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Original Article

Anaesthesia Section

Efficacy of Paracetamol Plus Lignocaine versus Lignocaine Alone for Pain on Propofol Injection: A Randomised Controlled Trial

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ABSTRACT

Introduction: Propofol triggers endothelial irritation and nociceptor activation, producing early injection pain. Lignocaine blunts this response but does not abolish it completely. A brief systemic analgesic may help close this residual gap. This randomised evaluation tested whether intravenous paracetamol added to lignocaine further reduces the frequency and intensity of pain during induction.

Aim: To assess the efficacy of paracetamol plus lignocaine versus lignocaine alone for propofol injection pain.

Materials and Methods: This double-blinded, randomised, parallel-group trial was conducted at a tertiary care centre in the Department of Anaesthesiology, Krishna Institute of Medical Sciences (Deemed to be University), Karad, Maharashtra, India, from May 2023 to August 2024 (16 months) {n=98; American Society of Anaesthesiologists (ASA) I-II adults, 20–60 years; Body Mass Index (BMI) 19-30 kg/m^2}. Group 1 received intravenous paracetamol 15 mg/kg infused over 10 minutes before theatre, plus lignocaine 2% (2 mL, diluted to 5 mL) with 2-minute venous occlusion. Group 2 received the identical lignocaine protocol without paracetamol (1:1, n=49 each). After tourniquet release, 25% of the propofol induction dose (2.5 mg/kg total) was injected over five seconds through the same cannula and pain was scored immediately on a 0-3 Verbal Rating Scale (VRS). Primary comparisons used risk ratio with 95% confidence intervals and Chi-square (χ^2); ordinal severity was analysed using a trend/non parametric test. Two-sided α=0.05; intention-to-treat analysis was applied.

Results: Baseline characteristics were similar between groups: age 38.2±10.1 vs 37.6±9.8 years; sex 28/21 vs 26/23 (M/F); BMI 24.9±2.8 vs 25.1±2.7 kg/m^2; ASA I/II 30/19 vs 32/17 (Group 1 vs Group 2). Pain occurred in 12/49 patients receiving paracetamol+lignocaine versus 28/49 receiving lignocaine alone {Relative Risk (RR) 0.43, 95% Confidence Interval (CI) 0.25-0.74; Absolute Risk Reduction (ARR) 32.7%; Number Needed to Treat (NNT=4); p=0.001). Severity distribution: none 37 vs 21; mild 10 vs 14; moderate 2 vs 10; severe 0 vs 4 (p=0.0013). No patient in either group developed injection-site complications (erythema, phlebitis, or swelling). Both regimens were well-tolerated.

Conclusion: Intravenous paracetamol, when added to standard lignocaine pretreatment, substantially decreases both the likelihood and intensity of propofol injection pain without causing new local adverse effects. This approach is simple, inexpensive and immediately transferable to routine practice.

Keywords: Analgesics, Injections, Intravenous, Non narcotic, Pain measurement, Perioperative care, Treatment outcome

INTRODUCTION

Propofol is a widely used intravenous anaesthetic for induction, maintenance, ICU and procedural sedation due to its rapid onset and recovery. However, pain on injection, reported in up to 70% of patients and described as burning, stinging, or aching, can undermine the patient experience at the outset of care [1]. Preventing this pain is clinically meaningful, improving patient satisfaction, dampening behavioural responses at induction and streamlining workflow [2].

Propofol injection pain is multifactorial. Although formulated as a near-neutral lipid emulsion, its aqueous phase may be relatively acidic. Contact with venous endothelium activates the kallikrein–kinin cascade, leading to bradykinin release and increased vascular permeability, as well as sensitisation of nociceptors [3,4]. C- and Aδ-fibre activation has been linked to Transient Receptor Potential Vanilloid 1 (TRPV1) channel stimulation (the “capsaicin-like” burn) [5,6], while inflammatory mediators (histamine, prostaglandins) and mechanical factors (distension/irritation in small, low-flow veins) amplify symptoms compared to larger antecubital sites [7].

