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Original Research Article

Evaluation of the effect of cold normal saline as a carrier fluid in reducing propofol induced pain

Murali Shankar Bhat[1], **Sheba Cherian**[2], **Raghavendra R Huchchannavar**[3], **Chethana Bolanthakodi**[4]*

[1]*Dept. of Anaesthesiology and Critical Care, K S Hegde Medical Academy, Mangalore, Karnataka, India*
[2]*Dept. of Anaesthesia and Operation Theatre Technology, Yenepoya School of Allied Health Care Professions, Bengaluru, Karnataka, India*
[3]*Dept. of Community Medicine, K S Hegde Medical Academy, Mangaluru, Karnataka, India*
[4]*Dept. of Obstetrics and Gynaecology, Father Mullers Medical College, Mangaluru, Karnataka, India*

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ABSTRACT

Background: Pain or discomfort during intravenous injection is a common unwanted result of Propofol, and can lead to dissatisfaction. Various methods are used to reduce 'pain on propofol injection' (POPI), among which mixing lignocaine with propofol is commonly used. However mixing lignocaine destabilises propofol, leading to reduced anaesthetic properties of propofol, warranting the use of other methods. Cold temperatures reduce nerve conduction velocity resulting in decreased pain signal transmission and have vasoconstrictive properties which reduce local tissue irritation, potentially minimizing pain.
Aim and Objective: To evaluate cold normal saline (at 4°C) as carrier fluid in reducing POPI compared to normal saline at room temperature, with a primary objective of assessing the incidence and severity of pain using a pain score and a secondary objective of assessing postoperative recall in both the groups.
Materials and Methods: A single-blinded prospective randomized controlled trial was conducted involving 76 patients undergoing general anaesthesia for elective surgeries. The patients were randomly assigned to two groups: Group C received cold saline (at 4°C) and Group R received room temperature saline as carrier fluids during propofol administration. Pain during injection was recorded using pain score, Heart rate changes before and after propofol administration, and Postoperative recall of injection pain was assessed.
Result: The incidence of pain was significantly lower in Group C (52.6%) compared to Group R (81.57%) (p=0.007). Group R had a higher severity of pain, with more patients experiencing moderate to severe pain. Group R also showed an increase in heart rate (3.46%) compared to Group C (0.27%) (p=0.027). Postoperative recall of injection pain was more frequent in Group R than in Group C.
Conclusion: Cold normal saline as a carrier fluid (at 4^0C) effectively reduces pain associated with propofol injection. This technique helps to enhance patient comfort and satisfaction, making it a valuable addition to clinical practice.

1. Introduction

Propofol is a popular intravenous anaesthetic drug for the induction and maintenance of anaesthesia, due to its smooth induction and faster recovery. One of the common issues encountered with propofol is that it causes

* *Corresponding author.*
E-mail address: muralishankarbhat@gmail.com (C. Bolanthakodi).

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discomfort or pain while injecting intravenously. Many patients attribute this as an unpleasant experience. Pain can be seen in as many as 70% of patients.[1] Propofol is an alkyl phenol. All phenols cause skin and mucous membrane irritation, which is why they can cause pain.[2] Irritation of venous adventitia can lead to the release of kininogen from the kinin cascade, further explaining the pain caused by propofol injection.[3] The frequency of pain after a propofol injection appears to be influenced by several variables like injection site, vein size, the speed of the injection, blood's ability to act as a buffer, speed of carrier fluid during injection, propofol temperature at the time of injection, the syringe material and the concurrent use of medications like opiates or local anaesthetics. Various methods were tried to reduce POPI (pain on propofol injection) including mixing lignocaine with propofol, pre-treatment with lignocaine, opioids, ketamine, midazolam, NSAIDS, magnesium sulphate etc.[4,5] Out of all the methods, adding lignocaine to propofol is one of the widely used, but mixing of lignocaine destabilizes the propofol emulsion and reduces the anaesthetic property of the propofol.[6,7] Furthermore, researchers have feared that the larger oil droplets formed due to destabilised propofol emulsion might pose the risk of pulmonary embolism.[8] This challenges the popular practice of mixing lignocaine and indicates the alternate methods.

