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Original Article

Evaluation of the Effectiveness of Lidocaine and Ketamine Injections in Reducing Pain from Propofol Injection in General Anesthesia

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Abstract

Background: Propofol is a widely used anaesthetic agent, known for its rapid onset and short duration of action. However, pain at the injection site remains a common side effect that may affect patient comfort and the overall quality of anaesthesia. Lidocaine and ketamine are commonly used adjuncts to reduce injection pain; however, their comparative effectiveness remains unclear. This study aimed to evaluate the efficacy of lidocaine and low-dose ketamine in reducing the pain associated with propofol injection. **Methods**: This double-blind, randomised controlled trial involved 50 adult patients randomly assigned to either the ketamine group (0.1 mg/kg) or lidocaine group (1 mg/kg). Both agents were administered intravenously before propofol injection (2 mg/kg). Pain intensity was assessed using the Verbal Rating Scale (VRS) at several intervals post-injection. Statistical analysis was performed using the Wilcoxon test for within-group comparisons and Mann-Whitney U test for between-group comparisons. **Results**: In the ketamine group, 52% of the participants reported no pain, 32% experienced mild pain, 12% experienced moderate pain, and 4% reported severe pain. In contrast, 76% of the lidocaine group reported no pain, 20% reported mild pain, and 4% reported moderate pain with no reports of severe pain. A significant difference was found between the two groups ($p = 0.001$ for lidocaine vs. $p = 0.012$ for ketamine), indicating that lidocaine was more effective at reducing injection pain. **Conclusion**: Lidocaine is more effective than ketamine in reducing the pain caused by propofol injection, providing superior analgesia. This suggests that lidocaine is the preferred option to prevent injection pain during anaesthesia induction.

Keywords: Propofol, Lidocaine, Ketamine, Injection pain, Anesthesia, Pain management

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INTRODUCTION

General anaesthesia is a pharmacologically induced state of reversible unconsciousness, typically achieved through the administration of intravenous agents, inhalational agents, or a combination thereof. Currently, intravenous induction agents, such as Propofol and Ketamine, are more frequently employed [1]. Propofol, a widely used intravenous anaesthetic, is integral to the induction and maintenance of general anaesthesia in routine clinical practice [2]. It is preferred because of its rapid onset, short duration of action, ease of titration, well-established side effect profile, and expedited recovery compared with other agents such as thiopental [3,4]. Despite its advantages, propofol administration is often associated with injection pain, characterised by a burning or sharp, intense sensation [5,6]. The incidence of propofol injection pain is reported to range from 28% to 90%. Studies by Scott et al. have documented that the incidence of injection pain varies from 25% to 74%, with severe pain reported in 32% to 52% of cases. Other studies have reported higher incidences of up to 91.7% [7-10].

The chemical mechanism of propofol-induced injection pain involves direct irritation through kininogen release upon contact with the vascular endothelium. This activates afferent nerve endings between the tunica media and intima of the blood vessels [11]. The oil-emulsifying vehicle of propofol may irritate blood vessel walls [5]. Kininogen release initiates a local kinin cascade that is amplified by prostaglandins [12]. Methods to reduce injection pain include altering the injection speed, modifying the vehicle, dilution, and using adjuncts such as lidocaine, although none are entirely effective [11, 5]. Combining lidocaine with propofol remains one of the most common strategies for alleviating injection pain [13,14].

This study evaluated the efficacy of lidocaine and low-dose ketamine in the alleviation of propofol-induced pain. Research shows that administering lidocaine (0.5 mg/kg with a tourniquet before propofol injection is most effective [5]. Ketamine has shown potential for reducing injection pain at small doses [13,15]. However, the results remain inconsistent and the optimal strategy remains undetermined. This study examined the pain scales following propofol injection, lidocaine pre-injection, and ketamine pre-injection in adult patients to assess the efficacy of these strategies.

MATERIALS AND METHODS

This study employed an experimental and analytical research design utilising a double-blind, randomised controlled trial methodology. This study aimed to investigate the effects of lidocaine and low-dose ketamine on the pain scale associated with propofol injection. A cohort of 50 patients scheduled for elective surgeries at a Regional Hospital in Thailand will be selected for participation. The participants will be randomly allocated into two groups. Group I received a lidocaine injection (1 mg/kg body weight) followed by propofol (2 mg/kg body weight), whereas Group II received a low-dose ketamine injection (0.1 mg/kg body weight) followed by propofol (2 mg/kg body weight). Post-injection pain intensity will be assessed using a Verbal Rating Scale (VRS) ranging from 0 to 3.

The sample size was determined using a statistical formula to ensure sufficient power to detect significant differences between the groups. Each group consisted of 21 participants, with an additional 20% included to account for potential attrition, resulting in 25 participants per group for a total of 50 participants. Inclusion criteria included patients aged 18 to 64 years, with ASA I-II physical status, scheduled for elective surgery under general anaesthesia, and without contraindications to lidocaine or ketamine. Exclusion criteria included allergies to the study drugs, serious neurological or psychiatric conditions, and specific health conditions, such as pregnancy or thrombophlebitis.

