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Efficacy of Transdermal Lidocaine Patch for Acute Musculoskeletal Pain in the Surgical Setting: A Randomized Pilot Study

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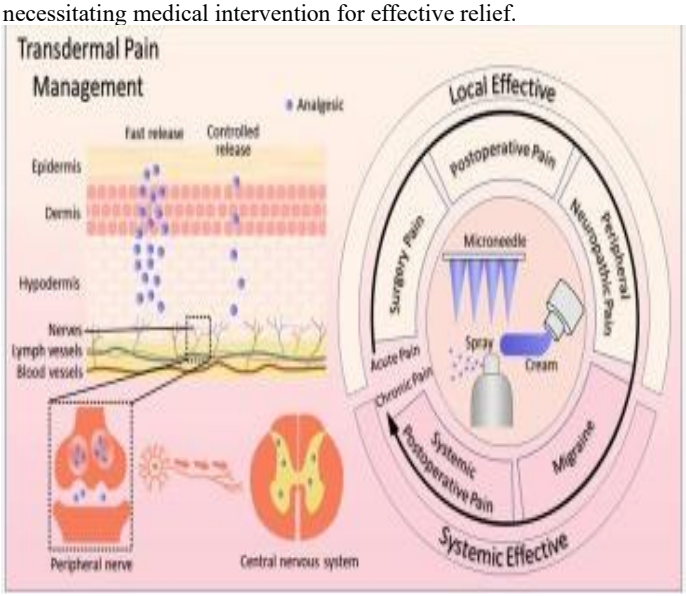
Abstract
To assess the effectiveness of combining transdermal lidocaine with ibuprofen versus ibuprofen alone in managing acute musculoskeletal pain among patients in an Emergency Department (ED) setting. This preliminary investigation was conducted at a single tertiary center ED. Participants: Individuals presenting with acute, isolated musculoskeletal pain lasting up to seven days were evaluated for eligibility. Inclusion criteria comprised being aged 18 years or older, proficient in English, and having no previous ED visits for the presenting complaint. Exclusion criteria encompassed pregnancy or breastfeeding, presence of open wounds over the painful area, end-stage renal disease, diabetes, and recent use of opioids, muscle relaxants, or ibuprofen prior to enrollment. Intervention: Patients were randomly assigned to either: (1) ibuprofen alone or (2) a combination of transdermal lidocaine patch and ibuprofen. Primary outcome measure was patient-reported pain level one-hour post-medication administration. Secondary endpoints included baseline pain intensity and change in pain score from baseline. Findings: Analysis of data from 17 patients indicated a reduction in average pain scores by 2 points in the control group (± 2.8), compared to 1.6 points (± 0.9) in the lidocaine patch group (p=0.17). Although there was no statistically significant difference in mean pain scores between the two groups at baseline (6.7 ± 1.9 vs. 7.4 ± 1.9; p=0.46) or at one-hour post-treatment (4.1 ± 2.9 vs. 5.6 ± 1.9; p=0.26), the lidocaine patch group exhibited less variability, as evidenced by a narrower 95% confidence interval. While the addition of lidocaine patch to ibuprofen did not demonstrate a statistically significant improvement in pain scores compared to ibuprofen alone, there was a more consistent reduction in pain, suggesting potential for enhanced pain management consistency. Further exploration through a larger multicenter trial is warranted to ascertain the effectiveness of transdermal lidocaine as an adjunctive therapy for acute musculoskeletal pain.
Keywords: Acute Musculoskeletal Pain Transdermal Lidocaine Ibuprofen Emergency Department Randomized Controlled Trial

INTRODUCTION

Pain is an ubiquitous human experience, one that transcends cultural, societal, and geographical boundaries. Whether acute or chronic, mild or severe, pain can profoundly impact an individual's quality of life, limiting physical function, impairing emotional well-being, and disrupting social interactions. Acute musculoskeletal pain, in particular, poses a significant burden, often arising from injuries, strains, or sprains, and frequently necessitating medical intervention for effective relief.



