Effect of Intramuscular and Intravenous Lidocaine on Propofol Induction Dose

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Key Words

Anaesthesia induction • Intravenous • Intramuscular • Lidocaine • Propofol dose

Abstract

Objective: Our purpose was to study whether or not intravenous (IV) administration of lidocaine reduces propofol dose requirement as intramuscular (IM) lidocaine in a placebo-controlled manner. **Subjects and Methods:** Seventy-five adult patients with American Society of Anesthesiologists physical status I and II, aged 20–60 years who were scheduled for surgery under general anaesthesia were included in the study. The patients were randomly allocated to 3 groups: IM: intramuscular administration; IV: intravenous administration and C: control. There were 25 patients in each group. The patients in group IM received lidocaine $1.5 \text{ mg} \cdot \text{kg}^{-1}$ administered into the deltoid muscle 10 min before anaesthesia induction. In group IV, the patients received IV lidocaine $1.5 \text{ mg} \cdot \text{kg}^{-1}$, 2 min before anaesthesia induction. Group C patients served as control group who received only propofol injection. Hypnosis after propofol administration was measured with response to verbal commands. **Results:** There were no statistical differences between group IM ($100.8 \pm 26.1 \text{ mg}$) and group IV ($110.8 \pm 30.1 \text{ mg}$) regarding the induction dose of propofol ($p > 0.05$). In group C, the required propofol dose ($151.2 \pm 27.4 \text{ mg}$) for anaesthesia induction was significantly higher than in the other groups ($p < 0.001$). No

side effect was observed in any patients. **Conclusion:** In this study, both IV and IM lidocaine administration were effective in reducing the hypnotic dose of propofol without any side effects. In addition, IV lidocaine may be more comfortable for awake patients.

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Introduction

Propofol is a potent intravenous (IV) hypnotic agent, which is widely used for induction and maintenance of anaesthesia and for sedation in the intensive-care unit. The major cardiovascular effect of propofol is a decrease in blood pressure owing to a drop in systemic vascular resistance, cardiac contractility and preload [1]. In order to reduce unwanted side effects of propofol, adjuvant agents may be used to decrease the propofol dose requirement during anaesthesia induction. For example, sedative drugs such as midazolam are known to interact additively with propofol and reduce the induction dose of propofol [2, 3]. Two recent articles also demonstrated that intramuscular (IM) administration of lidocaine reduced the induction dose of propofol [4, 5]. However, IM injection causes bias sensation in awake patients [6]. The purpose of this study was to investigate whether or not IV lidocaine administration can reduce propofol dose requirement as IM lidocaine in a placebo-controlled manner.

Table 1. Patient characteristics and propofol doses of all groups (means $\pm$ SD)

	Group IM	Group IV	Group C
Age, years	36.7 $\pm$ 13.9	40.4 $\pm$ 13.5	38.7 $\pm$ 15.7
Gender, F/M	16/9	15/10	17/8
Weight, kg	68.2 $\pm$ 9.0	71.0 $\pm$ 12.1	71.8 $\pm$ 13.3
ASA, I/II	20/5	20/5	21/4
Propofol dose, mg kg ⁻¹	1.4 $\pm$ 0.3	1.5 $\pm$ 0.3	2.1 $\pm$ 0.2*
Total propofol dose, mg	100.8 $\pm$ 26.1	110.8 $\pm$ 30.1	151.2 $\pm$ 27.4*

ASA = American Society of Anesthesiologists. * $p < 0.001$ vs. group IM and group IV.

Subjects and Methods

After institutional ethics committee approval and obtaining patients' written informed consent, 75 adult patients with American Society of Anesthesiologists physical status I and II, aged 20–60 years, weighting 50–85 kg, who were scheduled for surgery under general anaesthesia were included in the study between February and October 2006. Patients taking cardiovascular medication, with known hypersensitivity to local anaesthetics, neurological disorders, hypertension, baseline systolic arterial pressure (SAP) <100 mm Hg and heart rate (HR) <55 beats min⁻¹ were excluded.

