Original Article

A Comparative Study of Pain on Injection with Propofol Long-Chain Triglycerides versus Propofol Medium/Long-Chain Triglycerides with Lignocaine

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Abstract

Background: Propofol long-chain triglyceride (LCT) is the most commonly used intravenous anesthetic drug, which has pain on injection as its major disadvantage. Many drugs have been used to alleviate this pain with variable efficacy, among them lidocaine pretreatment is most popular. Propofol medium-chain triglyceride (MCT)/LCT emulsion has the ability to decrease pain on injection. The availability of propofol with two different formulations necessitates a comparison of pain on injection with lidocaine pretreatment. **Aim:** The aim of this study was to study the incidence and intensity of pain on injection with propofol LCTs versus propofol MCT/LCTs with lignocaine. **Materials and Methods:** This prospective, double-blind, and randomized controlled study included 120 American Society of Anesthesiology Grade I and II participants undergoing General Anesthesia. In Group A, patients were induced with 1% propofol LCT (2 mg/kg) with 2% lidocaine 2 ml and in Group B 1% propofol MCT/LCT (2 mg/kg) with 2% lidocaine 2 ml. Assessment of pain on injection was performed after 30% of total induction dose was injected at a rate of 1 ml/s by Verbal Rating Scale. **Results:** Group A reported an incidence of pain in 28.4% and Group B with 13.3%. There was a statistically significant difference in the incidence and intensity of pain with propofol MCT/LCT along with lignocaine. Sixteen patients in Group A and eight patients in Group B had mild pain, whereas one patient in Group A and none of them in Group B had moderate pain. **Conclusion:** Premixing lignocaine with MCT/LCT propofol significantly reduces both the incidence and intensity of pain as compared to LCT propofol with lignocaine.

Keywords: *Propofol, lignocaine, long-chain, medium-chain, pain on injection*

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Introduction

Propofol long-chain triglyceride (LCT) is the most commonly used intravenous (IV) anesthetic drug. Pain on injection is a major disadvantage and can be very distressing for the patient with propofol LCT. Incidence of pain varies between 28% and 90% in adults and may also be severe.[1,2] The mechanism of pain on injection has been postulated to be due to either irritant effect giving rise to an immediate sensation of pain or an indirect effect through the release of mediators, leading to the delayed onset.[3] Many drugs such as opioids, lidocaine, thiopentone, ketamine, or metoclopramide have been used to alleviate this pain after IV injection of propofol LCT with variable efficacy.[2,4-6] Among them, lidocaine pretreatment is the most popular method for reducing pain. A new formulation propofol medium-chain triglyceride (MCT)/LCT emulsion is being proposed for its ability to decrease the pain on injection.[7-11]

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Hence, the availability of propofol with two different formulations necessitates a comparison of pain on injection with lidocaine pretreatment.

In this prospective double-blind randomized controlled study, we compare pain on injection with propofol LCT and propofol MCT/LCT for induction of anesthesia.

Materials And Methods

It was a prospective, double-blind, randomized controlled study. A total of 120 participants were included in this study. The study population consists of normal adults aged between 18 and 60 years and of the American Society of Anesthesiology (ASA) Grade I and II. Patient refusal, emergency surgeries, known allergy to any of the test drugs, malignancies, pregnancy, cardiovascular, respiratory, neurological, psychological, hepatic, or renal disease, and diabetes mellitus were excluded from the study. After obtaining institutional ethical clearance, the participants were provided information sheet, and written informed consent was obtained. The study involves the assessment of pain using Verbal Rating Scale (VRS). The study population was randomly divided into two groups, 60 patients in each group by a computer-generated randomization table.

In Group A, patients were induced with 1% propofol LCT (2 mg/kg) with 2% lidocaine 2 ml, and in Group B, patients were induced with 1% propofol MCT/LCT (2 mg/kg) with 2% lidocaine 2 ml.

Assessment of pain on injection was performed after 30% of the total induction dose was injected at a rate of 1 ml/s by VRS. 0 – no pain (negative response to the question), 1 – mild pain (pain reported only in response to the question), 2 – moderate pain (pain reported in response to the question and accompanied by behavioral signs and pain reported spontaneously without question), and 3 – severe pain (strong vocal response or response accompanied by facial grimacing, arm withdrawal, and tears).

A day before the surgery, the preoperative visit was made, and a detailed history of the patient was obtained. A thorough clinical examination was conducted and necessary investigations were sent. Lidocaine test dose was given during the preoperative visit, if any allergy seen, injection hydrocortisone 100 mg and injection pheniramine maleate 25 mg were administered, and these patients were excluded from the study. Airway assessment was done using Modified Mallampatti Score on the day before surgery. All patients were kept nil per oral for 8 h before the surgery. They were premedicated with tablet ranitidine 150 mg at night on the day before surgery and also at 6 am in the morning of the surgery and tablet alprazolam 0.5 mg in the night before surgery.

