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RESEARCH ARTICLE

Comparative study between the effects of intravenous paracetamol versus lidocaine on the prevention of localised pain resulting from intravenous propofol injection during general anaesthesia

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Abstract: Propofol is a commonly used intravenous anaesthetic agent, but pain on injection remains a frequent adverse effect that can affect patient comfort. This study compared the effectiveness of intravenous paracetamol and lidocaine in reducing propofol-induced injection pain. A prospective, randomized, double-blind controlled trial was conducted at a tertiary care hospital involving 60 adult patients (ASA I–II) undergoing elective surgeries under general anaesthesia. Patients were randomly divided into two groups: one group received 1000 mg IV paracetamol 10 minutes before propofol injection, and the other received 40 mg IV lidocaine 30 seconds prior. Pain intensity was assessed immediately after injection using a Verbal Rating Scale (0–3), along with secondary outcomes including adverse effects, anaesthesia duration, and patient satisfaction. Demographic characteristics were similar across both groups. The incidence of injection pain was significantly lower in the lidocaine group (16.7%) compared to the paracetamol group (33.3%) ($p = 0.04$). Severe pain was observed only in the paracetamol group (3.3%). Patients in the lidocaine group reported higher satisfaction, with 60% being "very satisfied" compared to 40% in the paracetamol group ($p = 0.04$). There were no significant differences in adverse effects or anaesthesia duration. The findings indicate that intravenous lidocaine is more effective than paracetamol in reducing both the incidence and severity of propofol injection pain, along with better patient satisfaction. Although paracetamol offers modest benefit, lidocaine remains the preferred agent for minimizing injection-related discomfort during anaesthesia induction.

Keywords: Propofol injection pain; Lidocaine; Intravenous paracetamol; General anaesthesia; Randomized controlled trial; Patient comfort.

INTRODUCTION

Propofol, chemically known as 2,6-diisopropylphenol, is a short-acting, lipophilic intravenous anaesthetic agent that has gained widespread acceptance and utilization in modern anaesthetic practice since its introduction into clinical use. Its pharmacokinetic and pharmacodynamic properties make it an ideal agent for a broad range of clinical applications. These properties include a rapid onset of action, typically occurring within 30–40 seconds of administration, and a short duration of effect, due primarily to rapid redistribution and hepatic metabolism. These characteristics make propofol highly suitable for situations requiring quick titration, smooth induction, and prompt recovery from anaesthesia. Consequently, propofol has become one of the most widely administered drugs in both elective and emergency anaesthesia [1].

Propofol is routinely employed for the induction and maintenance of general anaesthesia, and it is also used extensively in the context of procedural sedation, particularly for short outpatient procedures such as endoscopy, cardioversion, and minor surgical interventions. In the intensive care unit (ICU), propofol is often used for the sedation of mechanically ventilated patients, given its favourable pharmacological profile, which allows for sustained sedation with minimal accumulation. Furthermore, its antiemetic properties, minimal residual sedation, and low incidence of postoperative nausea and vomiting contribute to enhanced patient outcomes and reduced recovery times, making it a cornerstone of day-case surgeries and fast-track anaesthesia protocols [2].

Despite these numerous clinical advantages, the administration of propofol is not without drawbacks. One of the most frequently encountered adverse effects associated with its use is pain on intravenous injection, which remains a significant source of patient discomfort. This side effect is not only common but also often described as intensely distressing, and in some cases, it can be the most painful part of the perioperative process for the patient. According to the literature, the incidence of propofol-induced injection pain can be as high as 90% when no preventive measures are employed [3,4]. This high prevalence underlines a substantial area of concern, particularly in vulnerable populations or in ambulatory surgical settings, where patient experience and satisfaction are integral to quality care.
The pain typically manifests immediately or shortly after the administration of propofol and is frequently described by patients as a burning, stinging, or aching sensation localized to the injection site. In certain instances, the discomfort may extend along the venous

pathway, potentially resulting in withdrawal reflexes or involuntary limb movements, thereby complicating the intravenous administration and necessitating repeated attempts or increased restraint. In paediatric and geriatric patients, this can significantly heighten anxiety levels. Moreover, for individuals undergoing multiple procedures or repeated intravenous anaesthesia, such pain can lead to anticipatory anxiety, reduced cooperation, and negative associations with anaesthesia, all of which can impair the overall perioperative experience [5].

