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A reliable method for preventing pain on injection of propofol

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Introduction

Pain on injection is the most common and well-known problem encountered when propofol is administered, and occurs in up to 90% of patients if a vein on the dorsum of the hand is used [1]. The results of several studies evaluating the effect of premixing lidocaine and propofol [2–4], prior administration of alfentanil [4–6], dilution with 5% glucose, intralipid [7], or 10% fat emulsion [8] on the incidence of pain are controversial.

One method of preventing injection pain due to propofol in adults is to use a large proximal vein. Although this method has been shown to reduce the incidence of pain, implying that dilution should help, the benefits of preinjection dilution of propofol or injection into a fast-running infusion are controversial. Therefore, we attempted to determine the exact incidence and severity of pain when propofol was injected into an antecubital or a large forearm vein, and the effect of an infusion rate of 0.9% NaCl on this incidence.

Materials and methods

After Faculty Ethic Committee approval and patients' written consent, 100 patients, American Society of Anesthesiologists' physical status classification (ASA) class I–II, aged between 20 and 60 years and scheduled for elective surgery under general anesthesia, were randomly assigned to two groups ($n = 50$). Exclusion criteria were a history of chronic pain syndromes, thrombophlebitis, and analgesic administration. No premedication was administered.

In all patients, 0.9% NaCl infusion was started from an antecubital or a large forearm vein with an 18-gauge teflon cannula before induction. The infusion rate was $100\,cc{\cdot}h^{-1}$ in the first group and $900\,cc{\cdot}h^{-1}$ in the second group. Anesthesia was induced with propofol i.v. at a rate of 10 mg in 5 s until loss of consciousness. Propofol was injected from a three-way stopcock connected to the cannula while keeping the infusion of the 0.9% NaCl solution running. In all patients, systolic, diastolic, and mean arterial pressure and heart rate were recorded before and after propofol injection. The patients were asked to grade pain according to a four-point verbal rating scale (0, no pain; 1, mild pain; 2, moderate pain; 3, severe pain). The propofol dose required for induction was also recorded.

The results were analyzed statistically with ANOVA, Student's t, Fisher's exact (incidence of pain), and Mann–Whitney (severity of pain) tests, and $P < 0.05$ was accepted as significant.

Results

There were no significant differences in the demographic characteristics of patients or in the amount of propofol administered between groups (Table 1). In all patients, systolic, diastolic, and mean arterial pressure decreased significantly after propofol injection ($P < 0.001$), but there was no significant difference in heart rate (Table 2). There was also no significant difference in hemodynamic parameters between groups. The incidence of pain reported by patients is shown in Table 3. The mean severity scores of pain were 0.12 ± 0.43 in group I and 0.08 ± 0.39 in group II. There was no significant difference in the incidence and severity of pain between groups ($P > 0.05$).

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Table 1. Demographic data and induction dose of propofol (mean ± SD)

	Group I	Group II
Age (years)	47.1 ± 6.31	46.4 ± 2.38
Weight (kg)	70.46 ± 1.77	69.72 ± 1.56
Sex (M/F)	26/24	22/28
Dose of propofol (mg)	120.2 ± 4.26	109.4 ± 3.12

$P > 0.05$, no significant difference between groups.

Table 3. The incidence of pain on injection of propofol (% in parentheses)

	Group I ($n = 50$)	Group II ($n = 50$)
No pain	46 (92)	48 (96)
Mild pain	2 (4)	0 (0)
Moderate pain	2 (4)	2 (4)
Severe pain	0 (0)	0 (0)

$P > 0.05$, no significant difference between groups.

Table 2. Hemodynamic parameters of patients before and after propofol injection (mean ± SD)

	Group I		Group II	
	Before	After	Before	After
Systolic pressure (mmHg)	137.36 ± 2.56	115.34 ± 2.42*	142.06 ± 3.29	113.24 ± 2.67*
Diastolic pressure (mmHg)	79.62 ± 2.33	65.4 ± 2.14*	78.98 ± 2.15	64.0 ± 2.02*
Mean pressure (mmHg)	98.58 ± 2.08	82.08 ± 2.14*	98.34 ± 2.02	79.82 ± 2.17*
Heart rate (beats·min^{-1})	108.18 ± 14.5	88.62 ± 2.22	114.3 ± 18.26	89.76 ± 2.36

* $P < 0.001$, systolic, diastolic, and mean arterial pressure decreased significantly after propofol injection in all patients.
No significant difference between groups.