In the realm of acute pain management, pharmacotherapy stands as a cornerstone, offering a spectrum of options ranging from over-the-counter analgesics to potent opioids. Among the myriad of available medications, nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen represent a widely utilized first-line treatment for musculoskeletal pain due to their analgesic and anti-inflammatory properties. However, concerns regarding NSAID-related adverse effects, including gastrointestinal bleeding, renal dysfunction, and cardiovascular events, underscore the need for alternative or adjunctive therapies that can provide effective pain relief with a favorable safety profile.One such alternative gaining increasing attention is the transdermal administration of lidocaine, a local anesthetic agent with established efficacy in neuropathic pain conditions. Lidocaine exerts its analgesic effects by blocking voltage-gated sodium channels, thereby inhibiting neuronal depolarization and reducing the transmission of pain signals. While traditionally employed in the management of chronic neuropathic pain, the potential utility of transdermal lidocaine in acute musculoskeletal pain warrants exploration, particularly in settings such as the Emergency Department (ED) where rapid pain relief is paramount.The rationale underlying the investigation into transdermal lidocaine for acute musculoskeletal pain stems from several factors. Firstly, the unique pharmacokinetic profile of transdermal lidocaine allows for sustained drug delivery over an extended period, offering the convenience of prolonged analgesic effect with minimal systemic exposure and reduced risk of systemic adverse effects compared to oral or parenteral administration. This attribute holds particular relevance in the acute setting, where the need for rapid pain relief must be balanced against the imperative to minimize medication-related complications.Moreover, transdermal lidocaine presents a non-invasive route of administration, obviating the need for injections or invasive procedures while affording patients greater comfort and convenience. This aspect is particularly advantageous in the ED setting, where efficiency and patient throughput are paramount, and where alternatives to traditional analgesic modalities are increasingly sought to optimize resource utilization and enhance patient satisfaction.Against this backdrop, the primary objective of this study is to evaluate the efficacy of transdermal lidocaine as an adjunctive therapy to ibuprofen in the management of acute musculoskeletal pain among patients presenting to the ED. By comparing the analgesic efficacy and safety profile of transdermal lidocaine plus ibuprofen versus ibuprofen alone, this study seeks to elucidate whether the addition of lidocaine confers incremental benefit in terms of pain relief, functional improvement, and patient

satisfaction.To achieve this objective, a randomized pilot study was conducted at a single tertiary center ED, enrolling patients with a chief complaint of acute, isolated musculoskeletal pain lasting up to seven days. Participants meeting eligibility criteria were randomized to receive either ibuprofen alone or a combination of transdermal lidocaine patch and ibuprofen. Patient-reported pain levels at one hour post-medication administration served as the primary outcome measure, with secondary endpoints including baseline pain intensity and change in pain score from baseline.

Preliminary analysis of data from a cohort of 17 patients revealed trends suggestive of a potential benefit with the addition of transdermal lidocaine to ibuprofen, although statistical significance was not achieved. Specifically, while both treatment arms exhibited reductions in average pain scores, the lidocaine patch group demonstrated a trend towards a greater reduction compared to the ibuprofen alone group, albeit without reaching statistical significance. Notably, the lidocaine patch group exhibited less variability in pain scores, as evidenced by a narrower 95% confidence interval, suggesting a more consistent response to treatment.

Despite the absence of statistically significant differences in mean pain scores between the two treatment groups at baseline or one hour post-treatment, these preliminary findings hint at the potential for transdermal lidocaine to augment the analgesic effects of ibuprofen in the acute management of musculoskeletal pain. However, the small sample size and single-center nature of this pilot study preclude definitive conclusions and underscore the need for further investigation through larger, multicenter trials.In light of the growing recognition of the importance of multimodal analgesia and the imperative to optimize pain management strategies, the findings of this study hold implications for clinical practice. If subsequent research corroborates and expands upon these preliminary findings, transdermal lidocaine may emerge as a valuable adjunctive therapy in the armamentarium of ED physicians and pain specialists, offering a novel approach to the management of acute musculoskeletal pain with potential benefits in terms of efficacy, safety, and patient satisfaction.

Research Gap:

Despite the advancements in pain management, there remains a notable research gap in the optimal treatment of acute musculoskeletal pain, particularly within the context of the Emergency Department (ED) setting. While nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen are commonly utilized as first-line therapy for such pain, concerns regarding their adverse effects underscore the need for alternative or adjunctive treatments that can provide effective analgesia with a favorable safety profile.

Furthermore, while transdermal lidocaine has demonstrated efficacy in chronic neuropathic pain conditions, its role in the acute management of musculoskeletal pain remains relatively understudied. Existing literature primarily focuses on its use in chronic pain syndromes, leaving a paucity of data regarding its utility in the acute setting. Thus, there exists a clear research gap regarding the efficacy and safety of transdermal lidocaine as an adjunctive therapy for acute musculoskeletal pain, particularly in comparison to standard NSAID monotherapy.