The pathophysiology of propofol injection pain is considered to be multifactorial and complex. One major contributing mechanism is thought to involve the direct irritant effect of the aqueous phase of the propofol emulsion on the vascular endothelium. As a lipophilic compound, propofol is formulated in an oil-in-water emulsion, where the aqueous component may interact unfavourably with the delicate endothelial lining, particularly in smaller peripheral veins where blood flow is slower and more susceptible to irritation [6]. In addition to this mechanical and chemical irritation, another important mechanism involves the activation of the kallikrein-kinin system, a component of the inflammatory response pathway. Upon injection, this system leads to the release of bradykinin, a potent inflammatory mediator that increases vascular permeability and vasodilation, thereby facilitating the leakage of emulsion components into the surrounding tissue and enhancing the stimulation of peripheral nociceptors [7,8]. This neurovascular cascade amplifies pain perception and contributes significantly to the discomfort experienced during injection.

Given the high prevalence and clinical significance of this adverse effect, numerous pharmacological and non-pharmacological strategies have been explored over the years to mitigate or prevent the pain associated with propofol injection. Among the most widely adopted and extensively studied pharmacological interventions is the use of lidocaine, a local anaesthetic agent with well-known efficacy in nerve conduction blockade. Lidocaine functions by stabilizing the neuronal membrane and blocking voltage-gated sodium channels, thereby preventing the initiation and propagation of action potentials. When administered intravenously before or mixed with propofol, lidocaine can blunt or eliminate the activation of peripheral nociceptors at the injection site. Clinically, lidocaine is either administered as a bolus prior to propofol injection (pretreatment) or mixed directly with propofol in the same syringe prior to administration. Numerous studies and meta-analyses have consistently shown that lidocaine, in both forms, significantly reduces the incidence, severity, and duration of propofol-induced injection pain, and is considered a standard intervention in anaesthetic protocols globally [9,10].

In recent years, interest has emerged in evaluating alternative or adjunctive pharmacological agents, including paracetamol (acetaminophen), for their potential role in the management of injection pain. Paracetamol is a centrally acting analgesic and antipyretic agent, most commonly used for the treatment of mild to moderate pain and fever. Its mechanism of action is distinct from that of local anaesthetics. It primarily involves the inhibition of central cyclooxygenase (COX) enzymes, particularly COX-2, leading to reduced synthesis of prostaglandins in the central nervous system (CNS) [11]. Additionally, paracetamol is thought to modulate the descending serotonergic pain inhibitory pathways, and may also interact with endocannabinoid and TRPA1 pathways, contributing to its analgesic effects [12,13]. The availability of intravenous formulations of paracetamol has made it a practical and increasingly utilized option in perioperative care, especially in multimodal analgesia regimens aimed at reducing opioid consumption.

Some researchers have hypothesized that the central analgesic effects of paracetamol, when administered intravenously prior to propofol injection, may indirectly help attenuate the perception of pain associated with the injection itself. Several clinical studies have tested this hypothesis and found that pre-treatment with IV paracetamol can reduce the subjective pain scores reported by patients during propofol injection, suggesting a systemic analgesic effect that may have peripheral implications [14,15,16]. Furthermore, paracetamol's potential anti-inflammatory properties may play a role in modulating the vascular and nociceptive responses triggered by the administration of propofol. However, its precise efficacy in this particular context, and the underlying mechanisms through which it might exert such effects, remain less clearly understood than those of lidocaine.

