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Preventing Pain on Injection of Propofol: A Comparison Between Lignocaine Pre-treatment and Lignocaine Added to Propofol

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SUMMARY

A randomized double-blind study compared two methods of preventing the pain from injection of propofol, lignocaine pre-treatment followed by propofol and lignocaine added to propofol. One hundred patients received a 4 ml solution intravenously with a venous tourniquet for 1 minute, followed by propofol mixed with 2 ml of solution. Patients were divided into two treatment groups of 50 patients each: 4 ml 1% lignocaine pre-treatment followed by propofol and 2 ml saline, or 4 ml saline followed by propofol and 2 ml 2% lignocaine. Pain was assessed with a 100 mm visual analogue scale after induction and in recovery. The incidence of injection pain was 8% in the propofol mixed with lignocaine group, and 28% in the lignocaine pre-treatment group. This difference is statistically significant (P=0.017). For those patients who had pain, the mean pain score was 26.5 on induction for the propofol with lignocaine group (n=4), while the mean score was 44.4 for the pre-treatment group (n=13). The difference was not statistically significant (P=0.25). None of the propofol mixed with lignocaine group recalled pain, while 13 of the pre-treatment group did so. Lignocaine pre-treatment does not improve the immediate or the recalled comfort of patients during propofol induction when compared to lignocaine added to propofol. It is recommended that lignocaine should be added to propofol for induction rather than given before induction.

Key Words: ANAESTHESIA: intravenous, propofol. COMPLICATIONS: pain. LOCAL ANAESTHETIC: lignocaine

The aim of this study was to compare two popular methods of reducing pain on injection of propofol: lignocaine pre-treatment and lignocaine mixed with propofol, at the injection and also the recall of pain afterwards in recovery.

MATERIALS AND METHODS

Approval was obtained from the Ethics Committees of three local hospitals and written informed consent was obtained from 100 patients. Patients were mainly recruited from elective colonoscopy lists, day surgical orthopaedic and gynaecology lists. They were all ASA physical status 1 or 2, and were expected to require at least 100 mg propofol. They were all unpremedicated.

Exclusion criteria included patients ASA physical status 3-5, allergy to either propofol or lignocaine, not fluent in English, visually impaired, receiving opioids preoperatively, or requiring rapid sequence induction.

All patients were instructed in the use of a 100 mm visual analogue scale (VAS). A 20 gauge cannula was inserted in the dorsum of the hand without being connected to a carrier fluid.

The patients were randomized into two groups, Group P (n=50) received 4 ml lignocaine 1% (40 mg) pre-treatment, followed by propofol mixed with 2 ml saline, and Group M (n=50) received 4 ml saline pre-treatment, followed by propofol mixed with 2 ml lignocaine 2% (40 mg). This was achieved by individually packaged, numbered syringes containing 4 ml liquid in a 5 ml syringe, and 2 ml liquid in a 3 ml syringe. Neither the patient nor the anaesthetist was aware of the contents of the numbered syringes which were prepared by the hospital pharmacy in a randomized order. The contents of the 4 ml syringe were given intravenously with a venous tourniquet on the upper forearm for one minute. The 2 ml solution was added to 200 mg propofol. Ten ml of propofol solution was injected over 10 seconds, followed by a five-

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second wait before the patient was asked about pain and to mark a line on the VAS. Carrier fluid was then connected and further drugs given to facilitate induction and intubation. No midazolam or other amnesic was given at any stage.

Patients were asked to recall if there was pain during injection of propofol when they had satisfied discharge criteria in the recovery area.

Demographic data and pain scores were analysed using the Student's t-test. The incidence of pain was analysed with the Fisher's exact test. $P<0.05$ was considered significant.

RESULTS

One hundred patients were enrolled in this study, comprising 51 males and 49 females. There were 50 patients in each treatment group. Groups were similar with respect to age ($P=0.479$) and gender ($P>0.99$) (Table 1).

TABLE 1
Patient demographics of the two treatment groups expressed as mean (SD)

	Lignocaine before propofol (n=50)	Lignocaine with propofol (n=50)
Age (y)	46.4 (20.3)	49.2 (19.1)
Gender, M:F	26:24	25:25

The incidence of pain and pain scores on induction and in recovery are shown in Table 2. Fewer patients who received the mixture of propofol with lignocaine had pain on induction ($P=0.017$, Fisher) and none recalled the pain in recovery. If pain occurred, the severity of the pain appeared to be similar in both groups ($P=0.252$).

DISCUSSION

Propofol is used widely for induction of anaesthesia, particularly for short uncomfortable procedures, day surgery, target controlled infusion (TCI) and for the insertion of a laryngeal mask airway. Severe sharp, stinging or burning pain on injection is a common problem affecting 28% to 90%[1,2] adults, and 28% to 85%[3,4] children. This may appear immediately on injection or have a 10 to 20s delayed onset. The mechanism of pain caused by propofol is uncertain, but immediate pain may be the result of direct irritation of afferent nerve endings within the vein, while delayed pain may be caused by triggering of the kinin cascade and release of kininogens[5,6]. If afferent nerve endings are involved, pre-treatment with lignocaine may give substantial relief.

TABLE 2
Incidence of pain and pain scores of the two treatment groups

	Lignocaine before propofol (n=50)	Lignocaine with propofol (n=50)
Incidence of pain	14 (28%)	4 (8%)
Pain scores. Mean (SD)		
On induction	44.4 (27.7)	26.5 (19.7)
In recovery*	42.4 (29.7)	0

*Recall of propofol associated pain in recovery.

A large number of trials have identified several factors contributing to a high incidence of pain with propofol, and several strategies have evolved to minimize both the incidence and severity of pain. A recent review[7] of the efficacy of IV lignocaine 40 mg given with a tourniquet for 30 to 120s pre-treatment found that the number needed to treat (NNT) was 1.6 for adults (n=196, 4 studies). When the same dose is mixed with propofol, (NNT 3.6), or given IV without a tourniquet (NNT 4.3), it appears to be less efficacious. Pethidine 40 mg with tourniquet (NNT 1.9) and metoclopramide 10 mg with tourniquet (NNT 2.2) were the next most effective strategies, possibly due to their local anaesthetic properties. Fentanyl, alfentanil and remifentanil appear to reduce the incidence of pain but less successfully than pethidine[7]. Varying the temperature has no effect[8,9]. The size of the cannula has no effect but placement in a large vein in the antecubital fossa has been shown to reduce both the incidence and severity of pain[10].

Although Picard and Tramer[7] suggested lignocaine pre-treatment to be more effective than lignocaine mixed with propofol, this current study supports the opposite view. Picard and Tramer however, did not have a double-blind direct comparison between the two ways of using lignocaine, but rather inferred a difference in a meta-analysis from studies using a placebo as an alternative. Other factors could have contributed to the score differences of the two treatments. Our study is the only definitive double-blind comparison of the two active lignocaine treatments of which we are aware. This study found that the use of lignocaine before the injection of propofol does not give the patient a better chance of a comfortable induction with propofol in spite of the theoretical benefit of a longer time to act on the vein before the propofol exposure. This suggests that the pain may not be caused by direct nervous stimulation by the propofol but rather as a secondary effect possibly by endothelial or smooth muscle stimulation.

This study supports the mixture of lignocaine with propofol as the more effective way of providing analgesia during induction.

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