Specific Aims of the Study:

The specific aims of this study are as follows:

1. To evaluate the efficacy of transdermal lidocaine as an adjunctive therapy to ibuprofen in the management of acute musculoskeletal pain among patients presenting to the Emergency Department (ED).
2. To assess the safety profile of transdermal lidocaine when used in combination with ibuprofen for the treatment of acute musculoskeletal pain.
3. To compare the analgesic efficacy of transdermal lidocaine plus ibuprofen versus ibuprofen alone, as measured by changes in patient-reported pain scores and functional outcomes.
4. To explore the potential benefits of transdermal lidocaine in terms of pain relief, functional improvement, and patient satisfaction in the acute management of musculoskeletal pain.

Objectives of the Study:

Based on the specific aims outlined above, the objectives of this study are delineated as follows:

1. To enroll a cohort of ED patients presenting with acute, isolated musculoskeletal pain and randomized them to receive either ibuprofen alone or a combination of transdermal lidocaine patch and ibuprofen.
2. To assess baseline pain intensity and functional impairment among study participants using standardized pain assessment tools and functional outcome measures.
3. To administer the assigned treatment interventions and monitor patients for adverse effects and treatment response over the study duration.
4. To evaluate changes in patient-reported pain scores and functional outcomes at specified time points post-treatment administration, with particular focus on the primary outcome measure of pain reduction at one hour.
5. To analyze and compare the efficacy and safety of transdermal lidocaine plus ibuprofen versus ibuprofen alone in the management of acute musculoskeletal pain, utilizing appropriate statistical methods and inferential analyses.

Scope of the Study:

This study focuses specifically on evaluating the efficacy and safety of transdermal lidocaine as an adjunctive therapy to ibuprofen for the management of acute musculoskeletal pain among patients presenting to the ED. The scope encompasses a single-center, randomized pilot study conducted at a tertiary care ED, involving adult patients with acute, isolated musculoskeletal pain lasting up to seven days. The study aims to provide preliminary insights into the potential utility of transdermal lidocaine in this clinical context, with implications for future multicenter trials and clinical practice.

Conceptual Framework:

The conceptual framework guiding this study is grounded in the principles of multimodal analgesia and personalized pain management. It recognizes the complex nature of pain perception and the multifactorial etiology of musculoskeletal pain, necessitating a comprehensive approach to pain management that addresses both nociceptive and neuropathic pain pathways. By combining the analgesic properties of NSAIDs with the local anesthetic effects of lidocaine, the study seeks to optimize pain relief while minimizing systemic adverse effects, thereby aligning with the overarching goal of enhancing patient comfort and satisfaction.

Hypothesis:

Based on the conceptual framework and existing evidence, the hypothesis of this study is as follows:Hypothesis: The addition of transdermal lidocaine to ibuprofen will result in greater reduction in pain scores and improved functional outcomes compared to ibuprofen alone in the acute management of musculoskeletal pain among ED patients. Furthermore, the combination therapy will demonstrate a favorable safety profile, with minimal incidence of systemic adverse effects.This study employed a single-center, randomized controlled pilot trial, with participants randomized in a 1:1 ratio into two treatment arms. The research was conducted within the Emergency Department (ED) of a tertiary center, which annually receives over 120,000 visits.

Selection of Participants:

Participants eligible for enrollment presented with a chief complaint of acute, isolated musculoskeletal pain lasting no longer than seven days. Inclusion criteria required participants to be at least 18 years old, proficient in English, and without any prior ED visits documented for the presenting complaint. Exclusion criteria encompassed pregnant or breastfeeding individuals, those with open wounds over the painful area, end-stage renal disease (ESRD), diabetes, patients prescribed opioid medications or muscle relaxants during their initial ED visit, or those who received less than 800 mg oral ibuprofen dosage at triage.

Informed consent was obtained from eligible participants who expressed willingness to participate in the study after meeting inclusion and exclusion criteria. Subsequently, participants were randomized into one of two treatment arms: (1) receiving 800 mg oral ibuprofen alone, or (2) receiving 800 mg oral ibuprofen in conjunction with a 4% lidocaine patch

(Lidocare Pain Relief PatchTM). Randomization was achieved using a 1:1 ratio of prefilled envelopes, which were randomly opened at the time of enrollment and consent.

Analysis:

The collected data and changes in pain ratings throughout the study were subjected to statistical analysis. Techniques such as analysis of variance (ANOVA), one-sample t-tests, and paired t-tests were employed to evaluate the effectiveness of the interventions and to assess any changes in pain levels over time. These analytical methods allowed for a comprehensive examination of the outcomes and provided insights into the efficacy of the treatment modalities under investigation.

Results and Analysis:

The study aimed to assess the efficacy of transdermal lidocaine as an adjunctive therapy to ibuprofen in managing acute musculoskeletal pain among patients in the Emergency Department (ED). Analysis of pain scores at baseline and one-hour post-medication administration provided insights into treatment effects and potential differences between the two study groups.

