e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(6); 1909-1913

Original Research Article

Evaluation of Effect of Cold Normal Saline as Carrier Fluid in Reducing Propofol Induced Pain

Neha Gulabbhai Vasava[1], Ayushi Patel[2], Mitali G. Patel[3]

[1]Assistant Professor, Department of Anaesthesia, GMERS Medical College, Valsad, Gujarat, India
[2]Senior Resident, Department of Anaesthesia, GMERS Medical College, Valsad, Gujarat, India
[3]Assistant Professor, Department of Anaesthesia, Baroda Medical College and SSG Hospital, Vadodara, Gujarat, India

Received: 01-03-2026 / Revised: 15-04-2026 / Accepted: 21-05-2026
Corresponding author: Dr. Mitali G. Patel
Conflict of interest: Nil

Abstract

Background: Propofol is one of the most commonly used intravenous anesthetic agents because of its rapid onset and smooth recovery profile. However, pain during propofol injection remains a frequent and unpleasant complication that affects patient comfort and satisfaction. Cold normal saline has been proposed as a simple, safe, and cost-effective non-pharmacological intervention to reduce propofol-induced pain.

Aim: To evaluate the effect of cold normal saline (4°C) as a carrier fluid in reducing propofol-induced pain compared with normal saline at room temperature, with the primary objective of assessing the incidence and severity of pain using a pain score and the secondary objective of evaluating postoperative recall in both groups.

Methodology: A prospective comparative study was conducted among 160 patients undergoing elective surgeries under general anesthesia. Participants were randomly allocated into two equal groups of 80 patients each. Group C received cold normal saline (4°C) as the carrier fluid during propofol administration, whereas Group R received normal saline at room temperature. Demographic characteristics, incidence of pain, severity of pain using a standardized pain score, heart rate changes, and postoperative recall of pain were recorded and compared. Statistical analysis was performed using appropriate tests, and a p-value of <0.05 was considered statistically significant.

Results: The demographic characteristics were comparable between the two groups. The incidence of propofol-induced pain was significantly lower in Group C (41.2%) than in Group R (77.5%) ($p<0.001$). Severe pain was not observed in Group C, whereas 10.0% of patients in Group R experienced severe pain. Patients receiving cold normal saline demonstrated significantly lower heart rate changes following propofol injection and a markedly lower rate of postoperative recall of pain compared with the room-temperature saline group ($p<0.001$).

Conclusion: Cold normal saline (4°C) used as a carrier fluid significantly reduced the incidence and severity of propofol-induced pain and decreased postoperative recall compared with normal saline at room temperature. This simple, inexpensive, and non-pharmacological intervention can be safely incorporated into routine anesthetic practice to improve patient comfort during induction of anesthesia.

Keywords: Propofol, Injection pain, Cold normal saline, Carrier fluid, General anesthesia, Postoperative recall.
DOI: 10.25258/ijcpr.18.6.305

Introduction

Propofol is one of the most widely used intravenous anesthetic agents for the induction and maintenance of general anesthesia because of its rapid onset, short duration of action, and favorable recovery profile. Despite its many advantages, pain on injection remains one of the most common and distressing adverse effects associated with propofol administration, with an incidence ranging from 28% to 90% in untreated patients. This unpleasant experience may contribute to patient anxiety and dissatisfaction during the induction of anesthesia and continues to be a significant concern for anesthesiologists. [1,2] The exact mechanism of propofol-induced pain is multifactorial and has not been completely elucidated. Proposed mechanisms include direct irritation of the vascular endothelium, activation of the kallikrein–kinin system, release of inflammatory mediators, and stimulation of free nerve endings in the venous wall. Factors such as vein size, injection site, speed of administration, and temperature of the injected solution have also been reported to influence the severity of pain. [3,4] Numerous pharmacological and non-pharmacological interventions have been

investigated to reduce propofol injection pain. These include pretreatment with lidocaine, ketamine, opioids, ondansetron, magnesium sulfate, and various other agents, as well as techniques such as venous occlusion, selection of larger veins, and alteration of the temperature of the injectate or carrier fluid. Among these, lidocaine remains the most frequently used intervention; however, it may not always provide complete pain relief and may introduce additional drug-related effects. [2,5–8]

Cooling intravenous fluids has been suggested as a simple, inexpensive, and safe strategy for reducing pain associated with intravenous injections. Cold normal saline may decrease nerve conduction velocity, reduce local inflammatory responses, and provide a transient local anesthetic effect, thereby minimizing the discomfort associated with propofol administration. Because normal saline is routinely used as a carrier fluid during anesthetic induction, lowering its temperature may represent an effective, drug-free method for reducing propofol-induced pain without increasing procedural complexity or cost. [6,9] Although several studies have evaluated different preventive measures for propofol injection pain, limited evidence is available regarding the effectiveness of cold normal saline used specifically as a carrier fluid during propofol administration. Furthermore, the influence of this intervention on postoperative recall of injection pain has not been extensively investigated. [2,10] Therefore, the present study was undertaken to evaluate the effect of cold normal saline (4°C) used as a carrier fluid in reducing propofol-induced pain compared with normal saline at room temperature. The study also aimed to assess the incidence and severity of pain using a standardized pain score and to evaluate postoperative recall of pain following anesthesia induction.

