Title:
EPA+DHA Therapy Reduces PMN Activity in Microenvironment of Venous Leg Ulcers: A Randomized Controlled Study

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Session Title:
Chronic Disease Management
Slot:
I 02: Monday, 30 October 2017: 3:45 PM-4:30 PM
Scheduled Time:
4:05 PM

Keywords:
Chronic inflammation, Chronic venous leg ulcers and EPA+DHA oral therapy

References:


Abstract Summary:
Compelling findings from a randomized controlled study will be presented that support the use of an oral adjuvant therapy containing the bioactive components of fish oil for reducing the persistent inflammation that delays healing of chronic venous leg ulcers, significant healthcare problems worldwide.

Learning Activity:
The learner will be able to describe why the worldwide healthcare problem of chronic venous leg ulcers (CVLUs) necessitates focused attention and research. Describe significance of worldwide problem of CVLUs including prevalence rates and details about financial and emotional burdens on patients, families and healthcare systems.

The learner will be able to summarize the basic scientific premise supporting the hypothesis that an oral therapy containing the bioactive components of fish oil (EPA+DHA) will improve healing outcomes for some patients with CVLUs. Describe pathobiology of CVLUS. Provide a brief summary of landmark studies supporting anti-inflammatory actions of EPA+DHA. Explain inflammation resolving actions of EPA+DHA, focusing on how they are proposed to reduce prolonged PMN activation in CVLU fluid and facilitate healing.

The learner will be able to summarize the current study design, methods, results and implications of findings. Describe purpose of current study, hypotheses, specific aims, study design, sample and setting. Summarize research methods and findings. Propose why the findings are important.

The learner will be able to deduce why a multidisciplinary team of nurses, dieticians and wound care clinicians is important when developing a plan of care for patients with CVLUs. Explain how a multidisciplinary team of nurses, dieticians and wound care clinicians could design and implement assessment plans that would help identify the CVLU patients most likely to benefit from EPA+DHA therapy.

Abstract Text:

Chronic venous leg ulcers (CVLU) are common, costly conditions in the aging population that have high recidivism rates and cause considerable morbidity. In the U.S. alone, the average annual incidence of venous leg ulcers in individuals aged 65+ is 2.2% with payer burden at nearly $15 billion, excluding other indirect costs such as lost productivity. Furthermore, the incidence of CVLUs is increasing dramatically due to their association with obesity and aging. CVLUs are very distressing for patients because of pain, reduced mobility, social isolation, and high health care costs related to protracted treatments that collectively reduce quality of life. Current strategies for treating CVLUs generally involve locally applied therapies such as compression (the gold standard) that are often ineffective or result in only short-term recovery. Therefore, novel adjuvant therapies targeting the underlying etiology of CVLUs are greatly needed to improve healing outcomes. The pathogenesis of CVLUs involves chronic inflammation and the persistent presence of activated polymorphonuclear leukocytes (PMNs) in the microenvironment secreting proteases that eventually destroy newly developed tissue and degrade growth factors, impeding the healing process. The bioactive components of fish oil, n-3 eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have strong inflammation-resolving actions and have been shown to assuage PMN activity, but have not been tested in CVLU patients. The purpose of this randomized, double-blind, controlled study of patients with CVLUs conducted at a large Midwest university clinical research center was to test the effectiveness of EPA+DHA oral therapy to reduce PMN activity in CVLU microenvironments and facilitate healing. Descriptive statistics, t-tests and Spearman’s rho correlation were used to assess the data. At Days 0, 28 and 56, EPA and DHA were measured in plasma and markers of PMNs (CD15) and activated PMNs (CD66b) were measured in the wound fluid collected from CVLU patients receiving standard compression therapy and 1) EPA+DHA therapy (n=16) or 2) placebo (n=19). By Day 56, the EPA+DHA Group had a significantly lower percentage of CD66b+ cells in CVLU fluid compared to Day 0 (p = 0.02) and to Day 28 (p= 0.05); a pattern not detected in the Control Group. Further, the EPA+DHA Group demonstrated a greater reduction in wound area by Day 28 (57% reduction) and Day 56 (76% reduction) than the Control Group (35% and 59%, respectively). Importantly,
reductions in wound area had significant negative correlations with CD15+ cells ($p < 0.05$) and CD66b+ cells ($p < 0.05$) in wound fluid at Days 28 and 56 and a positive correlation with plasma levels of EPA+DHA at Day 28 ($p = 0.05$). The collective results provide supplemental evidence that high levels of activated PMNs in CVLU microenvironments inhibit healing, and suggest that EPA+DHA oral therapy modulates PMN activity and facilitates healing. The findings support the value of designing larger, randomized clinical trials to further test EPA+DHA adjuvant therapy for people with high levels of activated PMNs and PMN-derived proteases in CVLU microenvironments to facilitate healing and perhaps help prevent ulcer recurrence. Potential advanced work could 1) evaluate “high” and “low” dose EPA+DHA therapy at weekly time points to determine the most effective dose and duration of therapy, 2) test adjuvant EPA+DHA therapy for preventing ulcer recurrence in patients with healed leg ulcers in a prospective long-term study, and 3) include patients with other types of chronic wounds associated with high levels of activated PMNs and PMN-derived proteases, such as diabetic foot ulcers. If EPA+DHA supplementation is found to be an effective adjuvant systemic therapy for reducing PMN activity, a multidisciplinary team of nurses, dieticians and wound care clinicians could design and implement assessment plans to identify the CVLU patients most likely to benefit from adding EPA+DHA therapy to standard wound care regimens.