While the data on paracetamol appear promising, the comparative efficacy of intravenous paracetamol and lidocaine in the specific context of propofol injection pain remains inconclusive and under-researched. A review of the existing literature reveals that direct comparative studies between these two agents are relatively scarce, and those that are available are often limited by small sample sizes, heterogeneous methodologies, and variability in the dosages and timing of administration. Additionally, the assessment tools used to evaluate pain (such as verbal rating scales, visual analogue scales, or categorical pain scores) vary widely between studies, making cross-study comparisons difficult and limiting the generalizability of the results [17,18,19].

This paucity of robust head-to-head comparative data represents a significant gap in the current clinical knowledge base, particularly given the routine and widespread use of propofol in surgical and procedural sedation across a wide range of patient demographics.

Understanding which agent—lidocaine or paracetamol—provides more effective pain relief during propofol injection could help improve patient comfort, reduce procedural anxiety, and ultimately enhance the overall anaesthetic experience.

Given the growing emphasis on patient-centred care, the minimization of perioperative distress, and the optimization of clinical protocols to ensure safety, comfort, and satisfaction, a direct and systematic comparison of the effects of intravenous lidocaine and intravenous paracetamol in the context of propofol-induced injection pain is both timely and clinically relevant. Such a study is essential for generating high-quality evidence that can inform evidence-based practice and guide the development of more refined, patient-focused anaesthetic protocols.

Therefore, the present study is designed to undertake a comprehensive, randomized, controlled comparative analysis of the analgesic efficacy of intravenous paracetamol versus lidocaine in preventing or reducing the pain associated with intravenous propofol injection during the induction phase of general anaesthesia. By employing a standardized pain assessment methodology, carefully controlled drug administration protocols, and rigorous statistical analysis, this investigation aims to provide meaningful and clinically applicable data. Previous studies involving other interventions, such as magnesium sulfate, suggest that exploring multiple strategies remains clinically relevant [20]. The study will evaluate not only the incidence and intensity of pain, but also secondary outcomes such as patient satisfaction, tolerability, and the occurrence of any adverse effects, thus offering a comprehensive assessment of the two agents. Ultimately, the findings of this study are intended to enhance our understanding of the most effective strategies for minimizing discomfort during propofol administration and improving the overall quality of anaesthetic care provided to patients.

MATERIAL AND METHODS

Study Design and Setting

A prospective, randomized, double-blind, controlled trial was conducted in the Department of Anaesthesiology at a tertiary care teaching hospital, over 6 6-month duration. Patients aged 18–60 years of either sex, classified as American Society of Anesthesiologists (ASA) physical status I or II, scheduled for elective surgeries under general anaesthesia were included.

Exclusion criteria included patients with:

- Hypersensitivity to study drugs (paracetamol, lidocaine, or propofol)
- Chronic pain conditions or regular use of analgesics
- Neurological or psychiatric disorders
- Difficultvenousaccess
- Pregnancy or lactation

Sample Size Calculation

Sample size was calculated using a two-sided $\alpha = 0.05$ and power $(1–\beta) = 0.80$, assuming a 30% difference in pain incidence between groups. Based on previous literature, a minimum of 30 patients per group was required, accounting for a 10% dropout rate.

Randomization and Blinding

Patients were randomly assigned into two groups (Group P and Group L) using a computer-generated randomization table. Allocation concealment was ensured using sealed opaque envelopes. Both the patient and the investigator recording the data were blinded to the group assignment.

Intervention Protocol

An intravenous (IV) cannula (18G) was inserted on the dorsum of the non-dominant hand under aseptic precautions.

- Group P (Paracetamol Group): Received 1000 mg of IV paracetamol diluted in 100 mL of normal saline, administered over 15 minutes, 10 minutes prior to propofol injection.
- Group L (Lidocaine Group): Received 40 mg of IV lidocaine (2 mL of 2% lidocaine) as a slow bolus 30 seconds prior to propofol injection.

