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Authors
Millsop, Jillian W
Bhatia, Bhavnit K
Debbaneh, Maya
et al.

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Diet and Psoriasis: Part 3. Role of Nutritional Supplements

Jillian W. Millsop, M.S[1,2,*], **Bhavnit K. Bhatia, B.A.**[1,3,*], **Maya Debbaneh, B.A.**[1,4], **John Koo, M.D.**[1], and **Wilson Liao, M.D.**[1]

Jillian W. Millsop: jillian.millsop@gmail.com; Bhavnit K. Bhatia: nitabhatia@post.harvard.edu; Maya Debbaneh: maya.debbaneh@gmail.com; John Koo: John.Koo@ucsfmedctr.org

[1]University of California, San Francisco, Department of Dermatology, San Francisco, CA

[2]University of Utah School of Medicine, Salt Lake City, UT

[3]Rush Medical College, Rush University Medical Center, Chicago, IL

[4]University of California, Irvine, School of Medicine, Irvine, CA

Abstract

Psoriasis patients are increasingly turning to the use of alternative and complementary medicine to manage their psoriasis. Patients often inquire about what dietary supplements may be beneficial, including the use of oral vitamin D, vitamin B12, selenium, and omega-3 fatty acids in fish oils. In this review we examine the extent to which each of these common nutritional interventions has been studied for the treatment of psoriasis. We weighed evidence from both controlled and uncontrolled prospective trials. The evidence of benefit was highest for fish oils. For other supplements, there is need for additional large, randomized clinical trials to establish evidence of efficacy.

Keywords

psoriasis; diet; nutrition; oral vitamin D; 1,25-$(OH)_2D_3$; 1,25-dihydroxycholecalciferol; 1,25-dihydroxyvitamin D3; vitamin B12; selenium; omega-3; fish oil

Introduction

The use of alternative and complementary medicine has soared in popularity with patients, not just for improvement of baseline health, but even in the management of chronic

Corresponding Author: Wilson Liao, liaowi@derm.ucsf.edu, 515 Spruce Street, San Francisco, CA 94118, Phone: (415) 476–4701, Fax: (415) 502–4126.
*these authors contributed equally to this work

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conditions like psoriasis [1, 2]. There is a growing body of popular and scientific literature for the use of nutritional supplementation in the treatment of psoriasis. With this information readily available, patients often perform independent research and ask their dermatologists about what they can add to their diets to make their condition more manageable. Here we sought to explore some of the most common nutritional supplements and explore to what extent the scientific literature has evaluated their respective clinical efficacies. We review studies that have examined oral vitamin D, vitamin B12, selenium, and omega-3 fatty acids.

Methods

We performed our literature search in June 2013 by searching the electronic MEDLINE database via PubMed. Search terms included “psoriasis” combined with “oral vitamin D”, “1,25-$(OH)_2D_3$”, “1,25-dihydroxyvitamin D3”, “1,25-dihydroxycholecalciferol”, “fish oil”, “omega”, “B12”, “vitamin B”, and “selenium”, respectively. In addition, abstracts containing the keywords “alternative therapies” and “nonstandard treatment” were reviewed. We limited our search to articles available in English and those published between 1960 and 2013. Manual searches of bibliographies of the articles were also performed to identify additional studies to be included. Exclusion criteria included topical regimens and studies that did not specify supplement dosage. The primary outcome evaluated was a statistically significant reduction in Psoriasis Area and Severity Index (PASI) and secondary outcomes were other reported clinical measures of improvement.

Results

Fish Oil

Oils of cold water fish rich in omega-3 polyunsaturated fatty acids, eicosapentaenoic acid (EPA) and docosahexanoic acid (DHA) have been considered for use in psoriasis treatment. We found a total of fifteen trials evaluating fish oil for the treatment of psoriasis (Table I). Although the populations studied and the outcomes assessed were heterogeneous, overall there was moderate evidence of benefit for the use of fish oil supplements in psoriasis, with 12 trials (6 controlled, 6 uncontrolled) showing clinical benefit in psoriasis and 3 trials (2 controlled, 1 uncontrolled) showing no benefit.