The study commenced with the acquisition of ethical approval from the Health Research Ethics Committee. Participants who satisfied the inclusion and exclusion criteria were randomly allocated to one of two groups. Upon obtaining informed consent, participants will be prepared in the operating room for standard monitoring procedures, including electrocardiography (ECG), non-invasive blood pressure measurement, and pulse oximetry. Once the participant was stabilised and monitoring was established, an 18-gauge catheter was inserted into the dorsal hand vein and a three-way stopcock was attached to facilitate the administration of fluids and medications. Normal saline was infused at a rate of 5 mL/kg/hour.

Prior to any injections, participants will be briefed on the pain assessment process using the Verbal Rating Scale (VRS), which evaluates pain intensity associated with propofol injection. The VRS categorises pain into four levels: 0 (no pain); 1 (mild pain); 2 (moderate pain); and 3 (severe pain). Once the setup was completed, the intervention proceeded.

A tourniquet was applied to the upper arm to induce temporary venous stasis, thereby prolonging the retention time of the injected drug in the vein. Subsequently, the three-way stopcock was closed to prevent entry of saline. In Group I, 1 mg/kg body weight of lidocaine will be administered intravenously over 15 s, whereas in Group II, 0.1 mg/kg body weight of ketamine was administered intravenously at the same rate. The tourniquet

will remain in place for 30 seconds to ensure adequate drug action before proceeding to the subsequent stage.

Following the designated time period, the tourniquet was released, and propofol (2 mg/kg body weight) was administered intravenously at a rate of 1 mL/s for 30 s. Subsequently, the three-way stopcock was opened to re-establish the flow of normal saline. Immediately after administration of propofol, the patient will be queried regarding any pain or discomfort experienced by the hand or arm. If the patient reports pain, the intensity will be assessed at 5-second intervals, with the highest pain score being documented. In the absence of reported pain, the pain score was 0.

Upon loss of consciousness, additional pharmacological agents were administered in accordance with the anaesthesia protocol. Fentanyl (2 μg/kg) and rocuronium (0.6 mg/kg) will be administered, followed by intubation for the surgical procedure. Anaesthesia was maintained appropriately and the patient was meticulously monitored throughout the procedure. Post-procedure, data pertaining to the patients' characteristics (age, sex, weight, ASA classification) and pain scale scores will be documented. These data will subsequently be subjected to statistical analysis to compare pain outcomes between the two groups.

The data will be analysed using appropriate statistical methods, including the Kruskal-Wallis test and Mann-Whitney U-test for pain intensity and the χ^2 test for pain incidence. Statistical significance was set than 0.05. The findings of this study are anticipated to contribute to the identification of effective strategies for mitigating propofol injection pain, which remains a prevalent challenge in anaesthesia practice.

RESULTS

This study was conducted from January to February 2019 at the Surgical Installation of the Regional Hospital in Thailand. This study compared pain intensity following lidocaine and low-dose ketamine injections administered before propofol injection. The study included 50 samples, with 25 participants receiving either lidocaine-propofol or ketamine-propofol. The characteristics of the sample are listed in Table 1.

Table 1 Sample Characteristics

Characteristic	Ketamine Group	%	Lidocaine Group	%	p-Value
Gender					0.043
Male	13	52	6	24	
Female	12	48	19	76	
Age					0.437
20-39 years	16	64	13	52	
40-59 years	9	36	12	48	
ASA					0.779
ASA 1	13	52	12	48	
ASA 2	12	48	13	52	
BMI					0.315
Normal	21	84	14	56	
Overweight	4	16	10	40	
Obesity	0	0	1	4	
Injection Site					0.641
Dorsum Hand	23	92	22	88	
Dorsum Foot	2	8	3	12	
Total	25	100	25	100	

Samples in both groups were homogeneous in terms of age, ASA classification, BMI, and injection site ($p>0.05$). The sex distribution differed significantly, with more females in the lidocaine group ($p = 0.043$). The 40-59 years age group included 9 participants (36%)

in the ketamine group and 12 (48%) in the lidocaine group, with older participants more frequently taking ketamine. In the ketamine group, 21 participants (84%) had a normal BMI, and 14 (56%) in lidocaine. The lidocaine group had more overweight participants (10, 40%) than the ketamine group (4, 16%).

Table 2. Pain Intensity Following Propofol Injection Preceded by Ketamine

Group	No Pain	Mild Pain	Moderate Pain	Severe Pain	p-Value
Ketamine	13	8	3	1	0.012*
	52%	32%	12%	4%	

Note: *Wilcoxon Test

As illustrated in Table 2, in the ketamine group, 13 participants (52%) reported an absence of pain, 8 participants (32%) experienced mild pain, 3 participants (12%) reported moderate pain, and 1 participant (4%) experienced severe pain. The distribution of pain intensity was statistically significant, as determined using the Wilcoxon test (p = 0.012).