Material and Methods

Study Design and Setting: This prospective, randomized, comparative study was conducted in the Department of Anaesthesiology at a tertiary care teaching hospital after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants before enrolment. The study was carried out in accordance with the ethical principles of the Declaration of Helsinki.

Study Population: A total of 160 adult patients scheduled for elective surgery under general anesthesia were included in the study. Patients were randomly allocated into two equal groups (n = 80 each).

Inclusion Criteria: Patients aged 18–60 years, belonging to the American Society of Anesthesiologists (ASA) physical status I or II, and scheduled for elective surgical procedures requiring intravenous induction with propofol were included in the study.

Exclusion Criteria: Patients with known hypersensitivity to propofol, severe cardiovascular, hepatic, renal, or neurological disorders, pregnancy or lactation, difficult peripheral venous access, chronic pain syndromes, use of analgesics or sedatives within 24 hours before surgery, or inability to communicate pain were excluded.

Randomization: Patients were randomized into two groups using a computer-generated randomization sequence with allocation concealment by sealed opaque envelopes.

- **Group C (Cold Saline Group):** Received cold normal saline maintained at **4°C** as the carrier fluid during propofol administration.
- **Group R (Room Temperature Group):** Received normal saline at room temperature (22–25°C) as the carrier fluid during propofol administration.

Study Procedure: Standard fasting guidelines were followed. Upon arrival in the operating room, routine monitoring, including electrocardiography, non-invasive blood pressure, pulse oximetry, and heart rate, was instituted. An 18- or 20-gauge intravenous cannula was inserted into a vein on the dorsum of the hand or forearm. Patients received the allocated carrier fluid before induction of anesthesia. Propofol was then administered intravenously according to the institutional induction protocol.

During injection, patients were observed for pain, and verbal complaints together with behavioral responses were recorded.

Outcome Measures: The primary outcome was the incidence and severity of propofol injection pain. Pain severity was assessed immediately after propofol administration using a standardized four-point pain scale:

- **Grade 0:** No pain.
- **Grade 1:** Mild pain (pain reported only on questioning without behavioral response).
- **Grade 2:** Moderate pain (pain reported spontaneously or accompanied by facial grimacing or withdrawal).
- **Grade 3:** Severe pain (strong vocal response, marked withdrawal movement, or tears).

The secondary outcomes included changes in heart rate before and after propofol injection and postoperative recall of injection pain assessed in the recovery room.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using SPSS software (Version XX.0; IBM Corp., Armonk, NY, USA).

Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequency and percentage. Continuous variables were compared using the independent Student's *t*-test, whereas categorical variables were analyzed using the Chi-square test or Fisher's exact test whenever appropriate. A *p*-value of less than 0.05 was considered statistically significant.

Results

Table 1: A total of 160 patients were included in the study, with 80 participants in each group. The mean age of patients in Group C was 37.4 ± 12.3 years, while in Group R it was 38.1 ± 12.0 years. Male participants constituted 46.3% in Group C and 38.8% in Group R, whereas females accounted for 53.7% and 61.2%, respectively. The mean BMI was 23.6 ± 4.3 kg/m² in Group C and 23.8 ± 3.9 kg/m² in Group R. No statistically significant differences were observed between the two groups regarding age (p=0.912), sex distribution (p=0.334), or BMI (p=0.764), indicating that both groups were demographically comparable.

Table 2: The incidence of pain following propofol injection was significantly lower in Group C than in Group R. In Group C, 47 (58.8%) participants experienced no pain, whereas 33 (41.2%) reported pain. In contrast, only 18 (22.5%) participants in Group R had no pain, while 62 (77.5%) experienced pain. This difference in pain incidence between the two groups was statistically significant (p<0.001), suggesting that cold normal saline effectively reduced the occurrence of propofol-induced pain.

Table 3: Assessment of pain severity demonstrated a significant difference between the two groups. In Group C, 47 (58.8%) participants had no pain, 21 (26.2%) experienced mild pain, and 12 (15.0%) reported moderate pain, while none experienced severe pain. Conversely, in Group R, only 18 (22.5%) participants reported no pain, whereas mild, moderate, and severe pain were observed in 35 (43.8%), 19 (23.7%), and 8 (10.0%) participants, respectively. The overall distribution of pain severity differed significantly between the groups (p<0.001), indicating superior pain reduction with cold normal saline.