Mitigation strategies include using larger veins, slower injection rates and cooled propofol [3]. Among pharmacological options, lignocaine is the most consistently effective single agent, administered either as a brief pretreatment (± venous occlusion) or premixed with propofol [8]. Its benefits reflect voltage-gated sodium channel blockade, endothelial stabilisation and TRPV1 modulation; meta-analyses and clinical trials demonstrate meaningful reductions in pain incidence and severity, particularly with premix or short occlusion [9]. Yet lignocaine alone does not abolish pain in all patients.

This has prompted multimodal, mechanism-based approaches pairing local perivenous control with centrally acting analgesia. Intravenous paracetamol exerts analgesic effects via central Cyclooxygenase inhibition (relative COX-2/putative COX-3), enhancement of descending serotonergic inhibition and TRPV1/Cannabinoid Receptor Type 1 (CB1) modulation via N-arachidonoylphenolamine (AM404) [10]. Preadministration has been associated with lower pain scores and fewer painful responses, with a favourable safety profile within recommended doses [10]. Mechanistically, lignocaine provides immediate local blockade and endothelial stabilisation, while paracetamol attenuates central sensitisation and further modulates TRPV1/CB1 signaling, addressing both early peripheral and sustained central components [11,12]. Evidence from reviews and randomised trials supports that the combination outperforms either agent alone and is inexpensive, simple and widely adoptable, including in ambulatory settings where patient experience is pivotal [11,13-15].

However, gaps remain: heterogeneous protocols (venous site, timing, dose, occlusion), inconsistent pain scales, an emphasis on incidence over ordinal severity and limited data on local tolerability when agents are combined [3,16]. Accordingly, the present study aimed to evaluate whether adding intravenous paracetamol to lignocaine pretreatment reduces propofol injection pain during anaesthetic induction. The primary objective was to compare the

incidence of pain (VRS ≥1) between paracetamol + lignocaine and lignocaine-alone groups. The secondary objectives were to: (i) compare the distribution of pain severity (VRS 0-3) and (ii) assess local injection-site tolerability (erythema, wheal, thrombophlebitis).

MATERIALS AND METHODS

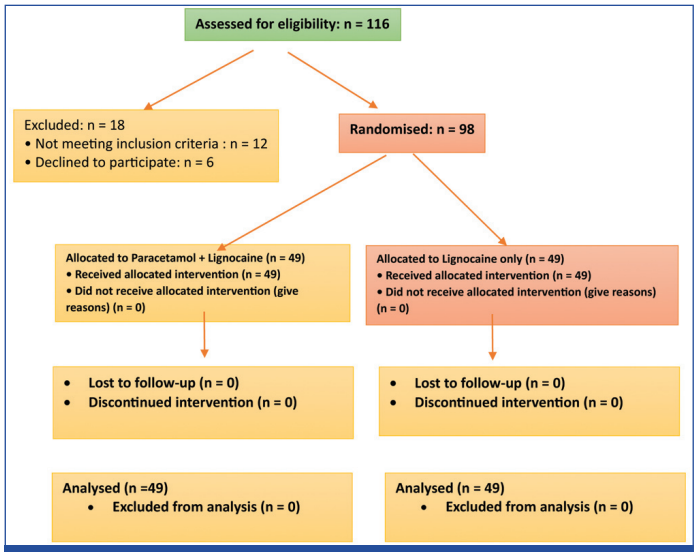
The present was a randomised, double-blind, parallel-group controlled trial conducted at a tertiary care centre in the Department of Anaesthesiology, Krishna Institute of Medical Sciences (Deemed to be University), Karad, Maharashtra, India, from May 2023 to August 2024 (16 months). "Double-blind" indicates that both participants and the outcome assessor were masked to group allocation; anaesthetists followed a standardised script. Ethical approval was obtained from KIMSDU/IEC/03/2023 (Protocol 346/2022-2023, dated 05-Apr-2023). All participants provided written informed consent.

Sample size calculation: A priori sample size was 98 (49 per arm) to detect a 20-percentage-point absolute reduction in pain incidence (26% to 6%) at α=0.05 with 80% power [17], computed using OpenEpi v3.01 and cross-checked in G*Power 3.1.

