriasis	Anthralin, tar, topical corticosteroids and UVB given to both groups regardless of alcohol intake history	Average of 23.1 days	M who drank >80 g of alcohol daily had less of an improvement in PASI score than M who drank <80 g alcohol daily ($P = .02$)
Behnam,[24] 2005	Review [a]			N/A	N/A	Alcohol intake is positively correlated with risk of developing psoriasis in M, and prolongs recovery time in M and W.
Tobin	Survey analysis	100	Alcohol-related liver abnormalities	N/A	N/A	Pts with liver conditions related to ETOH use may have increased risk of developing psoriasis (15%) vs controls (1% to 3%)
Jankovic,[23] 2009	Case-control study	110 pts + 200 controls	Psoriasis	N/A	N/A	Development of psoriasis is associated with alcohol intake (OR, 2.55)
Low-energy diet						
Rucevic,[30] 2003	Small prospective, PC study	82	Moderate psoriasis	Topical emollients and low-energy diet (855 kcal/d) or regular diet (2100 kcal/d)	4 weeks	Low-energy diet group: significant reduction in total chol ($P < .01$), TG ($P < .001$), LDL-C ($P < .01$) and clinical improvement
Lithell,[29] 1983	Small prospective trial	10	Psoriasis and arthritis	Fasting, vegan diet	Fasting for 11 days; vegan diet for 3-4 wks	No benefit with fasting; some improvement with vegan diet
Gisondi,[31] 2008	R, PC, SB trial	61	Moderate to severe psoriasis	CyA 2.5 mg/kg/d + regular diet or CyA + low-calorie diet (500 kcal below resting energy expenditure)	24 wks	Average PASI scores were significantly lower in the low-calorie diet group vs regular diet group ($P < .001$).
Gluten-free diet						
Michaelsson,[55] 2000	Small prospective	33 AGA-positive and 6 AGA-negative	Psoriasis	GFD	GFD for 3 mon, then ordinary diet for 3 mon	Significant ($P = .001$) decreased in PASI before and after GFD in pts with raised IgA and/or IgG AGA
Addolorato,[56] 2003	Case report	1	Psoriasis with celiac disease	GFD		Resolution of psoriasis

AGA, Antigliadin antibody; BSA, body surface area; *CyA,* cyclosporine A; *DB,* double-blind; *DHA,* docosahexanoic acid; *EPA,* eicosapentaenoic acid; *GFD,* gluten-free diet; *GFR,* glomerular filtration rate; *Ig,* immunoglobulin; *LDL-C,* low-density lipoprotein cholesterol; *M,* men; *MC,* multicenter; *N/A,* not applicable; *OR,* odds ratio; *PASI,* Psoriasis Area Severity Index; *PC,* placebo-controlled; *Pt,* patient; *PUFAs,* polyunsaturated fatty acids; *R,* randomized; *RAMBAs,* retinoic acid metabolism-blocking agents; *SB,* single-blind; *Se,* selenium; *SMR,* standardized mortality ratio; *TG,* triglycerides; *UVB,* ultraviolet B; *W,* women.

[a] Studies examining relationship between alcohol use and psoriasis from 1950 to 2004.

not produce a significant improvement in PASI score in well-designed clinical trials.[92]

Taurine in psoriasis

Although early observations suggested the amino acid taurine was involved in the pathogenesis of psoriasis, a series of studies failed to confirm that excessive or restricted taurine could exacerbate or ameliorate, respectively, the clinical course of psoriasis. In an initial study of 12 patients with chronic psoriasis treated with cholestyramine, a bile-acid sequestrant, all patients experienced clinical improvement and a concomitant increase in fecal taurine content. These results suggested that elimination of taurine might be related to clearing of psoriatic skin lesions.[93] Early studies showed that high doses of taurine in patients with psoriasis resulted in exacerbation of skin pruritus, erythema, and scaling within hours of ingestion. In patients without psoriasis, the same response was lacking.[94] Researchers also found that a regular diet contained an appreciable amount of taurine and postulated about whether dietary levels of taurine intake was involved in the pathogenesis of psoriasis. An early trial of a low-taurine diet in 15 patients with mild to severe psoriasis resulted in complete clearing of psoriasis in 9 patients and in partial clearing in the other 6 during a 3-month period.[95]

Another group of researchers 3 years later showed that among 13 patients with psoriasis receiving taurine in doses in excess of those found in a regular diet, only a few experienced an exacerbation of the underlying disease.[96] Furthermore, those on a low-protein/low-taurine diet failed to show a greater improvement than those on a regular or high-protein diet.[97] These authors also evaluated the effect of a low-calorie diet (restricted to 500 calories) and subsequent weight reduction in patients with psoriasis and found either no benefit or an exacerbation of disease with diet restriction.[98] These findings were particularly surprising, given that studies of people with psoriasis subjected to dietary restriction during World War I showed initial improvements, with a recurrence of skin lesions upon resumption of a normal diet.[95]

Conclusions

As summarized in Table 1, nutrition, nutritional supplements, low-calorie or gluten-free diets, and alcohol abstinence may have a role in the treatment of psoriasis and its comorbidities. Future investigations are merited, because these treatments are inexpensive and safer than immunosuppressives and biologics.

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