Mayser et al.[3] and Grimminger et al.[4] each conducted double-blind, randomized, controlled studies comparing the effect of intravenous omega-3 fatty acids (Omegaven) to omega-6 fatty acids (Lipoven) for the treatment of psoriasis. In the Mayser et al. study, 75 subjects with chronic plaque psoriasis subjects were randomized to a 14-day treatment with either intravenous omega-3 or omega-6. PASI scores decreased by 11.2 ± 9.8 in the omega-3 group versus 7.5 ± 8.8 in the omega-6 group ($p=0.048$), with significantly better improvement for the omega-3 group in erythema, scale, and induration. In Grimminger et al., 20 subjects with acute guttate psoriasis received either intravenous omega-3 or omega-6 for 10 days. The omega-3 group demonstrated greater improvement in erythema, scale, and induration compared to the omega-6 group ($p<0.05$ for all categories). This corresponded to a greater than ten-fold increase in favorable neutrophil leukotriene products seen in the omega-3 group but not in the omega-6 group.

In another double-blind placebo-controlled trial of 24 patients with chronic stable plaque psoriasis, the group that received 10 capsules of MaxEPA (1.8 g EPA, 1.2 g DHA) daily for 12 weeks showed more improvement in itching, erythema, scaling, and affected body surface area than the control group receiving 10 capsules of olive oil a day; however, only the improvement in erythema was statistically significant at 12 weeks[5]. Several uncontrolled, open studies have also shown that supplementation of fish oil, ranging from 0.54 to 13.5 grams EPA and 0 to 9.0 grams DHA daily for 6 weeks to 6 months, resulted in clinical improvement, measured by erythema, induration, and scaling[6-12]. These studies have also demonstrated clinical improvement associated with inhibition of leukotriene B4 production in peripheral leukocytes in vitro, decreases in platelet malondialdehyde production, changes in abnormalities of erythrocyte lipid membrane pattern, and increase in leukotriene B5 to leukotriene B4 ratio in peripheral blood neutrophils[6-9, 13].

Fish oil appears has also been studied in combination with other therapies. A double-blind, placebo-controlled study of 18 patients with severe stable plaque psoriasis demonstrated a statistically significant improvement of psoriasis on a regimen of fish oil with UVB therapy versus placebo olive oil with UVB[14]. An open investigation of 30 patients with mild-to-moderate plaque psoriasis who were given either tacalcitol, a synthetic vitamin D3 analog, or combined tacalcitol and Oravex (2.8 g EPA, 0.4mg DHA), showed highly significant improvement ($p<0.0001$) in the PASI score in the Oravex group compared to control after 8 weeks[15]. Another study of 40 patients with chronic stable plaque psoriasis reported better clinical improvement of psoriasis with fish oil in combination with oral etretinate compared to etretinate monotherapy[16].

There have also been several trials that have not shown significant improvement in psoriasis with fish oil (Table I). These studies utilized 1.8 to 3.2 g daily EPA and 1.2 to 2.2 g daily DHA[11, 17, 18]. In one randomized, double-blinded, controlled trial of 27 patients with psoriasis, there was no significant clinical difference between experimental fish oil group, which received 1.8 g EPA and 1.2 g DHA daily for eight weeks, and the control olive oil group[17]. Another randomized, double-blinded, controlled study of 145 patients with moderate to severe psoriasis showed no significant difference in PASI or patient reported subjective score between the group receiving fish oil and the placebo group receiving corn oil[18]. A third open study that included 21 patients with plaque psoriasis also showed no clinically significant improvement following fish oil supplementation for six to eight weeks, although a single patient with pustular psoriasis showed significant improvement[11].

The most common side effects of fish oil include nausea, which may be dose dependent, indigestion, diarrhea, and fishy taste in the mouth.

Vitamin D

Vitamin D deficiency associated with psoriasis has been reported[19-21]. We identified seven prospective trials of vitamin D3 supplementation in psoriasis and two trials in psoriatic arthritis (Table II). All were open-label uncontrolled studies except for one randomized, placebo-controlled trial. The forms of vitamin D3 used in these trials varied from 1,25-dihydroxyvitamin D3 (calcitriol, the physiologically active form of vitamin D) to 1-alpha-hydroxyvitamin D3 (alfacalcidol, requiring only liver metabolism to be converted to the

active form) to vitamin D3 (cholecalciferol, requiring both liver and kidney metabolism to become active).

