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Pain on Propofol Injection: Comparison of Multimodal Approach Via Antecubital Vein and Vein on Dorsum of Hand – an Observational Study

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ABSTRACT

Background: Pain on propofol injection (POPI) is one of the most common and unpleasant adverse effects encountered during induction of general anesthesia, with reported incidence ranging from 28% to 90%. Multiple pharmacological and non-pharmacological strategies have been proposed to reduce this discomfort; however, complete prevention remains challenging. Selection of an appropriate venous access site is a simple and practical factor that may influence the severity of injection pain by altering the dilution and endothelial exposure of propofol.
Objective: To compare the incidence and severity of pain on propofol injection when administered through the antecubital vein versus the vein on the dorsum of the hand using a multimodal anesthetic approach.
Methods: This prospective observational study included 146 adult patients with American Society of Anesthesiologists (ASA) physical status I–II undergoing elective surgery under general anesthesia. Patients were divided into two groups based on the site of intravenous cannulation: Group A (dorsum of hand vein) and Group B (antecubital vein). All patients received standardized multimodal premedication before induction. Pain was assessed using the Numerical Rating Scale after administration of approximately 30% of the calculated propofol dose. Hemodynamic parameters and recall of pain following recovery from anesthesia were also recorded and analyzed.
Results: The overall incidence of pain on propofol injection was 85.6%. Pain occurred significantly more frequently and with greater severity in patients receiving propofol through the dorsum of the hand compared with the antecubital vein. Severe pain was observed only in the dorsum of hand group. Hemodynamic parameters remained comparable between the two groups, and recall of injection pain was minimal and not statistically significant.
Conclusion: Administration of propofol through the antecubital vein significantly reduces the incidence and severity of injection pain compared with the dorsum of hand vein when used within a multimodal anesthetic regimen. Choosing a larger venous access site represents a simple and effective strategy to improve patient comfort during anesthesia induction.

Keywords: *Propofol injection pain; Antecubital vein; Dorsum of hand vein; Multimodal anesthesia; Numerical rating scale; General anesthesia.*

INTRODUCTION

Propofol is one of the most widely used intravenous anesthetic agents in contemporary anesthesia practice because of its rapid onset of action, short duration, favorable pharmacokinetic profile, and smooth recovery characteristics [1]. It is routinely used for induction and maintenance of general anesthesia, procedural sedation, and sedation in intensive care

settings [2]. Despite these advantages, pain on propofol injection (POPI) remains one of the most common and distressing adverse experiences encountered during induction of anesthesia. The reported incidence of POPI varies widely, ranging from 28% to 90%, depending on several factors including patient characteristics, venous access site, propofol formulation, and preventive strategies employed [3].

Chemically, propofol (2,6-diisopropylphenol) is a highly lipophilic alkylphenol compound that is insoluble in water and therefore formulated as an oil-in-water lipid emulsion. The commonly used propofol preparation contains soybean oil, glycerol, and egg phosphatide as an emulsifying agent, which produces the characteristic milky appearance of the drug solution [1,4]. Although this formulation allows rapid absorption and penetration across the blood–brain barrier, it also contributes to certain adverse effects, including pain during intravenous injection.

The precise mechanism of pain on propofol injection is complex and multifactorial. Immediate pain is believed to result from direct irritation of the venous endothelium and activation of nociceptive nerve endings by the free aqueous fraction of propofol present in the lipid emulsion. Delayed pain has been attributed to activation of the kallikrein–kinin system, leading to the release of bradykinin. Bradykinin causes venodilation and increased vascular permeability, allowing greater contact of propofol with nociceptive nerve endings in the vessel wall [3]. In addition, recent molecular studies have implicated the activation of transient receptor potential ion channels, particularly TRPA1 and TRPV1 receptors, which contribute to neurogenic inflammation and enhanced nociceptor sensitivity during propofol injection [5,6].

Various strategies have been proposed to reduce the incidence and severity of propofol injection pain. Pharmacological interventions such as intravenous lignocaine, opioids, benzodiazepines, ketamine, ondansetron, and non-steroidal anti-inflammatory drugs have been investigated for their analgesic effects during propofol administration [3,7]. Among these, lignocaine pretreatment is the most commonly used method; however, it does not completely eliminate injection pain, with reported failure rates ranging from 13% to 32% when used as a single intervention [3].

