KALISIAK, Jakub, TSCHUSCHKE, Max, CHOINKA, Martyna, LORENZ, Mikołaj, LEWANDOWSKI, Jędrzej, KONOPKA, Agata, SZCZEPANIAK, Zuzanna, WDOWIAK, Natalia, KOMARÓW, Małgorzata and KARASIŃSKA, Dominika. Lignocaine in Migraine Treatment: A Comprehensive Review. Quality in Sport. 2024;23:55066. eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2024.23.55066
https://apcz.umk.pl/QS/article/view/55066

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 10.09.2024. Revised: 19.09.2024. Accepted: 28.09.2024. Published: 30.09.2024.

Lignocaine in Migraine Treatment: A Comprehensive Review

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Abstract

Introduction: Migraine is a prevalent and debilitating neurological disorder characterized by recurrent headaches and associated symptoms such as nausea, photophobia, and phonophobia. While conventional treatments exist, a significant subset of patients suffers from refractory migraines, prompting the exploration of alternative therapies like lignocaine.

Purpose of the work: This review examines the mechanisms by which lignocaine modulatespain and underscores the potential of lignocaine as a therapeutic option for refractory migraines, while also highlighting the need for continued research to refine its clinical application.

Materials and methods: A comprehensive analysis of research papers available on PubMed, Google Scholar, Web of Science, Embase and Scopus was undertaken using the searchterms encompassing the following keywords: chronic migraine / lignocaine migraine / migraine treatment/ migraine pain mechanism / migraine chronic pain mechanism / lignocaine and ketamine migraine / lignocaine adverse effects / lignocaine safety / refractory migraine.
Results: Lignocainehas shown promise in alleviating both acute and chronic migraine pain. However, its use requires careful patient selection and monitoring due to potential side effects, such as cardiac and central nervous system toxicity. Despite these risks, the favorable safety profile and efficacy of lignocaine make it a valuable option in migraine management. Future research should focus on optimizing dosing protocols, evaluating long-term outcomes, and identifying biomarkers to guide patient selection.

Keywords: Migraine, Anesthesia, Lignocaine,Chronic pain, Pain Management, Refractory Migraine

1. Introduction

Migraine is a complex neurological disorder characterized by recurrent headaches that can be severely debilitating. Affecting approximately 15% of the global population, migraines significantly impair quality of life and are often associated with symptoms such as nausea, vomiting, photophobia, and phonophobia (Ashina et al., 2021) . Despite the availability of various pharmacological treatments, a significant proportion of patients suffer from refractory migraines, which are resistant to conventional therapies (Sacco et al., 2021) . This has led researchers and clinicians to explore alternative therapeutic options, including the use of lignocaine.

Lignocaine is a local anesthetic and antiarrhythmic drug that has been used in medical practice for decades. Its role in migraine management, particularly for refractory cases, has garnered increasing attention due to its potential to provide rapid and sustained pain relief. This review aims to provide a comprehensive analysis of the use of lignocaine in migraine

treatment, including its mechanisms of action, clinical efficacy, safety profile, and potential implications for future research and clinical practice.

2. Mechanisms of Action

A. Sodium Channel Blockade

Lignocaine's primary mechanism of action is the inhibition of voltage-gated sodium channels, which play a crucial role in the propagation of action potentials in neurons (Cummins, 2007). In the context of migraines, excessive activation of sodium channels in trigeminal nerve pathways can lead to heightened neuronal excitability and the generation of pain signals. By blocking these channels, lignocaine reduces the hyperexcitability of neurons, thereby dampening the transmission of nociceptive (pain-related) signals from the periphery to the central nervous system.

B. Modulation of NMDA Receptors

In addition to sodium channel blockade, lignocaine has been shown to modulate the function of N-methyl-D-aspartate (NMDA) receptors, which are involved in the process of central sensitization (Gronwald et al., 2011). Central sensitization refers to the amplification of pain signals within the central nervous system, a phenomenon that contributes to the persistence and chronicity of migraines. NMDA receptors play a key role in this process by facilitating the influx of calcium ions into neurons, leading to long-lasting changes in synaptic strength and neuronal excitability (Kalatharan & Al-Karagholi, 2023). Lignocaine's ability to inhibit NMDA receptor activity may help to mitigate central sensitization, thereby reducing the severity and frequency of migraines.