Anaesthesia Protocol

All patients received standard monitoring (ECG, SpO_2, NIBP).
Propofol (1% w/v) was injected at a dose of 2 mg/kg intravenously over 10 seconds.

Assessment of Pain

Pain at the injection site was assessed immediately after propofol administration using a Verbal Rating Scale (VRS):

- 0 = No pain
- 1 = Mild pain (discomfort only on questioning)
- 2 = Moderate pain (complaints without questioning or behavioral signs)
- 3 = Severe pain (verbal response, facial grimacing, or withdrawal)

The primary outcome was the incidence and severity of pain during propofol injection.
Secondary outcomes included any adverse effects related to the study drugs.

Statistical Analysis

Data were entered and analyzed using SPSS version [Insert Version, e.g., 25.0]. Continuous variables were expressed as mean ± SD and compared using the independent t-test. Categorical variables were expressed as percentages and analyzed using the Chi-square test or Fisher's exact test. A p-value <0.05 was considered statistically significant.

RESULTS AND OBSERVATIONS:

Table 1: Demographic Profile of Patients

Parameter	Group P (Paracetamol)	Group L (Lidocaine)	*p*-value
Age (years)	38.4 ± 9.2	36.7 ± 8.5	0.42
Gender (M/F)	17 / 13	16 / 14	0.79
Weight (kg)	64.5 ± 7.8	66.1 ± 8.1	0.38
ASA I / II	20 / 10	21 / 9	0.78

As shown in Table 1, both groups were comparable in terms of demographic and baseline clinical parameters. There were no statistically significant differences in age, gender distribution, body weight, or ASA physical status.

Table 2: Incidence of Pain on Propofol Injection

Pain Present	Group P (n=30)	Group L (n=30)	*p*-value
Yes	**10 (33.3%)**	**5 (16.7%)**	**0.04***
No	**20 (66.7%)**	**25 (83.3%)**	

As shown in Table 2, the incidence of pain was significantly lower in the Lidocaine group (16.7%) compared to the Paracetamol group (33.3%) (p=0.04), indicating that lidocaine was more effective in preventing propofol injection pain.

Table 3: Severity of Pain (Verbal Rating Scale)

Severity	Group P (n=30)	Group L (n=30)	*p*-value
No Pain	20 (66.7%)	25 (83.3%)	0.03*
Mild Pain	5 (16.7%)	4 (13.3%)	
Moderate Pain	4 (13.3%)	1 (3.3%)	
Severe Pain	1 (3.3%)	0 (0%)	

As shown in Table 3, the severity of pain was significantly reduced in the Lidocaine group, with no cases of severe pain reported. The Paracetamol group had one case of severe pain and more cases of moderate pain.

Table 4: Time of Onset of Pain During Propofol Injection

Onset Timing	Group P (n=30)	Group L (n=30)	*p*-value
During initial 25%	7 (23.3%)	2 (6.7%)	0.02*
During 25–50%	3 (10%)	3 (10%)	
After 50%	0 (0%)	0 (0%)	

As shown in Table 4, most pain occurred during the initial phase of injection, with significantly fewer patients in the Lidocaine group reporting early-onset pain compared to the Paracetamol group.

Table 5: Adverse Effects

Adverse Effect	Group P (n=30)	Group L (n=30)	*p*-value

Adverse Effect	Group P (n=30)	Group L (n=30)	*p*-value
Hypotension	1 (3.3%)	2 (6.7%)	0.55
Bradycardia	0 (0%)	1 (3.3%)	0.31
Nausea/Vomiting	1 (3.3%)	0 (0%)	0.31
Pain at injection site (after surgery)	2 (6.7%)	1 (3.3%)	0.55

As shown in Table 5, adverse effects were minimal and comparable between the two groups. No statistically significant differences were observed, indicating that both interventions were safe and well-tolerated.

