A Prospective Randomized Double Blind Study Comparing Propofol Medium Chain/Long Chain Triglyceride And Propofol Medium Chain/Long Chain Triglyceride With Lignocaine On Injection Pain

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Citation

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Abstract

A common drawback of propofol is pain on injection and lignocaine is commonly mixed with propofol to reduce its incidence and severity. In this study we sought to compare the effectiveness of propofol medium chain and long chain triglyceride (MCT/LCT) alone in comparison to propofol medium chain and long chain triglyceride (MCT/ LCT) premixed with lignocaine in preventing propofol pain on injection. 200 patients were randomly divided into two groups. Group A received propofol – MCT/LCT premixed with normal saline and group B received propofol- MCT/LCT premixed with 20 mg lignocaine. The incidence of pain in group A was 63% compared to 15% in group B (χ^2 = 48.242 ,p< 0.001). To conclude propofol MCT/LCT alone provides no advantage to reduce pain on injection in comparison to propofol MCT/LCT premixed with lignocaine.

INTRODUCTION

Propofol is a popular intravenous anaesthetic agent providing smooth induction and rapid recovery from anaesthesia. However pain on injection is a major disadvantage with a reported incidence of approximately 70% when a standard formulation of propofol is administered with no intervention to reduce pain.([1]) Several strategies have been applied to alleviate pain, such as previous administration of opioids or metoclopromide and adaptation of the temperature of the emulsion. The most frequently used method to reduce pain is the administration of lignocaine, either before propofol injection, with or without a tourniquet ([2]) or added to the propofol emulsion as a premixture.([1,3,4]) The mechanism of pain relief can be two fold ; first by reduction of propofol in the aqueous phase and second by lignocaine acting as a stabiliser in the kinin cascade.([5])

Injection pain has been attributed to the amount of free propofol in the aqueous phase of the emulsion. In 1997, Doenicke et al ([6]) advocated a reformulated lipid emulsion of propofol to alleviate injection pain. This reformulation of propofol contains both medium chain triglycerides (MCT) and long chain triglycerides (LCT) in equal proportions in contrast to usual LCT formulation. The amount of free propofol in a MCT/LCT emulsion is assumed to be less compared with propofol LCT thus causing less pain on injection. However recent studies have suggested that propofol MCT/LCT emulsion when used alone causes more pain on injection as compared to propofol LCT with lignocaine.([7,8,9])

The aim of this study was to determine whether propofol in a reformulated MCT/LCT emulsion without further addition was more effective in preventing pain on injection as compared to propofol MCT/LCT with lignocaine and more frequently used standard LCT propofol with a premixture of lignocaine.

MATERIAL AND METHODS

Following approval by the institutional ethics committee and written informed consent, 300 ASA I-III patients aged 18-65 years scheduled for elective surgery under general anaesthesia were recruited into this prospective randomised double blind study. Sample size was determined by performing a power analysis which showed that a minimum of 200 patients will be required for the study. Exclusion criteria were patients with ischemic heart disease and neurological problems, pregnant or lactating patients, those

who were taking any analgesics before surgery, or those with known hypersensitivity to propofol or to any of the constituents of the emulsion (soy-bean oil, MCT, glycerol, egg lecithin, sodium oleate or water for injection).

The drugs used were propofol –MCT/LCT (Propofol^{R}-Lipuro, B Braun Ltd, Melsungen, Germany) and lignocaine hydrochloride 2% (Xylocard^{R} , AstraZeneca, India).

The patients were assigned to 2 groups using computer generated randomizatiopn with 100 patients in each group. Group A received propofol – MCT/LCT premixed with normal saline (1 ml of normal saline added to 19 ml propofol-lipuro). Group B received propofol- MCT/LCT premixed with lignocaine (1 ml of 2% lignocaine added to 19 ml propofol- lipuro).

Patients received no premedication. On arrival at the operation theatre, routine monitoring was applied and a 20G cannula was inserted into a suitable vein on the dorsum of non- dominant hand. A blinded investigator injected 5 ml of the propofol solution at a constant rate over 15 secs and patients were asked to grade any associated pain or discomfort using a four-point verbal rating scale that had been previously described to them(Table 1).

Figure 1

Table 1: Verbal rating scale used by patients for assessment of propofol injection pain.

Pain Score	Description
0	No pain or discomfort at all.
1	Sensation of mild discomfort only.
2	Sensation of moderately severe pain.
3	Sensation of severe pain and/or grimacing or withdrawal of limb.

