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Review

Borage oil in the treatment of atopic dermatitis

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ABSTRACT

Nutritional supplementation with omega-6 essential fatty acids (ω-6 EFAs) is of potential interest in the treatment of atopic dermatitis. EFAs play a vital role in skin structure and physiology. EFA deficiency replicates the symptoms of atopic dermatitis, and patients with atopic dermatitis have been reported to have imbalances in EFA levels. Although direct proof is lacking, it has been hypothesized that patients with atopic dermatitis have impaired activity of the delta-6 desaturase enzyme, affecting metabolism of linoleic acid to gamma-linolenic acid (GLA). However, to date, studies of EFA supplementation in atopic dermatitis, most commonly using evening primrose oil, have produced conflicting results. Borage oil is of interest because it contains two to three times more GLA than evening primrose oil. This review identified 12 clinical trials of oral or topical borage oil for treatment of atopic dermatitis and one preventive trial. All studies were controlled and most were randomized and double-blind, but many were small and had other methodological limitations. The results of studies of borage oil for the treatment of atopic dermatitis were highly variable, with the effect reported to be significant in five studies, insignificant in five studies, and mixed in two studies. Borage oil given to at-risk neonates did not prevent development of atopic dermatitis. However, the majority of studies showed at least a small degree of efficacy or were not able to exclude the possibility that the oil produces a small benefit. Overall, the data suggest that nutritional supplementation with borage oil is unlikely to have a major clinical effect but may be useful in some individual patients with less severe atopic dermatitis who are seeking an alternative treatment. Which patients are likely to respond cannot yet be identified. Borage oil is well tolerated in the short term but no long-term tolerability data are available.

Introduction

Atopic dermatitis (atopic eczema) is a chronic-relapsing inflammatory skin condition that can be distressing and, when severe, can be functionally and socially disabling [1]. It affects up to 15–20% of children in developed countries, and the incidence is increasing [2,3]. The condition improves or resolves with age in most patients. However, many patients will require intermittent treatment for exacerbations through to early adulthood or beyond with agents such as topical corticosteroids that have significant adverse effects (Table 1) [2–4].

The pathogenesis of atopic dermatitis is multifactorial and involves a complex interaction between environmental, immunological, and genetic factors [1,5]. It is associated with hyperreactivity to environmental triggers. T-cell-mediated processes and various cytokines and chemokines play an essential role. Most, but not all, cases are IgE-mediated. Atopic dermatitis often co-occurs with other atopic conditions such as asthma and hayfever. The condition has been linked to various regulatory genes, and it is strongly linked to a family history of atopy. The pathophysiology of atopic dermatitis includes skin barrier defects causing increased transepidermal water loss (TEWL) and increased permeability to irritants and allergens. There is increased susceptibility to infection, and colonization of the skin with *Staphylococcus aureus* contributes to inflammation of the skin.

It has been proposed that atopic dermatitis is associated with an abnormality in essential fatty acid (EFA) metabolism, in particular, affecting production of gamma-linolenic acid (GLA), and possibly also impaired incorporation of EFAs into membrane phospholipids [6–8]. In the body, EFAs and their products, particularly those of the omega-6 (ω-6) series, are important for skin structure and physiology. EFAs play a crucial role in cell

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Table 1
Overview of treatments for atopic dermatitis (AD)*

Treatment	Role	Limitations
Emollients	Standard of care for both preventive and maintenance therapy Corticosteroid-sparing	Often underused. Need to be applied liberally at least 3–4 times daily
Topical corticosteroids	Standard of care for acute exacerbations Provide symptomatic relief	Recommended only for short-term or intermittent use Adverse cutaneous effects limit long-term use (e.g., striae, skin atrophy, telangiectasia) Specialist monitoring required for infants <2 years and with use of more potent steroids Concerns regarding systemic effects (e.g., HPA suppression, reduction of bone density, growth retardation in children)†
Topical calcineurin inhibitors	Second-line use only in patients who have failed to respond adequately to, or cannot be treated with, topical corticosteroids Reduce severity of symptoms Tacrolimus: moderate-to-severe AD Pimecrolimus: mild-to-moderate AD	Can be used only in patients aged ≥2 years Recommended only for short-term or intermittent use Fewer adverse cutaneous effects but can cause a transient burning sensation at site of application Concerns regarding malignancy with long-term continuous use†
Antihistamines	Sedating antihistamines may be useful when symptoms disrupt sleep	Nonsedating antihistamines have little effect on symptoms
Oral antibiotics	Treatment of secondary skin infections	In the absence of infection, reduction of skin bacterial colonization with use of antibiotics has little benefit in AD Resistance concerns with excessive use
Oral immunomodulators	Oral corticosteroids and cyclosporin Effective in refractory and severe AD	Rebound flaring/relapse when treatment discontinued Long-term use limited by serious adverse effects

