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Effect of lidocaine on pain caused by injection of propofol: Comparison of three methods at two injection rates

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Introduction

A number of reports have addressed the use of lidocaine for prevention of pain during injection of propofol. Two methods are widely used: preinjection of lidocaine and premixing of lidocaine with propofol. Although the premixing method can reduce the stability of propofol emulsion [1–5] and the efficacy of lidocaine [1], the premixing method is reported to be more effective for reduction of pain [1,6–8]. We planned two types of preinjection methods: a simple intravenous injection and an intravenous injection with the application of a rubber tourniquet, and compared them with a premixing method. We also considered the injection rate of propofol.

Patients and methods

With the patients' informed consent, and with approval from our institutional ethics committee one hundred and twenty patients, ASA grade I or II, aged 15–78 years, undergoing elective operations were randomly allocated to one of six groups.

Patients in group I ($n = 20$) received only propofol, at a rate of 1200 ml·h^{-1}. Patients in group II ($n = 20$) and group III ($n = 20$) received 2.5 ml of 2% lidocaine (50 mg) intravenously, followed immediately by propofol, at rates of 600 ml·h^{-1} and 1200 ml·h^{-1}, respectively. Patients in group IV ($n = 20$) and group V ($n = 20$) received 10 ml of 0.5% lidocaine (50 mg) intravenously, with a rubber tourniquet applied to the forearm about 5 cm distal to the elbow joint. The forearm was "kneaded" along the vein filled with lidocaine for about 15 s in order to infiltrate lidocaine into the vein wall, and propofol was injected, simultaneously with release of the tourniquet, at rates of 600 ml·h^{-1} and 1200 ml·h^{-1}, respectively. Patients in group VI ($n = 20$) received a premixed solution: 19 ml of propofol (190 mg) and 1 ml of 2% lidocaine (20 mg), mixed within 30 min before administration, given at a rate of 600 ml·h^{-1}.

All patients received midazolam 0.02–0.05 mg·kg^{-1} intramuscularly 30 min before transfer to the operating room and had a 20- to 22-G cannula inserted into a vein on the dorsum of the hand. Atropine 0.25–0.5 mg, propofol 2 mg·kg^{-1}, and vecuronium 0.15 mg·kg^{-1} were administered for induction of anesthesia. Propofol was injected directly from a syringe pump. Oxygen (100%) was given via a mask. Blood pressure and heart rate were recorded continuously until tracheal intubation.

During the injection of propofol and until they lost consciousness, the patients were continuously questioned about pain: its presence, the grade (mild or severe), and the site. To extract a subjective description of a sensation, we first asked patients, "Do you feel anything in your arm?" If the reply was "No," the same question was repeated. The grade of pain was scored as: 0, no pain; 1, mild pain; 2, severe pain.

Statistical analysis was performed using the χ^2 test for comparisons of the incidence of pain and the Mann-Whitney *U*-test was used to compare pain scores. Student's *t*-test was used to compare other data. $P < 0.05$ was considered significant.

Results

There were no significant differences in sex, age, and weight among the six groups (Table 1).

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Table 1. Demographic characteristics of study patients

Groups	I	II	III	IV	V	VI
No. of patients	20	20	20	20	20	20
Sex (M/F)	11/9	11/9	8/12	10/10	8/12	9/11
Age (years)	52 ± 18	54 ± 15	49 ± 17	50 ± 16	52 ± 17	53 ± 20
Weight (kg)	57 ± 10	56 ± 11	62 ± 13	55 ± 8	59 ± 12	57 ± 10

Values are means ± SD.
There were no significant differences among the six groups.

Table 2. Incidence, severity, and site of pain

Groups	I	II	III	IV	V	VI
Lidocaine	None	PI	PI	PIT	PIT	PM
Propofol (ml·h^{-1})	1200	600	1200	600	1200	600
Incidence and severity of pain			Number of patients (%)			
None	8 (40)	9 (45)	9 (45)	11 (55)	17 (85)*	17 (85)*
Mild	7 (35)	7 (35)	8 (40)	7 (35)	3 (15)	3 (15)
Severe	5 (25)	4 (20)	3 (15)	2 (10)	0 (0)	0 (0)
Pain score[a]	0.85 (0.79)	0.75 (0.77)	0.70 (0.71)	0.55 (0.67)	0.15* (0.36)	0.15* (0.36)
Site of pain			Number of patients			
Dorsum	9	5	9	6	3	2
Forearm	3	5	1	3	0	1
Elbow	0	1	1	0	0	0

*Significantly different from groups I, II, and III ($P < 0.01$) and from group IV ($P < 0.05$).
There was no significant difference in incidence and severity of pain among groups I, II, III, and IV.
No statistical analysis was performed for site of pain.
Values for pain score are means (SD).
PI, Preinjection of lidocaine; PIT, preinjection of lidocaine under tourniquet application; PM, premixed lidocaine.
[a]See text for details.