Once the assessment of injection pain had been made, induction of anaesthesia continued according to anaesthesiologists routine practice.

STATISTICS

Statistical analysis was conducted using SPSS version 11.5. Descriptive statistics such as mean, range and standard deviation have been used to summarize the baseline clinical and demographic profile of the patient. Categorical data was analyzed using Chi –square test and Fischer‘s exact test. Parametric data was analyzed using analysis of variance (ANOVA) with post hoc analysis (least square difference)

RESULTS

Both the groups were comparable with respect to age, weight and male:female ratio.(Table 2)

Figure 2

Table 2: Demographic data

	Group A (n=100)	Group B (n=100)
Age(years)	42.02±14.12	40.63± 13.71
Weight(kg)	68.6±9.46	65.4± 9.42
Male:Female	59:41	61:39

Values expressed as mean± SD
Group A= propofol MCT/LCT mixed with normal saline ; Group B= propofol MCT/LCT mixed with lignocaine

Patients in group A had significant pain compared to patients in groups B(Table 3).

Figure 3

Table 3: Incidence of pain

	Group A (n=100)	Group B (n=100)
No pain	37	85
Pain	63	15

X² = 58.021 , p= <0.001
MCT= medium-chain triglycerides; LCT= long chain triglycerides.
Group A= propofol MCT/LCT mixed with normal saline ; Group B= propofol MCT/LCT mixed with lignocaine.

In group A the incidence of pain was 63% compared to 15% in group B ($?^2$ = 48.242 ,p< 0.001). There was also significant difference in incidence of severity of pain between groups A and B (Table 4).

Figure 4

Table 4 : Incidence of severity of pain

Pain score	Group A (n=100)	Group B (n=100)
0= no pain or discomfort	37	85
1= mild discomfort	23	8
2= moderately painful	32	7
3 = severely painful	8	0

X² = 61.338, p< 0.001
MCT= medium-chain triglycerides; LCT= long chain triglycerides.
Group A= propofol MCT/LCT mixed with normal saline ; Group B= propofol MCT/LCT mixed with lignocaine

DISCUSSION

In this study patients receiving propofol MCT/LCT premixed with lignocaine had significantly less pain on injection than LCT/MCT formulations of propofol.

Several mechanisms of pain on injection have been suggested, but investigations have shown that the free concentration of propofol in the aqueous phase may be the most important factor.([6,10,11]) Emulsions of MCT/LCT, although maintaining similar pharmacological properties as standard propofol have smaller propofol concentrations in the aqueous phase.([5])

Rau et al.([12]) reported that 37.8% patients receiving propofol MCT/LCT were painfree and of the patients who had pain none graded it as severe. Kam et al.([13]) have reported a similar incidence of pain on injection, 38% in patients receiving propofol MCT/LCT compared to 36% in patients receiving propofol LCT. Larsen et al.([14]) have shown a lower incidence of pain on injection in patients receiving propofol MCT/LCT (37%) compared to patients receiving propofol LCT(64%).Yew et al.([15]) have reported a incidence of 24% in patients receiving propofol LCT premixed with lignocaine and propofol MCT/LCT emulsion.

In our study the incidence of pain with propofol MCT/LCT was 63%.

Schaub et al.([7]) have reported a 47% incidence of pain with propofol MCT/LCT compared to 24 % in patients receiving propofol LCT with lignocaine pretreatment. Nyman et al([8]) in their study in paediatric patients have reported 33.3% patients having pain free propofol injection in propofol MCT/LCT group compared to 61% patients having pain free propofol injection in propofol LCT premixed with lignocaine group. Adam et al.([9]) have reported that patients receiving propofol MCT/LCT had a higher verbal analogue scale(VAS) as compared to patients receiving propofol LCT with lignocaine.

We found that mixing propofol MCT/LCT with lignocaine was effective in significantly reducing the incidence of pain from 63% in propofol MCT/LCT to 15% in propofol MCT/LCT with lignocaine.

Yew et al([15]) have reported a decrease in pain on injection from 24% to 4% in patients receiving propofol MCT/LCT mixed with lignocaine. Kunitz et al.([16]) have also suggested that addition of lignocaine to propofol MCT/LCT seems to have an additive effect to reduce propofol injection pain.

In, conclusion propofol MCT/LCT alone does not provide any advantage to reduce pain on injection in comparison to propofol MCT/LCT premixed with lignocaine. Further studies need to be done to establish the role of this new propofol MCL/LCT emulsion on propofol injection pain.

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