Apart from pharmacological measures, several non-pharmacological techniques have also been evaluated. These include modification of the injection rate, dilution of propofol, cooling or warming the drug, and selection of an appropriate venous access site. Among these factors, the site of intravenous cannulation plays an important role in determining the intensity of injection pain. Administration of propofol through larger veins, such as the antecubital vein, allows rapid dilution of the drug within the bloodstream and reduces contact with the venous endothelium, thereby decreasing nociceptor stimulation and pain perception [3,4]. In contrast, smaller superficial veins on the dorsum of the hand have a lower blood flow and a higher density of sensory nerve endings, making them more susceptible to endothelial irritation and painful stimulation.

Recent evidence suggests that a multimodal approach combining pharmacological agents with appropriate injection techniques may provide better control of propofol injection pain compared with isolated interventions. Such an approach may reduce anxiety, modulate nociceptive pathways, and minimize endothelial irritation, thereby improving patient comfort during induction of anesthesia [3,7].

In routine clinical practice at our institution, propofol induction is often administered through larger veins in the antecubital region along with standardized multimodal premedication. This practice has been associated with a noticeably lower incidence of injection pain. However, limited published literature systematically evaluates the combined effect of venous site selection and multimodal anesthetic strategies in reducing POPI. Therefore, the present study was undertaken to compare the incidence and severity of pain on propofol injection when administered through the antecubital vein versus the vein on the dorsum of the hand using a multimodal approach. The study also aims to evaluate associated hemodynamic responses and patient-related factors influencing pain perception during propofol administration.

MATERIALS AND METHODS

Study Design and Setting: This prospective observational study was conducted in the Department of Anaesthesiology at Travancore Medical College, Kollam, Kerala. The study was carried out after obtaining approval from the Institutional Ethics Committee and written informed consent from all participating patients.

Study Population: All patients scheduled to undergo elective surgical procedures under general anesthesia were included in the study.

Inclusion Criteria

- Age between 18 and 60 years
- American Society of Anesthesiologists (ASA) physical status I or II
- Patients undergoing elective surgical procedures requiring general anesthesia with intravenous propofol induction

Exclusion Criteria

- Known allergy or hypersensitivity to propofol or any study medication
- Peripheral vascular disease
- History of chronic pain disorders or neuropathy
- Use of analgesics, sedatives, or opioids prior to induction
- Communication difficulties preventing accurate pain assessment
- Patients requiring rapid sequence induction

Sample Size: A total of 146 patients who met the inclusion criteria during the study period were enrolled. The patients were divided into two groups based on the site of intravenous cannulation.

Group Allocation : Patients were categorized into two groups depending on the site of venous access used for administration of propofol :

- **Group A :** Intravenous cannulation through the vein on the dorsum of the hand
- **Groupe B :** Intravenous cannulation through the antecubital vein

Both groups received standardized anesthetic management and multimodal premedication according to institutional protocol.

Preoperative Assessment: All patients underwent routine preoperative evaluation, including detailed medical history, physical examination, and necessary laboratory investigations. Demographic details such as age, gender, body weight, and body mass index (BMI) were recorded. ASA physical status classification was assigned according to standard guidelines. Patients were kept nil per os (NPO) as per institutional fasting guidelines before surgery.

Anesthetic Technique : Upon arrival in the operating room, standard monitoring was established for all patients, including electrocardiography (ECG), non-invasive blood pressure monitoring, pulse oximetry, and heart rate monitoring.

An intravenous cannula was secured either in the dorsum of the hand or the antecubital vein depending on group allocation. All patients received standardized multimodal premedication prior to induction of anesthesia.

Baseline hemodynamic parameters including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and peripheral oxygen saturation (SpO_2) were recorded before induction.

Propofol was administered intravenously for induction of anesthesia. Pain assessment was performed after administration of approximately 30% of the calculated induction dose of propofol, before loss of consciousness.

Pain Assessment: Pain on propofol injection was evaluated using the Numerical Rating Scale (NRS).
The pain scale ranged from 0 to 10, where:

- 0 – No pain
- 1–3 – Mild pain
- 4–6 – Moderate pain
- 7–10 – Severe pain

Patients were asked to verbally report their pain intensity immediately after receiving the initial portion of the propofol injection.

