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Original Article

Comparison of Cold Normal Saline and Lidocaine for Pain Relief During Propofol Injection

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Abstract

Background: Propofol is a commonly used anesthetic agent that frequently causes severe pain upon injection. Various pharmacological and non-pharmacological interventions have been employed to reduce the severity of this injection-related pain. The aim of this study was to compare the efficacy of intravenous cold normal saline with that of lidocaine in reducing pain during propofol injection.

Methods: Patients were randomly assigned to three groups of 40 using permuted block randomization. Each patient received one of the following interventions: Group A received intravenous (IV) cold normal saline (4°C); Group B received IV room-temperature normal saline (25°C); and Group C (control group) received IV lidocaine 0.5%. All groups subsequently received 50 mg of 1% propofol. Pain intensity was assessed using a visual analog scale (VAS) at baseline, and at 15 and 30 seconds after propofol injection. Heart rate and blood pressure were recorded before injection and continued for up to 15 minutes after drug administration. Data were presented as mean ± standard deviation (SD), and a *P*-value < 0.05 was considered statistically significant. All statistical analyses were performed using GraphPad Prism version 8.0.

Results: Pain intensity in patients receiving cold saline was lower than that in the other two groups; however, this difference did not reach statistical significance. Heart rate and blood pressure values remained within normal physiological ranges across all groups throughout the study period.

Conclusion: Cold normal saline may serve as a suitable and cost-effective alternative to lidocaine for reducing pain during propofol injection, given its comparable analgesic efficacy ($p = 0.12$).

Keywords: Propofol; Pain; Lidocaine; Cold Temperature; Sodium Chloride

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Introduction

Propofol is commonly used as an anesthetic agent for general anesthesia; however, it is associated with several adverse effects, including cardiovascular complications such as bradycardia and hypotension. Pain and discomfort at the injection site are among the most common adverse effects, occurring in approximately 46% of patients receiving propofol infusion[1, 2]. Various strategies have been employed to reduce this injection-related pain, including cooling or warming the propofol solution, diluting the propofol emulsion, administering propofol through a large vein, and pretreating patients with an intravenous (IV) injection of lidocaine [3].

Lidocaine is a local anesthetic commonly used to alleviate pain associated with propofol injection [4]. However, lidocaine administration is not without its own adverse effects, which may include neurological and cardiac disturbances such as dizziness, lightheadedness, hypotension, and cardiac arrhythmia [5]. Furthermore, the addition of lidocaine to propofol emulsions can disrupt emulsion stability and may potentially increase the risk of pulmonary embolism [6].

Cryotherapy is frequently utilized for pain relief in postoperative settings and sports injuries [7]. Cold temperature may reduce propofol injection pain by stimulating temperature-sensitive nerve endings, leading to suppression of pain at the spinal level [8-10].Despite these potential benefits, few studies have specifically investigated the effect of cold temperature on pain reduction following propofol injection. Given that lidocaine can cause significant adverse effects, the aim of the present study was to compare the efficacy of cold normal saline versus lidocaine in relieving pain induced by propofol injection, and to evaluate whether cold normal saline could serve as a suitable alternative to lidocaine

Methods

Study Design and Ethics Approval

This double-blind, randomized, controlled trial was approved by the Ethics Committee of the Research Vice Chancellor of Rohani Hospital, Babol University of Medical Sciences (IR.MUBABOL.REC.1399.426). Written informed consent was obtained from all participants prior to enrollment. This study was registered in the Iranian Registry of Clinical Trials (IRCT20141121020020N7).

Study Population and Eligibility Criteria

Inclusion criteria were age 18–60 years, American Society of Anesthesiologists (ASA) physical status class I or II, and candidacy for elective surgery under general anesthesia. A total of 120 patients were enrolled between March and May 2021. Exclusion criteria were a history of painful propofol injection, anxiety or non-cooperation, sensitivity to lidocaine or propofol, history of seizures, cardiovascular disorders, and psychiatric problems.

Sample Size and Randomization

Sample size was determined based on our pilot study ($\alpha = 0.05$, $\beta = 0.2$, effect size = 0.65). Patients were randomly assigned to three groups of 40 using a permuted block randomization method with a block size of 6. The three groups received either cold normal saline, room temperature (RT) normal saline, or lidocaine. Study medications and placebos were prepared in identical packaging with a randomization code. The study medications were administered by a nurse who was not involved in other aspects of the study.

Intervention and Drug Administration

After standardized monitoring, a 20-gauge cannula was inserted into a vein on the dorsum of the patient's non-dominant hand, and lactated Ringer's solution was infused. A tourniquet cuff was inflated to 70 mmHg. Patients then received one of the following pretreatment solutions: 10 mL of cold normal saline (Iranian Parenteral and Pharmaceutical Co.), 10 mL of RT normal saline, or 10 mL of 0.5% lidocaine (Caspian Tamin Pharmaceutical Co.). After one minute, the tourniquet was deflated. Subsequently, 50 mg of 1% propofol (DarmanYab Darou IRC) in 5 mL was administered over 5 seconds to all groups.