C. Anti-Inflammatory Effects

Inflammation is increasingly recognized as a contributing factor in migraine pathophysiology. Pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-1β (IL-1β), are elevated in patients with chronic migraines and are thought to contribute to the activation and sensitization of trigeminal nerve pathways (Edvinsson et al., 2019). Lignocaine has been shown to exert anti-inflammatory effects by inhibiting the release of these cytokines, thereby reducing neurogenic inflammation and its associated pain.

3. Effects on the Autonomic Nervous System

The autonomic nervous system (ANS) plays a crucial role in the regulation of physiological processes, including blood flow and vascular tone. Dysregulation of the ANS has been

implicated in the pathogenesis of migraines, particularly in the context of migraine with aura(Miglis, 2018). Lignocaine's effects on the ANS, including the stabilization of autonomic function and reduction of sympathetic nervous system hyperactivity, may contribute to its therapeutic efficacy in migraine treatment.

4. Clinical Efficacy

The clinical efficacy of lignocaine in migraine treatment has been investigated in a number of studies, including randomized controlled trials, observational studies, and retrospective analyses (Wang et al., 2023) . These studies have demonstrated that lignocaine can provide significant relief from migraine pain, particularly in patients with refractory migraines who have not responded to other treatments(Chi et al., 2019).

5. Acute Pain Relief

One of the primary benefits of lignocaine is its ability to provide rapid pain relief in acute migraine attacks. Several studies have reported that patients experience significant reductions in pain intensity within minutes to hours of receiving lignocaine. For example, a study published in the “Annals of Emergency Medicine” found that a single bolus of lignocaine provided rapid pain relief in patients presenting to the emergency department with severe migraines. The study reported that patients experienced a reduction in pain intensity within 15 minutes of lignocaine administration, with many patients achieving complete or near-complete pain relief within one hour(Vazirani & Knott, 2012).

Similarly, a study published in “Regional Anesthesia & Pain Medicine” demonstrated that continuous IV infusion of lignocaine resulted in significant pain relief in patients with chronic, refractory migraines. The study involved the administration of lignocaine over several hours, with patients reporting substantial reductions in pain intensity both during and after the infusion. Importantly, the study found that the effects of lignocaine were sustained for several weeks, with patients experiencing a reduction in both the frequency and severity of migraine attacks(Schwenk et al., 2022).

6. Long-Term Efficacy

In addition to providing acute pain relief, lignocaine has also been shown to have long-term benefits in the management of chronic migraines. A retrospective analysis conducted by Krause et al. examined the long-term outcomes of patients who received IV lignocaine infusions for chronic migraines. The study found that patients experienced significant

reductions in the frequency of migraine attacks and overall headache burden in the months following lignocaine treatment. These findings suggest that IV lignocaine may not only serve as an acute intervention but also contribute to long-term migraine prevention (Mojica et al., 2021).

A separate study published in "Headache: The Journal of Head and Face Pain" also supports the long-term efficacy of IV lignocaine in migraine treatment. The study reported that patients who received repeated lignocaine infusions over a period of several months experienced sustained improvements in headache frequency, pain intensity, and overall quality of life. The authors concluded that IV lignocaine represents a viable option for the long-term management of refractory migraines, particularly in patients who have exhausted other treatment options(Marmura et al., 2009).

7. Comparison with Other Treatments

While lignocaine has shown promise in the treatment of migraines, it is important to compare its efficacy with that of other available treatments. For example, in a study performed by Ray et. al, the efficacy of IV lignocaine was compared with that of IV ketamine, another NMDA receptor antagonist used in migraine treatment. The study found that both lignocaine and ketamine provided significant pain relief in patients with refractory migraines, but lignocaine was associated with a lower incidence of side effects and a more favorable safety profile(Ray et al., 2022).

8. Safety and Tolerability

Lidocaine works via binding to voltage-gated sodium channels, thereby inhibiting the propagation of action potentials, therefore the main target organs are the central nervous system (CNS) and the cardiovascular system (CVS). Thecentral nervous system(CNS) is more sensitive to these electrophysiological changes, so neurological symptoms typically occur before any cardiovascular symptoms appear(Ray et al., 2022).

The most commonly reported neurological side effects of IV lignocaine include dizziness, nausea, perioral numbness (numbness around the mouth), and a metallic taste in the mouth. These side effects are generally mild and transient, resolving shortly after the infusion is stopped. At higher doses, lignocaine can cause CNStoxicity, such as confusion, agitation, tremors, and, in severe cases, seizures(Hasan et al., 2017; Ray et al., 2022).