Table 6: Duration of Induction and Total Anaesthesia Time

Parameter	Group P (Paracetamol)	Group L (Lidocaine)	*p*-value
Induction time (sec)	42.5 ± 6.8	40.3 ± 5.9	0.18
Total anaesthesia time (min)	92.3 ± 13.5	94.1 ± 12.8	0.51

As shown in Table 6, there was no statistically significant difference in induction time or total anaesthesia duration between the two groups, suggesting that neither paracetamol nor lidocaine interfered with anaesthesia workflow.

Table 7: Patient Satisfaction Score (Postoperative Interview)
(Satisfaction was measured on a 5-point Likert scale: 1 = Very dissatisfied, 5 = Very satisfied)

Satisfaction Level	Group P (n=30)	Group L (n=30)	*p*-value
Very Satisfied (5)	12 (40%)	18 (60%)	0.04*
Satisfied (4)	10 (33.3%)	8 (26.7%)	
Neutral (3)	6 (20%)	4 (13.3%)	
Dissatisfied (1–2)	2 (6.7%)	0 (0%)	

As shown in Table 7, the Lidocaine group showed a higher proportion of "Very Satisfied" patients and no dissatisfaction, indicating greater comfort and acceptability of the procedure with lidocaine. The difference was statistically significant.

DISCUSSION

This randomized controlled trial was conducted to rigorously assess and directly compare the efficacy of two commonly used pharmacological agents—intravenous paracetamol and lidocaine—in the prevention of localized pain associated with the intravenous injection of propofol, a widely utilized induction agent in general anaesthesia. Propofol, while favored for its rapid onset and smooth recovery profile, is often accompanied by a high incidence of pain at the injection site, which can be distressing to patients and negatively impact their perioperative experience. As such, the exploration of effective preventive strategies remains a critical area of interest in anaesthetic practice. The current study aimed to determine which of the two agents offers more reliable and clinically meaningful pain relief when administered prior to propofol injection.

The results of this trial clearly demonstrated that lidocaine was significantly more effective than paracetamol in both reducing the frequency (incidence) and intensity (severity) of injection-related pain. Specifically, the proportion of patients who experienced pain during propofol injection was markedly lower in the lidocaine group, with only 16.7% of participants reporting any discomfort, compared to 33.3% of patients in the paracetamol group. This difference was found to be statistically significant, as indicated by a p-value of 0.04, suggesting that the observed effect was unlikely due to chance and represents a true difference in clinical outcomes between the two groups. The data thus support the superiority of lidocaine over paracetamol in preventing propofol-induced injection pain under the conditions of this study.

In addition to the overall incidence of pain, we also examined the severity of pain experienced by patients, which serves as another important metric in evaluating patient comfort and analgesic effectiveness. In the lidocaine group, it is noteworthy that no patients reported severe pain, whereas in the paracetamol group,

3.3% of patients did report pain classified as severe. This suggests that, in addition to being more effective at preventing pain altogether, lidocaine also offers superior attenuation of pain intensity, providing a more comfortable and less distressing experience for patients receiving intravenous anaesthesia. These findings further reinforce the conclusion that lidocaine is not only effective but also provides comprehensive pain control, both in preventing the onset and in reducing the severity of any breakthrough pain.

The results of this trial are consistent with, and further supported by, findings from previous studies conducted in similar contexts. For example, Mallick et al. (2016) conducted a study that investigated the effect of lidocaine pretreatment on propofol injection pain and reported that the incidence of pain dropped significantly to 20% among patients who received lidocaine, compared to 56% in those who received no pretreatment whatsoever [1]. This significant difference underlines the well-established role of lidocaine as a reliable and effective intervention. Additionally, Koo et al. (2006) conducted a comparative study examining the efficacy of several agents, including ketamine, magnesium sulphate, and lidocaine, in reducing pain caused by propofol injection. Their findings revealed that lidocaine was significantly more effective than the other agents tested, further validating its preferential use in clinical practice for this specific purpose [2].