Table 3. Pain Intensity Following Propofol Injection Preceded by Lidocaine

Group	No Pain	Mild Pain	Moderate Pain	Severe Pain	p-Value
Lidocaine	19	5	1	0	0.001*
	76%	20%	4%	0%	

Note: *Wilcoxon Test

In the lidocaine group, 19 participants (76%) had no pain, five (20%) had mild pain, and one (4%) had moderate pain, with no severe pain reported. The distribution of pain intensity was statistically significant (p = 0.001, Wilcoxon test).

Table 4 Comparison of Pain Intensity Between Lidocaine and Ketamine Groups

Pain Level	Ketamine Group	Lidocaine Group	Total	p-Value
No Pain	13 (52.0%)	19 (76.0%)	32	0.074
Mild Pain	8 (32.0%)	5 (20.0%)	13	
Moderate Pain	3 (12.0%)	1 (4.0%)	4	
Severe Pain	1 (4.0%)	0 (0.0%)	1	
Total	25 (100%)	25 (100%)	50	

Noted: *Mann-Whitney Test

Analysis of Table 4 shows that more participants in the lidocaine group reported no pain (76%) than in the ketamine group (52%). No severe pain was reported in the lidocaine group, whereas one ketamine participant (4%) reported severe pain. The Mann-Whitney test showed no statistically significant difference in pain levels between the groups (p = 0.074).

The findings showed that lidocaine administration before propofol injection resulted in lower pain intensity than ketamine administration. While both treatments reduced pain, lidocaine showed higher rates of pain absence, suggesting that it may be more effective for propofol injection. However, the lack of statistical significance warrants further investigation of the pain perception factors.

DISCUSSION

This study assessed pain intensity following propofol injection preceded by lidocaine and low-dose ketamine. Both agents are used to reduce pain during propofol injection under clinical anaesthesia. Lidocaine is used as a pre-injection agent or in combination

with propofol, whereas intravenous ketamine has shown effectiveness in preventing propofol-induced pain [15,16].

These findings substantiate the effectiveness of ketamine in the mitigation of propofol-induced pain. In the ketamine cohort, 52% of the participants reported no pain, while 32% experienced mild pain, which is consistent with previous observations [17]. Other studies have indicated that ketamine reduces postoperative pain and morphine requirement [18,19]. Administering ketamine at a dosage of 100 μg/kg prior to propofol injection is both safe and efficacious [20].

The lidocaine group exhibited greater pain reduction, with 76% of the patients reporting no pain and 4% reporting moderate pain. These results are in agreement with those of Picard and Tramer's meta-analysis, which identified lidocaine with a tourniquet before propofol injection as highly effective [21]. While previous studies reported a 40% pain incidence with lidocaine, this study demonstrated a lower incidence with no severe pain reported.

The mechanisms by which lidocaine and ketamine alleviate propofol-induced pain are based on their interactions with the pain pathways. Propofol is formulated as an oil-in-water emulsion containing soybean oil, glycerol, and egg phosphatide, which creates a biphasic structure capable of irritating endothelial cells in veins, thereby inducing pain through bradykinin release [22]. Bradykinin activates nociceptors in the venous endothelium, a process exacerbated by nitric oxide, which facilitates vasodilation and increases vascular permeability to both propofol and bradykinin, resulting in pain [23]. Ketamine, an NMDA receptor antagonist, inhibits central nervous system pain pathways, whereas lidocaine, a local anaesthetic, blocks sodium channels in peripheral nerves, thereby inhibiting pain transmission [24,25].

Both groups exhibited reduced pain intensity compared to no pre-treatment, but the lidocaine pre-injection group had the lowest incidence of severe pain, indicating that lidocaine with a tourniquet is more effective than ketamine. Previous studies have shown that lidocaine pre-injection offers superior pain relief compared with ketamine [26]. The mixed lidocaine-propofol solution reduced the non-lipophilic fraction of propofol responsible for the injection pain. Eriksson et al. found that mixing lidocaine with propofol decreases the solution pH, potentially reducing pain by diminishing bradykinin formation and modulating nitric oxide production [25]. Although this mixed approach reduces pain, it is less effective than pre-injection lidocaine, which acts locally to block pain transmission.

CONCLUSION

This study corroborates the finding that both lidocaine and ketamine are effective in mitigating the pain associated with propofol injection, with lidocaine administered in conjunction with a tourniquet offering superior analgesic efficacy. These findings underscore the significance of the pharmacological properties of drugs and the method of administration. Further research is warranted to determine the optimal dosing and timing to enhance anaesthesia practice and improve patient comfort.

Abbreviations: VRS, Verbal Rating Scale; ECG, Electrocardiography.

Supplementary Materials: The datasets generated or analysed during this research are available from the corresponding author upon request.

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Informed Consent Statement: Informed consent was obtained from all the subjects involved in the study.

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