Perez et al. performed a single center open trial to assess the safety and efficacy of oral 1,25-dihydroxyvitamin D3 for the treatment of psoriasis. Patients (n=85) were given 0.5 μg daily oral calcitriol, which was increased by 0.5 μg every 2 weeks as long as lab values were normal, for a period of six months to 36 months. Overall, 88% had some level of clinical improvement of psoriasis during the study period.[22] 26.5% had complete improvement, 36.2% had moderate improvement, 25.3% had slight improvement of psoriasis, and 12% had no improvement. Additionally, the mean PASI scores decreased from 18.4 at baseline to 9.7 at 6 months to 7.8 at 24 months of treatment ($p<0.001$).

Five additional open-label uncontrolled studies investigated the role of oral vitamin D supplementation in a smaller numbers of psoriasis patients ranging from seven to seventeen. In three of those trials, moderate or greater improvement in psoriasis was reported in at least 50% of subjects[23-25]. For the other two trials, one showed statistically significant improvement in mean PASI from baseline but results for individual subjects were not given[26], while in the other trial only 25% of patients showed moderate or better improvement[27]. Additionally, two small trials have shown benefit of oral vitamin D on psoriatic arthritis as measured by the Disease Activity Score (DAS28)[28] or tender joint count[29].

In the only randomized, placebo-controlled trial of vitamin D supplementation reported to date, 9/20 (45%) receiving 1 μg daily of 1-hydroxyvitamin D3 showed slight improvement versus 8/21 (38%) in the placebo group, which was not statistically significant[30].

Possible side effects of oral vitamin D supplementation include hypercalcemia, hypercalciuria, and kidney stones. Long-term vitamin D overdose can also lead to bone demineralization. Some studies reported an increase in blood levels of calcium and vitamin D or an increase of calcium in urine after starting oral supplementation[29-31], but no patient experienced adverse clinical side effects[29-34].

Vitamin B12

Vitamin B12 deficiency associated with psoriasis has been reported[31, 32]. A retrospective observational study of 98 patients with plaque psoriasis and 98 healthy controls demonstrated lower vitamin B12 levels in psoriasis patients compared to healthy controls[31]. However, few studies have investigated the role of intramuscular administration of vitamin B12 in the treatment of psoriasis. Ruedemann found favorable results with the administration of 1,000 g per cubic centimeter of vitamin B12 intramuscularly for 10 consecutive days, followed by a maintenance dose[33]. Thirty-two percent (11/34) of patients cleared their psoriasis lesions and 29% (10/34) reached PASI 75. Six of 34 patients initially reported severe pruritus, which resolved after two to three treatments. However, no baseline levels were taken prior to administering vitamin B12 to these subjects.

In contrast to these positive results, a double-blinded controlled study by Baker and Comaish showed no difference with the use of intramuscular vitamin B12 injections for

psoriasis[34]. In this study involving 73 patients, intramuscular injections of 1,000 ug vitamin B12 or placebo were administered five days weekly for three weeks. No statistically significant benefit in vitamin B12 group was observed compared to placebo.

Vitamin B12 has no common side effects reported. Rare side effects include hypersensitivity reaction, nausea, vomiting, myalgia and swelling.

Selenium

Selenium is an essential element with anti-proliferative and immunoregulatory properties. A prospective study by Serwin et al. found that a decline in serum selenium was related to increased psoriasis disease severity in patients with psoriasis for more than three years ($p<0.05$)[35]. Several trials have assessed the role of selenium supplementation in psoriasis. Kharaeva et al. enrolled 58 subjects in a double-blind placebo-controlled clinical study to compare the effects of combined selenium aspartate, coenzyme Q10, and Vitamin E versus placebo for the treatment of severe erythrodermic and arthropathic forms of psoriasis[36]. They found that supplementation with the combination of antioxidants showed statistically significant clinical improvement of psoriasis by PASI and Severity Score (SS), the latter which included symptom scoring for desquamation of plaques, plaque hyperemia, plaque inflammation, nail dystrophy, and joint pain ($p<0.05$). The study also showed decline in oxidative stress, measured through activity level of enzymes such as catalase and superoxide dismutase, with the antioxidant supplementation.

