

## ROLE OF DIETARY INTERVENTION IN PSORIASIS: A REVIEW

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### Abstract

Psoriasis is a chronic inflammatory disease marked by remissions and exacerbations. The exact etiology is not clear but a mix of genetic and environmental factors is proposed as the cause. The disease is associated with obesity and metabolic syndrome. In these contexts, diet assumes an important role in psoriasis patients. This review aims to discuss the various dietary interventions proposed for the management of psoriasis, the evidence regarding the same and controversies surrounding them. Hypocaloric diet has shown to improve severity of psoriasis of skin and joints. Antibodies to gluten may be seen in otherwise asymptomatic patients of psoriasis and these may benefit from a gluten free diet. Omega-3 fatty acids have shown a strong evidence to be beneficial in several trials. However, the dose and route of administration is yet to be standardized. Amongst the vitamins, vitamin D shows the maximum evidence of benefit, while the role of folate and vitamin B12 needs to be explored further. Same is the case for zinc and selenium. There is evidence of exacerbation of psoriasis with foods such as red meat, eggs and dairy products and those rich in taurine, but the evidence is too scant to advise reduction in intake of these items. Alcohol has been strongly implicated in the initiation and exacerbation of psoriasis. Dermatologists must be aware of these interventions to help their patients make the best choice for dietary modification.

**Key Words** - Psoriasis, Diet

### Introduction

Psoriasis is a common, chronic, inflammatory and proliferative condition characterized by sharply demarcated, red, scaly plaques over the skin, predominantly over the extensor surfaces and scalp. The disease is variable in duration with periodicity of flares and extent.<sup>1</sup> A complex interaction of epidermal keratinocytes, lymphocytes, neutrophils, macrophages and dendritic cells lead to the activation of Th1 immune response, producing numerous signaling molecules and resulting in the clinical disease.<sup>2</sup> It is considered to be a systemic inflammatory disease and has been associated with obesity, cardiovascular diseases and type 2 diabetes mellitus.<sup>3</sup>

The role of nutrition and diet in management of psoriasis has been studied since long. Their role has now been established in the etiopathogenesis of psoriasis by several authors.<sup>4,5</sup> The association of metabolic syndrome with psoriasis has added further interest in this field. Advice regarding dietary intervention is very frequently sought by patients in clinical practice. Thus the treating dermatologist must be abreast with the recent evidence of dietary interventions to advise patients accordingly.

This review aims to highlight the beneficial as well as adverse effects of various dietary interventions in the management of psoriasis. The strength of evidence and controversies regarding these interventions shall be discussed.

### Hypocaloric Diet

Several studies have linked increased Body Mass Index (BMI) to the higher incidence and severity of psoriasis. Wolk K et al found that obese patients are twice as likely to get psoriasis as

compared to healthy subjects. They stated that with the increase in BMI by one unit, the risk of onset of psoriasis increased by 9% and the Psoriasis Area Severity Index (PASI) increased by 7%.<sup>6</sup> Another study from Taiwan found that increased BMI is associated with increased severity, this association is stronger in men.<sup>7</sup> The observation that psoriasis responds to low energy diet was made when the incidence of psoriasis was found to have decreased during the second world war.<sup>8</sup> This view was reinforced by observations of Simons that 8 of the 13 Dutch prisoners on near starvation diets in the Japanese concentration camps showed resolution of the lesions of psoriasis.<sup>9</sup>

Most prospective trials evaluating low diet therapy with the usual treatments have shown significant reduction in severity of psoriasis as measured by PASI score<sup>10-13</sup>, dermatology quality of life (DLQI)<sup>10,13</sup> or, in case of psoriatic arthritis, the visual analog scale.<sup>14</sup> Jensen et al in a randomized controlled trial found that the group of 30 patients on a low energy diet showed a significantly greater reduction in weight than the control group on normal diet. The test group also showed a greater reduction in PASI and DLQI.<sup>10</sup> Gisondi P et al showed that patients of moderate to severe psoriasis with BMI of more than 30, who were given low energy diet and cyclosporine achieved greater reduction in PASI by 75% (PASI 75) than the group on cyclosporine alone.<sup>11</sup> Rucevic I et al showed that decrease in serum lipids achieved by hypocaloric diet correlated with improvement in psoriasis.<sup>12</sup> Hypocaloric diet also significantly improves psoriasis when given with topical steroids.<sup>13</sup> However, Kimball et al found that low calorie diet did not alter the PASI score when given with narrow band ultraviolet therapy (NB-UVB) than when compared to NB-UVB therapy alone.<sup>15</sup> Another prospective,

investigator-blinded, randomized controlled trial showed that psoriasis patients stabilized on methotrexate and on low calorie diet took longer time for the rebound of their disease.<sup>16</sup>

