Efficacy of Different Doses of Lidocaine in the Prevention of Pain Due to Propofol Injection: A Randomized, Open-Label Trial in 120 Patients

Halit Madenoglu, MD, Karam Mehmet Yildiz, MD, Kudret Dogru, MD, and Adem Boyaci, MD

Department of Anaesthesiology, Erciyes University Gevher Nesibe Hospital, Kayseri, Turkey

ABSTRACT

Background: The incidence of pain due to propofol injection is high, but the most efficacious method of preventing this pain has not been identified.

Objective: The aim of this study was to investigate the efficacy of lidocaine, at different doses and schedules, on propofol injection pain.

Methods: In this open-label study, conducted at the Department of Anaesthesiology, Erciyes University Gevher Nesibe Hospital (Kayseri, Turkey), patients with American Society of Anesthesiologists Patient Acuity Classification I-II (ASA I-II) (ie, patients with absent [I] or mild [II] underlying systemic disease) aged 18 to 60 years undergoing various types of surgery were eligible. Patients were randomized to 1 of 4 treatment groups: group 1 received propofol; group 2, a combination of propofol plus lidocaine 10 mg; group 3, lidocaine 10 mg 30 seconds before propofol administration; and group 4, lidocaine 1 mg/kg 30 seconds before propofol administration (all drugs were administered intravenously). After cessation of the standard replacement fluid infusion (isotonic saline), propofol was given at a rate of 2 mL every 5 seconds until a dose of 2 mg/kg was reached. The patients were asked to rate their pain according to the following scale: 0 = none, 1 = mild, 2 = moderate, and 3 = severe.

Results: A total of 120 patients (61 men, 59 women; mean [SD] age, 38.7 [8.9] years) were enrolled in the study ($n = 30$ patients in each group). The incidence of injection pain in groups 2 and 4 was significantly lower than that in groups 1 and 3 (all $P < 0.05$), but no significant difference in the incidence of pain was found between groups 1 and 3. The incidence of pain in group 2 was significantly lower than that in group 4 ($P < 0.05$).

Conclusions: In this study population, the addition of 10 mg of lidocaine to propofol 2 mg/kg, or the administration of 1 mg/kg of lidocaine 30 seconds

before the administration of propofol 2 mg/kg, effectively decreased pain caused by propofol injection. Furthermore, a lower dose of lidocaine could be used. Based on our results, we suggest mixing propofol with 10 mg of lidocaine to decrease pain due to propofol injection during anesthesia induction. (*Curr Ther Res Clin Exp.* 2003;64:310–316) Copyright © 2003 Excerpta Medica, Inc.

Key words: propofol, injection pain, lidocaine, local anesthetics.

INTRODUCTION

Injection pain is the most common undesired effect of the widely used anesthetic agent propofol.¹ The reported incidence of pain varies between 25% and 100%. The pain causes stress during the induction phase and is considered to be the most important disadvantage of propofol use.^{1–4} Although various pharmacologic^{3–5} and nonpharmacologic^{6,7} methods to decrease pain due to propofol injection have been tried, the most efficacious method has not been identified.⁸

The aim of this study was to investigate the efficacy of lidocaine at different doses and schedules on propofol injection pain.

PATIENTS AND METHODS

This randomized, open-label study was conducted at the Department of Anaesthesiology, Erciyes University Gevher Nesibe Hospital (Kayseri, Turkey). The protocol was approved by the faculty ethics committee.

Patients with American Society of Anesthesiologists Patient Acuity Classification I-II (ASA I-II) (ie, patients with absent [I] or mild [II] underlying systemic disease) aged 18 to 60 years were eligible for the study. Patients who had received analgesics in the 24 hours preceding the surgery or who had a history of drug allergy, chronic pain, or thrombophlebitis, or who were pregnant, possibly pregnant, or lactating were excluded. Premedication was not given to any patient. Verbal informed consent was obtained from all patients before they entered the study.

Patients were randomized to 1 of 4 treatment groups: group 1 received propofol; group 2, a combination of propofol plus lidocaine 10 mg; group 3, lidocaine 10 mg 30 seconds before propofol; and group 4, lidocaine 1 mg/kg 30 seconds before propofol (n = 30 patients in each group). All treatments were administered intravenously, and all propofol doses were 2 mg/kg. All medications were kept at room temperature (20–24°C) and were prepared 5 to 10 minutes before administration. All medications were injected in an open-labeled manner. The same investigator who administered the drug also questioned the patients about the pain after propofol administration. For patients in group 2, propofol and lidocaine were mixed by an assistant immediately before

injection. After the patients were taken to the surgical suite, electrocardiography (DII; right arm-left leg), blood pressure (by a noninvasive method), and pulse oximetry were monitored (Datex-Engstrom AS/3®, Datex Medical Instrumentation Corp., Helsinki, Finland). A standardized cannula (20-G), the site of venous cannulation (in the dorsum of the hand), and the speed of saline infusion (given at a rate of 2 mL every 5 seconds) were the same for all patients.