In contrast, a double-blind, parallel group study of 37 patients by Serwin, Wasowicz, and Chodynicka demonstrated that selenium supplementation plus narrowband UVB was not superior to placebo plus narrowband UVB for psoriasis treatment[37]. In another case-control study by Serwin et al., 22 patients received topical 5% salicylic acid ointment, 0.1% to 0.3% dithranol ointment, and 200 μg daily selenomethionine versus placebo for 4 weeks[38]. Both groups achieved almost complete remission, but the PASI score was higher in the selenium group ($p < 0.05$) and the TNF level was also higher in the selenium group. Another small prospective study involving 7 patients showed that 6 weeks of 400 μg daily selenium increased the number of dermal CD4+ cells, but did not result in any clinical improvement in the patients[39].

Side effects with selenium are quite uncommon and are observed at doses above 400 mcg/day. They include nausea, vomiting, nail changes, loss of energy, and irritability. Long-term selenium toxicity can mimic arsenic poisoning and can include nail changes, nausea, vomiting, garlic breath, metallic taste, and hair loss.

Discussion

Of the nutritional supplements reviewed, fish oil appears to be the most promising. Several studies suggest that omega-3 fatty acids may be beneficial as monotherapy or in combination with other therapeutic regimens in doses ranging from 0.45 to 13.5 g EPA and 0 to 9.0 g DHA daily for 6 weeks to 6 months. However, efficacy in shorter studies (2 weeks or less) required intravenous administration and oral supplementation was most effective in trials of 3 months or longer. An elevated arachidonic acid level has been implicated in

psoriasis, and its metabolite, leukotriene B4, is a known inflammatory mediator in this condition[14, 40]. Consumption of omega-3 fatty acids from fish oil forms leukotrienes and prostaglandins that are of odd-number, such as prostaglandin E3 and leukotriene B5[41], which oppose the even-numbered inflammatory mediators, decreasing overall inflammation[42, 43]. A high consumption of omega-3 fatty acids is found in the populations of the West African countries, and this dietary intake of omega-3 has been linked to a low incidence of psoriasis in this region.[44, 45] In this review, fish oil appeared to be efficacious in combination with other therapies such as UVB phototherapy, topical vitamin D analogs, and oral retinoids.

Oral vitamin D has also shown some promise, but only in uncontrolled studies. Thus, larger controlled studies are needed. Vitamin D derivatives have been widely used as a treatment for psoriasis in topical form. Vitamin D has been found to be a immune regulator that may benefit inflammatory diseases like psoriasis through its effects on T-lymphocytes type 1 (Th1) cells[46, 47]. Vitamin D3 acts through the vitamin D receptor, which activates transcription of genes that affect keratinocyte proliferation and differentiation[48, 49]. Genetic polymorphisms in the vitamin D receptor and vitamin D metabolic pathway may impact levels of circulating vitamin D3. Vitamin D has also been found to impair the capacity of human plasmacytoid dendritic cells to induce T-cell proliferation and secretion of the T-helper 1 cytokine interferon-gamma[50].

With regard to intramuscular administration of vitamin B12 and oral supplementation of selenium, we found few studies supporting efficacy in psoriasis. The results of the studies were often contradictory. Therefore, there is little evidence currently to support recommending vitamin B12 or selenium in psoriasis. Selenium has been hypothesized to regulate immune processes in psoriasis by increasing the number of $CD4_+$ T cells in the reticular dermis of plaques[39].

There were several limitations to this review. Several of the reported studies were not controlled or randomized, making it difficult to draw conclusion about true efficacy in these investigations. In addition, not all studies included a primary outcome of PASI improvement, and “clinical improvement” is a subjective measure that is difficult to standardize across multiple studies. Additionally, there was significant variability in the populations studied in terms of their psoriasis severity and concurrent therapies.

Conclusion

Of the nutritional supplements reviewed, fish oil showed the highest evidence of benefit in randomized, controlled trials. Oral vitamin D showed promise in open label studies, but additional controlled trials are needed. There was little evidence of benefit for selenium or B12 supplementation. Given high popular interest, dermatologists should familiarize themselves with the efficacy and safety of nutritional supplements in psoriasis to assist their patients in making informed decisions.