One of the nonpharmacological methods used to reduce pain is either using cold propofol or cold saline as a carrier fluid. The cold carrier fluid might provide a local anaesthetic effect on the vein wall, or it could delay the enzymatic reactions at the propofol injection site.[9] This can be a safe and effective method to reduce POPI. A few studies have been done to check the effectiveness of cold carrier fluid in reducing POPI, hence we decided to compare cold saline (at 4°C) with room temperature saline as a carrier fluid to reduce POPI, with a hypothesis that cold saline is beneficial in lowering POPI. This study aimed to evaluate cold normal saline (at 4^0C) as carrier fluid in reducing POPI compared to normal saline at room temperature, with a primary objective of assessing the incidence and severity of pain using a pain score and a secondary objective of assessing postoperative recall in both the groups.

2. Materials and Methods

A single-blinded prospective randomised control study was designed and approval from the institutional ethics committee (INST.EC/EC/037/2022 dated 29/4/2022) was obtained before the start of the study. Incidence of perceived pain at the site of injection from the study conducted by Barker et al. (cold saline group 30% and the control group 70%) was considered for the calculation of the sample size.[9] At 95% confidence interval and 95% power of the study, the minimum sample size required was 48 (24 in each group). However, we have included all the eligible cases during the study period (1 month). 80 patients undergoing general anaesthesia for elective surgeries with the age group 18-65 years were assessed, but 4 patients refused to participate, hence 76 were included in the study. (Diagram 1) The procedure was explained to them in detail and written informed consent was taken. Their demographical data were noted. They were divided into 2 groups containing 38 each in both the groups (Group C=38, Group R=38) with computer-generated random numbers. Group C received cold normal saline (at 4°C) as carrier fluid whereas Group R received normal saline at room temperature. On arrival into the operating room, patients were cannulated with a 20-gauge cannula into the largest visible vein, preferably on the dorsum of the hand as standard practice. Group C patients received 10 ml of cold normal saline and Group R patients received 10 ml of room temperature normal saline. After that, patients in both groups were given half the induction dose of propofol over 5 seconds, with their respective saline running. Then, patients were asked for any pain or discomfort at the injection limb and any signs of pain were observed. The pain score was graded from none to severe depending on the patient's response. Patients were graded as 'none' if they had no pain. If they said they had pain only on asking and there were no behavioural signs, then they were graded in 'mild pain'. If patients said they had pain without being questioned along with some mild behavioural signs, they were graded in 'moderate pain'. Patients were graded in severe pain if they showed strong responses verbally along with strong behavioural responses like tears or withdrawal of hand or grimacing of facial muscles etc.[10]

After the assessment of the pain score, the remaining dose of propofol was given. The heart rate was recorded before (HR1) and immediately after (HR2) the administration of propofol. Analgesia and muscle relaxation were given to facilitate intubation. Maintenance of anaesthesia and extubation was done as per standard protocol. After extubation, the patient was shifted to PACU. Once they were completely conscious and oriented in the PACU, patients were asked whether they had pain while injecting propofol (post-op recall).

2.1. Statistical analysis

Data was compiled in MS Excel. The statistical analysis was performed using SPSS software version 20 with Unpaired t-test and Chi-square test between the two groups. A 'p' value <0.05 was considered significant in this study.