After arrival in the operating room, a 20-gauge venous cannula was placed in a forearm vein and 500 ml of saline (0.9%) solution was infused. HR, non-invasive SAP and diastolic arterial pressure (DAP), and oxygen saturation were monitored preoperatively.

The patients did not receive premedication and were randomly allocated to 1 of the 3 groups [IM, IV and control (C)], 25 patients in each. The patients in group IM lidocaine received lidocaine 1.5 mg $\cdot$ kg⁻¹ intramuscularly (Aritmal 10% ampul, Biosel İlaç AŞ, Istanbul, Turkey) administered into the deltoid muscle 10 min before anaesthesia induction. In group IV, the patients received lidocaine 1.5 mg $\cdot$ kg⁻¹ intravenously, 2 min before anaesthesia induction. Group C patients served as control group who received neither IV nor IM lidocaine or anything else before propofol injection. A trained physician (D. K.) performed IV and IM lidocaine injections. Propofol (Fresenius, Fresenius Kabi, Australia GmbH) was administered IV over 5 s in doses of 0.2 mg $\cdot$ kg⁻¹ every 30 s in order to determine the minimum dose for hypnosis by another anaesthesiologist (S. B.) who was blinded to the treatment groups. Inability to respond to simple commands such as ('What is your name?', 'Where are you?') were used as the end-point for hypnosis. Response to verbal commands was evaluated 25 s after each injection. The total dose of propofol to achieve loss of response in each patient was recorded. Three minutes after a bolus dose of 0.2 mg $\cdot$ kg⁻¹ cisatracurium (Nimbex, GlaxoSmithKline SpA, Italy) the patient was intubated. Anaesthesia was continued and complemented with additional agents. If SAP and HR increased 20% from baseline after intubation, fentanyl 1 μ g $\cdot$ kg⁻¹ was given.

HR, non-invasive SAP, DAP and oxygen saturation were recorded before lidocaine administration, before and after propofol injection, and 1 and 3 min after intubation. The total dose of propofol to achieve loss of response in each patient was recorded.

If HR decreased 20% from baseline, atropine 0.5 mg was given. Hypotension was defined as decrease in SAP 20% of the baseline value and was treated by infusion of normal saline solution 3–5 ml $\cdot$ kg⁻¹, and if hypotension continued, ephedrine 5 mg IV was given. Side effects of local anaesthetics were recorded during the study.

Based on the study of Senturk et al. [5], in which IM lidocaine reduced the induction dose of propofol to 1.56 $\pm$ 0.24 mg $\cdot$ kg⁻¹, a sample size calculation with $\alpha = 0.05$ and requiring the study to have a power of 99% indicated that 21 patients would be required in each group.

The SPSS statistical package (version 10.0, SPSS Inc., Chicago, Ill., USA) was used for statistical analysis. Statistical analysis was performed with analysis of variance with repeated measures. Nominal data were analyzed and compared by using the χ^2 test for trend. A p value <0.05 was considered statistically significant. Values are given as means $\pm$ SD.

Results

The patient characteristics were similar between the groups ($p > 0.05$) (table 1). There were no statistical differences between group IM (1.4 $\pm$ 0.3 mg $\cdot$ kg⁻¹) and group IV (1.5 $\pm$ 0.3 mg $\cdot$ kg⁻¹) regarding the induction dose of propofol ($p > 0.05$). The required propofol dose (2.1 $\pm$ 0.2 mg $\cdot$ kg⁻¹) for anaesthesia induction was higher in group C than the other groups and the difference was statistically significant ($p < 0.001$).

In groups IM and IV, HR significantly increased 1 min after intubation according to baseline ($p < 0.05$) and returned to baseline values 3 min after intubation (fig. 1). In group C, HR decreased according to baseline after propofol injection ($p < 0.05$). HR was significantly different between groups IM (86.5 $\pm$ 12.1 beats min⁻¹) and IV (72.7 $\pm$ 14.3 beats min⁻¹) 1 min after intubation ($p < 0.05$). However, it was not clinically important. After propofol injection, SAP and DAP decreased significantly from baseline values in all groups ($p < 0.05$) (fig. 2).

