Section: Anesthesia

Original Research Article

INVESTIGATING THE ROLE OF COLD NORMAL SALINE IN REDUCING PROPOFOL-INDUCED PAIN.

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ABSTRACT

Background: Pain on injection is a common and distressing side effect of propofol. Various methods have been explored to minimize this discomfort. This study aimed to evaluate the effectiveness of normal cold saline (4°C) as a carrier fluid in reducing the incidence and severity of propofol-induced pain compared to room temperature saline.

Materials and Methods: A randomized controlled study was conducted on 100 patients divided into two groups of 50 each. Group C received 10 ml of cold saline, while Group R received saline at room temperature prior to propofol administration. Pain scores, postoperative recall, and heart rate changes were recorded and analyzed.

Results: Group C showed a significantly lower incidence and severity of pain compared to Group R. Postoperative recall of pain was also reduced in Group C, along with more stable heart rate readings, indicating reduced nociceptive stress.

Conclusion: Cold normal saline is a simple, effective, and safe method to reduce propofol-induced pain, improving overall patient comfort during induction.

Keywords: Propofol, Injection pain, Cold saline.

INTRODUCTION

Propofol (2,6-diisopropylphenol) is a widely utilized intravenous anesthetic agent owing to its rapid induction, short duration of action, and favorable recovery profile. It is commonly used for induction and maintenance of general anesthesia, as well as for sedation in various procedures and intensive care settings.[1] Despite its pharmacokinetic advantages, a significant drawback of propofol is the pain it induces upon intravenous injection, which can be distressing for patients and may affect their overall anesthetic experience.[2]

Pain on propofol injection (POPI) remains a common and bothersome problem, with reported incidences ranging from 28% to 90%, depending on numerous factors such as site of injection, rate of administration, presence of carrier fluids, and the patient's age and anxiety level.[3,4] This pain is believed to be due to direct irritation of the endothelial lining of veins, activation of the kallikrein-kinin system, and involvement of nociceptive nerve endings.[5] Moreover, the lipid emulsion vehicle used in propofol formulations may enhance its potential to cause endothelial irritation and subsequent pain.[6]

To alleviate POPI, several pharmacological and non-pharmacological strategies have been explored. These include the use of lidocaine pretreatment, dilution of propofol, change in injection speed, use of larger veins, and modification of the temperature of either propofol or the carrier fluid.[7] Among these, reducing the temperature of the drug or its carrier fluid has garnered attention as a simple and cost-effective method to reduce pain. The underlying mechanism is thought to involve reduced nerve conduction velocity, vasoconstriction, and decreased activation of pain receptors at lower temperatures.[8]

Cold saline, particularly at temperatures around 4°C, has been evaluated in a few studies as a carrier fluid for propofol administration, showing a potential reduction in both the incidence and intensity of injection pain.[9] However, the evidence is still evolving, and there is a lack of sufficient data from Indian populations, where variations in practice, patient demographics, and pain perception may yield

different results. Furthermore, assessing the postoperative recall of this pain adds a meaningful dimension, as it reflects the subjective impact of POPI on patient memory and satisfaction.[10]

Given these considerations, this study aims to evaluate the effectiveness of cold normal saline (at 4°C) as a carrier fluid in reducing propofol-induced pain compared to normal saline at room temperature in a tertiary care center in India. The primary objective is to assess the incidence and severity of pain using a standardized pain scoring system, while the secondary objective focuses on evaluating the postoperative recall of the injection pain in both groups.

MATERIALS AND METHODS

Study Design and Setting: This prospective, randomized, comparative study was conducted at a tertiary care institute in India over a period of one year. Ethical clearance was obtained from the Institutional Ethics Committee prior to the commencement of the study. Written informed consent was obtained from all participants.

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki and after obtaining approval from the Institutional Ethics Committee of the tertiary care institute. Written informed consent was obtained from all participants after explaining the nature, purpose, potential risks, and benefits of the study in a language they understood. Participants were assured of the confidentiality of their personal information and were informed of their right to withdraw from the study at any point without affecting their medical care. The intervention posed minimal risk, as both cold and room temperature normal saline are routinely used in clinical practice, and patient safety remained the utmost priority throughout the study.

Sample Size and Group Allocation: A total of 100 patients undergoing elective surgeries under general anesthesia were initially considered for participation. After applying inclusion and exclusion criteria, 76 patients were enrolled and randomized into two equal groups of 38 each using a computer-generated randomization list.

- Group C (Cold Saline Group): Received 10 ml of normal cold saline (4°C) as a carrier fluid.
- Group R (Room Temperature Saline Group): Received 10 ml of normal saline at room temperature (~22–25°C) as a carrier fluid.

Inclusion Criteria

- ASA Physical Status I and II
- Age 18–60 years
- Patients scheduled for elective surgical procedures under general anesthesia
- Written informed consent provided

Exclusion Criteria

- Known allergy to propofol
- Patients on chronic pain medication
- History of psychiatric illness or cognitive dysfunction
- Communication barriers preventing pain assessment
- Uncooperative or unwilling patients

Procedure: Upon arrival in the operating room, all patients were monitored according to standard ASA guidelines. A 20-gauge intravenous cannula was inserted into the most prominent vein, preferably on the dorsum of the hand, following institutional protocol.