3. Results

Both groups displayed comparable demographic data. (Table 1)

The incidence of pain was more in Group R (81.57%) compared to Group C (52.6%) which was statistically

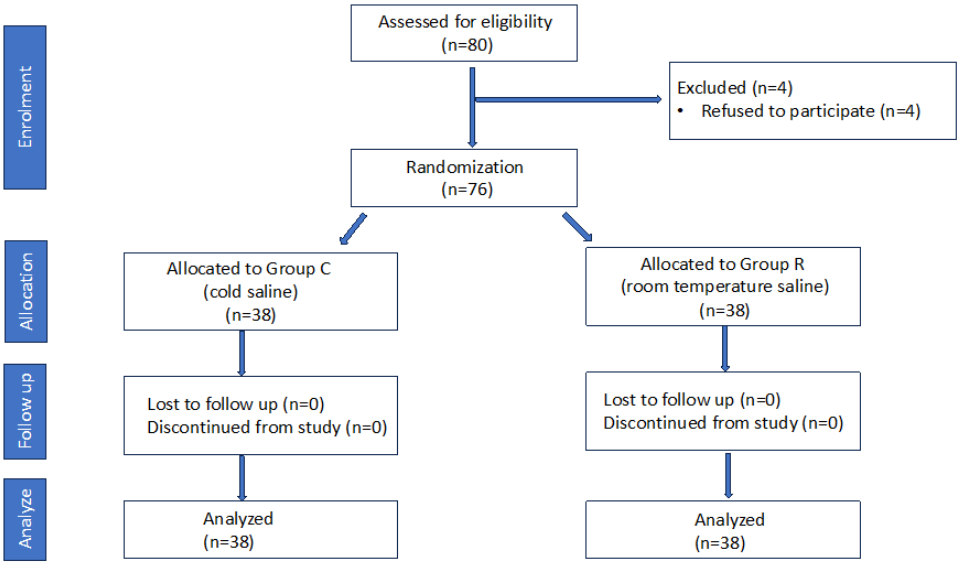

Diagram 1: Consort diagram

significant (p=0.007). (Figure 1) The severity of the pain was also more in Group R with more number of patients experiencing moderate to severe pain and higher pain score. (Figure 2)

There was a slight drop in heart rate after giving propofol in Group C (difference in heart rate 0.27%) which was statistically insignificant (p value=0.849), whereas there was an increase in heart rate in Group R (difference in heart rate 3.46%) with p value = 0.027 indicating that it was statistically significant. (Figure 3)

In the comparison of both groups based on post-op recall (Figure 4), a statistically significant difference ('p' value <0.05) was observed. Since 18 patients in Group C and 7 patients in Group R didn't have pain during the induction, they are not applicable for postoperative recall of propofol-induced pain.