Hemodynamic Monitoring: Hemodynamic parameters including heart rate, systolic blood pressure, diastolic blood pressure, and oxygen saturation were recorded at predefined intervals during induction to assess any physiological response to propofol injection pain.

Assessment of Pain Recall: After recovery from anesthesia, patients were asked whether they recalled experiencing pain during the propofol injection. The presence or absence of recall was documented.

Outcome Measures

Primary Outcome

- Incidence and severity of pain on propofol injection

Secondary Outcomes

- Hemodynamic changes during induction
- Recall of pain after recovery from anesthesia
- Association between pain severity and patient-related factors such as age, gender, BMI, and ASA physical status

Statistical Analysis: The collected data were entered into a spreadsheet and analyzed using appropriate statistical software. Continuous variables were expressed as mean ±standard deviation, while categorical variables were presented as frequency and percentage. Comparisons between the two groups were performed using appropriate statistical tests. The association between categorical variables was analyzed using the Chi-square test, while continuous variables were compared using the independent t-test where applicable. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 146 patients were included in the study and divided into two groups based on the site of venous cannulation. Group A (n=73) received propofol through the vein on the dorsum of the hand, while Group B (n=73) received propofol through the antecubital vein. The two groups were comparable with respect to age, gender distribution, BMI, and ASA physical status. No statistically significant difference was observed between the groups ($p > 0.05$), indicating that baseline characteristics were similar.(Table 1)

Table 1: Baseline Characteristics of Study Participants

Variable	Group A (Dorsum of Hand) (n=73)	Group B (Antecubital Vein) (n=73)	p-value
Age (years) Mean ± SD	36.4 ± 10.8	37.1 ± 11.2	0.72
Male n (%)	38 (52.1)	36 (49.3)	0.73
Female n (%)	35 (47.9)	37 (50.7)	
BMI (kg/m²) Mean ± SD	24.3 ± 3.2	24.7 ± 3.5	0.54
ASA I n (%)	46 (63.0)	44 (60.3)	0.74
ASA II n (%)	27 (37.0)	29 (39.7)	

Statistical test: Independent t-test for continuous variables and Chi-square test for categorical variables.

The overall incidence of pain on propofol injection was 85.6%. Pain occurred significantly more frequently in patients receiving propofol through the dorsum of the hand vein compared to the antecubital vein ($p < 0.001$).(Table 2)

Table 2: Incidence of Pain on Propofol Injection

Pain Presence	Group A (n=73)	Group B (n=73)	p-value
Pain Present	67 (91.8%)	58 (79.5%)	<0.001
No Pain	6 (8.2%)	15 (20.5%)	

Statistical test: Chi-square test.

Pain severity differed significantly between the two groups. Severe pain was observed exclusively in the dorsum of hand group, while the antecubital vein group had a greater proportion of patients experiencing either no pain or mild pain.(Table 3)

Table 3: Comparison of Pain Severity Between Study Groups (Numerical Rating Scale)

Pain Severity	Group A (n=73)	Group B (n=73)	p-value
No Pain	6 (8.2%)	15 (20.5%)	<0.001
Mild Pain	21 (28.8%)	34 (46.6%)	
Moderate Pain	31 (42.5%)	24 (32.9%)	
Severe Pain	15 (20.5%)	0 (0%)	

Statistical test: Chi-square test.

Hemodynamic parameters during induction were comparable between the two groups. There were no statistically significant differences in heart rate, systolic blood pressure, diastolic blood pressure, or oxygen saturation ($p > 0.05$).(Table 4)

Table 4: Comparison of Hemodynamic Parameters During Induction

Parameter	Group A Mean ± SD	Group B Mean ± SD	p-value
Heart Rate (beats/min)	84.2 ± 11.5	82.9 ± 10.8	0.48
Systolic BP (mmHg)	124.6 ± 13.2	123.1 ± 12.7	0.56
Diastolic BP (mmHg)	78.4 ± 9.1	77.6 ± 8.8	0.61
SpO_2 (%)	99.1 ± 0.7	99.2 ± 0.6	0.37

Statistical test: Independent t-test.