Patients in Group C received 10 ml of cold normal saline (at 4°C) through the IV line, while those in Group R received 10 ml of normal saline at room temperature. The saline was administered slowly, immediately prior to propofol administration.

Thereafter, half of the induction dose of propofol (1 mg/kg) was administered over 5 seconds, concurrently with the running saline. Following the propofol injection, patients were assessed for any signs or complaints of pain at the injection site.

Pain Assessment: Pain was evaluated based on both subjective patient responses and objective behavioral cues. The intensity of pain was graded using a four-point categorical scale:

- None: No pain or discomfort reported or observed.
- Mild: Patient reported pain only upon questioning, with no observable behavioral signs.
- Moderate: Patient voluntarily reported pain without prompting, accompanied by mild behavioral signs (e.g., facial grimace, slight hand movement).
- Severe: Patient expressed strong verbal response and demonstrated clear behavioral signs such as crying, hand withdrawal, or pronounced facial grimacing.

All assessments were conducted by an anesthesiologist blinded to group allocation, ensuring objective evaluation.

Postoperative Recall: To evaluate the secondary objective, patients were interviewed in the recovery room 1 hour postoperatively to determine whether they recalled any pain during the injection process. The presence or absence of such recall was noted.

Statistical Analysis: All collected data were compiled and analyzed using appropriate statistical software. Categorical variables such as pain scores and recall were expressed as frequencies and percentages. Intergroup comparisons were made using the Chi-square test or Fisher's exact test, as applicable. A p-value <0.05 was considered statistically significant.

RESULTS

[Figure 1] shows the comparison of the incidence of propofol-induced pain between Group C (cold saline) and Group R (room temperature saline). A higher number of patients in Group R (39 out of 50) experienced pain compared to Group C (26 out of

50), suggesting that cold normal saline as a carrier fluid may be more effective in reducing the incidence of injection pain.

[Figure 2] illustrates the degree of pain experienced by participants in both study groups. In Group C (cold saline), the majority reported no pain (24 participants), followed by mild (17), moderate (9), and no cases of severe pain. In contrast, Group R (room temperature saline) had a higher number of participants reporting mild (22), moderate (13), and severe pain (5), with only 9 participants reporting no pain. This distribution further supports the efficacy of cold saline in minimizing both the incidence and severity of propofol-induced pain.

[Figure 3] displays the change in heart rate before (HR 1) and after (HR 2) the administration of propofol in both study groups. In Group C (cold saline), the heart rate remained nearly stable (76.95 to 76.74 bpm), whereas Group R (room temperature saline) showed a noticeable increase from 79.97 to 82.74 bpm. This suggests that cold saline may help in attenuating the sympathetic response associated with propofol-induced pain.

[Figure 4] presents the data on postoperative recall of propofol injection pain. In Group C (cold saline), 18 participants reported the experience as not applicable (NA), 9 remembered the pain (Yes), and 11 reported no recall (No). In contrast, Group R (room temperature saline) had a greater number of patients (16) recalling the pain postoperatively, and only 7 participants reported NA. This suggests a higher likelihood of painful memory recall when room temperature saline was used as a carrier fluid for propofol administration.

[Table 1] shows the baseline demographic and clinical characteristics of the study participants in both groups. The mean age in Group C was 36.8 ± 13.2 years, while in Group R it was 37.2 ± 12.6 years, with no statistically significant difference between the groups ($p = 0.889$). The sex distribution was comparable, with a slightly higher proportion of females in both groups. The mean BMI was also similar between Group C (23.3 ± 4.1 kg/m²) and Group R (23.5 ± 4.3 kg/m²), with a p-value of 0.771, indicating no significant difference. These results confirm that the two groups were well-matched in terms of baseline characteristics.

