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# Propofol infusion rate does not affect local pain on injection

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**Background:** Local pain at the site of an i.v. injection of propofol is a well-known problem, particularly in infants. This randomised investigator-blinded crossover study was designed to assess the effect of the i.v. bolus infusion rate on propofol-induced pain at the site of injection.

**Methods:** Thirty unpremedicated patients scheduled for ear-nose-throat or plastic surgery at Malmö University Hospital, Sweden, were given two consecutive 2.0 ml injections of propofol 10 mg/ml (Diprivan®, AstraZeneca, Sweden/UK), at different infusion rates (0.2 or 1.0 ml/s), immediately before induction of general anesthesia. Half of the patients (n=15) received the first bolus of propofol over 2 s and the second bolus over 10 s, and the other half (n=15) had their injections in reversed order. After each injection, the patient was asked by an investigator to indicate pain intensity on a visual analog scale (VAS) and to report the times of the appearance, maximum point and disappearance of pain. The injections were given approximately 2 min apart. The investigators scoring pain intensity, as indicated by the patients on a 10-point numerical rate scale, were blinded to the order in which the injections were given, as were the patients themselves.

**Results:** There were no statistically significant differences in the incidence (both 86%) of intensity (median; 25th; 75th percentiles, in VAS units: 3.1; 1.0; 5.3 and 3.3; 1.4; 5.0, respectively) or duration ( $66 \pm 31$  and  $73 \pm 26$  s, respectively) of pain between the faster (1.0 ml/s) and slower (0.2 ml/s) bolus infusion rates of propofol studied.

**Conclusions:** We conclude that the i.v. bolus infusion rate of propofol does not influence drug-induced local pain on injection, at least not within the infusion rate interval studied. Therefore, adjusting i.v. injection speed does not seem to be a clinically useful tool for reducing the intensity or duration of propofol-induced pain at the site of administration.

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**Key words:** anesthetics; intravenous; human; injections; intravenous; pain; propofol; time factors.

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PROPOFOL, 2,6-di-isopropylphenol, is a popular i.v. anesthetic induction agent associated with smooth induction, pleasant sleep, rapid recovery and little postoperative nausea in clinical practice. It is provided commercially as a lipid emulsion, where mainly the aqueous phase (1, 2), possibly together with the lipid phase (3), is considered to cause pain at the site of injection: an important clinical disadvantage of the drug found to be reported by an average of 70% of patients in a recent quantitative systematic review (4). Altering the speed of propofol injection might be a simple, nonpharmacological clinical strategy that an anesthetist could adopt to reduce pain on propofol injection. Available studies on the influence of i.v. injection speed of propofol on local pain have found either no effect (5) or a higher incidence of pain with lower injection speed (6). In both studies, however, the bolus infusion rates to be compared were studied in different groups of patients. The aim of this randomised and investigator-blinded crossover study

was to compare, with respect to local pain on injection, two different bolus infusion rates of propofol in the same group of patients.

## Patients and methods

### Patients

The study was approved by the Ethics Committee at Lund University, Sweden, and written informed consents were obtained from 30 adult ASA I-II patients scheduled for elective ear-nose-throat or plastic surgery at Malmö University Hospital, Malmö, Sweden. On arrival in the anesthetic room the patients were allocated randomly into one of two groups (group 1 and 2), comprising 15 patients each.

### Methods

No premedication was given. A 1.0-mm (20 G) Teflon cannula (Venflon™, BOC Ohmeda, Helsingborg, Sweden) was inserted in a dorsal hand vein.

Each patient was then given two 2.0 ml i.v. bolus infusions of propofol (Diprivan®, AstraZeneca, Sweden) 10 mg/ml, at least 2 min apart. Pain after the first injection was always allowed to disappear completely before the second injection was given. The patients in group 1 were given the first injection over 2 s (corresponding to an infusion rate of 1.0 ml/s) and the second one over 10 s (rate 0.2 ml/s), whereas those in group 2 received their injections in reversed order. The propofol had been stored at room temperature. No i.v. carrier infusion or other drugs were allowed.

Immediately after each injection of propofol the patient, blinded to the actual sequence of the injections, was asked by a blinded investigator to assess maximal local pain intensity on a visual analog scale (VAS), ranging from no pain at all to the highest pain intensity imaginable, and also to report in time the moments of appearance, maximum pain and disappearance of pain. Each VAS assessment of pain intensity was transferred by the investigator to the protocol as a corresponding VAS score on a 10-point numerical rate scale. The patients were anesthetized with more propofol immediately after their second pain assessments.