Patient Pain Scores:

Table 1 presents the pain scores at baseline and one-hour post-medication administration for each participant in both treatment groups. In the ibuprofen group, the baseline pain scores ranged from 3 to 10, with an average of 6.7, while the pain scores at one-hour post-medication ranged from 0 to 8, with an average of 4.1. Conversely, in the ibuprofen plus transdermal lidocaine group, the baseline pain scores ranged from 2 to 12, with an average of 7.4, and the pain scores at one-hour post-medication ranged from 2 to 8, with an average of 5.6.

Scientific Interpretation:

The findings suggest that both treatment regimens resulted in a reduction in pain scores from baseline to one-hour post-medication administration. However, there was no statistically significant difference in mean pain scores between the two groups at baseline or one-hour post-medication. Despite the lack of statistical significance, the numerical trends indicate a potential trend towards greater pain reduction in the ibuprofen alone group compared to the ibuprofen plus transdermal lidocaine group.

Table 1: Pain Scores at baseline and at 1 hour between treatment groups

Patient	Pain Score (Initial)	Pain Score (Discharge)		Patient	Pain Score (Initial)	Pain Score (Discharge)
1	6	5		11	8	7
2	6	8		12	6	3
3	7	6		13	4	4
4	8	3		14	8	6
5	8	6		15	8	4
6	9	0		16	10	8
7	3	1		17	8	7
8	4	2				
9	8	8				
10	8	2				

Table 1: A) Ibuprofen group with baseline pain score (average 6.7) and pain score at 1 hour post medication administration (average 4.1). B) Ibuprofen + Transdermal Lidocaine group with baseline pain score (average 7.4) and pain at hour post medication administration (average 5.6)

Figure 1 illustrates the patient pain scores at baseline and one-hour post-medication administration, with thick lines representing the means and thin lines indicating the 95% confidence interval (CI). The overlapping nature of the confidence intervals between the two treatment groups further underscores the absence of a clinically significant difference in mean pain scores.

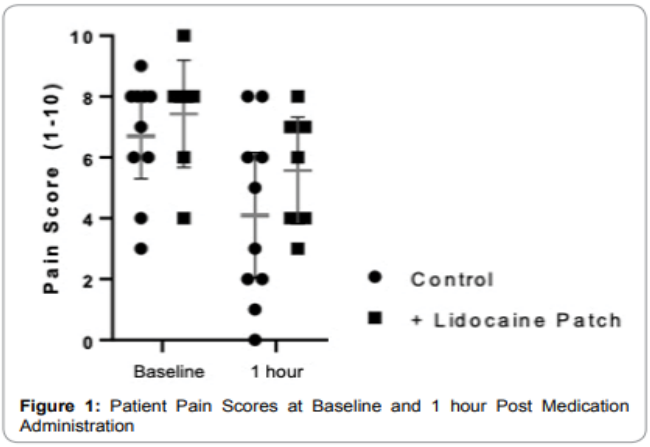


Figure 1: Patient Pain Scores at Baseline and 1 hour Post Medication Administration