Outcome Measures

Pain was assessed using a visual analog scale (VAS) with the following categories: 0–1 (no pain), 2–3 (mild pain), 4–5 (moderate pain), 6–7 (severe pain), 8–9 (very severe pain), and 10 (unbearable pain). Pain intensity, as the primary outcome, was recorded at baseline and at 15 and 30 seconds after propofol injection by an observer

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(an anesthesiologist) who was blinded to the treatment allocation. Anesthesia induction and intubation were performed using 2 mg of midazolam, 100 µg of fentanyl, 2.5 mg/kg of propofol, and 0.6 mg/kg of atracurium. Hemodynamic changes, as the secondary outcome, including heart rate and blood pressure, were monitored from the time of pretreatment with normal saline or lidocaine until 15 minutes after the start of surgery.

Statistical Analysis

Analysis of variance (ANOVA) was used to compare demographic data, hemodynamic changes, and mean pain intensity between groups. Data were presented as mean ± standard deviation (SD), and a p-value < 0.05 was considered statistically significant. All statistical analyses were performed using GraphPad Prism version 8.0.

Results

Between March and May 2021, 120 patients who met the eligibility criteria were enrolled. The three groups were comparable with respect to baseline demographic characteristics (Table 1).

Table 1: Comparison of patient characteristics between groups

Groups	Cold normal saline	RT Lidocaine	RT normal saline	P-value
Age	27.55±6.81	30.9±8.27	29.05±8.61	0.19
Sex M/F	25/15	25/15	27/12	0.86

Data are presented as mean ± SD or number, RT: room temperature

Pain severity following propofol injection is presented in Table 2 and Figure 1. Lower pain severity was observed in the group pretreated with cold normal saline compared to the other two groups; however, this difference was not statistically significant

Table 2: Visual analogue score for pain before injection, 15 and 30 second after injection between groups

Groups	Cold normal saline	Lidocaine	RT normal saline	p-value
Before Inj	1.37±0.47	1.42±0.54	1.35±0.48	0.79
15 sec after Inj	3.77±1.45	4.15±1.25	4.12±1.22	0.36
30 sec after Inj	3.47±1.26	3.95±1.21	4±1.28	0.12

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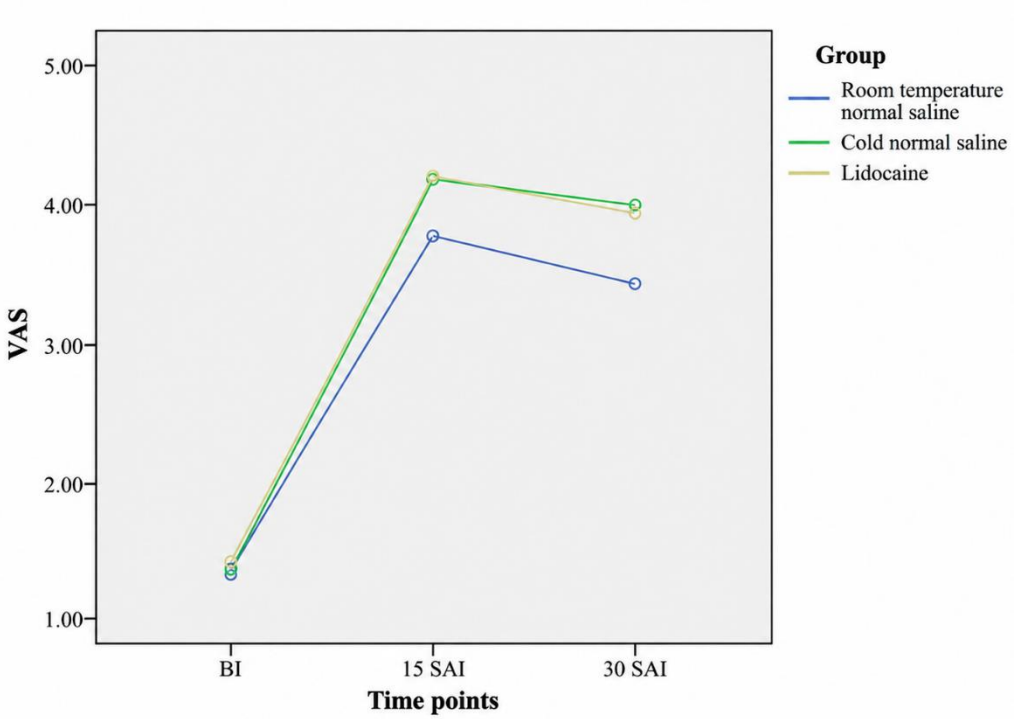

Figure 1: Propofol pain intensity in patients pretreated with room temperature normal saline, cold normal saline, and lidocaine at three time points; BI: before injection, 15 SAI: 15 seconds after injection, 30 SAI: 30 seconds after injection

Inter-group analysis revealed that blood pressure and heart rate remained within similar ranges across all groups at the different time points. Intra-group analysis showed a decreasing trend in blood pressure, which was remarkable at some time points. In contrast, heart rate increased during the follow-up period (Table 3). All changes in blood pressure and heart rate remained within the normal range.

