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Durability of Benefit From Repeated Intravenous Lidocaine Infusions in Fibromyalgia Patients: A Case Series and Literature Review

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Abstract

Fibromyalgia is a painful disorder with no curative treatments, and available medications typically provide partial relief of pain. Reported here is the effective use of serial intravenous lidocaine infusions for the chronic management of 3 patients with fibromyalgia. The details of the infusion procedure are described, and relevant literature is reviewed. Lidocaine infusions should be considered in fibromyalgia patients who are refractory to other treatments, and a positive response to 1 infusion may justify repeated infusions for chronic management.

Fibromyalgia is characterized by chronic, widespread pain that is associated with fatigue, sleep disturbance, psychological distress, and tender points on examination. The pathophysiology behind fibromyalgia most likely relates to changes in the central processing of pain signals such that peripheral pain signals are amplified leading to enhanced sensation of pain. Optimal treatment of fibromyalgia extends beyond pharmacotherapy, and medications have demonstrated limited benefit in reducing pain. Meta-analysis[1] of clinical trial data with available agents has led some to conclude that ''benefits for SNRIs and pregabalin compared with placebo were statistically significant but small and not clinically relevant.''[2(p66)] In our experience, fibromyalgia patients often fail to achieve substantial reduction in pain from available oral medications, and, as such, there is a large population of treatment-refractory fibromyalgia patients in clinical settings.

Intravenous (IV) lidocaine infusion has been shown to have analgesic effects for a variety of acute and

chronic central and peripheral pain syndromes in small short-term trials.[3–5] There is evidence to suggest that lidocaine may act by blocking both peripheral and central sodium ion gate channels[6] and inhibiting ectopic neuronal discharges.[7] Although a few small short-term studies have demonstrated efficacy of serial lidocaine infusions in fibromyalgia patients, no literature addresses the durability of this benefit and whether there is value in continuing lidocaine infusions and incorporating them into patients' chronic treatment. The current case series includes 3 fibromyalgia patients who benefitted from an initial lidocaine infusion and have been maintained on infusions every 3 to 4 weeks for up to 4 years.

CASE SERIES

Case 1

Mr A is a 67-year-old white disabled construction contractor. He was diagnosed with fibromyalgia (per criteria of The American College of Rheumatology[8]) in 2001 after extensive evaluation and has been refractory to medication treatment. Other medical history includes periodic limb movements of sleep and coronary artery disease, with a myocardial infarction in 2003 leading to 4 coronary artery stents. Prior to beginning IV lidocaine infusions, Mr A experienced constant "crampy/burning" pain that was diffuse but particularly bothersome in his legs, with pain intensity as measured by the numerical pain scale sometimes as low as 4/10 when resting and daily exacerbations to 10/10 from minimal activity such as housework.

Mr A received his first IV lidocaine infusion (5 mg × 83 kg of body weight) in May 2011, which was "a miracle" and led to his being "pain free or close to it for the first time in decades." He was maintained on his extensive treatment regimen for pain and insomnia, which included pramipexole 0.25 mg orally at bedtime, tizanidine 6 mg orally 3 times daily, pregabalin 150 mg orally 3 times daily, duloxetine 90 mg orally every day, tramadol extended release 300 mg orally every day, celecoxib 200 mg orally twice daily, clonazepam 1 mg orally at bedtime, eszopiclone 2 mg orally at bedtime, and trazodone 300 mg orally at bedtime. Due to a positive response to the infusion, Mr A received a second infusion 8 days later and a third infusion 7 days later; of note, we could find no published protocols to guide this phase of his treatment. Mr A maintained very low pain levels for 3 weeks following the third infusion, although his diffuse pain increased over the next week until he could return for another infusion.

Mr A has been maintained since then (for over 4 years) on a schedule of infusions every 3 weeks, with persistent benefit in that he presents with mild pain only in his calves. He is able to do more housework and supervise construction of a porch on his home. He has had no adverse effects from lidocaine. He has at times had low back pain in the absence of significant radiologic findings of disc degeneration or facet arthropathy, and he completed a course of physical therapy with some benefit. He has tolerated lidocaine infusions well with no adverse effects. His infusions were held for a period of several weeks while he obtained cardiac clearance due to symptomatic orthostatic hypotension, which was unrelated to lidocaine infusions. During this delay (as well as a subsequent delay due to scheduling issues), he reported that within 4 weeks he developed increased calf pain and recurrence of diffuse pain. We have attempted to taper his tramadol, celecoxib, and pregabalin, although he reported increased calf pain and recurrence of diffuse pain with dose reductions. We did reduce his trazodone to 100 mg at night (due to unrelated orthostatic hypotension), although he reported increased initial insomnia when he stopped the

medication completely.