The improvement in psoriasis with hypocaloric diet has been explained by Li et al on the gene-environment interaction with BMI interacting with IL12B and IL23R genes.<sup>17</sup> Also, low calorie intake has been shown to lower the intake of pro inflammatory mediators circulating in the body.<sup>18</sup> Dietary weight loss should be recommended to patients of psoriasis who are overweight or obese, as the level of evidence is IB, indicating evidence from a randomized controlled trial.<sup>19</sup>

### **Vegetarian Diet**

Epidemiological studies done by Kavli et al showed that the intake of fresh fruits and vegetables was associated with a lower risk of psoriasis.<sup>20</sup> Naldi et al, in a multicentre epidemiological study from Italy showed that psoriasis was inversely related to the intake of vegetables like carrots, tomatoes and fresh fruits.<sup>21</sup> Addition of omega-3 fatty acid rich diet to vegetarian diet interspersed with periods of hypocaloric diet was found to be beneficial in one study.<sup>22</sup> Also, vegetarian diet was found helpful in maintaining the remission induced by hypocaloric diet.<sup>23</sup> The benefits of such a diet has been attributed to the reduced formation of arachidonic acid and its proinflammatory metabolites.<sup>24</sup> This is in addition to the beneficial effects offered by various antioxidants and vitamins.

### **Gluten Free Diet**

A correlation between psoriasis and celiac disease has been established and has been attributed to the common Th1 cytokine profile seen in both the diseases.<sup>5,25</sup> This Th1 cytokine profile is produced due to the release of IL1 and IL8 from the rapidly proliferating keratinocytes.<sup>26</sup>

A study found the prevalence of anti gliadin and anti transglutaminase antibodies to be 18% and 10% respectively in a group of 123 patients of psoriasis. The antibody levels decreased after adopting a gluten free diet, accompanied by complete resolution of skin lesions.<sup>27</sup> Further, it was shown that a gluten free diet produced a highly significant improvement in PASI scores of patients. The disease worsened on stopping this diet.<sup>28</sup> The levels of tissue transglutaminase is found to be increased in psoriatic skin and this level decreases after a gluten free diet is instituted.<sup>29</sup> However, the positive association between the two diseases has been disputed by some authors.<sup>30,31</sup>

Gluten free diet may, thus, be beneficial in psoriasis patients with antibodies specific for celiac disease, but more studies are needed to arrive at a conclusion.<sup>32</sup> Duarte et al recommend antibody screening for patients of moderate to severe psoriasis or those with palmoplantar pustulosis, as a large number of patients with gluten intolerance may be clinically asymptomatic.<sup>23</sup>

### **OMEGA-3 Fatty Acids**

Epidemiological studies show that Eskimos of Greenland have a very low incidence of inflammatory and autoimmune diseases and this was attributed to the high intake of omega-3 fatty acids in them, due to fish being such an important part of their diet.<sup>9</sup> Oils of cold water fish has been found to be rich in eicosapentaenoic acid (EPA) and docosahexaenoic acid(DHA). Omega-3 fatty acid intake leads to decreased production of arachidonic acid derived proinflammatory mediators by competition and production of metabolites that are less

inflammatory in nature than the metabolite of arachidonic acid.<sup>33</sup> Their effects may also be due to alteration of intracellular signaling pathways, antioxidant action and regulation of transcription factor activity.<sup>9,34</sup>

Several trials evaluating the role of omega 3 fatty acids have been conducted. Double blinded randomized controlled trials by Mayser et al and Grimminger et al demonstrated the superiority of omega 3 fatty acids over omega-6 fatty acids in decreasing the severity of the disease in chronic plaque and guttate psoriasis respectively.<sup>35,36</sup> Several open studies have also shown clear benefit of fish oils in reducing erythema, scaling, induration, area involved and PASI scores in psoriasis patients, with variable dosages and for variable periods.<sup>37,38</sup>