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Abbreviations and Acronyms

EPA	Eicosapentaenoic acid
DHA	Docosahexaenoic acid
PASI	Psoriasis Area Severity Index
SS	Severity scale
VAS	Visual analogue scale
DAS28	Disease activity score

Table I

Studies examining the efficacy of fish oil supplementation in psoriasis

Study	Region	Study Design	Length	Number of Patients	EPA Dose (g/day)	DHA Dose (g/day)	Results	Comments
Mayser et al. 1998	8 European Centers	Prospective, randomized, double-blind, controlled	14 days	75	4.2	4.2	PASI score decreased by 11.2 ± 9.8 in the omega-3 group and by 7.5 ± 8.8 in the omega-6 group (p = 0.048)	Treatment group (n=42, intravenous omega-3) vs control group (n=33, intravenous omega-6)
Bittiner et al. 1988	England	Prospective, double-blind, placebo-controlled	8-12 weeks	28 at 8 weeks; 24 at 12 weeks	1.8	1.2	Improvement in: erythema p<0.05 at 8 and 12 weeks; itching at 8 weeks p<0.05 in treatment group vs control	Treatment (omega-3) vs control (olive oil)
Grimminger et al. 1993	Germany	Prospective, randomized, double-blind, controlled	10 days	20	2.1	2.1	Greater improvement in erythema, infiltration, desquamation in omega-3 group compared to omega-6 group (p<0.05 for all categories)	Treatment group (n=9, intravenous omega-3) vs control group (n=11, intravenous omega-6); Only adjunct therapy allowed was topical vaseline
Lassus et al. 1990	Finland	Prospective, uncontrolled	8 weeks	76	1.1	0.8	Decrease in mean PASI after 4 and 8 wks (p<0.001); 7 pts with complete response; 13 pts with greater than 75% improvement; 14 pts with poor response	34 patients also had psoriatic arthritis

Study	Region	Study Design	Length	Number of Patients	EPA Dose (g/day)	DHA Dose (g/day)	Results	Comments
Kragballe and Fogh 1989	Denmark	Prospective, uncontrolled	4 months	26	5.4	3.6	Moderate-excellent improvement in 15/26 (58%) of pts; mild improvement in 5/26 (19%) of pts; no change in 6/26 (23%) of pts	Pts put on low-fat diet avoiding fats, oils, red meats, whole-milk dairy products, baked goods, egg yolks, salad dressings, nuts
Kragballe 1989	Denmark	Prospective, uncontrolled	4 months	17	0.54	0.36	Moderate-excellent improvement in 10 pts; mild improvement in 4; no change in 3 pts	Pts also given 100 μg selenium daily and placed on low-fat diet (see Kragballe and Fogh 1989)
Ziboh et al. 1986	United States	Prospective, uncontrolled	8 weeks	13	10.8-13.5	7.2-9.0	Improvement in: scaling ($p<0.001$); erythema ($p<0.02$); thickness ($p<0.004$). 8/13 (62%) of subjects demonstrated “clinically significant” improvement.	Subjects also engaged in a special diet in which fats, oils, red meat, and whole milk were excluded
Maurice et al. 1987	United Kingdom	Prospective, uncontrolled	6 weeks	10	12.0	8.0	8/10 (80%) showed modest improvement in erythema in scale	Enrolled subjects were resistant to topical treatment
Kojima et al. 1989	Japan	Prospective, uncontrolled	3-6 months	9	3.6	-	At 6 months, 2/7 (29%) showed marked improvement, 4/7 (57%) showed moderate improvement, and 1/7 (14%)	

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Study	Region	Study Design	Length	Number of Patients	EPA Dose (g/day)	DHA Dose (g/day)	Results	Comments
							no improvement no improvement	
Danno and Sugie 1998	Japan	Prospective, randomized, controlled	12 weeks	40	1.8	-	Greater number of patients showed “excellent clinical improvement” by >75% reduction in clinical scores in treatment group	All patients also on 20 mg etretinate daily
Balbas et al. 2011	Spain	Prospective, controlled	8 weeks	30	5.6	0.8	Improvement statistically greater in treatment group compared to control for PASI ($p<0.0001$), DLQI ($p=0.0056$), pruritis ($p<0.0001$)	Treatment group (n=15, omega-3 + topical tacalcitol) vs control group (n=15, topical tacalcitol only)
Gupta et al. 1989	United States	Prospective, randomized, double-blind, controlled	15 weeks	18	3.6	2.4	Fish oil group improved greater than olive oil group in erythema ($p=0.02$), thickness ($p=0.006$), scale ($p=0.008$), and total body surface area ($p=0.0001$)	Treatment group (n=8, fish oil plus UVB phototherapy) vs control group (n=10, olive oil plus UVB phototherapy)