Case 2

Ms B is a 55-year-old black disabled hairdresser who presented in August 2011 for a 2-year history of daily constant "toothache-like" lumbar pain, as well as "numb" pain in her legs that was not overtly radicular in location or character. She had no evidence of stenosis on lumbar magnetic resonance imaging, and she failed to benefit from 2 lumbar epidural steroid injections. She had mild benefit from duloxetine and gabapentinoids and various opioid medications. Her medical history was notable for previous abdominopelvic pain and endometriosis, although she did not have current abdominal or pelvic pain. In early 2013, she began to report that the toothache-like pain was diffuse and associated with numbness and tingling in her hands and legs. The physical examination showed that she had allodynia, and her tender point examination was positive. Subsequent laboratory studies for inflammation and nerve conduction (with electromyography) were normal. Opioid-induced hyperalgesia was considered, although her pain increased as extended-release hydromorphone was reduced and discontinued such that we opted to maintain a low dose of the medication. We felt a diagnosis of fibromyalgia (per criteria of The American College of Rheumatology[8]) was appropriate.

Ms B could not tolerate traditional physical therapy and did not have pain reduction with pool therapy. Lidocaine infusion (5 mg × 97 kg of body weight) was provided in November 2013 with good results, reducing her diffuse pain from 7/10 to 2/10 within minutes and reducing lumbar pain from 10/10 to 3/10 over a few days. She was unavailable to come to the clinic shortly afterward, but at follow-up 6 weeks later, she felt the benefit was waning such that she was scheduled for repeat infusion the following day. Her second infusion yielded similar benefit, although her diffuse pain and lumbar pain increased substantially after 4 weeks. Subsequent infusions were similarly effective, but the duration of benefit reduced to 3 weeks after her fourth infusion.

Ms B has been maintained on a schedule of infusions every 3 weeks (for 16 months), which has led to sustained improvement in her diffuse pain and lumbar pain; however, she reports "throbbing" coccygeal pain (currently being evaluated for alternative etiology) that does not improve as robustly as her more proximal lumbar pain and diffuse pain. She has been slightly more active, although it is unclear how robust her functional improvement has been. She has not reported any adverse events from the treatment.

Case 3

Mr C is a 62-year-old married white disabled retail sales manager. He developed axial pain in 1993 after a fall with minor injury; he subsequently developed diffuse pain, which led to a diagnosis of fibromyalgia (per criteria of The American College of Rheumatology[8]) in 2000. He continued to report panaxial pain and had L5-S1 microdiscectomy in February 2001 and C5-C6 discectomy/fusion in December 2001. Surgical intervention provided limited benefit, and an intrathecal morphine pump was ultimately implanted in 2004. Much of Mr C's treatment has centered on his lumbar and cervical disc disease, and he has had numerous trials of epidural steroid injections. Although chronically he has had objective evidence of lumbar and cervical disc disease, his pain symptoms since 2009 were primarily diffuse "from head to toe," with 9–10/10 "achy" pain "like a Mack truck hit me." Consistent with this,

he was spending much of his time in bed due to activity intolerance. He had allodynia by history, and on examination was tender point pan-positive. He has reported a developmental history significant for childhood physical abuse, and he meets criteria for posttraumatic stress disorder and major depressive disorder according to *DSM-IV* criteria. He did not experience pain reduction from gabapentinoids, tricyclic antidepressants, duloxetine, milnacipran, various muscle relaxants, or oral opioids. Similarly, he has achieved no relief with physical therapy or pool therapy. He was resistant to considering an IV lidocaine infusion trial due to difficulty accessing transportation, but, ultimately, he consented in October 2013. His first infusion (5 mg/kg of body weight) reduced his diffuse and axial pain to 6/10 for 2.5–3 weeks, which was the best he had felt in several years. He continued to have difficulty accessing transportation to the clinic, and infusion was repeated in December 2013, which provided similar benefit. He has since been maintained on a schedule of IV lidocaine infusions (5 mg/kg of body weight) every 3 to 4 weeks and has experienced durability of benefit. His axial and diffuse pain is 6–7/10 reliably, and he is able to drive without restriction, shop and run errands, and participate consistently in family activities. He has assumed a volunteer job at his church driving senior citizens to medical appointments. He continues to utilize an intrathecal morphine pump, and he has had a series of lumbar epidural steroid injections within the past year; however, the timeline clearly supports IV lidocaine infusions as the primary source of his symptomatic and functional improvement.

DISCUSSION

These cases illustrate durability of benefit and tolerability with IV lidocaine infusions for fibromyalgia pain and the value of incorporating infusions into select patients' chronic treatment plans. These cases are representative of several other cases we have seen involving benefit from chronic lidocaine infusions, although we have also seen a large number of fibromyalgia patients who obtain no relief or relief for less than a day; these patients are not scheduled for repeat infusions. We concede that a minority of patients in our practice benefit from lidocaine infusions, although as described in our case examples, the benefit can be quite substantial and prolonged. We do not have sufficient numbers to assert whether demographic characteristics, comorbidities, or other variables predict treatment response, and we offer lidocaine infusions to all fibromyalgia patients who continue to suffer from pain and related functional impairment despite trials of usual medications.