Inclusion criteria: Adults aged 20-60 years, ASA I–II, BMI 19-30 kg/m^2, scheduled for elective surgery under general anaesthesia, with peripheral IV access suitable for dorsal-hand or forearm cannulation were included in the study.

Exclusion criteria: Refusal to participate; hypersensitivity to propofol, lignocaine (lidocaine), or paracetamol (acetaminophen); egg/soy allergy; chronic pain or regular analgesic use; significant cardiovascular, hepatic, or renal disease; pregnancy; ASA ≥III; or any condition judged to increase risk.

Of 116 patients screened, 18 were excluded (12 ineligible, 6 declined participation) and 98 were randomised (49 per arm). No patients were lost to follow-up; all 98 were analysed [Table/Fig-1].



[Table/Fig-1]: Consolidated Standards of Reporting Trials (CONSORT) diagram.

Study Procedure

Concealment: A computer-generated 1:1 sequence with permuted blocks (sizes undisclosed) was prepared by an independent pharmacist [Table/Fig-1]. Allocation was concealed using sequentially numbered, opaque, sealed envelopes. Masking was preserved with identical syringes matched for appearance and volume; the pharmacist retained the code until database lock.

Study arms:

- Control arm: Lignocaine only.
- Intervention arm: Paracetamol + Lignocaine.

Peri-anaesthetic management: Institutional fasting protocols were followed. Premedication in the preoperative area included ranitidine 0.5 mg/kg i.v., metoclopramide 0.15 mg/kg i.v., glycopyrrolate 0.004 mg/kg i.v. and midazolam 0.05 mg/kg i.v.

In theatre, Electrocardiogram (ECG), non invasive blood pressure and pulse oximetry were applied; a wide-bore peripheral cannula was inserted; Ringer's lactate 10 mL/kg was commenced; and oxygen 6 L/min was administered via a Hudson mask.

Interventions: Both groups underwent a uniform short venous-occlusion lignocaine pretreatment in the vein planned for propofol injection.

Paracetamol + Lignocaine (Intervention): Paracetamol 15 mg/kg i.v. (maximum 1 g) was infused over 10 minutes before theatre entry. In theatre, 2 mL of 2% lignocaine, diluted with normal saline to 5 mL, was prepared for venous pretreatment.

Lignocaine only (Control): The same lignocaine preparation (2 mL of 2% diluted to 5 mL) was used; no paracetamol was administered.

Venous-occlusion technique (both arms): A pneumatic tourniquet or elastic band was placed approximately 20 cm proximal to the i.v. site to achieve venous occlusion. The 5 mL lignocaine was injected and the tourniquet was released after two minutes [11].

Propofol test dose and pain scoring: Immediately after tourniquet release, 25% of a 2.5 mg/kg propofol induction dose was injected over five seconds through the same cannula to standardise early nociceptive exposure. Pain on injection was recorded immediately using a 0-3 Verbal Rating Scale (VRS):

0= None

1= Mild (on questioning, no behavioural sign)

2= Moderate (on questioning with behavioural sign)

3= Severe (vocal response, facial grimace, or arm withdrawal)

The i.v. site was inspected for erythema, wheal, induration and tenderness. Anaesthesia then proceeded with the remaining 75% of the propofol dose until loss of responsiveness. Fentanyl 1-2 µg/kg i.v. and vecuronium 0.08-0.1 mg/kg i.v. were administered for tracheal intubation as per institutional practice.

Outcomes:

Primary outcome: Incidence of propofol injection pain, defined as VRS ≥1 after the standardised test bolus.

Secondary outcomes:

1. Severity distribution across VRS 0-3, with emphasis on moderate–severe pain (VRS 2-3)
2. Local injection-site reactions (immediate and within 24 hours)
3. Peri-induction hemodynamics for safety: heart rate (beats/min) and mean arterial pressure (mmHg) at predefined timepoints:

T0: Baseline (pre-drug)

T1: Post-occlusion, pre-propofol bolus

T2: 1 min after 25% propofol test bolus

T3: Pre-laryngoscopy

T4: 1 min post-intubation

Safety thresholds were predefined as follows: hypotension {Mean Arterial Pressure (MAP) <65 mmHg or ≥20% fall from T0}, bradycardia {Heart Rate (HR) <50 bpm or ≥20% fall}, tachycardia (HR >120 bpm or ≥20% rise). Any threshold crossing and need for rescue interventions (fluids, vasopressors, or atropine) were recorded.