Study	Region	Study Design	Length	Number of Patients	EPA Dose (g/day)	DHA Dose (g/day)	Results	Comments
Soyland et al. 1993	Norway	Prospective, randomized, double-blind, placebo-controlled	4 month	145	3.1	1.9	No significant difference in change in PASI, scaling, erythema, infiltration of selected area between treatment vs. control group	Treatment (fish oil) vs control (corn oil). Pts advised to reduce intake of whole-milk products, meat, margarine
Bjorneboe et al. 1988	Norway	Prospective, randomized, double-blind, placebo-controlled	8 weeks	27	1.8	1.2	No significant change in clinical scores of erythema, infiltration, desquamation, and surface area in either group	Treatment (fish oil) vs control (olive oil)
Kettler et al. 1988	United States	Prospective, uncontrolled	6-8 weeks	23	3.2	2.2	Significant improvement only in the 1 pustular pso patient; minimal improvement in 8 pts; no change in 10 pts; mild worsening in 5 pts	21 plaque, 1 pustular, 1 palmoplantar pts enrolled; diets with more fish/ chicken than beef/pork more likely to show improvement

Legend

PASI = Psoriasis Area Severity Index
DLQI = Dermatology Life Quality Index
EPA = Eicosapentaenoic acid
DHA = Docosahexaenoic acid
DPA = Docosapentaenoic acid
LA = Linoleic acid
GLA = Gamma-linolenic acid

Table II

Studies examining the efficacy of vitamin D supplementation in psoriasis and psoriatic arthritis

Study	Disease	Region	Study Design	Length	Number of Patients	Vitamin D3 Form Dose (microgram/day)	Results
Perez et al. 1996	Psoriasis	United States	Prospective, uncontrolled	6 months to 3 years	85	**1,25-dihydroxy** Started at 0.5 and increased by 0.5 every 2 weeks as long as 24 hour urinary calcium concentrations remained normal	26.5% had complete improvement 36.2% had moderate improvement 25.3% had slight improvement Mean PASI 18.4 ± 1.0 at baseline, 9.7 ± 0.8 at 6 months, 7.8 ± 1.3 at 24 months
Siddiqui et al. 1990	Psoriasis	Saudi Arabia	Prospective, randomized, double-blind placebo controlled	3 months	41	**1-hydroxy** 1.0	9/20 (45%) on Vit D showed slight improvement vs 8/21 (38%) on placebo showed slight improvement, no statistically significant difference
Morimoto et al. 1986	Psoriasis	Japan	Prospective, uncontrolled	6 months	17	**1-hydroxy** 1.0	76% of patients displayed moderate or greater improvement after 2.7 ± 0.6 months
Smith et al. 1988	Psoriasis	United States	Prospective, uncontrolled	6 to 12 months	14	**1,25-dihydroxy** 0.5 to 2.0	7/14 (50%) improved greater than 75% 3/14 (21%) improved 25-50% 4/14 (29%) patient improved 0-25%
Finamor et al. 2013	Psoriasis	Brazil	Prospective, uncontrolled	6 months	9	**cholecalciferol** 875.0	There was a statistically significant improvement in PASI scores from baseline to 6 months ($p<0.01$); PASI scores inversely correlated with serum 25-hydroxyvitamin D3 levels ($p<0.001$)
El-Azhary et al. 1993	Psoriasis	United States	Prospective, uncontrolled	6 months	8	**1,25-dihydroxy** 0.5 to 2.0	1/8 (12.5%) improved markedly 1/8 (12.5%) improved moderately 6/8 (75%) with no or mild improvement
Takamoto et al. 1986	Psoriasis	Japan	Prospective, uncontrolled	6 months	7	**1-hydroxy** 1.0	2/7 (29%) showed complete remission 2/7 (29%) showed marked improvement 3/7 (43%) showed no improvement
Gaal et al. 2009	Psoriatic arthritis	Hungary	Prospective, uncontrolled	6 months	19	**1-hydroxy** 0.5	DAS28 score decreased from a mean of 45 ± 11 to 29 ± 10
Huckins et al. 1990	Psoriatic arthritis	United States	Prospective, uncontrolled	6 months	10	**1,25-dihydroxy** 2.0	4/10 (40%) improved 50% or more in tender joint count; 3/10 (30%) improved 25-50% in the tender joint count. 2/10 (20%) unable to receive therapeutic doses because of hypercalciuria.