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## **Lidocaine in fibromyalgia: A systematic review**

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### **Abstract**

#### **BACKGROUND**

Fibromyalgia (FM) patients are treated with antidepressants, and in most cases, these drugs lose efficacy or present side effects. Intravenous lidocaine (IL) is an anesthetic drug used in some FM trials.

#### **AIM**

To systematically review the safety and efficacy of IL in FM patients.

#### **METHODS**

To systematically search PubMed for articles in English, Spanish, and Japanese with English Abstracts on FM and lidocaine between 1966 and February 2021. This study was registered at PROSPERO.

#### **RESULTS**

We found only ten articles published in this field, with a total of 461 patients. Females predominated varying from 95% to 100% in the studies. Age varied from 40.9 to 55 years old. Disease duration varied from 1 mo to 6.4 years. Lidocaine dose varied from 2 to 7.5 mg/kg *via* intravenous infusion. Follow-up period varied from 65.7 to 90 days. Regarding outcomes, most studies used the visual analogue scale (VAS) for pain; before short-term lidocaine administration, VAS was between 6.1 and 8.1 and after treatment was between 1.7 and 4.5 mm. Concerning long term lidocaine, VAS varied from 30% to 35.4% after lidocaine infusion. Side effects were observed in 0% to 39.6% of cases, they were usually mild or moderate.

#### **CONCLUSION**

This study demonstrates the short-term effectiveness and safety of intravenous lidocaine in FM patients. However, more studies, including long-term follow-up, are still needed.

**Key Words:** Lidocaine; Fibromyalgia; Pain; Intravenous infusions

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**Core Tip:** This is the first systematic review on lidocaine studies in fibromyalgia patients.

## **INTRODUCTION**

Fibromyalgia is a painful chronic disease characterized by diffuse pain for over three months with associated co-morbidities including headaches, irritable bowel syndrome, anxiety, depression, and others<sup>[1]</sup>. FM is the third most common musculoskeletal condition and may affect 0.4% (in Greece) to 8.8% (in Turkey) of a population and has a global prevalence of 2.7%<sup>[1]</sup>.

Standard treatments for FM include physical exercise, psychological intervention, and medication. Regarding pharmacological treatment, antidepressants are the leading choice for this condition. However, adverse effects can lead to dropouts, which range from 9% to 23% in short-term studies and from 11.4% to 27.2% in long-term studies<sup>[2]</sup>. Lack of efficacy is also observed during FM treatment, which can reach between 50 to 60% of cases<sup>[2]</sup>. Thus, different treatment modalities are desired for unresponsive patients or who present side effects with drugs.

Lidocaine is a topical anesthetic drug used worldwide to treat specific clinical situations such as systemic sclerosis. It is used intravenously in chronic pain and arrhythmia cases<sup>[3]</sup>. Intravenous lidocaine has been shown to control the symptoms of diabetic neuropathy<sup>[4]</sup>; there are some studies on intravenous lidocaine use in FM patients with controversial results<sup>[5-14]</sup>.

In light of this, the objective of this article is to perform a systematic review of the safety and efficacy of lidocaine in FM patients.

## **MATERIALS AND METHODS**

### ***Literature review***

We performed a systematic search of articles published in PubMed/MEDLINE, Web of Sciences, LILACS, and Scielo from 1966 to November 2020 using the following MeSH entry terms: "lidocaine" and "fibromyalgia." We used equivalent strategies in other databases. All related articles are based on "lidocaine" and "fibromyalgia" without language restriction. The reference lists in the selected articles were analyzed to identify other publications. Initially, two authors (JFC and TLS) performed the literature search and independently selected the study abstracts. In the second stage, the same reviewers independently read the full-text articles selected by abstracts. Disagreements arising in consensus meetings were resolved by a third reviewer. The authors followed PRISMA guidelines<sup>[15]</sup>. We designed a standardized form to extract the following information from relevant articles regarding authors, year of

publication, number of patients studied, demographic data, disease duration, study follow-up, pre- and post-intervention VAS, lidocaine posology, and outcomes (Figure 1).

This study was registered at PROSPERO under number CRD42021227210.

## **RESULTS**

Demographic and clinical data and pre- and post-lidocaine treatment VAS scores for FM patients are shown in Table 1.

