



A Trial of Low Dose Naltrexone and Ketamine Cream for Diffuse Cutaneous Neuropathic Pain

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INTRODUCTION

- Neuropathic pain is “initiated or caused by a primary lesion or dysfunction in the nervous system”. Managing neuropathic pain can be challenging
- Low-dose naltrexone has seen recent use in central neuropathic pain states such as: fibromyalgia, complex regional pain syndrome, diabetic neuropathy, and multiple sclerosis (MS).
- Topical ketamine has been used off label for these same conditions.
- We describe a rare case of diffuse cutaneous neuropathic pain that, after failing several different neuropathic agents, was trialed on low-dose naltrexone, and ultimately managed with compounded cream.

METHODS

- Case report is devoid of patient identifiable information and is exempt from IRB review requirements
- Informed consent was obtained from the patient.

CASE REPORT

- 57-year-old female with a history of hypertension, well controlled type 2 diabetes, and hyperlipidemia, was seen for severe burning sensation on the skin of her back
- Symptoms began after a mechanical fall down the stairs 3 years ago
- Symptoms spanned the back from the level of bra line to the buttocks bilaterally including the flanks and sides of the abdomen and chest
- Pain described as a “rug burn”, was worse with contact and at the end of the day
- Relieving factors: warm water, showers and swimming.
- Pain was not triggered by any position, no radiation to the extremities, and range of motion and gait were unaffected.
- Physical exam: Allodynia and hyperalgesia with light touch. No muscle spasms, no hyperpigmentation or lichenification.
- MRI total spine from two months after injury was unremarkable
- Working diagnosis of notalgia paresthetica
- Unsuccessfully treated with multiple medications including: gabapentin, amitriptyline, oxcarbazepine, duloxetine, and lidocaine patches
- We suspected a peripheral neuropathic pain syndrome
 - Trialed low-dose naltrexone and a compounded cream with ketamine, lidocaine, gabapentin, in a 10/5/6% combination
 - Cream alone gave 50% relief within 1 month
 - Naltrexone at 1 mg BID failed to provide relief at 1 month
 - Naltrexone at 3 mg daily for the next month had no significant benefit.
- Patient discontinued the naltrexone and decided to rely on the cream

CONCLUSION

- We attributed her symptoms to a **post traumatic cutaneous neuropathic pain syndrome of unknown etiology**
- **Trialed low-dose naltrexone:**
- **At 1-5 mg naltrexone** follows alternate pathways and inhibits microglial activation
- This antagonist activity reduces the inflammatory response
- Also results in increased endogenous opioid production via transient opioid receptor blockade (3).
- Topical ketamine works via NMDA antagonism
- Use in topical form is supported by only case studies (4).
- **Our patient had no effect at a moderately high dose of naltrexone but did have relief with compounded cream. Larger studies are needed to assess efficacy of compounded creams containing ketamine for recalcitrant neuropathic pain states**

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DISCUSSION

- Notalgia paresthetica: a chronic neuropathic dysesthesia
 - Characterized by pruritus along the medial border of the inferior scapula, typically unilateral, in older females
 - Studies attribute the primary etiology to spinal nerve compression- potentially from muscle spasm
 - No primary cutaneous lesions- only secondary changes due to pruritis (1).
 - Our patient had a diagnosis of this condition but denied pruritis, had bilateral symptoms in a broader location than typically described, and had an unremarkable MRI
- We attributed her symptoms to a post traumatic cutaneous neuropathic pain syndrome of unknown etiology
- Her symptoms resembled more like what has been described in a small subset of patients with long COVID (2).
 - The subjective perception of generalized burning cutaneous pain, in a non-dermatomal fashion, and apparently unrelated to objective skin lesions.
 - Histopathology shows dermal nerve fiber hypertrophy
 - Electroneurography reveals disturbances of A-delta and C fibers.
 - Most patients respond to three months of low-dose gabapentin and achieve remission by 6 months.
- Our patient however had no known exposure to Covid around the time of her fall and denied associated symptoms. Pain failed to respond to multiple treatments, compounded cream came to the rescue

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