Propofol injection was started after cessation of the standard replacement fluid infusion (isotonic saline) until a dose of 2 mg/kg was reached. Until loss of consciousness, patients were asked whether they had pain and, if so, of what magnitude. The pain was assessed and recorded according to a standard scale⁶ (0 = none, 1 = mild, 2 = moderate, 3 = severe).

Statistical Analysis

Statistical analysis was performed with the Statistical Package for Social Sciences version 9.0 (SPSS Inc., Chicago, Illinois). The demographic data were assessed using 1-way analysis of variance and (post hoc) the Duncan multiple-range test. The incidence of pain was assessed using the Kruskal-Wallis test, and the Mann-Whitney *U* test when a significant difference was found between groups. $P \leq 0.05$ was considered significant.

RESULTS

A total of 120 (61 men, 59 women; mean [SD] age, 38.7 [8.9] years) were included in the study ($n = 30$ patients in each group). No significant differences were

Table I. Demographic and clinical characteristics of study patients ($N = 120$).*

Characteristic	Group 1 ($n = 30$)	Group 2 ($n = 30$)	Group 3 ($n = 30$)	Group 4 ($n = 30$)
Age, mean (SD), y	37.4 (9.5)	38.4 (8.1)	39.3 (8.9)	39.8 (9.2)
Sex, no. (%)				
Men	16 (53.3)	15 (50.0)	14 (46.7)	16 (53.3)
Women	14 (46.7)	15 (50.0)	16 (53.3)	14 (46.7)
Body weight, mean (SD), kg	78.33 (6.81)	82.13 (6.20)	80.70 (6.03)	78.33 (6.68)
Height, mean (SD), cm	168.20 (6.81)	169.66 (4.32)	168.10 (4.27)	170.10 (5.12)

*Group 1 received propofol only; group 2 received a mixture of propofol and lidocaine 10 mg; group 3 received lidocaine 10 mg 30 seconds before propofol; and group 4 received lidocaine 1 mg/kg 30 seconds before propofol.

found between the groups with respect to age, sex, body weight, or height (Table I).

In group 1, 66.7% (20/30) of patients experienced pain. This rate was 60.0% (18/30) in group 3, 30.0% (9/30) in group 4, and 16.7% (5/30) in group 2 (Table II). In group 2, no patients experienced severe pain; the incidence of patients who experienced severe pain was 16.7% (5/30) in group 1, 13.3% (4/30) in group 3, and 3.3% (1/30) in group 4. The incidence of injection pain in groups 2 and 4 was significantly lower than in groups 1 and 3 (all $P < 0.05$). The incidence of pain was similar in groups 1 and 3. The incidence of pain in group 2 was significantly lower than in group 4 ($P < 0.05$).

No precipitation of the mixture of propofol and lidocaine, vessel damage, or arrhythmia was observed.

DISCUSSION

A calm and tranquil anesthesia induction phase is important for patient comfort and compliance. Unpleasant experiences during induction adversely affect the subsequent stages of anesthesia. Propofol, which induces rapid and comfortable loss of consciousness, has the significant disadvantage of causing a burning pain sensation during injection.¹ This pain sometimes causes unnecessary stress during the induction phase.⁸

Although the exact mechanism of pain due to propofol administration has not been determined, the direct irritation of the vessel wall by the oil-emulsifying vehicle^{9,10} and the activation of kininogen-like pain mediators in the vessel wall have been implicated.^{2,9,11} A latent period for pain after propofol injection has

Table II. Incidence of pain (no. [%] of patients) in study population (N = 120).*

Pain Score [†]	Group 1 (n = 30)	Group 2 (n = 30)	Group 3 (n = 30)	Group 4 (n = 30)
0	10 (33.3)	25 (83.3)	12 (40.0)	21 (70.0)
1	7 (23.3)	3 (10.0)	8 (26.7)	5 (16.7)
2	8 (26.7)	2 (6.7)	6 (20.0)	3 (10.0)
3	5 (16.7)	0 (0.0)	4 (13.3)	1 (3.3)
1 + 2 + 3 [‡]	20 (66.7)	5 (16.7)	18 (60.0)	9 (30.0)

*Group 1 received propofol only; group 2 received a mixture of propofol and lidocaine 10 mg; group 3 received lidocaine 10 mg 30 seconds before propofol; and group 4 received lidocaine 1 mg/kg 30 seconds before propofol. All medication was administered intravenously, and all propofol was given at a dose of 2 mg/kg.

