Using Olivamine-Containing Products to Reduce Pruritic Symptoms Associated With Localized Lymphedema

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Lymphedema is a chronic condition characterized by edema that is usually localized in the limbs, trunk, and genitalia.[1] The World Health Organization estimates that 45 million people have symptoms associated with lymphedema.[2] The recent literature has focused on treating massive localized lymphedema in patients who are morbidly obese.[3,4] Such lymphedema is most common in the legs and the abdominal pannus.[5] Swelling induces chronic venous insufficiency. Initially, the lymphatic system compensates, but continual overload results in lymphatic failure and gives rise to venous and lymphatic edema.

Localized lymphedema in patients who are obese results in symptoms associated with skin breakdown. One symptom affecting the patient being treated is pruritus, or itch. Understanding and managing the pathology of lymphedema has become increasingly relevant to symptoms associated with lymphedema in the extended care setting.[6,7] The reduction of lymphatic drainage causes a build up of inflammatory mediators in the skin. The accumulation of immune proteins and cytokines, along with venous and lymphatic edema, results in barrier dysfunction.[8] Improper barrier function eventually leads to infection and dermatitis, which may cause an intense pruritic response.[9,10] This response involves several communication cascades between biochemical mediators and the peripheral nervous system.

BACKGROUND

The pruritic response can be intense, causing severe pain and discomfort for long periods.[11] The prominent biochemical triggers for pruritus are the degranulation of dermal mast cells (DMCs) and the subsequent release of histamine or imidazolylethylamine.[12,13] Histamine is a biogenic amine in numerous metachromatic granules in DMCs. When released, histamine acts on endothelial histamine-1 (H1)-nerve receptors and elevates the concentration of cyclic adenosine monophosphate (cAMP) in the primary neurons. The capillaries expand, local edema occurs, and the volume of the vascular bed increases. The cAMP signaling pathway excites pruritic C-nerve fibers near the dermal-epidermal junction, inducing pruritus.[14,15] Circulating histamine is eventually inactivated by the liver via several methylation and oxidation reactions.

The secondary biochemical factors in the infected, inflamed skin lower the threshold for DMC degranulation and potentiate the itch provoked by histamine. Prostaglandin E2 (PGE2) is a biologically active carbon-20 unsaturated fatty acid and short-range autocoid. PGE2 is a metabolite of arachidonic acid (AA) produced via the prostaglandin (PG) pathway.[14,16] AA is a polyunsaturated fatty acid derived from dietary sources and stored in the cell-membrane fraction. The acid is primarily esterified to the phospholipids at the sn-2 position until phospholipase catalyzes its release.[17,18] Cyclooxygenase enzymes oxidize AA along the PG pathway to form prostaglandin D2 (PGD2), PGE2, and prostaglandin F2 (PGF2). Once released, PGE2 dilates the local capillary system and lowers the threshold for histamine release.[19]

Similarly, leukotriene B4 (LTB4), leukotriene C4 (LTC4), leukotriene D4 (LTD4), and leukotriene E4 (LTE4) are all AA metabolites and chemical mediators for inflammation and pruritus. However, unlike PGs, which can play important roles as biologic regulators, leukotrienes appear to be exclusively pathologic. Leukotrienes are synthesized by the enzymatic oxidation of AA through the 5-lipoxygenase pathway.[17,18] Leukotrienes contain a slow-releasing substance discharged by DMCs after an immunoglobulin E–antigen reaction.[20] LTB4, LTC4, LTD4, and LTE4 bind to cysteinyl-leukotriene receptor-1 and cysteinyl-leukotriene receptor-2, causing inflammation and pruritus. In particular, LTB4 agitates pruritic C-nerve fibers and lowers the threshold for DMC degranulation.[14,21]

CASE STUDY

Over a 6-month period, 9 patients who are morbidly obese, with mild to severe pruritus associated with localized lymphedema, were evaluated. The localized lymphedema presented on the legs or the abdominal pannus. Pruritic symptoms were evaluated on an initial physician visit and

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followed carefully throughout the study period. A final evaluation was given by the physician at the end of the 6-month period.

TREATMENT APPROACH

All patients were treated in the office and given products to take home for self-care. Physician and patient followed a regimen based on the location and severity of lymphedema and the intensity of the patient's skin breakdown and associated pruritus.

The regimen was as follows:

1. Clean the area with Olivamine-based cleansing lotion and then pat dry.
2. Spray the area with Olivamine-based antimicrobial spray.
3. If the skin is macerated and infected, apply Olivamine-based Calazime Protectant Paste (Medline Industries, Mundelein, IL). Or if the skin is dry and flaky, use gentle strokes to apply a small amount of Olivamine-based skin repair cream followed by Olivamine-based Remedy Nutrashield Cream (Medline Industries, Mundelein, IL).
4. Lightly dust the area with antifungal powder, as indicated.

DISCUSSION

About 95% of the pruritic symptoms were completely resolved in 6 months. In fact, 7 out of 9 patients reported that their pruritic symptoms disappeared in a matter of days. The average evaluation score for pruritus intensity before treatment was 2.22, which corresponds to a discomfort level between mild-moderate and moderate. After treatment with Olivamine-based advanced skin care products, the average evaluation score was 0.11, which corresponds to a discomfort level scarcely above absent (Tables 1 and 2; Figure 1).