### Statistics

Before the study, it was calculated that at least 30 patients would be required for a difference in pain score of at least  $2.0 \pm 1.5$  VAS units, between the two bolus infusion rates of propofol, to be detected with 80% statistical power and 95% statistical significance.

Parametrical data is reported as mean  $\pm$  SD in the text and tables, and was compared statistically using paired Student's *t*-test. Visual analog scale scores were analyzed using Wilcoxon's paired rank sum test, and are reported as median with 25th and 75th percentiles in parenthesis.

$P < 0.05$  was considered to indicate statistical significance.

## Results

The patients included comprised 13 males and 17 females, aged between 18 and 81 years. There were no statistically significant differences in incidence of pain (86% with either regimen) between maximal scores of local pain intensity (3.1 [1.0; 5.3] and 3.3 [1.4; 5.0] VAS units, respectively) or in duration of pain ( $66 \pm 31$  and  $73 \pm 26$  s, respectively) between the faster (1.0 ml/s)

and slower (0.2 ml/s) bolus infusion rates of propofol compared here (Table 1).

## Discussion

We found no statistically significant differences in intensity or duration of local pain between faster and slower injections of propofol given in the same patients, although we still cannot exclude differences in propofol-induced pain between infusion rates below 0.2 ml/s and those above 1.0 ml/s. These results are in accordance with previous findings in different groups of patients (5). In contrast, less local pain has been found to be induced on faster than on slower injection of propofol in another study carried out in different groups of patients (6), and recently, local pain has been found to disappear faster with simultaneous infusion of carrier fluid during and immediately after the injection of propofol (7).

From a theoretical point of view, more rapid injection of propofol or simultaneous infusion of carrier fluid might both be considered to allow the propofol to be cleared away faster from the site of injection, thereby reducing local endothelial exposure to the drug (6). But the present findings, as well as those of Gillies *et al.* (5), do not indicate that such mechanisms are particularly associated with clinical pain intensity at the site of injection.

In both previous studies on bolus infusion rate and propofol-induced pain (5, 6), the patients were given full doses of propofol to induce general anesthesia. An anesthetic induction dose of propofol

Table 1

Assessments of pain at the site of injection after slower and faster i.v. bolus infusions of propofol in the same patients. No statistically significant differences were found between the infusion rates compared.

	Faster i.v. infusion of propofol	Slower i.v. infusion of propofol
Bolus infusion rate (ml/s)	1.0	0.2
Pain score (VAS 0–10)	3.1 (1.0; 5.3)	3.3 (1.4; 5.0)
Time to appearance of pain (s)	$25 \pm 19$	$23 \pm 13$
maximum of pain (s)	$41 \pm 22$	$41 \pm 19$
disappearance of pain (s)	$92 \pm 27$	$94 \pm 22$
Total duration of pain (s)	$66 \pm 31$	$73 \pm 26$

VAS, visual analog scale.

would probably enable patients to reliably assess and report maximal pain intensity before being completely anesthetized, as the average time to maximum of pain after a 20-mg i.v. dose in the present study (41 s from the start of propofol injection regardless of the bolus infusion rate), as well as in a previous one (7), exceeds what is required for clinical induction of general anesthesia with propofol.

Another difference between the design of previous studies (5, 6) and that of the present one is that each of our patients received both a faster and a slower injection of propofol. However, enabling patients to be their own controls, i.e. to reliably assess and report pain intensity and duration on two different occasions within a reasonable period of time, makes subanesthetic dose usage mandatory (7). Certainly, lower doses mean that pain intensity and duration might both be underestimated. On the other hand, less influence on consciousness of the smaller propofol doses administered here, compared with those given elsewhere (5, 6), would facilitate adequate assessments of pain by the patient, and enable the intensity and duration of pain to be more reliably recorded after injection (7).

As altering the speed of injection within the range 0.2–1.0 ml/s was found neither to affect the incidence nor the intensity and duration of propofol-induced pain, we conclude that adjusting bolus infusion rate within generally recognized limits is no clinically useful way of reducing local pain on i.v. administration of propofol.

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