Pain recall after recovery from anesthesia was relatively low in both groups. Although slightly more patients in the dorsum of hand group reported recall of pain, the difference between the groups was not statistically significant ($p > 0.05$).(Table 5)

Table 5: Pain Recall After Recovery from Anesthesia

Pain Recall	Group A (n=73)	Group B (n=73)	p-value
Present	8 (11.0%)	5 (6.8%)	0.38
Absent	65 (89.0%)	68 (93.2%)	

Statistical test: Chi-square test.

Association of Pain with Patient Characteristics

The association between pain severity and demographic characteristics was also evaluated. Pain scores were slightly higher among female patients compared to males; however, this difference was not statistically significant. Similarly, age, BMI, and ASA physical status did not demonstrate a statistically significant association with pain severity.

These findings indicate that venous access through the antecubital vein significantly reduces the severity of propofol injection pain compared to the dorsum of the hand vein.

DISCUSSION

Pain on propofol injection (POPI) continues to be one of the most frequently encountered adverse effects during induction of general anesthesia despite the widespread use of the drug in modern anesthetic practice. Propofol is favored for its rapid onset, predictable pharmacokinetics, smooth induction, and rapid recovery profile; however, the occurrence of injection pain can significantly affect patient comfort and overall perioperative experience [1,2]. The incidence of POPI has been reported to range from 28% to 90%, making it one of the most common complications associated with propofol administration [3]. The present study was conducted to compare the incidence and severity of pain on propofol injection when administered through the antecubital vein versus the vein on the dorsum of the hand using a multimodal anesthetic approach.

In the present study, the overall incidence of pain on propofol injection was 85.6%. This finding is consistent with previous literature which reports a high incidence of injection pain associated with propofol, particularly when administered through smaller peripheral veins [3]. The wide variability in reported incidence is primarily attributed to differences in study population, injection techniques, venous access sites, and preventive strategies used in various studies.

The results of the present study demonstrated that the incidence and severity of pain were significantly higher when propofol was injected through the dorsum of the hand compared with the antecubital vein. Severe pain was observed exclusively in patients receiving propofol through the dorsum of hand veins. These findings support the hypothesis that the site of intravenous cannulation plays a crucial role in determining the intensity of propofol injection pain.

The difference in pain perception between the two venous sites can be explained by anatomical and physiological factors. Veins on the dorsum of the hand are smaller in diameter and have relatively lower blood flow compared with the antecubital veins. Smaller veins result in slower dilution of the injected drug, thereby increasing the exposure of the venous endothelium to the free aqueous fraction of propofol. This increased contact can lead to greater endothelial irritation and activation of nociceptive nerve endings, resulting in higher pain intensity [3,4].

In contrast, the antecubital veins are larger and have higher blood flow, which allows rapid dilution of propofol within the bloodstream. This rapid dilution reduces the concentration of free aqueous propofol contacting the vascular endothelium and sensory nerve endings, thereby reducing the activation of nociceptors and decreasing the severity of pain [3,4]. These physiological differences provide a plausible explanation for the significantly lower pain scores observed in the antecubital vein group in the present study.

The pathophysiology of propofol injection pain is multifactorial. Immediate pain is believed to occur due to direct chemical irritation of the venous endothelium and activation of peripheral nociceptors by the free aqueous fraction of propofol in the lipid emulsion [8-10]. In addition to direct irritation, delayed pain may occur through activation of the kallikrein–kinin system, which leads to the production of bradykinin. Bradykinin causes venodilation and increases vascular permeability, thereby facilitating greater contact between propofol and sensory nerve endings within the vascular wall [3,11].

Recent advances in molecular research have also identified the role of transient receptor potential ion channels, particularly TRPA1 and TRPV1 receptors, in mediating propofol injection pain. These receptors are expressed on peripheral sensory neurons and are activated by chemical irritants and inflammatory mediators. Activation of these receptors leads to influx of calcium and sodium ions, resulting in depolarization of nociceptive fibers and transmission of pain signals [12,13]. The activation of these nociceptive pathways contributes to the characteristic burning or stinging sensation reported during propofol injection.

Several pharmacological strategies have been investigated to reduce the incidence and severity of propofol injection pain. Among these, intravenous lignocaine pretreatment is considered one of the most commonly used methods; however, it has been shown to have incomplete efficacy when used alone, with reported failure rates ranging from 13% to 32% [3]. Therefore, recent clinical practice increasingly favors a multimodal approach combining pharmacological and non-pharmacological measures to achieve better pain control.

