ABSTRACT

Neuropathic pain is a pathological and chronic condition characterized by hyperalgesia (enhanced perception of painful stimuli) and allodynia (innocuous stimuli perceived as painful). The underlying pathology of neuropathic pain is poorly understood. Ultra-low-dose opioid antagonists can enhance opioid analgesia and prevent tolerance in rodent nociceptive pain assays. The current work examined morphine plus ultra-low-dose naltrexone (NTX) in the rat L5/L6 spinal nerve ligation (SNL) model.  All morphine + NTX groups produced significant anti-hyperalgesia or analgesia compared to vehicle (p<0.001 through Day 7). The increased and prolonged efficacy compared to morphine alone, along with the anti-allodynic effect, suggests that this combination holds promise as an improved treatment for neuropathic pain.

RESULTS

Morphine + NTX at 1:33,000: 92, 75, 79, 65 and 77% anti-hyperalgesia on Days 1 - 7, respectively (Fig. 2), as well as anti-allodynia (81% on Day 1, 58% on Days 2-7). The combination of morphine + NTX at 1:33,000 was significantly different from vehicle (p<0.001) on Days 1-7. Importantly, it is well known that i.th. morphine alone has no anti-allodynic effect (similar to what is reported clinically), yet morphine + NTX at this dose resulted in anti-allodynia (81% on Day 1, 58% on Days 2-7). The % anti-hyperalgesic effects of morphine (MS) alone or in combination with NTX in the L5/L6 SNL model. All morphine + NTX groups produced significant anti-hyperalgesia compared to vehicle (p<0.001 through Day 7).

METHODS

Male Sprague-Dawley 200g rats underwent intrathecal (i.th.) catheterization and were contained in Plexiglas compartments and a radiant heat source aimed at the hindpaw was used to assess antinociception. The withdrawal latency was measured by a sensor that detects both light and movement when the paw is withdrawn. Antinociception was calculated as follows:

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\text{Percent antinociception} = \left( \frac{\text{Withdrawal latency of the injured paw} - \text{Pre-injury baseline}}{\text{Withdrawal latency of the unjured paw} - \text{SNL baseline}} \right) \times 100
\]

\[
\text{Time (day)} = \left( \text{Treatment-induced latency} - \text{Pre-injury baseline} \right) \div \left( \text{Withdrawal latency of the unjured paw} - \text{SNL baseline} \right)
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REFERENCES


Powell KJ, Abul-Husn NS, Jhamandas A, Olmstead MC, Beninger RJ, Jhamandas K. (2002). Paradoxical effects of morphine in the spared nerve injury model: the increased and prolonged efficacy compared to morphine alone, along with the anti-allodynic effect, suggests that this combination holds promise as an improved treatment for neuropathic pain.

DISCUSSION

While opioids remain the primary drugs of choice for moderate to severe pain, there is no current consensus for moderate to severe pain. Ultra-low doses of morphine have been shown to provide opioid analgesia, to reduce pain sensitivity, and to improve overall pain management.