Effectiveness of Mexiletine for Treatment of Neuropahthic Pain: A Retrospective Chart Review

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INTRODUCTION

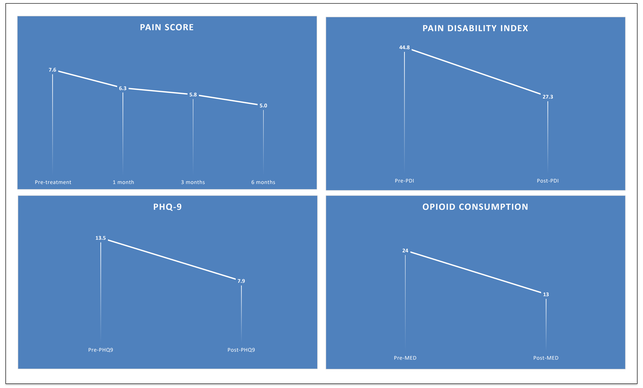
Neuropathic pain, often severe and disabling, is defined as pain produced by disorders of the nervous system (1). Pain as a manifestation of peripheral or central nerve injuries remain a major clinical problem today, interfering with daily activities (1). The prevalence of neuropathic pain is estimated to be between 4% and 8% of the population in developed countries however the long term benefits of chronic pain treatments have been difficult to demonstrate (2, 3). Many studies have shown that patients with chronic pain do not obtain adequate relief from existing treatment. However, literature review reports positive outcomes and long-term benefits with mexiletine use for neuropathic pain. Therefore, we would like to propose the use of mexiletine as an adjuvant for patients with neuropathic pain (1,2).

MATERIALS AND METHODS

This is an IRB approved retrospective chart review from August 2015 – August 2016, studying the safety and effectiveness of mexiletine as an adjuvant for treatment of neuropathic pain. All patients who presented during the time frame to three Henry Ford Health System sites with neuralgia who were started on mexiletine were included in the study. The neuropathic pain was due to various etiologies but all patients were initially started on first line agents, mainly gabapentin and tricyclic's. Pain that was not well controlled by these first line agents were recommended for trial lidocaine infusions. Two successful infusions with lidocaine identified patients most likely to benefit from mexiletine therapy. Patients without an analgesic response to lidocaine were not offered mexiletine and those with any decrease in pain scores following lidocaine infusions were offered ongoing treatment with oral mexiletine. All patients were started at 150mg daily for one week, then increased to 150mg twice a day, and then finally increased to 150mg three times a day assuming the patient did not experience any side effects. Before each dose increase the patients Qtc was obtained from a 12 lead EKG. The effectiveness of the treatment was evaluated through follow up appointment documentation with evaluation of recorded pain scores, pain disability index, PHQ-9 score, daily milligrams of morphine equivalents (MME), and side effects. The primary outcome was defined as any documented subjective amendment to neuralgic symptoms after receiving mexiletine, accompanied by improvement in overall function, related to neuralgia. All data related to this study were maintained on HFHS approved password-protected IronKey USB devices.

RESULTS

Of the 77 patients who were candidates to start on oral mexilitine 65 agreed to proceed with the treatment. Sixty nine percent of patients concomitantly took an anticonvulsant or TCA. All study patients had pre-treatment and 1 month pain scores recorded however only 85% and 50% had 3 month and 6 month pain scores recorded, respectively. Pain disability index and PHQ-9 scores were available for 23 patients and showed decreasing scores after 6 months of mexilitine treatment. MME consumption also decreased over that time and one third of the patients who started on mexilitine while also taking an opioid were no longer taking opioids after 6 months.



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DISCUSSION

We present a retrospective study approach for evaluating mexiletine as an adjuvant oral analgesic drug for chronic neuropathic pain and evaluating it's performance through the course of the treatment. Prior studies assessing the analgesic properties of oral mexiletine treatment have shown limited effectiveness but with prominent side effects limiting its use as an analgesic. However, recent studies such as Tremont-Lukats et al. revealed mexiletine's analgesic efficacy for neuropathic pain in a meta-analysis (4). However, the mean decrease in pain score was 5-10% leading to question the use of mexelitine as a sole analgesic, but to possibly be used as adjuvant analgesic therapy, with its other clinical use (3,4).

This study is retrospective study and subject to bias inherent in such studies. Selection bias was minimized by including all patients presenting to HFHS Pain clinic with chronic neuropathic pain and were started on mexiletine following profound analgesic response to IV lidocaine infusion. Given that it is a retrospective study and IV lidocaine assignment was at the discretion of the treating physician individualized to patient specific treatment, we thus refrain from contrasting those who were prescribed mexiletine to those patients not prescribed mexiletine following the lidocaine infusion.

Recommendations for treatment are based on degree of evidence of analgesic efficacy, safety, ease of use and cost-effectiveness (5). Analgesic agents recommended for first-line treatments for Neuropathic pain are certain antidepressants (tricyclics) and anticonvulsants (gabapentin and pregabalin) (2,6). Second-line treatments recommended are serotonin noradrenaline reuptake inhibitors and topical lidocaine (2,6). Opioid analgesics are not recommended as part of a treatment regimen due to lesser evidence of efficacy (2, 3). However, our retrospective chart review supports mexiletine as an adjuvant with improved analgesic response profile on various neuropathic pain syndromes for prolonged analgesia in patients with various types neuralgia. However, further work is needed to evaluate the relative acceptance of mexiletine against other treatments of neuropathic pain and estimate predictors of mexiletine acceptance and evaluate prospectively if other drugs are better accepted than mexiletine (4).

Our retrospective chart review supports mexiletine as an adjuvant therapy to treat neuropathic pain with improved patient reported pain scores, pain disability index, PHQ-9 scores, and lower daily MME use. Further work is needed including a larger prospective study to evaluate mexiletine therapy against a control population and to evaluate prospectively if other drugs are better accepted than mexiletine (4,5,6).