Low-dose naltrexone: a novel adjunctive treatment in symptomatic alopecias?

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Abstract

Naltrexone is a competitive antagonist of μ, k and γ opioid receptors, used for treatment of alcoholism and opioid addiction. Low-dose naltrexone (LDN) is defined as daily doses ranging from 1mg to 5mg. This is purported to have a paradoxical effect that leads to an increase in endogenous opioids, including beta-endorphins, which have anti-inflammatory properties. Theses mechanisms may also justify their possible role in the treatment of inflammatory conditions. The aim of this article is to discuss the use of LDN as an adjuvant therapeutic option in symptomatic alopecias presenting with trichodynia. Trichodynia is defined as scalp discomfort of variable intensity presenting as diffuse or localized dysesthesia and may be described by patients as pain, pruritus, or burning. These are common symptoms in patients with hair loss that negatively impacts quality of life. Scalp discomfort may be refractory to conventional therapies and does not yet have a specific therapeutic guideline. For these cases, LDN would be a possible alternative to be added to the therapeutic arsenal owing to its anti-inflammatory properties, analgesic potential, low cost, and few adverse effects described. Further studies are needed to standardize dosing, better understand its mechanism of action, and evaluate its potential therapeutic indications.

Keywords: alopecia, naltrexone, hair diseases, trichodynia

Introduction

Naltrexone is a competitive antagonist of μ, k, and γ opioid receptors, synthesized in 1963 and approved by FDA in 1984 for treatment of alcoholism and opioid addiction [1]. It is a fat-soluble substance absorbed from the gastrointestinal tract and bio-transformed in the liver into 6-betanaltrexol, its active metabolite, which crosses the blood-brain barrier, promoting attenuation or complete and reversible blockade of the opioid effects. Naltrexone is rapidly distributed to tissues and has a plasma half-life is of 13 hours. It has a slow terminal elimination-phase half-life of 96 hours, predominantly involving urinary excretion [1-3]. It is routinely available in 50mg tablets and can be administered by subcutaneous, intravenous, or intramuscular injections. In dermatological conditions, it has been used off-label in trichotillomania and refractory pruritus [1,2]. Recently, low-dose naltrexone (LDN), defined as up to 1/10 of the regular dose used for treatment of opioid dependence, has been reported to be helpful in a wide variety of diseases. The use of naltrexone at doses lower than 5mg daily has a paradoxical effect, leading to an increase in endogenous

opioids, including beta-endorphins, which have anti-inflammatory properties [2,3]. Low-dose naltrexone also plays a role in modulating the neuroimmune axis by its action on maturation of dendritic cells and in mitochondrial apoptosis. It inhibits proliferation of T and B lymphocytes and toll-like receptor 4 (TLR4) and reduces release of IL1, IL6, IL10, TNF, IFNβ, and nitric oxide. These mechanisms may also justify their possible role in the treatment of inflammatory conditions [3]. Therefore, it has become a potential adjuvant therapy in multiple sclerosis, fibromyalgia, Crohn disease, and Hailey-Hailey disease [1,2]. The

aim of this article is to discuss the use of LDN as an adjuvant therapeutic option in symptomatic alopecias presenting with trichodynia.

Discussion

Trichodynia is defined as scalp discomfort of variable intensity. It seems to be related to release of substance P and perifollicular inflammation may be a possible causative agent. Women are more often affected, presenting with diffuse or localized dysesthesia and these symptoms may be described by patients as pain, pruritus, or burning [4]. It has been previously associated with alopecia areata (AA), telogen effluvium, lupus erythematosus, dermatomyositis, folliculitis decalvans, and lichen planus pilaris (LPP) and its variants [2,4,5]. Trichodynia is a common symptom in patients with hair loss that negatively impacts quality of life [4]. It may be refractory to conventional therapies and does not yet have a specific therapeutic guideline. For these cases, LDN would be a possible alternative to be added to the standard therapeutic regimen.

Regarding alopecias, the use of LDN has already been reported in LPP and AA [2,6], with included benefits being reduction of symptoms of pruritus, clinical evidence of decreased scalp inflammation, and inhibition of disease progression [2]. In the authors' experience, the use of LDN has produced a remarkable improvement in trichodynia, but as opposed to a report by Strazzulla et al. [2], we did not observe a change in inflammation and disease status. In clinical practice, although without consensus, the suggested dose ranges from 1 to 5mg/day, usually starting at 3mg and increasing gradually to 5mg/day. Because many opioid receptors are located in the same nuclei that are active in sleep regulation, nocturnal use is recommended [1,7]. Vivid dreams and insomnia are possible side effects, which can be mitigated by changing drug administration from bedtime to morning [3, 8]. Pregnancy and opioid dependence are absolute contraindications. It is important to note that LDN can hypersensitize patients to exogenous opioids. Thus, physicians should be aware of drug interactions in patients taking opioid analgesics [7,8]. Nonetheless, LDN has no drug interactions described with the drugs commonly used for the treatment of alopecias presenting with trichodynia, which include systemic corticosteroids, methotrexate, hydroxychloroquine, and cyclosporine [8].

Conclusion

Owing to its anti-inflammatory properties, analgesic potential, low cost, and few adverse effects described, LDN seems to be a complementary option in the therapeutic arsenal for alopecias presenting with trichodynia [2-4]. Although patients report improvement of symptoms, it is not known how much the anti-inflammatory action aids in the course of the underlying disease. Further studies with larger number of patients are needed to standardize dosing, better understand its mechanism of action, and evaluate its potential therapeutic indications.

Potential conflicts of interest

The authors declare no conflicts of interests.

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