

## OPTIMAL DOSE OF LIGNOCAINE FOR PREVENTING PAIN ON INJECTION OF PROPOFOL

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### SUMMARY

*The purpose of this study was to define the optimum dose of lignocaine required to reduce pain on injection of propofol. We conducted a prospective, randomized, double-blind trial on 310 patients undergoing anaesthesia. Patients were allocated to four groups according to the lignocaine dosage: group A (control), no lignocaine; group B, lignocaine 0.1 mg kg<sup>-1</sup>; group C, lignocaine 0.2 mg kg<sup>-1</sup>; group D, lignocaine 0.4 mg kg<sup>-1</sup>. Our results showed that a dose of lignocaine 0.1 mg kg<sup>-1</sup> significantly reduced the incidence of pain and that there was no improvement when the dose was increased.*

### KEY WORDS

*Anaesthetics, intravenous: propofol. Complications: pain.*

Propofol is a rapidly acting i.v. agent used for induction of anaesthesia. It has many advantages and a low incidence of side effects [1]; but pain induced by injection of propofol limits its use [2, 3]. The pain was attributed first to the solubilizing agent, Cremophor EL, which is implicated in anaphylactoid reactions, but it persisted when this was replaced by soya bean oil [4, 5]. Several authors have shown that i.v. lignocaine given before or with propofol reduced the frequency of pain [4, 6, 7], but did not suppress it completely. The dose of lignocaine used varied and was based on the doses used in prevention of pain induced by other anaesthetic drugs such as etomidate [8]. The purpose of this study was to evaluate the optimal dose of lignocaine for reducing pain associated with i.v. administration of propofol.

### PATIENTS AND METHODS

The study comprised a prospective, randomized, double-blind trial, approved by the Hospital Ethics Committee. All patients gave their informed written consent and none had a history of adverse response to propofol or lignocaine. We studied 310 patients (150 male) aged 18–80 yr (mean 53.1 yr), ASA class I or II, undergoing a general anaesthesia for diagnostic procedures or minor surgery. Except for premedication, patients received no analgesic or sedative drug in the 12 h before the study. One hour before anaesthesia, patients were premedicated with hydroxyzine 100 mg i.m. and cimetidine 400 mg orally (PM1), or with midazolam 5 mg and atropine 0.5 mg i.m. (PM2). In the operating room, an 18-gauge i.v. cannula was inserted into a large forearm vein and standard monitoring commenced. Anaesthesia was induced with propofol 2.5 mg kg<sup>-1</sup>, mixed in the syringe (20 ml) with sodium chloride (group A), or lignocaine 0.1 mg kg<sup>-1</sup> (group B), 0.2 mg kg<sup>-1</sup> (group C) or 0.4 mg kg<sup>-1</sup> (group D). In all groups the syringe was filled to 20 ml with sodium chloride. The solution was injected slowly (30 s) within 30 min of preparation of the mixture. Three different members of the anaesthesia team took responsibility for anaesthesia, preparation of the mixture, and recording of pain on injection. Anaesthesia was maintained with a continuous perfusion of propofol without lignocaine and with 50% nitrous oxide in oxygen.

Arterial pressure, heart rate and Sp<sub>o</sub><sub>2</sub> were

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recorded every 5 min (HP52801) and the ECG was monitored continuously. At initial injection, the degree of pain experienced by the patient was scored as follows: 0 = no pain complained of even when asked about after injection; 1 = patient complained of pain when asked after injection of 50 % of the total dose; 2 = spontaneous complaint by patient before injection of 50 % of total dose; 3 = reported pain was associated with grimacing, withdrawal movement of the forearm, or both.

Data were analysed by chi-square test (sex ratio, ASA, PM1/PM2, degree of pain), Student's *t* test (age, weight, duration of anaesthesia, arterial pressure, heart rate) and a non-parametric test (Mann-Whitney test) when the groups studied were too small.  $P < 0.05$  was considered significant.

### RESULTS

There were no significant differences between the four groups in age, weight, sex, ASA physical

TABLE I. Patient characteristics (number or mean (SD)). PM1 = Premedication with hydroxyzine 100 mg i.m. plus cimetidine 400 mg orally; PM2 = premedication with midazolam 5 mg and atropine 0.5 mg i.m. No significant difference between the four groups

	Group A (n = 77)	Group B (n = 86)	Group C (n = 71)	Group D (n = 76)
Age (yr)	50.5 (9.4)	51.2 (8.6)	50.9 (10.5)	52.0 (9.6)
Weight (kg)	60.6 (9.7)	58.2 (9.5)	62.2 (9.9)	59.1 (8.1)
Sex (M/F)	40/37	44/42	37/34	36/30
ASA I/II	62/15	75/11	57/14	64/12
PM1/PM2	60/17	74/12	56/15	62/14
Duration of anaesthesia (min)	20.9 (6.9)	18.9 (7.5)	19.1 (8.2)	21.1 (5.3)

