EFFECTIVENESS OF KETOPROFEN AND KETAMINE TOPICAL CREAM IN NEUROPATHIC PAIN. A PILOT STUDY

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Introduction:
Neuropathic pain (NP) is produced by a primary lesion or dysfunction of the Central Nervous System (CNS). NP remains complex and includes peripheral manifestations that contribute to the symptoms experienced by many chronic pain sufferers. Traditionally these symptoms have been targeted with the use of oral medications with some efficacy. A modern concept of a interactive network between cutaneous nerves, the neuroendocrine axis and the immune system has been established. This concept considers the skin as a Neuroimmunoneuroendocrine organ. The interaction of the skin and nervous system offers the possibility for new therapies for the treatment of NP. On this basis, we propose a treatment for NP symptoms with a topical cream.

Objectives:
- Determine the effectiveness of a topical ketoprofen / ketamine based cream in the treatment of neuropathic pain symptoms.
- Identify side effects of the analgesic cream.

Methods:
Prospective pilot study. Performed at the HTB Injury Rehabilitation Centre, Montreal-Canada between January 2005 and January 2006. A total of 80 patients participated in this study, but only 55 patients finished the protocol with 4 visits.

Inclusion criteria:
- Older than 18 years,
- More than 3 months history of NP symptoms and manifestations,
- 5 or more points in the Verbal Numerical Scale (VNS) for intensity,
- Patient able to distinguish between nociceptive pain and NP on history,
- 3 or more of the following: dysesthesia, allodynia, hypersensitivity, tingling, burning or electric-like hyperalgesia.

Exclusion criteria:
- Allergy to any of the components of the preparation,
- Pregnancy,
- Absence of neuropathic pain manifestations,
- Unable to distinguish between the symptoms of NP and nociceptive pain.

Intervention: 15% ketoprofen and 5-20% ketamine analgesic cream applied 3 times/day on affected area for 3 weeks. This cream was prepared by pharmacists Pearson and Alter.

All patients were already receiving opioids (87% Oxycodone; 7.3% Transdermal Fentanyl; 3.6% Morphine LA; 1.81% Methadone) and 75% of patients were receiving Gabapentin.

4 consultations with each patient:
- Visit 1: Initial evaluation for assessment of pain
- Visit 2: 1 week later. Instructions and cream delivered to patients,
- Visit 3: Evaluation 2 weeks after start of treatment. Increase of ketamine dose in cream for patients reporting less than 10% in symptom reduction,
- Visit 4: Final evaluation at 3 weeks after treatment start to assess maintenance of improvement.

Assessment scales:
- VNS: at first and third consultation, 0=No pain 10=maximum pain possible,
- Perceptual Improvement Scale (PIS) at visit 3 and 4.

Results:
- 55 patients: 24 ♀ & 31 ♂. Mean age: 42±10.15 years.

<table>
<thead>
<tr>
<th>Pain level</th>
<th>Average pain intensity referred on the VNS</th>
</tr>
</thead>
<tbody>
<tr>
<td>0% (no improvement)</td>
<td>8</td>
</tr>
<tr>
<td>1-20%</td>
<td>16</td>
</tr>
<tr>
<td>21-40%</td>
<td>15</td>
</tr>
<tr>
<td>41-60%</td>
<td>10</td>
</tr>
<tr>
<td>61-80%</td>
<td>3</td>
</tr>
<tr>
<td>81-100%</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>55</td>
</tr>
</tbody>
</table>

- Mean pain reduction on VNS: 2.48±1.77 points (p<0.0001). This represents a 32.84% improvement which is similar to the mean improvement obtained on the PIS (31.04±24.06%). Both genders show significant symptom reduction (p<0.0001).
- Half of the patients (27 of 55) manifested an improvement of at least 30%.

The patients with pathologies closely related to a neuropathic origin show greater pain reduction.

Side effects observed:
- Photosensitivity reaction in two patients,
- Dizziness and minor cognitive impairment in one patient.
- Seven patients (12.72%) required an increase in the ketamine dose present in the preparation; to 10% in three patients, to 15% in three patients and to 20% in one patient. Two patients whose ketamine dose was increased suspended the progressive increment of opioid dose they were previously requiring.

Conclusion:
The concept of the skin as a Neuroimmunoneuroendocrine organ suggests the possibility for new therapies for the treatment of NP. This study illustrates the use of topical treatments for the peripheral symptoms of NP as an effective alternative to be associated to conventional therapy without major side effects.