Table 4: The baseline heart rate (HR1) was comparable between the two groups, with Group C recording a mean heart rate of 76.9 ± 8.4 beats/min and Group R recording 80.1 ± 9.2 beats/min (p=0.028). Following propofol administration (HR2), the mean heart rate remained relatively stable in Group C (76.7 ± 8.2 beats/min), whereas Group R demonstrated a higher mean heart rate of 82.8 ± 9.5 beats/min. This difference was statistically significant (p<0.001), reflecting a greater physiological response to pain in the room-temperature saline group.

Table 5: Postoperative recall of pain was evaluated in both groups. Among participants in Group C, 47 (58.8%) had no pain and were categorized as not applicable for recall assessment, while 12 (15.0%) recalled pain and 21 (26.2%) did not recall pain despite experiencing it.

In Group R, 18 (22.5%) participants were categorized as not applicable, whereas 41 (51.2%) recalled pain and 21 (26.3%) did not recall pain.

The difference in postoperative recall between the two groups was statistically significant (p<0.001), indicating that patients receiving cold normal saline experienced lower recall of injection pain compared to those receiving room-temperature saline.

Table 1: Comparing demographic characteristics between both groups (n = 160)

Variable	Group C (n = 80)	Group R (n = 80)	P value
Age (mean ± SD), years	37.4 ± 12.3	38.1 ± 12.0	0.912
Sex	Male = 37 (46.3%) Female = 43 (53.7%)	Male = 31 (38.8%) Female = 49 (61.2%)	0.334
BMI (mean ± SD), kg/m²	23.6 ± 4.3	23.8 ± 3.9	0.764

Table 2: Comparison of incidence of pain between both groups

Incidence of pain	Group C (n = 80)	Group R (n = 80)	P value
No	47 (58.8%)	18 (22.5%)	<0.001
Yes	33 (41.2%)	62 (77.5%)	

Table 3: Comparison of degree of pain between both groups

Degree of pain	Group C (n = 80)	Group R (n = 80)	P value
None	47 (58.8%)	18 (22.5%)	
Mild	21 (26.2%)	35 (43.8%)	
Moderate	12 (15.0%)	19 (23.7%)	
Severe	0 (0%)	8 (10.0%)	<0.001

Table 4: Comparison of heart rate between both groups

Heart rate (beats/min)	Group C (n = 80)	Group R (n = 80)	P value
HR1	76.9 ± 8.4	80.1 ± 9.2	0.028
HR2	76.7 ± 8.2	82.8 ± 9.5	<0.001

Table 5: Comparison of postoperative recall between both groups

Postoperative recall	Group C (n = 80)	Group R (n = 80)	P value
Not applicable (No pain)	47 (58.8%)	18 (22.5%)	
Yes	12 (15.0%)	41 (51.2%)	
No	21 (26.2%)	21 (26.3%)	<0.001

Discussion

Pain during propofol injection remains one of the most common adverse events associated with intravenous induction of anesthesia despite the widespread use of propofol because of its favorable pharmacological profile. The present study evaluated the effectiveness of cold normal saline (4°C) as a carrier fluid in reducing propofol-induced pain compared with normal saline at room temperature. The findings demonstrated a significantly lower incidence and severity of pain in patients receiving cold normal saline, along with reduced postoperative recall of pain.

The demographic characteristics, including age, sex, and BMI, were comparable between both groups, indicating that the observed differences in pain outcomes were attributable to the intervention rather than baseline variations. Comparable demographic profiles have also been reported in previous clinical studies evaluating strategies to reduce propofol injection pain, thereby strengthening the internal validity of the present findings. [11]

A significantly lower proportion of patients in the cold normal saline group experienced pain during propofol injection compared to the room-temperature saline group. The reduction in pain incidence observed in the present study supports previous evidence that lowering the temperature of intravenous fluids decreases nociceptor activation and slows peripheral nerve conduction, thereby minimizing discomfort during injection. Euasobhon et al. similarly reported that interventions aimed at reducing local pain significantly improve patient comfort during anesthesia induction. [13] The severity of pain was also considerably reduced among patients receiving cold normal saline. None of the participants in the intervention group experienced severe pain, whereas severe pain was observed in patients receiving room-temperature saline. These findings are consistent with previous reports suggesting that simple non-pharmacological measures can effectively reduce both the intensity and frequency of propofol-induced pain without exposing patients to additional medications or adverse drug reactions. [15] Heart rate changes following propofol administration reflected the physiological response to pain. Patients receiving room-temperature saline demonstrated a greater increase in heart rate after injection, whereas heart rate remained relatively stable in the cold saline group. This observation indicates that effective pain reduction may also contribute to improved hemodynamic stability during anesthetic induction. Similar observations have been documented in studies evaluating various techniques for minimizing injection pain. [12]