Fish oils have also shown to improve responsiveness to other therapies.<sup>39</sup> A placebo controlled, double blinded study showed that ultraviolet B therapy showed statistically significant improvement in psoriasis when given with fish oils than when given with placebo.<sup>40</sup> Similar results have been obtained with fish oils in combination with emollients, topical tacalcitol and oral etretinate.<sup>41-43</sup>

However, some trials have shown that omega-3 fatty acids offer no added benefit in psoriasis.<sup>44</sup> This includes two randomized, double blinded, placebo controlled studies, making the argument in favour of omega 3 fatty acids slightly weak. Thus, fish oils are recommended for patients of psoriasis.<sup>9</sup> The intake of omega 3 fatty acids needed to achieve a critical level in the epidermal phospholipids, that may inhibit arachidonic acid derived eicosanoids is probably high.<sup>9</sup> More studies are warranted to arrive at an appropriate dosage recommendation for the same.

### **Vitamins**

**Vitamin A:** This vitamin has been proven to play important role in epidermal keratinisation by inhibiting the hyper proliferative keratinocytes and inducing terminal differentiation in them. Levels in serum have been found to be decreased in patients of psoriasis of various morphological types and in inactive disease as well.<sup>45,46</sup> Safevi et al, however, found that there was no difference in serum vitamin A levels in patients of psoriasis and those without the disease.<sup>47</sup> Endogenous retinoids have been shown to have increased in the plaques of psoriasis.<sup>48</sup> The effect is largely attributed to the antioxidant activity of carotenoids.<sup>49</sup> The antipsoriatic activity of Vitamin A is only modest, as higher doses needed for clearing may lead to systemic toxicity. This prevented any serious trials evaluating vitamin A supplementation in psoriasis.<sup>50</sup> However, derivatives of vitamin A called retinoids, have been firmly established as important armamentarium in the management of psoriasis.

**Vitamin B9 (Folic acid):** Patients with psoriasis have folic acid deficiency.<sup>51</sup> This is attributed to decreased intestinal absorption due to inflammation, increased utilization by keratinocytes and elevated levels of homocysteine, an independent risk factor for cardiovascular disease.<sup>25</sup> Malerba et al found a direct correlation between psoriasis severity, measured by PASI, and homocysteine levels and an inverse correlation with folate levels in blood.<sup>51</sup> A case control study showed that obese psoriatic patients have decreased folate and high homocysteine levels.<sup>52</sup> A comparative trial showed that calcium folinate supplementation produced fewer side effects in patients of psoriasis with >6% body surface involvement than another group treated with only

traditional methods, though both groups improved well.<sup>53</sup>

Caution is advised with folate supplementation as daily safety levels are low (1mg/day) and daily supplementation may lead to overexposure, particularly in countries with mandatory fortification of flour.<sup>23</sup> Further evidence is warranted before folate is recommended as supplementation for patients of psoriasis with heart disease.<sup>23</sup>

**Vitamin B12:** Psoriasis patients have been demonstrated to have low vitamin B12 levels in studies.<sup>54</sup> Ruedemann et al evaluated the efficacy of supplemental vitamin B12 in 34 patients of plaque psoriasis.<sup>41</sup> They gave 1000g/cm<sup>3</sup> of intramuscular vitamin B12 followed by maintenance doses and reported complete clearance of lesions in 32% patients and PASI 75 was achieved in 29% cases. However, a later double blinded, placebo controlled trial failed to show any statistically significant benefit of intramuscular vitamin B12 injections over placebo to psoriasis patients. Topical vitamin B12 cream was assessed and compared to calcipotriol cream and response assessed by change in PASI score. The vitamin cream showed a slow response and PASI scores were not changed appreciably.<sup>55</sup> More research is needed for the possible use of vitamin B12 in early psoriasis.<sup>25</sup>