STATISTICAL ANALYSIS

Analyses followed the intention-to-treat principle. Categorical outcomes were expressed as risk ratios (95% CI) and compared using χ^2 (Fisher's-exact test where appropriate). Ordinal VRS severity was compared using the Mann-Whitney U test (primary), with a prespecified Cochran-Armitage trend test yielding concordant inference. Baseline continuous variables were tested for normality (Shapiro-Wilk) and compared using t-test or Mann-Whitney U as appropriate. Two-sided α=0.05 was applied. No data

imputation was performed. Statistical analyses were conducted using Statistical Package for the Social Sciences (SPSS) version 22.0 and Excel v16.

RESULTS

A total of 98 patients were enrolled and randomly assigned equally into two groups: Group 1 (Paracetamol + Lignocaine 2%, n=49) and Group 2 (Lignocaine 2% alone, n=49). All participants completed the study protocol without dropouts.

Baseline characteristics: Demographic and clinical variables (age, gender distribution, BMI, ASA physical status) were comparable between groups, with no statistically significant differences (all p>0.05), confirming effective randomisation [Table/Fig-2].

Variables	Group 1 (Paracetamol + Lignocaine) (n=49)	Group 2 (Lignocaine alone) (n=49)	p-value
Age (years, mean±SD)	38.2±10.1	37.6±9.8	0.74[1]
Gender (M/F)	28/21	26/23	0.68[2]
BMI (kg/m², mean±SD)	24.9±2.8	25.1±2.7	0.62[1]
ASA I/II	30/19	32/17	0.71[2]

[Table/Fig-2]: Baseline demographic and clinical characteristics.
[1]Student's t-test (two-tailed), df = 96; [2] Chi-square test (df = 1).

Incidence of propofol injection pain: Pain incidence was significantly lower in Group 1 than in Group 2: 12/49 (24.5%) vs 28/49 (57.1%). The between-group difference was statistically significant (Pearson's χ^2=10.81, df=1, p=0.001) [Table/Fig-3]. The Relative Risk (RR) was 0.43 (95% CI 0.25-0.74), corresponding to an absolute risk reduction of 32.7% and a Number Needed to Treat (NNT) of approximately 4.

Pain occurrence	Group 1 (n=49)	Group 2 (n=49)
Pain present	12 (24.5%)	28 (57.1%)
No pain	37 (75.5%)	21 (42.9%)

[Table/Fig-3]: Incidence of pain during propofol injection.
Pearson's Chi-square test: χ^2=10.81, df=1, p=0.001; Values presented in n (%).

Severity of pain: Pain severity (0=none; 1=mild; 2=moderate; 3=severe) differed significantly between groups. Group 1 predominantly experienced no or mild pain (none: 75.5%; mild: 20.4%), with two cases of moderate pain (4.1%) and no severe pain. Group 2 showed higher rates of moderate and severe pain (moderate: 20.4%; severe: 8.1%), with fewer patients reporting no pain (42.9%). The distribution of severity scores was significantly lower in Group 1 (Mann-Whitney U=748.5; z=-3.21; p=0.0013), indicating a medium effect size (Cliff's delta ≈ -0.38) [Table/Fig-4].

Pain severity	Group 1 (n=49)	Group 2 (n=49)
None (0)	37 (75.5%)	21 (42.9%)
Mild (1)	10 (20.4%)	14 (28.6%)
Moderate (2)	2 (4.1%)	10 (20.4%)
Severe (3)	0 (0%)	4 (8.1%)

[Table/Fig-4]: Distribution of pain severity.
Overall comparison: Mann-Whitney U=748.5; z=-3.21; p =0.0013 (two-tailed); Values presented in n (%).

Peri-induction haemodynamics: Event rates were low and similar between arms across T0-T4. Timepoint-wise tests within each safety domain were multiplicity-adjusted using the Holm-Bonferroni method; no between-group differences were significant (all adjusted p>0.05). Median maximal deviation from baseline remained within ~20% for both heart rate and mean arterial pressure in both groups [Table/Fig-5].