One of the most significant risks associated with IV lignocaine is cardiac toxicity, particularly in the context of high doses or prolonged infusions. Lignocaine can cause a range of cardiac

effects, including bradycardia, arrhythmias, and, in severe cases, cardiac arrest (Digala& Lucchese, 2020; Tierney et al., 2016). Therefore, careful patient selection and monitoring are essential when using IV lignocaine for migraine treatment.

9. Allergic Reactions

Although rare, allergic reactions to lignocaine can occur, particularly in patients with a history of hypersensitivity to local anesthetics. Allergic reactions may manifest as skin rash, pruritus, angioedema, or anaphylaxis. Patients with a known allergy to lignocaine or other amide-type local anesthetics should not receive IV lignocaine (Bahar & Yoon, 2021). In cases where an allergic reaction is suspected, lignocaine administration should be stopped immediately, and appropriate medical treatment should be initiated, because it may be dangerous to the patient's life(Chan, 2016).

10. Future Directions and Research

While the existing evidence supports the use of lignocaine in the treatment of refractory migraines, several questions remain unanswered, and further research is needed to optimize its use in clinical practice.

A. Optimization of Dosing Protocols

One of the key areas for future research is the optimization of dosing protocols for IV lignocaine. While current protocols vary widely in terms of dose, infusion rate, and duration, more standardized guidelines are needed to ensure consistent and effective treatment outcomes. Future studies should aim to identify the optimal dosing regimen for different patient populations, taking into account factors such as age, comorbidities, and the severity of migraines. Additionally, research should explore the potential benefits of titration strategies, where the dose of lignocaine is gradually increased based on the patient's response to treatment and tolerability.

B. Long-Term Efficacy and Safety

Another important area for future research is the long-term efficacy and safety of IV lignocaine in migraine treatment. While existing studies suggest that lignocaine can provide sustained relief from migraines, more long-term follow-up studies are needed to confirm these findings and assess the durability of treatment effects (Marmura et al., 2009). Additionally, research should explore the potential for long-term side effects, particularly in patients receiving repeated lignocaine infusions over an extended period.

C. Comparative Effectiveness

Comparative effectiveness research is also needed to determine how IV lignocaine compares to other treatments for refractory migraines, such as IV ketamine, occipital nerve blocks, or onabotulinumtoxinA (Botox) injections. These studies should evaluate not only the efficacy of lignocaine in relieving migraine pain but also its impact on patient quality of life, functional outcomes, and healthcare utilization. Additionally, comparative studies should assess the safety profiles of different treatments, particularly in terms of the risk of serious adverse events.

D. Biomarkers and Patient Selection

The identification of biomarkers that predict response to IV lignocaine is another important area for future research. Currently, there is limited understanding of which patients are most likely to benefit from lignocaine treatment, and patient selection is often based on clinical judgment and trial-and-error. Biomarkers, such as genetic polymorphisms, neuroimaging findings, or biochemical markers, could help to identify patients who are more likely to respond to lignocaine, allowing for more personalized and targeted treatment approaches.

E. Alternative Administration Routes

Finally, research should explore alternative routes of lignocaine administration, such as subcutaneous, intranasal, or transdermal delivery, which may offer similar benefits with a lower risk of systemic side effects. For example, a study conducted by Szperka et al. provides significant proof of treating migraine symptoms using occipital nerve blockade via lidocaine injections. Similar studies could be conducted in patients with migraines to assess the feasibility and efficacy of alternative administration routes(Szperka et al., 2024).

11. Conclusion

Intravenous lignocaine represents a promising treatment option for patients with refractory migraines, particularly those who have not responded to conventional therapies. Its ability to provide rapid and sustained pain relief, combined with its relatively favorable safety profile, makes it an attractive option in both acute and chronic migraine management. However, the use of IV lignocaine must be carefully managed, with appropriate patient selection, dosing, and monitoring to minimize the risk of adverse effects.

While the existing evidence supports the efficacy of IV lignocaine in migraine treatment, further research is needed to optimize its use in clinical practice. Future studies should focus on refining dosing protocols, evaluating long-term efficacy and safety, and identifying

biomarkers that predict treatment response. Additionally, comparative effectiveness research and investigations into alternative administration routes could help to expand the use of lignocaine in migraine treatment and improve outcomes for patients with this challenging and debilitating condition.

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Disclosures:
No disclosures.
Funding statement:
The study did not receive special funding.
Institutional review board statement:
Not applicable.
Informed consent statement:
Not applicable.
Data availability statement:
Not applicable.
Conflict of interest:
The authors declare no conflict of interest

All authors have read and agreed with the published version of the manuscript.

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