The incidence and the severity of pain in each group are shown in Table 2. The premixing method (group VI) was significantly effective for reducing the incidence and severity of pain. The incidence and severity of pain in patients who had lidocaine preinjected with the application of a tourniquet significantly decreased when propofol was injected at the faster rate (groups IV and V). However, there was no significant difference between groups II and III.

The sites of pain in each group are also shown in Table 2. The sites seemed to have varied insignificantly; no statistical analysis was performed.

The percent changes in systolic and diastolic arterial pressure and heart rate during induction of anesthesia (before tracheal intubation) were −19 ± 11%, −16 ± 11%, +7 ± 11% (mean ± SD) in the groups with propofol injected at 600 ml·h^{-1}, and −20 ± 10%, −15 ± 11%, +12 ± 17% in the groups injected with propofol at 1200 ml·h^{-1}, respectively. Hemodynamic changes did not significantly differ at the two injection rates of propofol.

Discussion

The chemical basis for the cause of the pain experienced during propofol injection remains unknown, but it may be associated with the activation of pain mediators. Several factors are, however, known to be responsible for the pain. Scott et al. [7] reported that the duration of exposure to the vein wall, which mostly depends on the injection rate, is of importance, and that this hypothesis is compatible with the time lag in the onset of the pain and suggests an association with pain mediators such as kininogens. They also reported that injecting into a large vein reduced pain and that this was, presumably, because of the low concentration of propofol due to dilution with blood; however, the effect and the mechanism of diluted propofol are still controversial [9–11]. The effect of the temperature of propofol is also not yet clear [12,13].

In our study, propofol was injected at rates of 600 and 1200 ml·h^{-1}, the range that propofol should be given to adults according to the manufacturer's recommended

rate ($0.5\,mg \cdot kg^{-1} \cdot 10\,s^{-1}$). However, as we considered that it would show a higher incidence of pain and the consequent disadvantage of patients, we did not give propofol to the control group at the slower rate. And considering that it would show a still lower incidence of pain, we did not study group with the premixing and with the faster rate. We believe that the data obtained from these six groups provided sufficient basis or which determine the clinical tactics to use with lidocaine for preventing the pain caused by propofol injection.

It is presumed that lidocaine acts on the pain caused by propofol in two ways: as a local anesthetic and as a stabilizer for pain mediators [7], and that premixed lidocaine acts mostly in the latter fashion. We confirmed that premixed lidocaine was significantly effective even when propofol was injected into a small vein at a relatively slow rate, a result that further confirms the pain mediator theory. Although premixed lidocaine has been reported to reduce the stability of propofol emulsion because moves into the lipid phase of propofol, we confirmed, as in previous studies, that this is not of clinical concern if the mixture is used immediately or within 30 min. However, it is presumed that preinjected lidocaine acts mostly as a local anesthetic. We noted that this action was not effective in reducing the pain of propofol injection except when a tourniquet was used and propofol was injected at the faster rate. It is not easy to explain the relation between the tourniquet application, the faster injection rate of propofol, and the action of preinjected lidocaine. We consider that our results simply indicate that the action of lidocaine as a local anesthetic may still have a place in the prevention of the pain caused by propofol.

A tourniquet was also used by Scott et al. [7], but they reported that it was not very effective. In our study, along with the use of the tourniquet, we kneaded the forearm along the vein filled with lidocaine to infiltrate lidocaine into the vein wall. However, our data are insufficient to assess the effect of this procedure. Also, we must admit that this method leaves much to be studied, such as where to apply the tourniquet, how to knead the vein, and how long to keep doing it.

We found no significant difference in hemodynamic changes between the two injection rates of propofol. In terms of pain reduction, therefore, we recommend that propofol should be injected at $1200\,ml \cdot h^{-1}$. However, a more rapid injection usually leads to a shorter induction time, which we noticed in this study but did not record. For a further study, we consider that analyzing the relation between induction time, the time lag in pain onset, and the pain data may be of interest.

In summary, the prominent pain-reducing effect of premixed lidocaine was confirmed in our study. We also noted that the analgesic effect of preinjected lidocaine increased when a tourniquet was used concomitantly. Intravenous lidocaine with transient tourniquet application could be an alternative for those practitioners who do not wish to premix propofol with other drugs.

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