Local injection-site tolerability: No patient in either group developed injection-site complications (erythema, phlebitis, or swelling). Both regimens were well tolerated.

Event	T0	T1	T2	T3	T4
Hypotension (MAP <65 or ≥20%↓) - Combo	0/49 (0.0)	2/49 (4.1)	3/49 (6.1)	1/49 (2.0)	0/49 (0.0)
Hypotension-Lignocaine	0/49 (0.0)	3/49 (6.1)	4/49 (8.2)	2/49 (4.1)	0/49 (0.0)
Bradycardia (HR <50 or ≥20%↓)-Combo	0/49 (0.0)	0/49 (0.0)	1/49 (2.0)	1/49 (2.0)	0/49 (0.0)
Bradycardia-Lignocaine	0/49 (0.0)	0/49 (0.0)	2/49 (4.1)	0/49 (0.0)	0/49 (0.0)
Tachycardia (HR >120 or ≥20%↑)-Combo	0/49 (0.0)	2/49 (4.1)	1/49 (2.0)	0/49 (0.0)	0/49 (0.0)
Tachycardia-Lignocaine	0/49 (0.0)	3/49 (6.1)	1/49 (2.0)	0/49 (0.0)	0/49 (0.0)
Any rescue (fluids/vasopressor/atropine)-Combo	0/49 (0.0)	1/49 (2.0)	1/49 (2.0)	0/49 (0.0)	0/49 (0.0)
Any rescue-Lignocaine	0/49 (0.0)	1/49 (2.0)	2/49 (4.1)	0/49 (0.0)	0/49 (0.0)

[Table/Fig-5]: Safety haemodynamic events by group and timepoint (n/N, %).
Notes: T0 = pre-induction baseline; T1 = post-tourniquet lignocaine (pre-propofol); T2 = 1 min after the 25% propofol test bolus; T3 = pre-laryngoscopy; T4 = 1 min post-intubation. Definitions-Hypotension: MAP <65 mmHg or ≥20% fall from baseline; Bradycardia: HR <50 bpm or ≥20% fall; Tachycardia: HR > 120 bpm or ≥20% rise. "Total (unique)" counts patients with ≥1 event at any timepoint; timepoint cells are per-timepoint counts. At T0, only absolute thresholds apply (%-change criteria are not applicable). Rescue intervention: any fluids, vasopressor, or atropine. Within-domain comparisons across timepoints used Holm–Bonferroni adjustment; all adjusted p>0.05.

DISCUSSION

In the present randomised trial, both groups were similar at baseline (age, sex, BMI, ASA class), so any observed differences in pain are likely attributable to the treatment rather than baseline imbalance. This profile is consistent with most studies on propofol injection pain, which focus on technique-related factors—such as vein site, brief venous occlusion and injection speed—rather than patient demographics. Our small subgroup analyses did not show meaningful interactions by age, sex, or BMI, supporting the view that vein size/location and timing are more influential than routine demographic factors [3,14,18].

Adding intravenous paracetamol to short-occlusion lignocaine significantly reduced the likelihood of pain during the propofol test dose: 12/49 (24.5%) with the combination versus 28/49 (57.1%) with lignocaine alone {$\chi^2(1)$ = 10.81, p=0.001; RR 0.43, 95% CI 0.25-0.74; ARR 32.7%; NNT ≈ 4}. The control rate aligns with reports indicating that lignocaine alone reduces but does not eliminate pain in many patients [14,18]. The magnitude of benefit observed here is consistent with studies showing that paracetamol plus lignocaine outperforms either drug alone [11,17]. By contrast, paracetamol alone is less effective than lignocaine when the painful stimulus is immediate; head-to-head comparisons report approximately 89% pain with paracetamol versus about 35% with lignocaine under similar conditions [19]. Differences in vein site, tourniquet use and timing likely explain inter-study variation [3,14].