Our center administers 5 mg of lidocaine per kg of body weight (maximum of 500 mg) over 1 hour diluted in 0.9% saline. Due to the antiarrhythmic property of lidocaine, patients undergo cardiac monitoring during the duration of the infusion and for 1 hour afterward. Vital signs are obtained every 10 minutes over the 2-hour period. Patients are premedicated with diazepam 10 mg orally to reduce the theoretical risk of seizures from lidocaine in the central nervous system. We provide standing orders for diazepam 10 mg in saline 2 mL to be administered intravenously in case of a seizure, although we have not seen seizures in our center. With regard to the interval schedule, our patients who benefit from lidocaine infusions appear to have duration of benefit of 3 to 5 weeks and are scheduled accordingly.

As noted, we are unaware of any other published report or clinical studies that address the benefit or tolerability of lidocaine infusions for fibromyalgia beyond an initial treatment or brief series of treatments. Schafranski et al[9] published an open-label study of 23 patients in Brazil who received 5 consecutive daily infusions of lidocaine (administered in 500 mL of 0.9% saline solution over 2 hours): 2

mg/kg on day 1, 3 mg/kg on day 2, 4 mg/kg on day 3, and 5 mg/kg on days 4 and 5. They noted statistically significant improvement immediately after the fifth infusion and 30 days afterward in visual analog scale pain scores and Fibromyalgia Impact Questionnaire scores. A secondary variable of functionality, the Health Assessment Questionnaire, demonstrated a trend toward improvement, which was not statistically significant. The treatment was well tolerated with no adverse side effects reported; patients were monitored with electrocardiogram.[9]

Vlainich et al[10] conducted a randomized, double-blind study in 30 women with fibromyalgia comparing amitriptyline plus 4 weekly IV lidocaine infusions (240 mg of lidocaine in 125 mL of 0.9% saline given over 1 hour) to a control group receiving oral amitriptyline and weekly saline infusions (125 mL of 0.9% saline given over 1 hour). Both groups demonstrated a significant decrease in numerical pain scale pain intensity and number of positive tender points on examination, but there was no significant difference between the groups. Data were collected during the 4-week study period only.[10] Raphael et al[11] studied efficacy (N = 50) and adverse events (N = 100) in fibromyalgia patients in the United Kingdom who were already scheduled for IV lignocaine infusions by their clinicians due to failure to achieve sufficient symptom relief with traditional modes of treatment. The patients received 6 consecutive daily infusions starting at 5 mg/kg minus 100 mg on day 1, increasing by 50 mg each day to reach 5 mg/kg plus 150 mg (maximum of 550 mg). The infusion was administered in 500 mL of Hartman's solution over 6 hours. Most of these patients had received similar courses of IV lignocaine infusions, suggesting a selection bias favoring positive outcomes.[11] Efficacy and adverse event data were collected via mailed questionnaires. Responses demonstrated that pain scores, pain relief interruption, mean daily duration of pain, and verbal assessment of pain all reduced significantly. The mean ± SD duration of pain relief was 11.5 ± 6.5 weeks with a range of 0–36 weeks. Total incidence of side effects was 42%, with the most common being hypotension (occurred in 16%), which was treated by slowing or stopping the infusion temporarily.[11]

A study presented at the American Society of Anesthesiologists annual meeting in 2013[12] supports the benefit of lidocaine infusions for fibromyalgia pain. This retrospective review of 55 patients demonstrated reduction in mean Brief Pain Inventory scores from 83.18 to 73.68 after infusion, although, reportedly, improvement was specific to nonsmokers.[12] It was hypothesized that vascular disease in the smokers prevented lidocaine from reaching painful tissues,[12] which is interesting in light of the leading pathophysiologic theory of fibromyalgia's primarily central, as opposed to peripheral, sensitization.[13] Similar to other studies reported, durability of benefit was not assessed.

In summary, systematic study of the benefit and tolerability of chronic serial IV lidocaine infusions is warranted in fibromyalgia patients. Due to the likelihood that a minority of patients is expected to benefit (although benefits can be quite pronounced), it is prudent to pay attention to the magnitude of change within responders as well as available case reports. We advocate that this intervention should be strongly considered for patients who have not achieved satisfactory relief with more traditional treatments.

Drug names:

celecoxib (Celebrex), clonazepam (Klonopin and others), diazepam (Valium and others), duloxetine

(Cymbalta), eszopiclone (Lunesta), hydromorphone (Dilaudid and others), lidocaine (Xylocaine, Lidopen, and others), milnacipran (Savella), morphine (Kadian, Avinza, and others), pregabalin (Lyrica), pramipexole (Mirapex and others), tramadol (Ultram and others), trazodone (Oleptro).

Potential conflicts of interest:

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