[†]Scale⁶: 0 = none; 1 = mild; 2 = moderate; 3 = severe.

[‡]Total number of patients experiencing pain ($P < 0.05$ [chi-square = 20.90] between all groups except group 1 vs group 3).

been reported.^{9,12} This observation suggests that propofol injection results in the release of a mediator, supporting the kininogen hypothesis.¹¹ Administration of propofol with an IV infusion fluid increases the pain, but cessation of infusion decreases the pain.¹³ Two authors^{14,15} have argued that the size of the contact area between the drug and the endothelium is more important than the absolute concentration of the drug.

Various methods, such as the administration of opioids^{4,16}; local anesthetics^{9,10}; cold saline and topical nitroglycerin^{7,8}; cooling the propofol to 4°C^{6,8}; ketamine⁷; antiemetics³; coinduction with thiopental sodium, tourniquet application, or lidocaine–prilocaine cream⁸; topical lidocaine¹⁷; aspirin¹⁸; and nonsteroidal anti-inflammatory drugs¹² have been tried. However, Picard and Tramer⁸ emphasized that the best method for controlling pain due to propofol injection has not been determined. In this study, we investigated the efficacy of different lidocaine applications on pain due to propofol injection.

Picard and Tramer⁸ carried out a meta-analysis of 56 studies (N = 6264 patients) of the prevention or mitigation of pain due to propofol injection and concluded that lidocaine administration is the most efficacious method for minimizing pain due to propofol injection. IV administration of lidocaine 10 to 30 seconds before propofol administration appears to lessen the pain, whereas after periods longer than 30 seconds, the drug is less effective or ineffective. Picard and Tramer⁸ reported the incidence of pain as 70%. Scott et al⁹ reported the incidence of pain of various severity levels as 25% to 74% and the incidence of moderate or severe pain as 32% to 52%. King et al² reported the incidence of pain as 73%; Ho et al,¹¹ as 91.7%; and Yokota et al,¹⁷ as 87%. In our study, the incidence of pain was 66.7%. However, 33.3% of the patients in the group given no lidocaine experienced no pain.

Gehan et al,¹⁹ in a study investigating the optimal dose of lidocaine for the prevention of injection pain due to propofol, found that the addition of 0.1 mg/kg of lidocaine to 2.5 mg/kg of propofol decreased the pain, whereas increasing the dose of lidocaine to 0.2 or 0.4 mg/kg did not bring additional benefit. King et al² reported that adding 5 mg of lidocaine to propofol was ineffective, whereas 10 mg and 20 mg of lidocaine were equally effective. Ho et al¹¹ argued that the addition of 10 mg/kg of lidocaine to propofol does not adequately decrease the pain and that the optimal dose of lidocaine is 20 mg/kg. In our study, mixing propofol with 10 mg of lidocaine and injecting 1 mg/kg of lidocaine 30 seconds before propofol administration were the most effective methods of decreasing injection pain. None of the patients who received the mixture of propofol and lidocaine 10 mg experienced severe pain.

Yokota et al¹⁷ reported that applying tape containing 60% lidocaine to the injection site decreased the incidence of pain from 87% to 33%, and that mixing 40 mg of lidocaine with propofol decreased the incidence of pain to 30%. We believe that using a mixture of propofol plus lidocaine is simple and inexpensive. In our study, the combination of propofol plus lidocaine 10 mg decreased the incidence of pain from 66.7% to 16.7%.

CONCLUSIONS

In this study population, the addition of 10 mg of lidocaine to propofol 2 mg/kg, or the administration of 1 mg/kg of lidocaine 30 seconds before the administration of propofol 2 mg/kg, effectively decreased pain caused by propofol injection. Furthermore, a lower dose of lidocaine could be used. Based on our results, we suggest mixing propofol with 10 mg of lidocaine to decrease pain due to propofol injection during anesthesia induction.

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Address correspondence to:

Halit Madenoglu, MD
Yildirim Bayazit Mah. Sivas Cad.
Ozkar Sitesi No. 192/3
Melikgazi
Kayseri 38039
Turkey
E-mail: halitm@erciyes.edu.tr