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Opiate-free Pain Therapy using Carbamazepine-Loaded Microparticles Provides up to Two Weeks of Pain Relief in a Neuropathic Pain Model

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Introduction

As evidenced by the ongoing opioid crisis, there is a great unmet medical need for alternative treatments for patients suffering from pain that do not result in addiction or adverse side effects. Anticonvulsants are effective in managing pain, though high systemic dosing creates unwanted side effects limiting its usage. We hypothesized a biodegradable poly(lactide-co-glycolide) microparticle formulation incorporating the anticonvulsant carbamazepine would provide prolonged pain relief while limiting unwanted systemic side effects.

Methods

All animals underwent induction of the chronic constriction injury model to induce neuropathic pain states. Animals were randomly divided into a control group receiving injections of saline, bupivacaine, carbamazepine, or unloaded microparticles or into a treatment group receiving either 10mg or 20mg of carbamazepine-loaded microparticles suspended in sterile saline. Mechanical and thermal behavioral testing was conducted using von Frey and plantar based measurements, respectively. Behavioral measurements were taken before surgery for normal baseline, 3 days after induction of the CCI model for ligation baseline, and at multiple time-points following injections for up to 21 days.

Results

Only the carbamazepine control group demonstrated a significant difference from other control groups though only for up to 4 hours post-injection. Both treatment groups demonstrated a rapid analgesic response that persisted for 14 days before returning to similar sensitivity levels as the control animals.

Conclusions

This two-component drug-delivery system has been specifically engineering to release a controlled amount of carbamazepine over a 14 day period demonstrating significant anti-nociceptive behavior with no toxicological or observable adverse events via behavioral or histochemical analysis.

Learning Objectives

By the conclusion of this session, participants should be able to: 1) Consider anticonvulsants as an alternative to opioids as an analgesic 2) View the power of local drug delivery to achieve potentcy and limit systemic side effects 3) Identify novel applications for locally applied antiepileptic to mitigate pain perception