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Thank you for entrusting in the compounding services at Madison Medical Compounding Pharmacy to help meet the unique medication needs of your patients. We are excited to share our monthly newsletter with you and look forward to working with you. Please don't hesitate to let us know how we can assist you and your practice.

LeAnn Chambers, Pharm.D. and Matthew Chambers, Pharm.D.

Low Dose Naltrexone (LDN) in Dermatology

Naltrexone is an opioid receptor antagonist that originally was approved by the FDA to treat addiction to alcohol, opiates, and heroin. The dose of naltrexone to treat addiction ranges from 50 to 100 mg/day; however, Low Dose Naltrexone (LDN) doses range from 1.5 to 4.5 mg/day.¹

LDN is a treatment option for a variety of inflammatory skin conditions, such as Hailey-Hailey disease, lichen planopilaris, various types of pruritus, and has a potential application in the treatment of atopic dermatitis (AD).² LDN is often used at the University of Wisconsin (Madison) to treat patients with psoriasis. "Ekelem et al. also discussed patients with skin conditions that either had no response or worsened with naltrexone treatment, including various types of pruritus (ie, uremic, mycosis fungoides related, other causes of pruritus). Importantly, in the majority of cases without an improved response, the dose used was 50 mg/d. Higher doses of naltrexone are not known to have anti-inflammatory effects. Low-dose naltrexone can be considered as a treatment option in patients with contraindications to other systemic anti-inflammatory treatments; for example, patients with a history of malignancy may prefer to avoid treatment with biologic agents. Low-dose naltrexone also can be considered as a treatment option in patients who are uncomfortable with the side-effect profiles of other systemic anti-inflammatory treatments, such as the risk for leukemias and lymphomas associated with biologic agents, the risk for liver toxicity with methotrexate, or the risk for hyperlipidemia with acitretin."¹ Anti-inflammatory effects have not been observed at the standard higher doses of naltrexone.



LDN can alter thyroid hormone levels, especially in patients with autoimmune thyroid disease, so a TSH level should be considered as well as regular monitoring in patients with thyroid disease. Low-dose naltrexone has minimal side effects with the most common being sleep disturbance with vivid dreams.¹

In addition to oral LDN therapy, topical naltrexone has also shown promise for dermatologic conditions. In one study, a 1% naltrexone cream was compared to vehicle alone for the treatment of pruritus. Patients using this topical cream reported a 30% decrease in scores on the visual analog scale for acute and chronic pain. Patients with chronic episodes of pruritus responded better than those with acute episodes.³

Chronic pruritic disorders such as atopic dermatitis (AD) demonstrate downregulation of the μ -opioid receptor. "Given the well-established role of both immune dysfunction and pruritus in AD, the idea of LDN as a potential treatment is intriguing... Topically administered naltrexone has been shown to cause upregulation of the μ -opioid receptor and provide better relief of pruritic symptoms relative to placebo. A trial of a topical formulation of 1% naltrexone in 40 patients with severe atopic dermatitis revealed a 29% improvement in pruritus after just two weeks of use."³

While there are no large, randomized clinical trials for the multiple disease states for which LDN has been investigated, there are a number of smaller studies, and the evidence is growing... "It has been suggested that in addition to influencing opioid receptors and the TLR signaling pathway, the possible mechanism for this successful treatment may involve improved keratinocyte differentiation and wound healing."⁴

Topical naltrexone for dermatological applications has often been prescribed in combination with one or more other active ingredients, such as antihistamines, mast cell stabilizers, corticosteroids, calcineurin inhibitors, and/or sodium channel blockers for a myriad of conditions. Ask our compounding pharmacist for more information.

Metformin For Dermatology

Metformin therapy for psoriasis and cutaneous malignancies has shown promising results. And, because of its role in improving hyperinsulinemia, metformin has proven beneficial in hormonal acne, hidradenitis suppurativa (HS), and acanthosis nigricans.

Topical metformin has also been used in hyperpigmentation disorders. Metformin acts on three melanogenic proteins and reduces their expression, and also inhibits the activity of PKC- β .⁵ Inhibiting PKC activity in vivo selectively blocks tanning and reduces basal pigmentation in the epidermis and in anagen hair shafts.⁶

Topical Metformin for Hirsutism

Metformin's antiandrogenic properties may help with the management of hirsutism associated with polycystic ovarian syndrome (PCOS). Hirsutism refers to excess growth of pigmented hair in women, typically in androgen-sensitive areas such as the lips, chin, and chest. Although long term treatment can involve balancing the hormones or treating metabolic disorders, women can appreciate a faster solution to this problem which can detract from their femininity and negatively impact their self-esteem.

In approximately 90% of hirsute females, the cause is idiopathic or there is underlying PCOS. It has been proposed that reduction in circulating insulin levels leads to a decrease in the concentration of free circulating levels of androgens which can decrease the occurrence of excess hair in women.

Topical Metformin: Therapy Against Skin Photodamage

Excessive inflammation and cell death induced by ultraviolet (UV) cause skin photodamage (premature aging). Topical metformin possesses anti-inflammatory and cytoprotective effects and can inhibit inflammation and cell death in UVB-induced acute skin damage. Cell viability and cell death of keratinocytes were evaluated upon UVB irradiation in the presence or absence of metformin. Topical metformin 0.6% cream was applied topically on UVB-irradiated

mice, and the cream alleviated UVB-induced skin damage. These findings indicate the potential value of metformin topical therapy against skin photodamage.⁷

Topical metformin is an option that is not commercially available but can be compounded by prescription.

Our compounding professionals can customize medications to meet your patient's unique needs.

References

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