In the present study, all patients received standardized multimodal premedication prior to induction. The use of multimodal anesthesia may contribute to the reduction of anxiety, modulation of nociceptive pathways, and overall improvement in patient comfort during induction of anesthesia [3,7]. Despite the use of multimodal premedication, the incidence of injection pain remained significantly higher in the dorsum of hand group compared with the antecubital vein group, emphasizing the importance of venous access site selection as an independent factor influencing pain perception.

Hemodynamic parameters including heart rate, systolic blood pressure, diastolic blood pressure, and oxygen saturation remained stable and comparable between the two groups during induction of anesthesia. This suggests that the choice of venous access site does not significantly influence hemodynamic stability during propofol administration. The findings indicate that the use of antecubital veins for propofol injection can improve patient comfort without causing any adverse hemodynamic effects.

Another aspect evaluated in this study was recall of injection pain following recovery from anesthesia. The proportion of patients reporting recall of pain was relatively low in both groups and did not differ significantly. This observation may be explained by the rapid onset of unconsciousness produced by propofol and the amnestic effects of anesthetic agents administered during induction.

Patient-related factors such as age, gender, and body mass index were also assessed in relation to pain severity. Although some studies have suggested that younger patients and female patients may experience higher pain intensity during propofol injection due to differences in nociceptive sensitivity, no statistically significant association was observed in the present study. These findings suggest that venous access site may have a greater influence on injection pain than individual demographic characteristics.

Overall, the findings of this study highlight the importance of venous site selection as a simple and effective strategy for reducing propofol injection pain. While various pharmacological interventions have been proposed to minimize this adverse effect, selecting a larger vein such as the antecubital vein represents a practical and cost-effective measure that can be easily implemented in routine anesthetic practice.

The present study demonstrates that administration of propofol through the antecubital vein significantly reduces both the incidence and severity of injection pain compared with the dorsum of hand vein when used as part of a multimodal anesthetic approach. These findings reinforce the role of venous access site selection as an important component of strategies aimed at improving patient comfort during induction of general anesthesia.

This study has certain limitations. It was conducted at a single tertiary care center with a relatively limited sample size, which may restrict the generalizability of the findings to broader populations. Blinding of the investigator was not feasible because the site of venous cannulation was visibly identifiable, which may have introduced observer bias. Additionally, psychological factors such as preoperative anxiety and individual pain thresholds, which can influence pain perception, were not objectively quantified in this study. Future multicentric studies with larger sample sizes and more comprehensive assessment of patient-related factors may provide further insights into strategies for reducing pain on propofol injection.

CONCLUSION

Pain on propofol injection remains a frequent and distressing adverse event during induction of general anesthesia. The present study evaluated the influence of venous cannulation site on the incidence and severity of propofol injection pain when administered as part of a multimodal anesthetic approach. The findings demonstrated that the incidence and intensity of pain were significantly higher when propofol was injected through the vein on the dorsum of the hand compared with the antecubital vein. Severe pain was observed exclusively in patients receiving the drug through the dorsum of hand veins. In contrast, administration through the antecubital vein resulted in a greater proportion of patients experiencing either mild pain or no pain. Hemodynamic parameters remained stable and comparable between the two groups, indicating that the choice of venous access site does not adversely affect physiological responses during induction. These results suggest that selecting a larger vein, such as the antecubital vein, represents a simple, safe, and effective strategy for reducing propofol injection pain and improving patient comfort during anesthesia induction.

Declarations

Ethical Approval and Consent to Participate

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Institutional Ethics Committee of Travancore Medical College, Kollam, prior to the commencement of the study. Written informed consent was obtained from all participants before their inclusion in the study.

Availability of Data and Materials

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Competing Interests

The authors declare that they have no competing interests.

Funding

The authors declare that no external funding was received for the conduct of this study.

Authors 'Contributions

The first author conceptualized the study, collected the data, performed the analysis, and prepared the initial manuscript draft. The guide and co-guides contributed to study design, supervision, data interpretation, and critical revision of the manuscript. All authors read and approved the final manuscript.

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