Olivamine-based skin care products contain several specialized nutrients that effectively modulate the biochemical abnormalities associated with pruritus. The antipruritic nutrients include hydroxytyrosol, or 3,4-dihydroxyphenyl ethanol, which is a simple phenol found mainly in *Olea europaea*, or the olive plant. Hydroxytyrosol is an extremely potent free-radical scavenger that stimulates significant anti-inflammatory activity in the skin.[22] Numerous studies have established that topically applied antioxidants substantially reduce pruritus by inhibiting the secondary biochemical factors in infected, inflamed skin.[23] Hydroxytyrosol inhibits LTB4 generation by modulating the enzymatic oxidation of AA through the 5-lipoxygenase pathway.[24,25] Altogether, the phenolics in hydroxytyrosol

Table 1.

TREATMENT EVALUATION

Pruritus Intensity	Lymphedema Severity[2,7]
0 Absent	1 Mild (<20% increase)
1 Mild	2 Moderate (20–30% increase)
2 Mild-Moderate	3 Severe (>30% increase)
3 Moderate	
4 Moderate-Severe	
5 Severe	

Pruritic intensity was evaluated subjectively based on patient description and attending physician's notes. Lymphedema severity was determined by the percent increase of edema in the specified location.[2,7]

Table 2.

PRURITIC SYMPTOMS

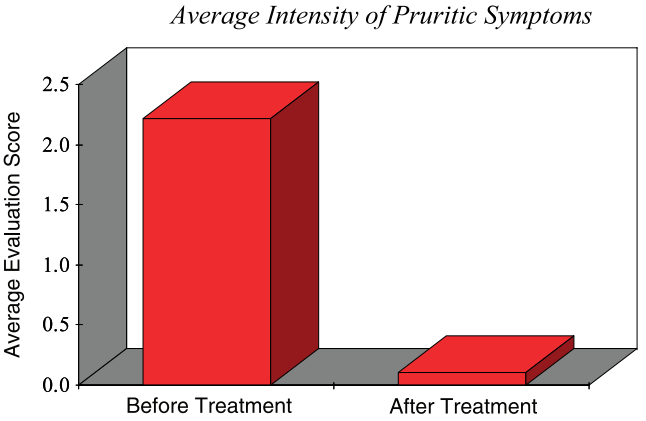
Patient	Lymphedema Location	Lymphedema Severity	Pruritus Intensity (Before Treatment)	Pruritus Intensity (After Treatment)
B.B.	Legs	2	3	0
R.F.	Pannus	3	3	0
L.K.	Legs	2	5	0
H.M.	Pannus	3	1	0
E.M.	Pannus	1	1	0
D.M.	Pannus	3	2	0
D.V.	Pannus	3	1	0
E.R.W.	Legs	3	1	0
E.W.	Legs	3	3	1

The pruritic symptoms of 9 patients who are obese and suffering from localized lymphedema were evaluated over a 6-month period. The lymphedema presented on the legs or the abdominal pannus. Pruritic symptoms were evaluated on an initial and final physician visit as well as throughout the study.

Figure 1.

AVERAGE INTENSITY OF PRURITIC SYMPTOMS

About 95% of all pruritic symptoms were completely resolved in 6 months. The average evaluation score for pruritus intensity before treatment was 2.22, which corresponds to a discomfort level between mild-moderate and moderate. After treatment, the average evaluation score was 0.11, which corresponds to a discomfort level just above absent.



have an array of beneficial LT-inhibitory, PG-sparing, and antioxidant properties.[26]

Olivamine-containing products also provide aloe barbadensis leaf juice, niacinamide, pyridoxine, and retinyl palmitate. Aloe barbadensis leaf juice contains the glycoprotein alprogen, which inhibits signals throughout the biochemical cascade responsible for DMC degranulation. Most notably, alprogen inhibits histamine activity and prevents the release of LTB4.[27,28] Niacinamide and pyridoxine also inhibit DMC degranulation and histamine release.[29,30] Furthermore, niacinamide has been shown to significantly inhibit cAMP at the dermal-epidermal junction, thus reducing the excitation of pruritic C-nerve fibers.[31,32] Retinyl palmitate reduces pruritic symptoms associated with vitamin A-deficient inflammation. Numerous studies show that vitamin A deficiency aggravates the clinical manifestations of inflammatory reactions, thereby increasing the release of pruritic-inducing PGs and LTs.[33,34] The topical application of retinyl palmitate prevents vitamin A deficiency and subsequently reduces inflammation and pruritus.

Remedy Nutrashield Cream and Skin Repair Cream (Medline Industries, Mundelein, IL) are composed of advanced silicones that prevent the excessive transepidermal water loss (TEWL) responsible for dry, irritated skin. TEWL, a measure of cutaneous barrier function that reflects skin water content, is defined as grams of water lost per square meter of skin per hour.[35] TEWL decreases stratum corneum hydration and activates a pruritic inflammatory response in the epidermis and dermis.[36] Scratching dry, irritated skin further increases TEWL and intensifies the associated pruritus.[37] An independent in vitro study found that silicone-based Nutrashield Cream and Skin Repair Cream significantly reduced excessive TEWL, conserving nearly 4 times the quantity of water as the control.[38] Reducing TEWL and conserving stratum corneum hydration is the key to reducing the dry, irritated skin responsible for inflammation and pruritus.[39]

SUMMARY

Olivamine-containing skin care products effectively treat the pruritic symptoms associated with localized lymphedema. In fact, 95% of the pruritic symptoms reported by the patients were completely dissolved at the end of 6 months. Most patients who had experienced chronic lymphedema-induced pruritic symptoms for several years drastically improved in a matter of days. Olivamine-based products provide numerous beneficial nutrients that reduce overall histamine activity, while inhibiting the secondary biochemical mediators associated with pruritus. An Olivamine-based treatment regimen significantly improved patient quality of life by diminishing the discomfort that accompanies lymphedema-induced pruritus. Further research is suggested to determine the most effective regimen for treating pruritic symptoms associated with localized lymphedema. ●

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