Pain intensity also shifted favourably. With the combination, most patients reported no pain or only mild pain and moderate-to-severe pain was rare (none: 37 vs 21; mild: 10 vs 14; moderate: 2 vs 10; severe: 0 vs 4). This pattern mirrors findings from trials and reviews in which lignocaine reduces both the incidence and severity of pain and where a dual-pathway strategy confers additional benefit [11,13,14,17]. Clinically, this makes induction smoother and communication easier, as patients either feel no discomfort or only brief, low-level pain.

Mechanistically, lignocaine acts locally and rapidly via sodium-channel blockade and endothelial stabilisation, with additional TRPV1 dampening at the cannula site [6,8]. Paracetamol contributes central effects, including COX inhibition, enhanced descending serotonergic tone and AM404-mediated TRPV1/CB1 modulation, raising the pain threshold when its peak coincides with injection [20,21]. The pre-theatre infusion and early 25% propofol test bolus were timed to match these pharmacodynamic profiles. Not all adjuncts

are effective: adding fentanyl to lignocaine has not consistently outperformed lignocaine alone, likely due to onset/peak mismatch for this brief, awake stimulus [22]. Oral paracetamol demonstrates mixed, dose-dependent results [15], whereas intravenous dosing is more reliable and, when combined with lignocaine, provides the most consistent reductions [11,17,23].

Safety and practicality were reassuring. No injection-site complications were observed and peri-induction haemodynamics did not differ significantly between groups, consistent with reports that intravenous paracetamol is well tolerated and does not exacerbate hypotension compared with other alternatives [23]. Strengths of the present study include concealed randomisation, double-blinding with identical syringes, a uniform short-occlusion protocol and immediate 0-3 VRS scoring after a standardised early test dose.

Two practical signals are noteworthy: the low NNT (~4) and excellent tolerability. No injection-site reactions were observed and there were no concerning deviations in peri-induction haemodynamics, supporting the safety of the combination regimen. Future research should explore generalisability through multicenter trials, stratify by hand versus forearm access, incorporate patient-reported outcomes and cost-utility measures and refine timing and dosing to optimise central-peripheral synergy.

Limitation(s)

The present single-centre randomised trial in ASA I–II elective adults used short venous occlusion with a 25% propofol test bolus, which limits generalisability to older adults, ASA ≥III patients, extremes of BMI, pediatric or Intensive Care Unit (ICU) cohorts and settings with different cannulation workflows. We did not stratify by venous site, cannula gauge, or vein caliber—factors known to affect propofol injection pain. Although participants and assessors were blinded, pre-theatre intravenous paracetamol could introduce performance bias if the control arm lacked a visually identical placebo; masking procedures and matched volumes are now clarified. Outcomes were limited to immediate 0-3 VRS pain after the test bolus; postoperative recall, patient satisfaction and cost-utility were not captured. The study was not powered for rare haemodynamic events, assessed safety only peri-induction and did not include biochemical monitoring after a single paracetamol dose. Only one paracetamol dose and timing were tested, with potential minor exposure variability and we did not compare against a lignocaine-propofol premix; head-to-head evaluation is warranted.

CONCLUSION(S)

Intravenous paracetamol, when added to short-occlusion lignocaine, significantly reduces propofol injection pain and shifts severity toward none or mild, without adding complexity or new safety concerns. The regimen uses familiar, inexpensive drugs and integrates seamlessly into pre-induction routines. Taken alongside literature showing residual pain with lignocaine alone and the mechanistic rationale for central-peripheral pairing, these findings support adopting the combination where propofol injection pain is anticipated. Future multicentre validation, venous-site stratification, patient-reported outcomes and cost-utility analyses should be conducted to enhance generalisability and inform clinical practice.