Table 3: Changes in the blood pressure and heart rate in all groups during the follow-up time

		Blood pressure					Heat ratio			
	Baseline	**Before induction**	**After intubation**	**5 min after intubation**	**15 min after intubation**	**Baseline**	**Before induction**	**After intubation**	**5 min after intubation**	**15 min after intubation**
Cold normal saline	109.3±14.16	106.3±11	106±10	99.9±10.86	97.12±9.6	74.9±6.7	76.7±6.13	85±6.7	88.6±8	89.7±6.9
RT normal saline	109.6±11.8	107±10.4	103.12±10.4	98±12.3	96.7±11.21	74.4±6.9	77.3±6.6	84.6±6.7	90.6±10.7	91±10.12
lidocaine	109.7±9.7	107.3±7.8	106±10.22	100±11	97.5±8.8	73.4±4.5	76.15±5.8	81.7±7.5	86.4±7.5	88±6.9

Data are presented as mean ± SD. MAP, mean arterial pressure; HR, heart rate; RT, room temperature; min, minutes. No statistically significant differences were observed among the three groups at any of the evaluated time points (P > 0.05).

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Discussion

Cold temperature alleviates pain through several mechanisms, including vasoconstriction, reduction of nerve conduction velocity, and inhibition of the kinin–kallikrein pathway [8, 11]. However, limited research has investigated the effect of cold exposure on reducing pain during intravenous (IV) propofol injection.

In the present study, cold normal saline had a better, albeit non-significant, effect on alleviating pain intensity after propofol injection compared to room-temperature normal saline and lidocaine. Furthermore, we observed a declining trend in blood pressure accompanied by an increase in heart rate. The vasodilatory and hypotensive effects of propofol have been extensively reported [12, 13]. In our study, the elevation in heart rate may represent a compensatory response to the decline in blood pressure following propofol induction.

Our results are consistent with those of Barker et al., who reported that in patients undergoing elective surgery, administration of cold saline significantly reduced pain intensity following 2.5 mg/kg propofol compared to unmodified propofol alone. Moreover, comparison of cold saline with cold propofol and propofol premixed with lidocaine showed no discernible effect on pain reduction during propofol injection [14]. Despite these findings, two previous studies indicated that cold propofol alone has no pain-relieving effect compared to combination therapy of propofol with analgesics

This discrepancy may be explained by small sample sizes. It has been reported that cold propofol was associated with an increased incidence of pain compared to room-temperature propofol premixed with lidocaine [15]. Similarly, Cho et al. observed that 2 mg/kg cold propofol alone had no effect on pain relief, whereas the combination of remifentanil with cold propofol significantly minimized propofol-induced pain [16]. This suggests that cold normal saline may be more effective in reducing pain than cold propofol.

It appears that a better pain-relieving effect occurs when cold is applied to the vein prior to propofol injection. In our study, a one-minute interval was maintained between cold normal saline and propofol administration.

Our results are also in line with Kamal et al, who reported that patients receiving cold normal saline (4°C) experienced significantly less pain during propofol injection compared to those in the control group [17, 18].

Consistent with our study, Aggarwal et al. and Seangrung et al. reported hypotension with increased pulse rate after induction of anesthesia with propofol [12] . The differences between those studies and our findings may be attributed to the higher doses of propofol used in other studies. It is noteworthy that all hemodynamic variations remained within normal limits in patients receiving cold normal saline, similar to the lidocaine group.

Conclusion

Considering the safety, efficacy, and cost effectiveness of cold normal saline, it may serve as a suitable alternative to lidocaine for reducing propofol induced pain. Given that lidocaine is associated with cardiovascular and neurological side effects, cold normal saline offers a potentially safer option. However, larger scale studies with greater sample sizes are warranted to confirm these findings.

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Conflict of Interests

The authors declare no financial and non-financial conflict of interest

Author's contribution

S.S. did study design, M.Y. collected the data and prepared the manuscript, M.M. analyzed the data and reviewed the article.

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Ethics statement

This double-blind, randomized, controlled trial was approved by the Ethics Committee of the Research Vice

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Clinical Trial Registry

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