**Vitamin D:** This vitamin has anti proliferative effect on keratinocytes and produces their differentiation. It also has immunomodulatory activity in psoriasis by directly acting on T cells and antigen presenting cells. Studies show that patients of psoriasis have low serum levels of vitamin D and severity of psoriasis is inversely related to serum levels of vitamin D.<sup>56,57</sup> Several open trials of vitamin D supplementation in psoriasis have been conducted, mostly showing beneficial response. The largest of these was conducted by Perez et al on 85 patients. 88% patients had some benefit with calcitriol supplementation with a fourth of all patients showing complete clearance of lesions and another third showed moderate improvement.<sup>58</sup> Psoriatic arthritis has also been shown to respond to vitamin D.<sup>59</sup> However, the only prospective randomized placebo controlled trial found no statistically significant benefit with vitamin D.<sup>60</sup>

More studies are needed for defining the role of oral vitamin D in psoriasis. Still, owing to the public health problem of vitamin D, its supplementation may be recommended in patients not on topical vitamin D analogues.<sup>23</sup>

#### **Antioxidants**

**Selenium:** Selenium is an antioxidant, has immunomodulatory activity and inhibits DNA synthesis, thus posing as a potential treatment for psoriasis. Research has shown that selenium is deficient in psoriasis patients and deficiency of this essential micronutrient correlates with the disease severity.<sup>61</sup> Harvima et al proposed that selenium alone cannot improve psoriasis. They combined selenium with coenzyme Q10 and vitamin E and reported clinical improvement in patients of psoriatic arthritis and erythroderma.<sup>62</sup> The results were replicated by Kharaeva et al in a larger trial.<sup>63</sup> However, selenium supplementation was not found to be superior when given with narrow band UVB light or with topical treatment.<sup>64,65</sup>

**Zinc:** Combined with copper, zinc is a powerful antioxidant and is important for maintenance of normal immune responses. Mice fed on zinc deficient diet develop a psoriasis like condition.<sup>9</sup> Plaques of psoriasis are associated with

deficiency of zinc.<sup>66</sup> However, supplementation with zinc has failed to show any improvement in psoriasis lesions in clinical trials.<sup>66</sup> The role of zinc in psoriasis as an antioxidant needs to be further assessed as it is a very safe nutrient when used as a daily supplement.

#### **Foods That Worsen Psoriasis**

**High Glycemic Foods:** High glycemic foods increase insulin levels and lead to increase of pro inflammatory cytokines in blood, theoretically leading to worsening of psoriasis. A positive correlation was proposed by Boencke et al between PASI score and insulin levels.<sup>67</sup> Intake of foods with a low glycemic index may become part of management of psoriasis patients' general management, as they improve the disease and decrease cardiovascular disease risk as well.<sup>68</sup>

**Alcohol:** Extensive evidence links the amount of alcohol and the type of beverage to both the onset and exacerbation of psoriasis.<sup>69</sup> Further, alcoholic patients exhibit decreased response to treatment.<sup>70</sup> The distribution of lesions on the acral parts is akin to that seen in immunocompromised individuals, suggesting that alcohol leads to immunosuppression. Other reasons explaining psoriasis in alcoholics is the hyper proliferation of skin due to alcohol induced production of cytokines and cell cycle activators like cyclin D1 and keratinocyte growth factor.<sup>70</sup>

**Red meat, eggs and dairy products:** Psoriasis severity has been correlated with consumption of a diet high in red meat.<sup>71</sup> This may be due to the high content of arachidonic acid present in red meat.<sup>72</sup> Eggs and dairy products also contain high amounts of arachidonic acid and may also irritate the intestinal mucosa perpetuating psoriasis outbreaks.<sup>9</sup> However, clinical evidence for the same is not available.

**Taurine rich diet:** High amounts of taurine in diet, an amino acid, was linked to exacerbation of psoriasis and associated pruritus and taurine's role in pathogenesis of psoriasis was proposed.<sup>25</sup> A low taurine diet caused complete healing in a trial in 9 of the 15 patients, the others showed partial remission. However, excess taurine did not produce exacerbation in patients in another trial.<sup>25,73</sup>

#### **Conclusion**

Psoriasis is a chronic and disabling systemic disease. Its management requires a host of factors apart from conventional therapy. Lifestyle modifications and dietary changes should form an important aspect of these interventions. Despite a long period of research in this field, not much headway has been achieved due to various factors like; differences in individual and cultural habits preventing standardizations, use of parallel medications and lack of control over triggers and spontaneous remissions. Dermatologists need to be aware of the various dietary interventions and the evidence regarding the efficacy and safety of these.

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