Treatment of psoriasis vulgaris using low-dose naltrexone

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INTRODUCTION

Psoriasis is a common, immune-mediated skin disease affecting 3.1% of the US population.[1] Psoriasis negatively impacts health-related quality of life and is associated with multiple physical and mental health comorbidities[2] in addition to symptoms such as pain, itching, and bleeding. Psoriasis also imparts substantial burden on the national economy, including high health care resource use and direct and indirect costs and contributes to work impairment, presenteeism, and employment status changes because of symptoms.[3]

A variety of treatments have been developed over the last several decades for the treatment of psoriasis. Exogenous therapies include topical corticosteroids, vitamin D derivatives, retinoids, and ultraviolet (UV) therapy. Systemic therapies include disease-modifying antirheumatic drugs, such as methotrexate or cyclosporine, and biologic medications such as adalimumab, ustekinumab, and secukinumab. Unfortunately, although psoriasis treatments are becoming increasingly safe and efficacious, they may not always be successful, affordable, or tolerable.

Naltrexone, a μ-opioid receptor antagonist commonly used for opioid overdose,[4] is typically well tolerated with minimal side effects, and does not have the potential for abuse or physical dependence.[5] Low-dose naltrexone has not yet been formally studied in the treatment of psoriasis; however, it may have anti-inflammatory and immunoregulatory properties because of its blockade of macrophage-released tumor necrosis factor (TNF).[6] In this report, we present the successful treatment of moderate plaque psoriasis with low-dose naltrexone over a period of 6 months.

Abbreviations used:

BSA:	body surface area
NBUVB:	narrow-band ultraviolet B phototherapy
PASI:	psoriasis activity severity index
TNF:	tumor necrosis factor
UV:	ultraviolet

CASE REPORT

A 60-year-old white woman presented to clinic with a history of moderate, generalized plaque psoriasis covering 10% of her body surface area (BSA). Her medical history was significant for mild osteoarthritis, but she did not have a history of active joint pains or swelling. She was not taking any medications and had no known drug allergies. On physical examination, the patient had well-demarcated, scaly, erythematous plaques covering 10% of her BSA. The patient reported symptoms of pruritus but no pain.

The patient did not have private drug coverage and did not qualify for a government-supported drug plan. In the past, she had some success with narrow-band UVB phototherapy (NBUVB), and we subsequently treated her 3 times per week for 3 to 6 months on 2 different occasions (Fig 1). The treatment course of NBUVB was supplemented with

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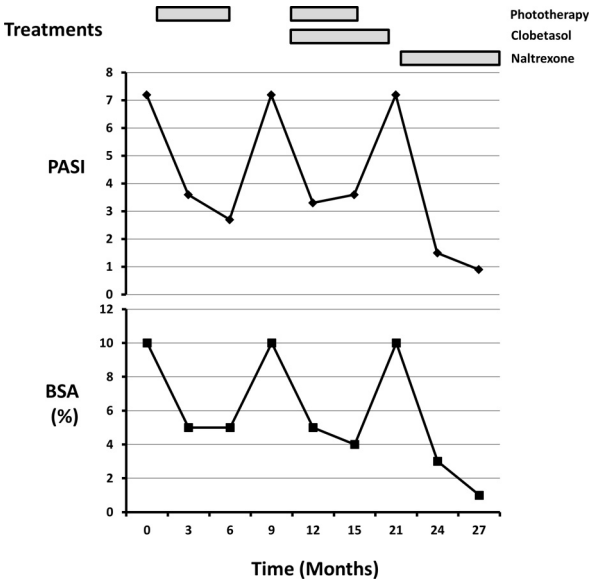

Fig 1. Clinical response of psoriasis to low-dose naltrexone. Psoriasis disease status as measured by BSA and PASI in relation to treatments over 27-month timeline.

clobetasol ointment applied to lesions on the arms, body, and legs. After a change in scheduling and the inability to attend NBUVB treatments and concern about long-term use of high-potency steroids, the patient wanted to try a systemic therapy. After researching low-dose naltrexone as a potential therapy for psoriasis, the patient suggested this treatment. After discussing the risks and benefits, the patient began low-dose naltrexone, 4.5 mg daily. Naltrexone is supplied as 50-mg tablets; therefore, the patient had to procure 4.5-mg tablets compounded by a specialty pharmacy. The patient's psoriatic lesions were significantly improved at 3 months, and the affected BSA had decreased from 10% to 1% after 6 months of treatment. The calculated PASI (psoriasis area severity index) score decreased from 7.2 to 0.9 after 6 months of treatment. Symptoms of pruritus also improved with naltrexone. No other adjuvant medications were used during this period. No side effects from the treatment were reported. As of this writing, the patient has continued therapy with low-dose naltrexone without any adverse effects and with continued success.

DISCUSSION

Psoriasis is mainly a dendritic and T-cell–mediated immunologic disease with increased intralesional levels of T-helper cells, interleukins, dendritic cells, and TNF.[7] As such, many new therapies have emerged over the last few decades for the treatment of psoriasis, most notably immune-modulating biologics such as ustekinumab, etanercept, and infliximab. However, not all patients benefit from or can tolerate these medications, leading to experimentation with unconventional anti-inflammatory drugs such as low-dose naltrexone.

Low-dose naltrexone (less than 5 mg/d, or approximately one-tenth the dose used for substance use disorders) antagonizes both μ-opioid receptors and nonopioid Toll-like receptors that are found on macrophages.[8] These effects, respectively, are coupled to produce both pain-relieving and anti-inflammatory properties by paradoxically increasing endogenous opioid release (in turn increasing ß-endorphin levels) and by mitigating the pro-inflammatory cascade promoted by macrophage-induced TNF activation.[8] In support of these remarks, 2 recent case series identify low-dose naltrexone as a successful treatment for lichen planopilaris[6] and for Hailey-Hailey disease.[9] Low-dose naltrexone has also been successfully used in the treatment of multiple sclerosis, Crohn's disease, and fibromyalgia and is associated with reduced levels of pro-inflammatory cytokines and other markers of immunodysregulation after treatment.[10]

Low-dose naltrexone significantly improved our patient's affected BSA from 10% to 1% over a span of 6 months, with continued remission to date. The likely mechanisms of action in this case are: (1) reduction of pro-inflammatory markers via inactivation of macrophage-produced TNF and (2) pain and pruritus control via increased circulating endogenous opioids such as ß-endorphin owing to paradoxical endogenous opioid release by low-dose naltrexone. Clinically, this result may have implications for patients who cannot tolerate other therapies or for whom other treatments have not been successful. Although it is typically not possible to establish cause and effect with a single case, this is an interesting and novel finding that warrants further study. Treatment of psoriasis with low-dose naltrexone may be appealing because of its low side-effect profile, low cost, and its efficacy in patients with chronic inflammatory conditions.

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