British Journal of Anaesthesia 1994; 72: 342–344

SHORT COMMUNICATIONS

Pretreatment with alfentanil reduces pain caused by propofol

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SUMMARY

We have compared two groups (n = 22) of unpremedicated patients to determine if the pain caused by injection of propofol could be modified by alfentanil. In group I, alfentanil 1 mg was given as a bolus i.v. injection 15 s before administration of propofol i.v., while group II received saline. Propofol was given in 20-mg increments every 4 s. All injections were given through the same i.v. cannula on the dorsum of one hand. We found that alfentanil pretreatment reduced pain on injection of propofol (P = 0.001). (Br. J. Anaesth. 1994; **72**: 342–344)

KEY WORDS

Anaesthetics, i.v.: propofol. Analgesics, opioid: alfentanil. Pain: injection.

When propofol is injected into a vein on the dorsum of the hand, up to 67% of patients feel pain in the arm [1, 2]. The incidence of pain relates to the size of the vein, the speed of injection and the temperature and concentration of propofol [1, 3]. Various methods have been described to reduce the pain. The most popular and effective method is to add lignocaine to propofol, immediately before injection, although this fails to prevent pain in some patients [1, 4].

We have noted in our daily practice that if the opioid alfentanil is given immediately before injection of propofol, very few patients experience any pain in the arm, even in the absence of lignocaine. This has been noted previously, although only in premedicated patients, or when there was a long interval between administration of alfentanil and administration of propofol [2, 5].

We have studied the effect of alfentanil on the incidence of pain during injection of propofol, using an anaesthetic technique suitable for unpremedicated patients.

METHODS AND RESULTS

Ethics Committee approval was obtained for the study and all patients gave informed consent. Patients were informed that the anaesthetic they would receive may cause a burning or stinging sensation in the arm into which it was injected. They were told also that while some patients felt no discomfort, others found that the pain was severe, although of brief duration, as they fell asleep.

Forty-four patients, ASA I–II, aged 18–70 yr, undergoing elective outpatient or minor inpatient surgery were allocated randomly to one of two groups ($n = 22$). Patients in group I received alfentanil 1 mg (2 ml) i.v. followed 15 s later by propofol i.v., whilst patients in group II received saline 2 ml followed 15 s later by propofol i.v. All drugs were administered through a 22-gauge i.v. cannula (Venflon) on the dorsum of one hand.

The study was conducted in a double-blind manner. All patients were unpremedicated. Propofol and alfentanil were stored and presented at 21–23 °C. Propofol was injected at a rate of 2 ml (20 mg) every 4 s.

Every 8 s during injection of propofol, the patients were asked if they had any discomfort in their arm. If they answered "yes" they were asked if it was "severe" or "mild". Patients were questioned until they fell asleep. If a patient reported pain which was severe, anaesthesia was hastened by more rapid injection of propofol, as indicated clinically. In this study, severe pain, considered to be unacceptable clinically, was based both on the patients' comments and the presence of features such as grimacing or limb withdrawal. Mild pain was defined as discomfort in the arm or hand, but which was not a cause of any distress, and was considered to be clinically acceptable.

After operation, the patients were asked if they remembered any pain during induction, and if so was it severe or mild.

Data were analysed statistically with the unpaired t test and chi-square test (using Yates' correction). Data are shown as mean (SD) unless otherwise specified. Results were considered significant when $P < 0.05$. Data published previously have shown that the incidence of pain after injection of propofol is 67% [1, 2]. We sought a reduction in the incidence of pain to 13% (i.e. comparable with the use of lignocaine [1]). Power analysis showed that 44 patients were needed for the study to have a power of 95% at a P value of 0.05.

The two groups were of similar age (alfentanil group 40.2 (15.6) yr, saline group 38.6 (17.7) yr), weight (alfentanil group 75.6 (10.0) kg, saline group 74.6 (15.8) kg) and gender distribution (male/female, alfentanil group 17/5, saline group 14/8).

Analysis of the worst pain reported by patients showed that those who received alfentanil before injection of propofol had less pain than those who

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TABLE I. *Distribution of "worst reported pain" between groups (No. of patients (%)). Patients in the saline group reported more pain after injection of propofol than patients in the alfentanil group* (P = *0.001; chi-square*)

	Alfentanil ($n = 22$)	Saline ($n = 22$)
None	14 (64)	3 (14)
Mild	7 (32)	10 (45)
Severe	1 (4)	9 (41)

TABLE II. *Number of patients who were asleep or reporting none, mild or severe pain when questioned at 8-s intervals after beginning injection of propofol. Each column shows the distribution of the 22 patients at each time point*

	Time (s)					
	8	16	24	32	40	48
Alfentanil ($n = 22$)						
Asleep	0	0	0	5	17	20
None	22	16	17	12	3	1
Mild	0	6	4	4	2	1
Severe	0	0	1	1	0	0
Saline ($n = 22$)						
Asleep	0	0	0	8	13	17
None	19	9	4	5	3	2
Mild	3	10	11	5	3	2
Severe	0	3	7	4	3	1

received saline ($P = 0.001$; chi-square). The incidence of clinically unacceptable severe pain, compared with the incidence of clinically acceptable mild or no pain, was also different between the two groups ($P = 0.012$; chi-square), as was the presence of any pain, mild or severe, compared with the absence of pain ($P = 0.002$; chi-square) (table I).