TABLE II. Mean (SD), mean arterial pressure (MAP) and heart rate (HR) just before and 5 and 10 min after induction of anaesthesia. No significant difference between the four groups

	Group A (n = 77)	Group B (n = 86)	Group C (n = 71)	Group D (n = 76)
Before induction				
MAP (mm Hg)	92 (14)	91 (13)	95 (10)	91 (15)
HR (beat min <sup>-1</sup> )	82 (15)	78 (13)	81 (14)	80 (11)
5 min after induction				
MAP (mm Hg)	70 (15)	69 (11)	71 (10)	68 (9)
HR (beat min <sup>-1</sup> )	66 (12)	66 (10)	64 (11)	67 (8)
10 min after induction				
MAP (mm Hg)	82 (12)	84 (13)	80 (16)	85 (11)
HR (beat min <sup>-1</sup> )	62 (11)	68 (11)	65 (12)	63 (10)

TABLE III. Patients feeling pain on i.v. injection of propofol in the control and lignocaine groups. For each score of pain, a significant difference ( $P < 0.05$ ) was found between group A (control group) and the other groups, but no significant difference was found between group B (lignocaine 0.1 mg kg<sup>-1</sup>), group C (lignocaine 0.2 mg kg<sup>-1</sup>) and group D (lignocaine 0.4 mg kg<sup>-1</sup>)

Pain score	Group A (n = 77)		Group B (n = 86)		Group C (n = 71)		Group D (n = 76)		Total (n = 310)	
	No.	%	No.	%	No.	%	No.	%	No.	%
0	49	63.6	73	84.8	58	81.6	62	81.5	242	78
1	16	20.7	7	8.1	7	9.8	8	10.5	38	12.2
2	8	10.3	5	5.8	6	8.4	6	7.8	25	8
3	4	5.1	1	1.1	0	0	0	0	5	1.6

status, premedication and duration of anaesthesia (table I). Haemodynamic changes were similar in the four groups (table II) and no patient developed cardiac events associated with lignocaine. Injection of propofol alone (group A) induced pain scores of 1, 2 and 3 in 20.7%, 10.3% and 5.1% of patients, respectively. In group B (lignocaine 0.1 mg kg<sup>-1</sup>), the incidence of pain was reduced significantly. There was no significant difference between group B and groups C (lignocaine 0.2 mg kg<sup>-1</sup>) and D (lignocaine 0.4 mg kg<sup>-1</sup>) (table III).

### DISCUSSION

We have shown that a dose of lignocaine 0.1 mg kg<sup>-1</sup> injected with propofol was associated with a significantly smaller incidence of pain than that in the control group and that an increase in dose did not provide better results. Pain on injection of propofol is a well recognized problem, with a high frequency (30–80%) [7, 9]. Our patients in group A confirmed these data (36.3%). Reformulation in soya bean oil to replace the solvent Cremophor EL (which has been implicated in the incidence of pain) was shown to have little effect with propofol [2, 10], although this almost completely prevented pain with diazepam [11] and etomidate [12].

Factors such as the vein used and the rate of injection have been studied previously: injection into a vein on the dorsum of the hand is more painful than injection into a large vein in the antecubital fossa [3, 10, 13]. If injected slowly, however, propofol causes more pain, which usually does not occur immediately after injection [10]. Thus pain on injection of propofol results not only from a direct effect on the vein wall, but

involves mediators such as kininogens [10, 14]. This is confirmed by the infrequent occurrence of thrombophlebitis and the wide variation between animal species in the pain response to injection of propofol [10].

Several attempts have been made to reduce the incidence of pain, such as prior administration of opioids [15] or aspirin [16], the use of a large-gauge cannula [10], injection into a large vein rather than one on the dorsum of the hand [5], 50% dilution in a glucose solution [14], and the use of EMLA cream applied to the skin 1 h before cannulation [6]. The data from all these studies are difficult to compare because of variation in study design. In our study, propofol was administered to all patients in the same manner, with standardization of rate of injection, site of injection in the antecubital fossa and size of cannula. Injection into the dorsum of the hand would have given more striking results but could have changed the rate of administration in some cases.

The use of lignocaine was found to reduce the incidence of pain to 5% when propofol was injected into a vein on the dorsum of the hand [4, 6, 7], provided that lignocaine was injected in combination with, and not before, the propofol—suggesting that an indirect mechanism is involved [4, 5]. Although the incidence of pain in our study was greater (15–18%), our method differed from that of other studies: no patient received opioids, and injection was slower and performed in a large vein of the forearm.

We conclude that the incidence of pain on injection of propofol may be reduced by addition of lignocaine. The optimum dose of lignocaine was found to be  $0.1 \text{ mg kg}^{-1}$  and its action may involve stabilization of pain mediators such as kininogens.

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