Only 5 patients in group C required fentanyl after intubation. None of the patients were given fentanyl in groups IM and IV ($p > 0.05$). No signs of local anaesthetic toxicity and side effects were observed in any patient.

Discussion

In this study, both 1.5 mg $\cdot$ kg⁻¹ lidocaine intravenously 2 min before propofol administration and 1.5 mg $\cdot$ kg⁻¹ lidocaine intramuscularly 10 min before propofol administration were effective in reducing the hypnotic dose of propofol without any clinically important side effects.

Fig. 1. HR values of groups (means $\pm$ SD). ^a $p < 0.05$ in group C vs. baseline; ^b $p < 0.05$ in groups IM and IV vs. baseline.

Fig. 2. SAP and DAP values of groups (means $\pm$ SD). ^a $p < 0.05$ in all groups vs. baseline.

In previous studies [4, 5], it was shown that IM administration of lidocaine 10 min before anaesthesia induction reduced the induction dose of propofol. Senturk et al. [5] demonstrated that $2 \text{ mg} \cdot \text{kg}^{-1}$ IM lidocaine with $1 \mu\text{g} \cdot \text{kg}^{-1}$ fentanyl resulted in a significant decrease in propofol induction dose according to group C ($1.56 \pm 0.24 \text{ mg} \cdot \text{kg}^{-1}$, $2.03 \pm 0.3 \text{ mg} \cdot \text{kg}^{-1}$, respectively). Similarly, Ben-Shlomo et al. [4] had shown that the hypnotic effect of IV propofol was enhanced by IM administration of lidocaine at least $1 \text{ mg} \cdot \text{kg}^{-1}$ or above. Our study confirmed these results. However, Stoneham et al. [7] showed that insertion of the laryngeal mask following induction of anaesthesia with propofol may be made easier by pre-treatment with $1.5 \text{ mg} \cdot \text{kg}^{-1}$ lidocaine administered intravenously, but, there was no significant difference between the lidocaine and control groups with respect to induction dose of propofol ($2.3 \pm 0.6 \text{ mg} \cdot \text{kg}^{-1}$, $2.3 \pm 0.5 \text{ mg} \cdot \text{kg}^{-1}$, respectively). In this study, the syringe dropping method for determining the propofol induction dose was used. In our study, the induction dose of propofol was $1.5 \pm 0.3 \text{ mg} \cdot \text{kg}^{-1}$ in the IV lidocaine group. The difference in mean propofol doses may be the result of different methods which were used for obtaining the hypnotic dose of propofol.

Although injection of lidocaine through both routes reduced the propofol dose requirement, the unwanted side effects of IM injection such as myonecrosis, interstitial and myoseptal oedema at the injection site may limit its use [8]. In addition, IM injection is painful and causes an unpleasant sensation in most awake patients. We observed that most people disliked IM injections during the study period. Equally importantly, IV administration of

lidocaine had an additional advantage of reducing pain associated with propofol injection [9].

Hemodynamic changes during the study period were not clinically significant between the groups. We did not observe any side effects attributed to IV or IM lidocaine.

The effects of propofol on the central nervous system involve pre- and postsynaptic effects, resulting from actions at multiple cellular and molecular sites [10]. The major action of propofol appears to be mediated by facilitation of inhibitory transmission by activating the postsynaptic GABA_A receptor-chloride ionophore complex [10–12]. Calcium influx is also modulated through slow calcium channels and inhibits voltage-gated sodium currents [10, 13, 14]. Lidocaine stabilizes the neuronal membrane by inhibiting the ionic fluxes required for the initiation and conduction of impulses, thereby effecting local anaesthetic action. Local anaesthetics also potentiate GABA-mediated Cl^- currents by inhibiting GABA uptake [15]. Similar mechanisms of action of both propofol and lidocaine may explain the additive effect of these agents in reducing the hypnotic dose.

Conclusion

Lidocaine administration by IM and IV routes decreased the induction dose of propofol significantly. However, IM injection caused unpleasant sensation for awake patients. Therefore, IV lidocaine administration before propofol injection may be a good choice for awake patients for reducing the propofol induction dose.

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