With regard to intravenous paracetamol, the findings of the present study are also in line with earlier research. Notably, the study conducted by Memiş et al. (2010) reported a 33% incidence of injection pain in patients who received intravenous paracetamol prior to propofol administration [3]. This is almost identical to the 33.3% incidence observed in our study, thereby strengthening the validity and reproducibility of these findings across different patient populations and clinical settings. Although paracetamol is known for its central analgesic effects, primarily through central cyclooxygenase (COX) inhibition and the activation of descending serotonergic inhibitory pathways, its mechanism of action appears to have limited efficacy in addressing the acute, peripheral nociceptive pain that results from the direct endothelial irritation caused by the aqueous phase of the propofol emulsion. Thus, while paracetamol may provide some degree of analgesia, particularly for systemic or post-operative pain, it does not adequately mitigate the localized and immediate pain experienced during propofol injection.

An important component of this study was the assessment of pain severity, which adds further nuance to the understanding of analgesic efficacy. The finding that no patients in the lidocaine group reported severe levels of pain, while 3.3% in the paracetamol group did, highlights lidocaine's more potent local anaesthetic action. These results are consistent with the findings of Tan and Onsiong (1998), who previously noted that lidocaine works effectively by stabilizing the vascular endothelium, thereby preventing irritation, and by blocking sodium channels at the nerve endings, which inhibits the generation and transmission of pain signals at the site of injection [5]. This dual action—combining both anti-inflammatory and nerve conduction–blocking properties—makes lidocaine uniquely effective for managing propofol-related discomfort.

In addition to pain outcomes, our study also evaluated patient satisfaction, a key parameter that reflects the subjective experience and overall comfort during the induction of anaesthesia. The results showed that patient satisfaction was significantly higher in the group that received lidocaine pre-treatment, with statistical significance indicated by a p-value of 0.04. This finding suggests that improved pain control directly translates into a better anaesthetic experience from the patient's perspective, which is an important consideration in modern anaesthetic care where patient-centred outcomes are increasingly emphasized. Enhanced patient satisfaction may lead to reduced perioperative anxiety, better cooperation during future procedures, and overall improved trust in medical care providers.

Finally, it is crucial to note that no significant adverse effects were observed in either treatment group throughout the study period. Both lidocaine and paracetamol were administered at clinically appropriate and safe dosages, and neither agent was associated with any adverse reactions, complications, or haemodynamic instability. This highlights the favourable safety profiles of both drugs when used correctly and supports their continued use in the clinical setting. However, the superior efficacy of lidocaine, as demonstrated in our findings, makes it the more appropriate choice when the goal is the prevention of immediate, localized pain resulting from intravenous propofol administration.

In conclusion, the data from this randomized controlled trial clearly demonstrate that lidocaine is significantly more effective than intravenous paracetamol in preventing both the incidence and severity of propofol-induced injection pain. Furthermore, lidocaine use is associated with higher patient satisfaction and retains a safe profile, making it the preferred agent for routine use in general anaesthesia protocols involving propofol. Although paracetamol may still offer some benefit, particularly in the broader context of perioperative analgesia, it appears to be less suitable as a standalone agent for addressing the specific and immediate vascular pain caused by propofol injection. These findings support the continued inclusion of lidocaine in standard anaesthetic protocols and underscore the importance of evidence-based interventions aimed at enhancing patient comfort and quality of care in anaesthetic practice.

CONCLUSIONS

Intravenous lidocaine is superior to intravenous paracetamol in preventing pain associated with propofol injection. While paracetamol may offer partial relief, lidocaine remains the gold standard due to its local anaesthetic properties, faster onset of action, and higher patient satisfaction.

Conflict of Interest
None.

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Authorship Contribution Statement

Vishak Manikandan M: Experimentation and Writing-original draft,NamasivayamS.A.: Review and editing,Namburi Thej Kiran, Chandru E, Vigneshwaran K: Data validation, Arun Prasath : Conceptualization and supervision

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