REFERENCES

[1] Sahinovic MM, Struys MMRF, Absalom AR. Clinical pharmacokinetics and pharmacodynamics of propofol. Clin Pharmacokinet. 2018;57(12):1539-58.
[2] Mubita WM, Richardson C, Briggs M. Patient satisfaction with pain relief following major abdominal surgery is influenced by good communication, pain relief and empathic caring: A qualitative interview study. Br J Pain. 2020;14(1):14-22.
[3] Desousa KA. Pain on propofol injection: Causes and remedies. Indian J Pharmacol. 2016;48(6):617-23.
[4] Sim JY, Lee SH, Park DY, Jung JA, Ki KH, Lee DH, et al. Pain on injection with microemulsion propofol. Br J Clin Pharmacol. 2009;67(3):316-25.
[5] Abdel-Salam, O.M., Mózsik, G. Capsaicin, the vanilloid receptor TRPV1 agonist in neuroprotection: Mechanisms involved and significance. Neurochem Res. 2023;48:3296-315.
[6] Premkumar LS, Sikand P. TRPV1: A target for next generation analgesics. Curr Neuropharmacol. 2008;6(2):151-63.
[7] Abdulkhaleq LA, Assi MA, Abdullah R, Zamri-Saad M, Taufiq-Yap YH, Hezmee MNM. The crucial roles of inflammatory mediators in inflammation: A review. Vet World. 2018;11(5):627-35.
[8] Becker DE, Reed KL. Local anesthetics: Review of pharmacological considerations. Anesth Prog. 2012;59(2):90-102.
[9] Dib-Hajj SD, Black JA, Waxman SG. Voltage-gated sodium channels: Therapeutic targets for pain. Pain Med. 2009;10(7):1260-69.
[10] Graham GG, Scott KF. Mechanism of action of paracetamol. Am J Ther. 2005;12(1):46-55.
[11] Hayat M, Afshan G, Nasir M, Asghar S, Monem A. Efficacy of intravenous paracetamol in combination with lidocaine pretreatment for reducing pain during injection of propofol. Cureus. 2020;12(2):e6926.
[12] Reddy A, Kumar S, Mahajan S. A well-known but rarely seen interaction: Propofol with lignocaine. Ain-Shams J Anesthesiol. 2023;15(1):4.
[13] Bakhtiari E, Mousavi SH, Gharavi Fard M. Pharmacological control of pain during propofol injection: A systematic review and meta-analysis. Expert Rev Clin Pharmacol. 2021;14(7):889-99.
[14] Jalota L, Kalira V, George E, Shi YY, Hornuss C, Radke O, et al. Prevention of pain on injection of propofol: Systematic review and meta-analysis. BMJ. 2011;342(6):01-18.
[15] Nimmaanrat S, Jongjidpranitarn M, Prathep S, Oofuvong M. Premedication with oral paracetamol for reduction of propofol injection pain: A randomized placebo-controlled trial. BMC Anesthesiol. 2019;19(1):100.
[16] Sumalatha GB, Dodawad RR, Pandarpurkar S, Jajee PR. A comparative study of attenuation of propofol-induced pain by lignocaine, ondansetron, and ramosetron. Indian J Anaesth. 2016;60(1):25-29.
[17] Borazan H, Erdem TB, Kececioglu M, Otelcioglu S. Prevention of pain on injection of propofol: A comparison of lidocaine with different doses of paracetamol. Eur J Anaesthesiol. 2010;27(3):253-57.
[18] Picard P, Tramèr MR. Prevention of pain on injection with propofol: A quantitative systematic review. Anesth Analg. 2000;90(4):963-69.
[19] Ahuja H, Cherian JJ. propofol induced pain: Comparison of efficacy of pre-treatment with paracetamol and lidocaine. IJPCR. 2023;15(9):247-50.
[20] Polomeni MM, Huguet T, Mariotti M, Larcher C, Delort F, Minville V, et al. Avoiding pain during propofol injection in pediatric anesthesia: Hypnoanalgesia of the hand versus intravenous lidocaine. Paediatr Anaesth. 2024;34(8):742-49.
[21] Mallet C, Desmeules J, Pegahi R, Eschalier A. An updated review on the metabolite (AM404)-mediated central mechanism of action of paracetamol (Acetaminophen): Experimental evidence and potential clinical impact. J Pain Res. 2023;16:1081-94.
[22] El-Radaideh KM. Effect of pretreatment with lidocaine, intravenous paracetamol and lidocaine-fentanyl on propofol injection pain. Comparative study. Rev Bras Anestesiol. 2007;57(1):32-38.
[23] Alipour M, Tabari M, Alipour M. Paracetamol, ondansetron, granisetron, magnesium sulfate and lidocaine and reduced propofol injection pain. Iran Red Crescent Med J. 2014;16(3):e16086.

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