Discussion

Although many different agents and methods have been studied for preventing pain on injection of propofol, the most frequently investigated agents are lidocaine and alfentanil [2–6]. Several authors have shown that i.v. lidocaine given before or with propofol reduced the frequency of pain but did not suppress it completely. While King et al. [2] found 20.5% pain with 20 mg premixed lidocaine with propofol injected on the dorsum of the hand, Gehan et al. [3] reported that the incidence of pain was 15% with the addition of 0.1 mg·kg^{-1} lidocaine to propofol injected into an antecubital vein. Nathanson et al. [4], who found an incidence of 13% with 40 mg lidocaine, concluded that mixtures of propofol and lidocaine are unstable, and therefore the mixture must be used within 30 min as after this time the lidocaine enters the lipid phase of propofol and is no longer effective.

Prior administration of alfentanil has been shown to reduce the injection pain of propofol [4–6]. In the study by Fletcher et al. [5], the incidence of pain decreased to 36% with a bolus of alfentanil 1 mg administered 15 s prior to propofol, while Saarnivara and Klemola [6] found that alfentanil 30 μg·kg^{-1} given 30 s before propofol abolishes pain on injection. However, all patients received oxycodone as a premedicant, and the authors did not mentioned the size of cannulae they used for the propofol injection. Besides these conflicting results, Nathanson et al. [4], who found an incidence of 24% pain with preadministered 1 mg alfentanil, concluded that alfentanil may not be a suitable drug to reduce the pain of propofol injection if the use of a potent opioid drug leading to possible respiratory depression is to be avoided.

Studies about the cause of pain with the injection of propofol have shown that high concentrations of free propofol in the aqueous phase of an emulsion are associated with pain on injection [7,8]. Klement and Arndt [7] examined the relationship between pain intensity and concentration by perfusing serial dilutions of propofol, and concluded that pain occured earlier and lasted longer with increasing concentrations and a lesser degree of pain was induced by dilutions of propofol with Intralipid compared with those with 5% glucose. Doenicke et al. [8] also studied the effect of a new formulation of 1% propofol in a 10% fat emulsion (Lipofundin). They observed that the incidence of pain was reduced from 91% to 66%. The currently available strategy for reducing pain by diluting the propofol emulsion has the disadvantage of requiring additional manipulation and the risk of contamination of the diluted propofol preparation, thus increasing the risk of infection. The injection of propofol into a large vein is a simple and safe method of diluting and reducing the amount of propofol in the aqueous phase of emulsion. Although the exact mechanism is not known, the dilutional effect of high blood flow and a larger surface area which free propofol can contact are the main reasons for a reduced incidence of pain by injecting into a large vein. In our study, propofol was injected into an antecubital or a large forearm vein, and the incidence of pain of slow injection of propofol was only 4%. However, we could not observe any additional beneficial

effect of fast 0.9% NaCl infusion in reducing pain by a dilutional effect as there was no difference in the incidence and severity of pain between groups.

As well as the conflicting results of the studies using local anesthetics or opioids, and the fact that none of them suppress the pain completely, there are associated complications such as unstable mixtures, respiratory depression, and the risk of contamination and infection. Most of the authors of these studies mentioned that injection into a larger proximal vein causes less pain, but carries the risk of arterial injection. There is no risk of intraarterial injection when the large forearm veins are used for cannulation. Also, it is difficult to put a cannula into an artery without knowing. Seddon [9] also criticized the use of pharmacological agents for the prevention of injection pain of propofol, and stated that if an appropriate injection site (proximal large vein) is used, the injection pain of propofol will not be a problem.

In summary, we attempted to determine the exact incidence and severity of pain when propofol was injected into an antecubital or a large forearm vein, and the effect of the rate of 0.9% NaCl infusion ($100\,cc{\cdot}h^{-1}$, slow; $900\,cc{\cdot}h^{-1}$, fast) on this incidence. Although there was no difference in the incidence and severity of pain between the fast and slow infusion of 0.9% NaCl solution, the incidence of pain was only 4%, and we concluded that the injection of propofol into a large forearm or an antecubital vein is a reliable way to decrease the incidence of injection pain of propofol.

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