There were only ten articles published in this field, with a total of 461 patients. Females predominated varying from 95% to 100% in the studies. Age varied from 40.9 to 55 years old. Disease duration varied from 1 month to 6.4 years.

Lidocaine IV dosage varied from 2 to 7.5 mg/kg. Follow-up was from 65.7 to 90 d.

Regarding outcome, most studies evaluated VAS. Before lidocaine, VAS ranged from 6.1 to 8.1 and after treatment, from 1.7 to 4.5 mm in the short term. Concerning long term after lidocaine infusion, VAS varied 30% to 35.4%.

Side effects were observed in 0% to 39.6% of cases, usually with mild or moderate repercussions. These effects were dizziness, nausea, vomiting, hyperglycemia, headache, lip numbness, mild dyspnea, paresthesia, dry mouth, and increasing pain. The significant effects were pulmonary edema and supraventricular tachycardia.

## **DISCUSSION**

This is the first study to systematically review the therapeutic effects of intravenous lidocaine in FM patients.

The study strengths are: (1) The inclusion of studies with patients with international criteria for FM; and (2) The exclusion of case reports, case series, and observational studies. Prospective studies present a higher degree of evidence.

The analgesic properties of intravenous lidocaine were first observed in 1962 when used to treat postoperative pain<sup>[16]</sup>. Thirty-six years later, a study demonstrated that lidocaine might be used to treat postoperative pain, reducing hospital stay in patients who had undergone radical prostatectomy<sup>[17]</sup>. Lidocaine acts by blocking sodium channels on the neuronal membrane that may play a role in the pathogenesis of inflammatory and neuropathic pain<sup>[6]</sup>.

Previous studies have demonstrated the efficacy of intravenous lidocaine in FM patients. Bennett and Tai<sup>[13]</sup> described improvement in pain scores were maintained

even 30 d after lidocaine infusion. Furthermore, Sörensen *et al*<sup>[14]</sup> evaluating 12 fibromyalgia patients showed improvements in VAS pain scores during and 15 min after a 30 min infusion of lidocaine in a double-blind placebo-controlled crossover study. Three of the 12 patients who responded to lidocaine had their pain reduced. The authors reported no statistically significant differences between FM and placebo groups in tender points, muscle strength (hip flexors and handgrip), and muscle endurance. However, the lidocaine group exhibited a significant improvement in wrist dorsiflexion muscle strength<sup>[14]</sup>.

Raphael *et al*<sup>[12]</sup> conducted a prospective study of the adverse effects of lidocaine in 106 patients with FM and a retrospective questionnaire study of the efficacy of this drug in 50 FM patients. Serial infusions of IV lidocaine were administered for six consecutive days at 5 mg/kg minus 100 mg and increased by 50 mg/d to 5 mg/kg plus 150 mg over 6 h, with the maximum allowable dose being 550 mg. Pain was measured using an 11-point VAS, in a 4-point verbal scale of pain severity (none, mild, moderate, severe), and according to the average number of hours per day in pain. Pain relief was also measured on the 11-point VAS along with pain relief duration. The psychological and social impact of the pain were evaluated by measuring depression, coping ability, dependency, and several other items using the 11-point scales. Pain score and relief interruption, pain mean duration, and verbal assessment were significantly reduced following lidocaine treatment. Mean pain relief duration was  $11.5 \pm 6.5$  wk, ranging from 0 to 36 wk. Psychosocial measurements significantly improved after lidocaine treatment in all parameters except work status.

Schafranski *et al*<sup>[11]</sup>, in an open trial, showed similar results after five sequential lidocaine infusions with rising dosages (2-5 mg/kg, days 1-5). The Fibromyalgia Impact Questionnaire (FIQ) and a VAS for pain were applied before lidocaine infusion and immediately, and 30 d after the 5th infusion. They observed significant reductions in FIQ and VAS after the fifth infusion which were maintained after 30 d<sup>[11]</sup>.

Finally, some limitations were observed in our study. For instance, no comparison between lidocaine and classical antidepressants used in FM were available in literature. The number of participants was low and future studies should include large patient samples with more long-term follow-up; this would enable a better

understanding of the course of this therapeutic modality in FM.

### **CONCLUSION**

The present study was a systematic review of all prospective studies that evaluated the role of lidocaine in FM patients and found excellent short-term efficacy. Future studies using larger FM patient samples and long-term follow-up which address the safety and efficacy of lidocaine are needed.

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