When studied by male/female gender, similar results were found. For the female subgroup, none of the five patients who received alfentanil reported any pain, whereas four of the eight patients who received saline reported severe pain and four reported mild pain ($P < 0.002$; Fisher's exact test, no pain/any pain). For the male subgroup, determination of statistical significance was not possible as a result of reduced numbers, although the original trend was maintained.

No patient had pain that increased or decreased by more than one level between time points (e.g. changed from none to severe in 8 s). Two patients in each group reported pain (three mild, one severe) which decreased subsequently to none before loss of consciousness. All but three patients (one in the alfentanil group, two in the saline group) reported their maximum pain score by 24 s. Early onset of pain appeared to be associated with increased severity. Although the number of patients who were asleep by 32 s was greater in the alfentanil group ($n = 17$) than the saline group ($n = 13$), the difference was not significant ($P = 0.3$; chi-square). The effect of time on the pain scores of the two treatment groups is shown in table II.

After operation, 87% of patients recalled accurately their degree of pain during induction. Of the remainder, all but one recalled that pain was mild, whereas at the time they had stated that the pain was severe.

COMMENT

Discomfort during induction of anaesthesia is undesirable. Lignocaine, added to or given before injection of methohexitone, etomidate and propofol has been shown previously to be effective in reducing pain in the arm caused by these drugs. However, protection is not complete, with a failure rate of between 13% and 32% reported for propofol combined with lignocaine [1, 4].

Two previous reports have shown a decreased incidence of pain when propofol is preceded by alfentanil. The incidence of pain varied from 39 to 67% without alfentanil, and this was reduced to 0–16% when alfentanil preceded administration of propofol [2, 5]. In our study the incidence of pain was 84% when no alfentanil was given and this declined to 36% when alfentanil preceded propofol. However, these previous studies differed from ours in methodology, in using either premedication or a time interval of 2 min between administration of alfentanil and administration of propofol. It is possible that in our patients, alfentanil had not reached its maximum effect by the time propofol was administered. In addition, the absence of premedication and asking direct questions about pain may account for the increased incidence of pain in both groups of our study compared with other reports. However, using our methodology, only one patient reported clinically unacceptable severe pain in the alfentanil group compared with seven in the saline group.

We asked patients direct questions about pain in order not to exclude those who may have felt pain but not reported it spontaneously during induction. This was in addition to the necessary information given to patients at the time of consent about pain on injection of propofol. In a previous similar study, patients given unmodified propofol did not report pain spontaneously during injection of propofol, although when asked directly, 67% stated that they were in pain [2]. Thus our method of enquiry may account for the incidence of pain in patients receiving propofol alone (86%) being greater than reported previously. Direct questioning, applied equally to both groups, was advantageous because it is unlikely that any patients in the alfentanil group experienced pain that went unnoticed. Thus our results are not likely to have overestimated the efficacy of pretreatment using alfentanil.

Previous studies assessing various methods to reduce the pain caused by injection of propofol have not discussed the effect of male/female gender. Although we did not set out to study this interaction, our results suggest that females benefited more from pretreatment with alfentanil than males. Two possible explanations for this are that the dose of alfentanil *per kilogram* was greater in females (average weight 64 kg) than males (average weight 79 kg) or that females may show a greater or more rapid pharmacodynamic effect from alfentanil.

The lack of effect of alfentanil on induction time or dose of propofol was not surprising. We sought to determine the worst pain reported by a patient. When a patient had reported severe pain, induction

of anaesthesia was hastened by more rapid administration of propofol. This resulted in more patients in the saline group with a more rapid induction of anaesthesia than in the alfentanil group. It is unlikely that patients in the alfentanil group reported less pain simply because they tended to fall asleep more rapidly. This is supported by the observation that all but three patients had reported their worst pain by 24 s, even though no patient was asleep by that time.

We examined specifically a common clinical situation where unpremedicated patients present for anaesthesia on a list where unnecessary delays are undesirable. We did not observe clinically important problems attributable to alfentanil and despite the fact that half of our patients received alfentanil 1 mg, all began spontaneous ventilation before surgery started.

The ability of our patients to recall the degree of pain that they had as they fell asleep supports the findings of other studies that propofol has a minimal retrograde amnesic effect.

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