GLA, gamma-linolenic acid; HPA, hypothalamic-pituitary-adrenal axis
* Based on guidelines from the American Academy of Dermatology [4] and the Primary Care Dermatology Society and British Association of Dermatologists [3].
† Data regarding the risk of these effects with topical application are inconclusive and such events are rare, but caution is warranted with extensive or long-term use.

membrane fluidity and flexibility and affect activity of membrane-associated proteins such as receptors and enzymes. Notably, EFAs are key components in the membrane systems that maintain the structural integrity of the skin and epidermal function as a permeability barrier. Furthermore, EFAs are metabolized to highly active eicosanoid products, such as prostaglandins and leukotrienes, that modulate inflammatory, immunologic, and proliferative responses including those of the skin cells [6,8–10].

In states of EFA deficiency, skin changes similar to those of atopic dermatitis are replicated [6,8]. The skin becomes inflamed with dry, scaly, red, and weeping lesions. There is an increased rate of proliferation of epidermal cells, metabolic activity, and formation of sterol esters and abnormal keratinocytes. The skin's normal function as a barrier to water loss becomes markedly impaired [6,8]. There is increased colonization with *S. aureus* [11]. This atopic dermatitis-like skin disorder is reversed by treatment with ω-6 EFAs [9].

There remains controversy over the exact importance of EFA disturbances as a pathophysiological factor in atopic dermatitis, and current data fall short of direct proof. Nevertheless, the finding that EFA abnormalities can be detected prior to the development of atopic dermatitis does support a causative role [12]. EFA abnormalities could contribute to atopic dermatitis in two ways: first, through a direct effect on the skin structure and function, and, second, by affecting maturation and sensitization of the immune system affecting the skin [6]. The abnormalities in EFA metabolism could potentially reduce levels of the prostaglandin PGE_1, resulting in reduced levels of cyclic AMP, and thereby affecting parts of the immune system causing selective hyperactivity.

Such data have stimulated interest in whether EFA-containing oils, particularly oils such as evening primrose oil that are rich in the ω-6 EFAs, are of value in the treatment of atopic dermatitis. More recently, borage oil (also known as starflower oil) has become of interest because of its high GLA content, which is two to three times higher than that of evening primrose oil [13,14].

While there have been a number of reviews on the use of evening primrose oil in atopic dermatitis, there have been very few, if any, comprehensive reviews focused solely on borage oil. One meta-analysis [15] considered all types of EFA supplementation including borage oil but was published several years ago and does not include more recent important data. The aim of this article is to outline the rationale behind the interest in the potential use of borage oil in atopic dermatitis and to review the clinical data on its use in this indication. This review focuses only on data relating to borage oil specifically. Studies testing GLA alone or other GLA-containing oils may not be applicable to borage oil because activity of different GLA-containing oils is potentially affected not only by the GLA content but also by the position of the GLA on the triglyceride and the balance between ω-6, ω-3, ω-9, and other fatty acids present in the oil [9,13,14].

Rationale for borage oil supplementation in atopic dermatitis

Borage oil contains high levels of the ω-6 series EFAs that are particularly important in skin structure and function, among other functions [8]. Borage oil does not contain significant amounts of the ω-3 series EFAs; while the ω-3 EFAs have some role in maintaining skin health, they are more important for neuronal development and are of particular importance in the retina, brain, and cardiovascular systems [16].

Within the body, the ω-6 series of EFAs derives from linoleic acid, which is converted to GLA and subsequently other important EFAs such as dihomo-gamma-linolenic acid (DGLA) and arachidonic acid, as shown in Figure 1. (Within the body, EFAs are present as unesterified fatty acids or as components of cholesterol esters, triacylglycerols, and phospholipids. For simplicity, such distinctions will not be made in this article except where specifically necessary.) For both ω-6 and ω-3 EFAs, metabolism involves alternating steps of desaturation and elongation. Binding to the desaturase enzymes is competitive and thus increasing the levels of ω-6 EFAs can affect metabolism of the ω-3 EFAs and vice versa.