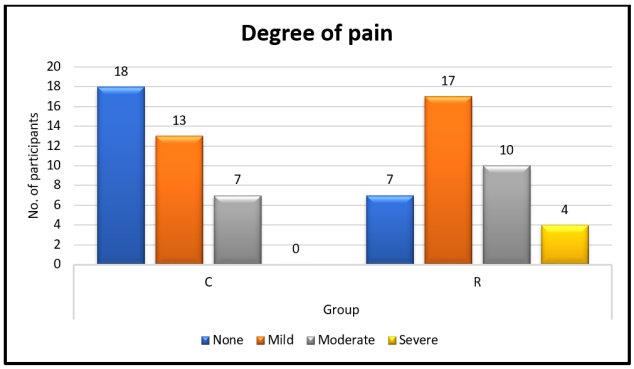

Figure 2: Showing the degree of pain in both groups

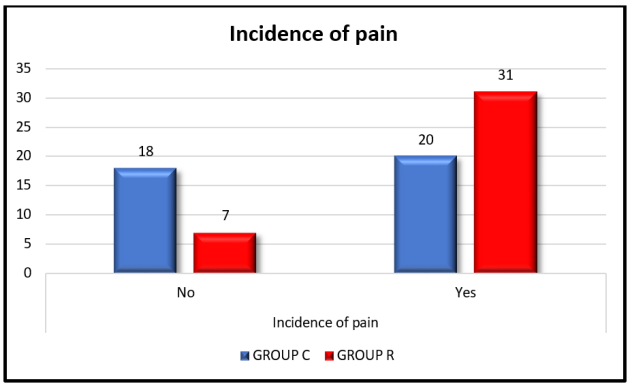

Figure 1: Showing incidence of pain in both groups

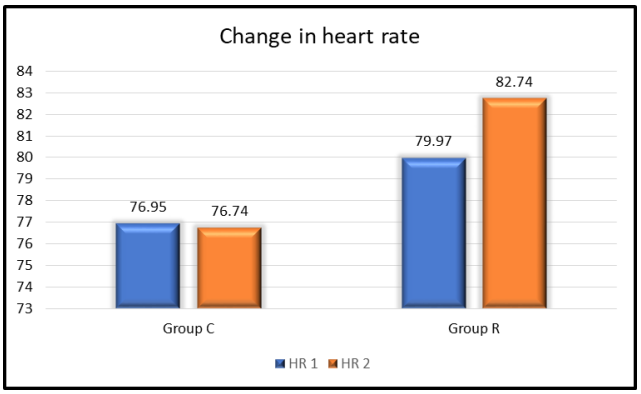

Figure 3: Showing heart rate change in both groups

In Group C, for those who experienced pain (20 patients out of 38), 9 patients (45%) recalled that they had pain and in Group R, for those who experienced pain (31 patients out of 38), 16 patients (51.6%) recalled that they had pain.

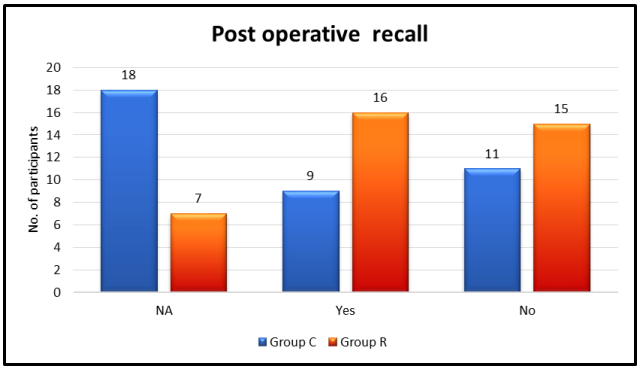

Figure 4: Showing post-operative recall in both groups. (NA = not applicable)

Table 1: Comparing demographic data in both groups

Group	C (n=38)	R (n=38)	P value
Age (mean ± SD) in years	37 ± 12.9	38 ± 12.2	0.906
Sex	Male = 44.7% Female = 55.3%	Male = 36.8% Female = 63.2%	
BMI (mean ± SD) in kg/m2	23.4 ± 4.4	23.6 ± 3.9	0.758

4. Discussion

Propofol-induced pain that occurs during the induction of anaesthesia is a widely acknowledged and commonly experienced problem in clinical practice. Some patients recall the propofol injection was the most discomforting and painful part of their anaesthesia experience.[11] The discomfort and distress of this adverse event can lead to patient dissatisfaction and may even impact the overall perioperative experience.