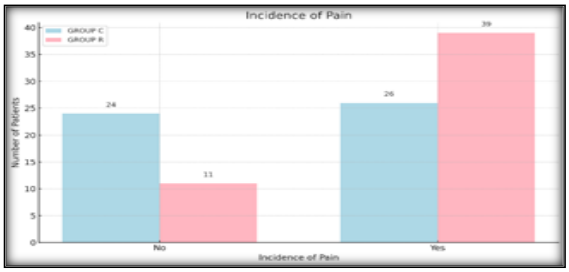

Figure 1: Showing incidence of pain in both groups

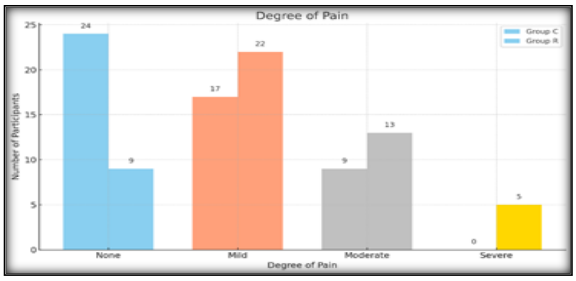

Figure 2: Showing the degree of pain in both groups

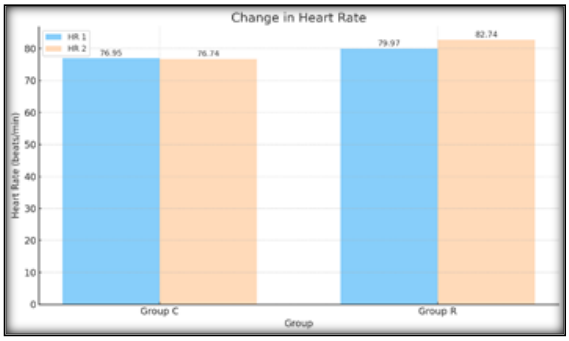

Figure 3: heart rate change in both groups

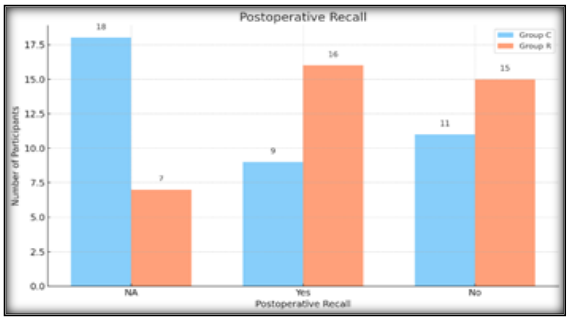

Figure 4: Showing post-operative recall in both groups. (NA = not applicable)

Table 1: Comparing demographic data in both groups

Variable	Group C (n=50)	Group R (n=50)	P value
Age (mean Â± SD) in years	36.8 ± 13.2	37.2 ± 12.6	0.889
Sex			
Male	46%	40%	
Female	54%	60%	
BMI (mean Â± SD) in kg/mÂ²	23.3 ± 4.1	23.5 ± 4.3	0.771

DISCUSSION

Pain on injection with propofol continues to be a significant concern in clinical anesthesia, often leading to discomfort, negative patient experiences, and, in some cases, apprehension about future anesthesia procedures. In this study, we evaluated the effectiveness of cold normal saline (4°C) as a carrier fluid in reducing the incidence and severity of propofol-induced pain, compared to room temperature saline. The findings suggest that cold saline significantly reduces both the occurrence and intensity of pain on injection.

The overall incidence of pain was lower in Group C (52%) compared to Group R (78%), affirming the analgesic effect of cold saline. These results are consistent with the findings of Ganta and colleagues, who demonstrated a statistically significant reduction in pain when cold propofol was used for induction.[11] The probable mechanism is vasoconstriction at lower temperatures, leading to reduced activation of pain receptors and decreased endothelial irritation.[12]

In terms of pain severity, the majority of patients in Group C reported either no pain or mild pain, while moderate and severe pain were more frequent in Group R. Similar trends were observed in the study by Honarmand and Safavi, where pretreatment with cold saline notably reduced the incidence of moderate-to-severe pain.[13] It is hypothesized that the cold temperature reduces the velocity of nociceptive signal transmission and modulates peripheral nerve endings.[14]

Postoperative recall of pain was another focus of this study. Fewer participants in Group C recalled experiencing injection pain compared to Group R. This is clinically relevant, as studies suggest that negative recall of anesthetic events can influence perioperative anxiety and satisfaction scores.[15] Cold saline may attenuate the emotional imprint of pain by blunting the initial nociceptive response, thereby reducing the chance of it being stored in long-term memory.

Heart rate variation served as a physiological indicator of nociceptive stress. A minimal change was observed in Group C, whereas a significant increase was noted in Group R, indicating a possible stress response to pain. This aligns with the findings of Ismail et al., who noted significant hemodynamic responses in patients reporting higher injection pain scores.[16] Controlling these fluctuations is important, especially in patients with cardiovascular comorbidities.

Although the study was conducted in a controlled environment and randomization was applied, certain limitations must be acknowledged. Firstly, the pain assessment was partly subjective, despite efforts to incorporate behavioral cues. Secondly, only a single dose of saline and propofol was evaluated, and potential synergistic effects with agents like lidocaine were not explored. Additionally, long-term patient satisfaction and anxiety parameters were beyond the scope of this study.

Nevertheless, our findings are supported by similar research from multiple centers. Lim et al. found that the combination of pre-cooling and slow injection of propofol significantly improved pain outcomes.[17] These results emphasize the potential of using cold saline—a simple, low-cost, and safe method—to enhance patient comfort during induction.

CONCLUSION

This study demonstrates that using cold normal saline (at 4°C) as a carrier fluid significantly reduces the incidence and severity of propofol-induced pain compared to normal saline at room temperature. Additionally, patients receiving cold saline showed lower postoperative recall of pain and more stable heart rate responses during induction. As a simple, cost-effective, and non-pharmacological intervention, cold saline can be a valuable addition to routine anesthesia practice to enhance patient comfort and satisfaction during propofol administration. Further studies on larger populations and in varied clinical settings are recommended to validate these findings and explore synergistic effects with other pain-relieving agents.

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