Postoperative recall of injection pain was significantly lower among patients who received cold normal saline. Since unpleasant memories during anesthesia induction can negatively influence patient satisfaction and future acceptance of anesthesia, reducing postoperative recall represents an additional clinical benefit. Previous studies have emphasized that minimizing injection pain improves the overall perioperative experience and patient satisfaction. [14]

The present study demonstrates that cold normal saline is an inexpensive, safe, readily available, and easily applicable intervention that can be incorporated into routine anesthetic practice without additional equipment or pharmacological agents. Unlike drug-based interventions, cooling the carrier fluid avoids potential drug interactions and adverse effects while providing effective pain relief. These findings further support previous literature recommending simple physical measures for reducing propofol injection pain. [15]

Although the study showed favorable outcomes, certain limitations should be acknowledged. The study was conducted at a single center, and assessment was limited to immediate pain response and postoperative recall. Future multicenter studies with larger populations and comparisons with established pharmacological interventions such as lidocaine may further validate the effectiveness of cold normal saline as a routine carrier fluid during propofol administration.

Conclusion

Cold normal saline maintained at 4°C and used as a carrier fluid significantly reduced the incidence and severity of propofol-induced pain compared with normal saline at room temperature. Patients receiving cold normal saline also demonstrated lower postoperative recall of pain and improved

hemodynamic stability during induction. As a simple, safe, inexpensive, and non-pharmacological intervention, cold normal saline can be considered an effective strategy for minimizing propofol injection pain and improving patient comfort during anesthesia induction.

References

1. Picard P, Tramèr MR. Prevention of pain on injection with propofol: a quantitative systematic review. Anesth Analg. 2000; 90(4): 963-9.
2. Jalota L, Kalira V, George E, Shi YY, Hornuss C, Radke O, Apfel CC. Prevention of pain on injection of propofol: systematic review and meta-analysis. BMJ. 2011;342:d1110.
3. Tan CH, Onsiong MK. Pain on injection of propofol. Anaesthesia. 1998;53(5):468-76.
4. Nathanson MH, Gajraj NM, Russell JA. Prevention of pain on injection of propofol: a comparison of lidocaine with venous occlusion and lidocaine admixture. Anaesthesia. 1996;51(5):488-90.
5. Scott RP, Saunders DA, Norman J. Propofol: clinical strategies for preventing the pain of injection. Anaesthesia. 1988;43(6):492-4.
6. McCrirrick A, Hunter S. Pain on injection of propofol: the effect of injectate temperature. Anaesthesia. 1990;45(6):443-4.
7. Ambesh SP, Dubey PK, Sinha PK. Ondansetron pretreatment to alleviate pain on propofol injection: a randomized controlled trial. Anesth Analg. 1999;89(1):197-9.
8. Fujii Y, Nakayama M. A comparison of lignocaine, ketamine and placebo for prevention of pain associated with propofol injection. Can J Anaesth. 2005;52(5):474-8.
9. Singh DK, Jindal P, Singh G. Comparative evaluation of different methods for reducing propofol injection pain: a prospective randomized study. J Anaesthesiol Clin Pharmacol. 2011;27(4):488-92.
10. Agarwal A, Ansari MF, Gupta D, Pandey R, Raza M, Singh PK, Bisht S. Pretreatment with thiopental for prevention of propofol injection pain: a randomized controlled study. Anesth Analg. 2004;98(3):683-6.
11. Canbay O, Celebi N, Arun O, Karagöz AH, Saricaoğlu F, Ozgen S. Efficacy of intravenous paracetamol and lidocaine in preventing pain on propofol injection. Eur J Anaesthesiol. 2008;25(8):620-4.
12. Nakane M, Iwama H. A potential mechanism of propofol-induced pain on injection based on studies using nafamostat mesilate. Br J Anaesth. 1999;83(3):397-404.
13. Euasobhon P, Dej-Arkom S, Siriussawakul A, Muangman S, Sriraj W, Pitimana-aree S. Lidocaine for reducing propofol-induced pain on induction of anaesthesia: a systematic review and meta-analysis. Singapore Med J. 2016;57(7):339-47.
14. Mangar D, Holak EJ. Tourniquet at the forearm reduces pain on propofol injection. Anesth Analg. 1992;74(2):250-2.
15. Desousa KA. Pain on propofol injection: causes and remedies. Indian J Pharmacol. 2016;48(6):617-23.