TRANSDERMAL CANNABIS AND PAIN

Very little is available in the scientific literature about the efficacy of transdermal cannabinoids for the treatment of local pain. There is a plethora of over the counter CBD oils and ointments claiming benefit, but very few clinical trials exist for this form of cannabinoid delivery. It stands to reason that given cannabinoids proved beneficial effects in neuropathic pain when administered through inhalational, oral mucosal, and oral routes, that transdermal administration has the potential for patient benefit. An open-label trial confirmed monotherapy with nabilone was as effective as gabapentin in relieving pain in peripheral neuropathy.[i]

Pain is generally described as nociceptive or neuropathic. Nociceptive pain is the more typical pain due to the stimulation of specialized neurons that respond to noxious stimuli, most commonly inflammatory mediators. CB2 receptor activation has been shown to have a beneficial effect on the modulation of inflammation. Neuropathic pain is seen less commonly but more severe. It is caused by dysfunction or damage to the somatosensory nervous system. Neuropathic pain is further classified as peripheral or central in origin. It represents one of the significant clinical challenges in medicine.

Peripheral neuropathy is a common cause of neuropathic pain, and it is only partially responsive to analgesics, including opiates. CB1 receptors had initially been thought to be concentrated primarily in the central nervous system, and CB2 concentrated in the immune cells. However, more recently, a functional ECS has been shown to be expressed in healthy and diseased skin.[ii] CB1, CB2, and TRP receptors are found in the basement membrane, dermis, subcutaneous layer and associated with nerve endings and sensory receptors within the dermis.[iii]

Because the endocannabinoid system is nearly ubiquitous in its receptor distribution, both CB1 and CB2 receptors in the skin are prime targets for pain modulation. Patients with diabetic and other forms of peripheral neuropathy are candidates for transdermal treatment because they have pain with inflammatory changes affecting skin integrity. Previous work has shown benefits with ectopic dermatitis and other inflammatory skin changes.[iv]

Research has shown an association between the nervous system and skin cannabis. Not only is there a functional ECS system in healthy skin, there is also a functional mu opiate receptor system in healthy skin, suggesting that beta-endorphins play a role in modulating skin integrity.[v] Transdermal delivery of opiates is well established as a treatment for severe pain. Transdermal opiate delivery does not remain limited to the local site resulting in systemic absorption. Systemic opioids are associated with well-known complications. Because cannabinoids have a much higher safety profile than opiates, circulatory absorption is much less problematic.

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[i] Bestard,Jennifer., et al An Open-Label Comparison of Nabilone and Gabapentin as Adjuvant Therapy or Monotherapy in the Management of Neuropathic Pain in Patients with Peripheral Neuropathy. PAIN PRACTICE, Jul/Aug2011; 11(4): 353-368. (16p)

[ii] T. Biro, B.I. Toth, G. Hasko, R. Paus, P. Pacher, The endocannabinoid system of the skin in health and disease: novel perspectives and therapeutic opportunities, Trends Pharmacol. Sci. 30 (8) (2009) 411–420.

[iii],[iv] Carmen del Río et al. The endocannabinoid system of the skin. A potential approach for the treatment of skin disorders. Biochemical Pharmacology Volume 157, November 2018, Pages 122-133

[v] Paul L.Bigliardi1 Expression of μ-Opiate Receptor in Human Epidermis and Keratinocytes**.** Journal of Investigative DermatologyVolume 111, Issue 2, August 1998, Pages 297-301