Cooling agents have been used effectively in clinical practice for superficial procedures and to decrease the pain of tissues affected by trauma or surgery.[12–14] Application of cold temperature is a common clinical practice by using vapocoolent spray for IV cannulation, small incision drainage procedures, etc., which numbs the site where it is applied.[15] The Application of cold compression (using ice packs) helps reduce pain and oedema of soft tissue and musculoskeletal injuries, which is a common clinical practice.[16] The cold temperature reduces the nerve conduction velocity, thereby diminishing the transmission of pain signals. Also, the vasoconstrictive properties of cold temperatures may help minimise local tissue irritation upon propofol injection. Cold temperatures have been shown to induce temporary numbness and decrease sensitivity at the injection site. This analgesic property may also be attributed to the 'gate control theory of pain', which could be another reason for the reduced pain perception associated with propofol administration.[17] As seen in our study, patients who received room temperature saline as carrier fluid had more pain than those who received cold saline. The above reasoning explains the lesser number of people experiencing pain who received cold saline as a carrier fluid; also, the severity of the pain was less than those who received room temperature saline as a carrier fluid. In clinical practice, most of the time, preservative-free lignocaine is used either pretreatment or mixed with propofol to reduce POPI. Barker P et al. compared 4 groups - unmodified propofol, propofol with 0.05% lignocaine, cold propofol at 4°C, and 10 ml of normal saline at 4°C pretreatment followed by unmodified propofol and assessed pain after propofol injection. They found that 10 ml of normal saline at 4°C pretreatment group had the least incidence of POPI (22%), followed by propofol at 4°C (33%) and propofol with lignocaine (44%).[9] This study showed that cold temperature reduced POPI better than mixing with lignocaine, and pretreatment and using cold saline as a carrier fluid has better pain relief than just cold propofol. Furthermore, many studies, like Masaki et al. Lilley et al. and Park et al. questioned the popular practice of mixing propofol with lignocaine since lignocaine destabilises propofol emulsion and can reduce its anaesthetic property and can cause complications.[6–8] So, adding lignocaine to reduce POPI should be avoided. That is why, non-pharmacological methods like cold temperature, which is used in our study, have an advantage over adding lignocaine.

Propofol depresses the baroreceptor. So, the heart rate should have been similar to the baseline heart rate even though propofol can induce hypotension.[10] But pain or stress can induce sympathetic stimulation, which can lead to an increase in the heart rate.[18] In our study, patients who received cold normal saline as carrier fluid did not show much change in heart rate after induction compared to baseline, but those who received room temperature saline as a carrier fluid showed significantly higher heart rates than the baseline. This also indicates the higher degree of pain they experienced and thus further solidifies our observation that the patient had more pain with room temperature saline as a carrier fluid since heart rate is not subjected to participant bias.

Several factors such as the site and size of the IV cannula, speed of injecting propofol, dose of propofol used, dose of analgesics, and use of other sedatives can affect the outcome of the study. Hence these factors are addressed by standardizing these factors in our methodology.

This study re-confirms the analgesic properties of cold temperatures and the use of cold normal saline in reducing POPI. This method is easy to practice and inexpensive. The knowledge from the study gives us the confidence to use non-pharmacological methods like cold saline as a carrier fluid for propofol injection. This can be incorporated into our routine anaesthesia practice as it is shown in the methodology, or along with other pharmacological methods like adding additives to propofol such as ketamine, opioids or pretreatment of lignocaine before propofol injection, for which future studies can be conducted to confirm the benefit of combining different methods. The usage of two different methods non-pharmacological and pharmacological may provide the best pain relief to the patients.

5. Limitations

This was a single blinded study. Since patients can differentiate between cold saline and room temperature saline, double blinding cannot be done.

Variations in individual pain thresholds and responses to propofol injection may have influenced the results. Grading of pain is subjective and depends on the complaint of the patient and is also subjected to the documentation of the observer. Even though cold saline decreased POPI compared to room temperature saline, still 52.6% of participants experienced pain.

6. Future Scope

Further research is needed combining non-pharmacological methods like cold saline as a carrier fluid, with pharmacological methods like lignocaine, ketamine, NSAIDs pretreatment, mixing of ketamine with propofol to see whether combining non-pharmacological method along with pharmacological methods improves the pain relief for POPI.

7. Conclusion

Cold normal saline as a carrier fluid (at 4°C) effectively reduces pain associated with propofol injection. This technique helps to enhance patient comfort and satisfaction, making it a valuable addition to clinical practice.

8. Source of Funding

None.

9. Conflict of Interest

None.

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Author's biography

Murali Shankar Bhat, Associate Professor https://orcid.org/0000-0002-7437-1539

Sheba Cherian, Assistant Professor https://orcid.org/0009-0001-2437-7844

Raghavendra R Huchchannavar, Assistant Professor https://orcid.org/0000-0003-2601-514X

Chethana Bolanthakodi, Assistant Professor https://orcid.org/0000-0003-4040-9049

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