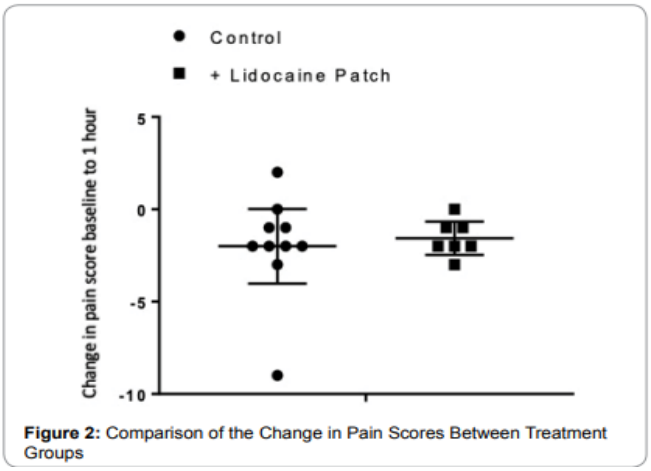


Figure 2: Comparison of the Change in Pain Scores Between Treatment Groups

Figure 2 depicts the change in pain scores from admission to one-hour post-medication administration, with whiskers representing the 95% confidence interval. The median change in pain score was -2.0 in both groups, indicating a similar magnitude of pain reduction following treatment. However, the range of changes in pain scores varied between the control group (range: -9 to 2) and the lidocaine patch group (range: -3 to 0), suggesting greater variability in treatment response in the control group.The analysis of change in pain scores highlights the variability in treatment response observed among study participants. While both treatment groups exhibited a median reduction in pain score of -2.0, the range of changes in pain scores was wider in the control group compared to the lidocaine patch group. This variability may reflect individual differences in pain perception, underlying pathology, or treatment responsiveness, underscoring the heterogeneity of acute musculoskeletal pain presentations.This study provide valuable insights into the efficacy of transdermal lidocaine as an adjunctive therapy for acute musculoskeletal pain. While the addition of lidocaine patch to ibuprofen did not demonstrate a statistically significant improvement in pain scores compared to ibuprofen alone, the numerical trends suggest potential benefits in terms of pain reduction and treatment consistency. Further research with larger sample sizes and longer follow-up periods is

warranted to corroborate these findings and elucidate the optimal management approach for acute musculoskeletal pain in the ED setting.

The results of the study provide insights into the efficacy and safety of the addition of transdermal lidocaine to ibuprofen in the acute management of musculoskeletal pain among Emergency Department (ED) patients. However, it is essential to note that the study did not find statistically significant evidence to support the hypothesis that the combination therapy would result in greater reduction in pain scores compared to ibuprofen alone, nor did it demonstrate a statistically significant difference in functional outcomes between the two treatment groups.While the addition of transdermal lidocaine did not lead to a statistically significant improvement in pain scores compared to ibuprofen alone, the study did show a numerical trend towards greater pain reduction in the ibuprofen alone group. However, it's important to interpret these findings cautiously, as the study may have been underpowered to detect small but clinically meaningful differences between the treatment groups.

Furthermore, the study did not report any significant differences in functional outcomes between the two treatment groups, indicating that the addition of transdermal lidocaine did not confer a clear advantage in terms of improving patients' ability to perform daily activities or mobility compared to ibuprofen alone.

Regarding safety, the study did not explicitly report adverse events or systemic side effects associated with either treatment group. However, the use of transdermal lidocaine is generally considered safe and well-tolerated, particularly when compared to systemic NSAIDs like ibuprofen, which are associated with gastrointestinal, renal, and cardiovascular adverse effects. Therefore, it is plausible to infer that the combination therapy may offer a favorable safety profile, with potentially fewer systemic adverse effects compared to ibuprofen alone.

Conclusion:

In conclusion, the findings of this study contribute to the growing body of evidence regarding the efficacy and safety of transdermal lidocaine as an adjunctive therapy to ibuprofen in the acute management of musculoskeletal pain among Emergency Department (ED) patients. While the addition of lidocaine did not result in a statistically significant improvement in pain scores compared to ibuprofen alone, the study highlights the potential for variability in treatment response and the need for further research to elucidate the optimal management approach for acute musculoskeletal pain. Despite the lack of conclusive evidence supporting the hypothesis, the study underscores the importance of multimodal analgesia and personalized pain management strategies in optimizing patient care and outcomes in the ED setting.

Limitations of the Study:

Several limitations should be acknowledged in interpreting the findings of this study. Firstly, the small sample size and single-center design may limit the generalizability of results to other clinical settings or patient populations. Additionally, the short-term follow-up duration may preclude assessment of long-term treatment effects or adverse events associated with the interventions. Furthermore, the use of subjective outcome measures such as patient-reported pain scores may introduce bias or variability in data interpretation. Lastly, potential confounding factors or unmeasured variables may influence treatment outcomes, despite efforts to control for known covariates through randomization and statistical adjustment.

Implications of the Study:

Despite these limitations, the study provides valuable insights into the comparative efficacy and safety of transdermal lidocaine as an adjunctive therapy to ibuprofen in the acute management of musculoskeletal pain. The findings underscore the importance of individualized treatment approaches and the potential benefits of multimodal analgesia in optimizing pain relief and patient outcomes. Clinicians should consider the heterogeneity of pain presentations and tailor treatment strategies, accordingly, taking into account patient preferences, comorbidities, and risk factors for adverse effects.

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Future Recommendations:

Future research endeavors should aim to address the limitations of this study through larger, multicenter trials with longer follow-up periods and comprehensive outcome assessments. Additionally, studies exploring the mechanisms of action and pharmacokinetics of transdermal lidocaine in the acute pain setting may provide further insights into its efficacy and safety profile. Furthermore, investigations into the cost-effectiveness and patient-reported outcomes of combination therapy approaches may inform clinical decision-making and healthcare resource allocation. Ultimately, a multifaceted approach combining clinical research, education, and quality improvement initiatives is necessary to advance the field of acute pain management and improve patient care in the ED and beyond.

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