Influence of ω-3 Fatty Acids on Triglyceride Levels in Patients Using Isotretinoin

The effect of ω-3 fatty acid (ω-3FA) supplementation on triglyceride levels was assessed in a retrospective study of patients taking isotretinoin for acne. Oral isotretinoin (13-cisretinoic acid) is commonly used in the treatment of severe and recalcitrant acne.1-3 This treatment commonly results in complete clearance of acne with long-term remission; however, treatment is associated with a number of adverse effects, including hypertriglyceridemia.4 At high levels of isotretinoin, hypertriglyceridemia may lead to acute pancreatitis.2,3 As many as 44% of patients with baseline triglyceride levels within the reference range who are treated with isotretinoin develop hypertriglyceridemia.4 Elevations in triglyceride levels during isotretinoin treatment can force dosage reductions or discontinuation of treatment. For less marked elevations, dietary modification or therapy to lower lipid levels may be used.

Methods | Patients were recruited from the dermatology clinic at the University of California, Los Angeles, and all study activities were approved by the university’s institutional review board. All the study participants provided written informed consent. Longitudinal survey data were obtained for 39 patients with acne who were treated with isotretinoin for a median of 5.87 months, and triglyceride levels during therapy were reviewed retrospectively. Nineteen patients reported consistent voluntary intake and 20 patients reported no use of ω-3FA supplements. Patients were grouped as follows: triglyceride levels within the reference range at baseline and throughout treatment; triglyceride levels within the reference range at baseline and elevated during treatment; or elevated triglyceride levels at baseline and during treatment. The mean percentage change in triglyceride levels for patients with measurements within the reference range at baseline and during treatment, triglyceride levels within the reference range at baseline and elevated during treatment, and triglyceride levels elevated at baseline and during treatment stratified by use of ω-3FA supplements are presented in the Figure.

Results | Comparison of the mean percentage increase in triglyceride levels in patients with and without ω-3FA supplement use and with preexisting elevated triglyceride levels demonstrated that patients not using the supplements had a greater increase in triglyceride levels during treatment from baseline compared with patients using the supplements. In this group, patients who did not use ω-3FA supplements experienced a mean increase of 49% in triglyceride levels during treatment, whereas patients using ω-3FA supplements only experienced a mean increase of 13.91% (P = .04). Thus, ω-3FA supplements stabilized the expected increase in triglyceride levels during isotretinoin therapy in patients with preexisting hypertriglyceridemia. This finding could be clinically significant. Adjunctive treatment with ω-3FA could permit maximal therapeutic dosing of isotretinoin while avoiding the necessity of using an agent to lower lipid levels.

Discussion | Supplements of ω-3FA may be a useful adjunct to the management of lipid levels during isotretinoin therapy. A future prospective, randomized placebo-controlled trial using a standard dose and formulation of ω-3FA is required to confirm this hypothesis.

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Accepted for Publication: July 13, 2014.


Author Contributions: Drs Krishna and C. Kim had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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OBSERVATION

Pregabalin for the Treatment of Painful Hand-Foot Skin Reaction Associated With Dabrafenib

Cutaneous adverse effects are one of the most frequent adverse events (AEs) associated with the use of BRAF inhibitors, reported in 92% to 95% of patients.1 Such dermatologic reactions include maculopapular eruptions, photosensitivity, verrucous keratoses, keratosis pilaris–like eruptions, keratoacanthomas, and melanocytic proliferations.2 Hand-foot skin reaction (HFSR) occurs in 19% to 60% of patients taking BRAF inhibitors1,3 and presents as tender, erythematous patches on the palms and soles.3 Painful hyperkeratotic plaques develop over pressure points. Although 88% of patients have grade 1 symptoms,4 pain can be severe.

The pathogenesis is unknown, but the reaction is dose dependent and so may be due to direct toxic effects of the drug. It has also been postulated that blockage of receptors for vascular endothelial growth factor and platelet-derived growth factor leads to reduced ability to repair vasculature that is subclinically traumatized in the skin. Previously described therapies include emollient creams, keratolytic creams, topical corticosteroids, pyridoxine, COX-2 inhibitors, phototherapy, and decreased chemotherapy dose.

Report of a Case | A man in his 50s with BRAF V600E–mutated metastatic melanoma treated with twice-daily dabrafenib, 150 mg, developed grade 2 HFSR on his feet after 1 week of treatment, which progressed to grade 3 within a month (grading based on Common Terminology Criteria for Adverse Events, v4.03; http://evs.nci.nih.gov/ftp1/CTCAE/About.html). This was his first treatment for metastatic disease. On the palms and soles bilaterally, he had thick, yellow, hyperkeratotic plaques with erythematous borders most pronounced on the weight-bearing areas, including the metacarpophalangeal joints of the hands, heels, and balls of the feet (Figure). These plaques caused significant pain, interfering with performance of activities of daily living.

Minimal improvement was seen after treatment with topical tazarotene, 0.05%, ointment, lidocaine, 5%, ointment, urea, 40%, ointment, and clobetasol, 0.05%, ointment under occlusion. For pain relief, he required use of long-acting oxycodone, 10 mg, every 12 hours, and oxycodone, 5 mg, every 4 hours, which provided mild pain control. He experienced significant improvement after halting treatment with dabrafenib for 2 weeks and subsequently resuming a reduced-dose dabrafenib regimen at 150 mg/d, but he still required narcotics for pain control.

After 2 weeks of low-dose dabrafenib, he started therapy with pregabalin, 50 mg, 3 times daily. Within a week and without any other change in his lifestyle or activity level, the pain in his feet dramatically decreased to the point where he no longer required narcotics and was able to participate in his previous activities. After 45 weeks, he continued to take pregabalin with continuous pain relief in his feet despite unchanged persistent thickened plaques on the soles, for which the topical therapies provided little therapeutic benefit. Of note, the patient had a lifelong history of bipolar disorder and had been taking bupropion, fluoxetine, lamotrigine, and quetiapine throughout this period.

Discussion | Pregabalin is an anticonvulsant widely used as first-line therapy for neuropathic pain secondary to a variety of