On the day of surgery, the procedure was explained to the participants, and written informed consent was obtained from each participant. IV access was secured, and infusion of Ringer's lactate solutions was started. Patients were then shifted to the operating room after which routine noninvasive monitors were applied, and vital signs were monitored. Injection glycopyrrolate 0.01 mg/kg and injection fentanyl 2 mcg/kg were given as premedicants, and then patients were randomly allocated into two groups, 60 patients in each group by a computer-generated randomization table to receive either 1% propofol LCT (2 mg/kg) with 2% lidocaine 2 ml or 1%propofol MCT/LCT (2 mg/kg) with 2% lidocaine 2 ml, pain was assessed using VRS after 30% of the induction dose was administered. The rest of the drug was administered following which mask ventilation was confirmed and then tracheal intubation was facilitated by injection scoline 2 mg/kg and maintained with injection vecuronium 0.1 mg/kg. Ventilation will be controlled with 50% O_2 and N_2O. Vitals were recorded before and after the propofol injection and were monitored throughout the surgery. In case of hypotension (systolic blood pressure <30% of baseline) following propofol, IV fluid boluses were given, if uncorrected injection mephentermine 6 mg increments were given. After completion of surgery, residual neuromuscular blockade was reversed with injection neostigmine 0.05 mg/kg, injection glycopyrrolate 0.01 mg/kg, and patients were extubated.

Statistical analysis

Data were entered into Microsoft Excel datasheet and were analyzed using SSPS software version 22 (IBM, Chicago, USA). Categorical data were represented in the form of frequencies and proportions. Chi-square test was used as a test of significance for qualitative data. Continuous data were represented as mean and standard deviation. Independent *t*-test was used as a test of significance to identify the mean difference between two quantitative variables. MS Excel and MS word were used to obtain various types of graphs such as bar diagram. *P* value (Probability that the result is true) of <0.05 was considered statistically significant after assuming all the rules of statistical tests.

Results

In Group A, the majority were in the age group of 31–40 years, and in Group B, the majority were in the age group <30 years. There was no significant difference in age distribution between two groups as shown in Table 1.

In Group A, 55% were males and 45% were females, and in Group B, 51.7% were males and 48.3% were females. There was no significant difference in gender distribution between two groups as shown in Table 2.

In Group A, 63.3% had ASA Grade 1 and 36.7% had ASA Grade 2. In Group B, 50% had ASA Grade 1 and 50% had ASA Grade 2. There was no significant difference in ASA grade between two groups. $\chi^2 = 2.172$, df = 1, $P = 0.141$ [Figure 1].

In Group A, the majority 45% were obese, and in Group B, the majority were overweight (46.7%). There was no significant difference in body mass index distribution between two groups as represented in Table 3.

There was no significant difference in the vitals before and after administering propofol in both the groups as shown in Table 4.

There was a statistically significant difference in VRS grade between the two groups. Sixteen patients in Group A have a VRS score of 1 whereas eight patients in Group B. One patient in Group A had a VRS score of 2, whereas no patients in Group B had VRS score of 2 as shown in Table 5.

Discussion

Propofol is an excellent IV induction agent with a speedy recovery. The first clinical trial on this drug happened in 1977.[12] Since then, it has been observed that pain on IV injection is its major setback. Numerous studies were performed to reduce the pain caused by propofol injection.[6,13-16] New formulation MCT/LCT propofol is found to reduce the incidence and intensity of pain on injection.[17]

It has been studied that the most important factor for the pain on injection is the free concentration of propofol in the aqueous phase.[15,18,19] Maintaining similar pharmacological properties as standard propofol, emulsions of MCT/LCT have smaller propofol concentrations in the aqueous phase.[20] There was a drastic reduction in the incidence of pain from 24% to 4% in a study done by Yew *et al*., and from 63% to 15% in Sethi *et al*. on premixing lignocaine with MCT/LCT.[21,22] Hence, we decided to premix lignocaine with MCT/LCT in our study.

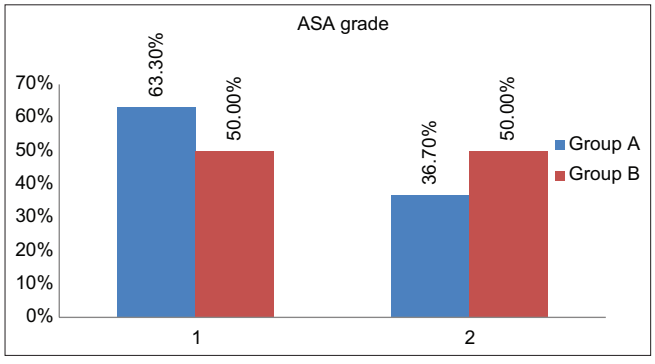

Figure 1: Bar diagram showing ASA grade distribution comparison between two groups

Table 1: Age distribution comparison between two groups

Age (years)	Group, count (%)	
	Group A	Group B
<30	17 (28.3)	21 (35.0)
31-40	21 (35.0)	17 (28.3)
41-50	10 (16.7)	12 (20.0)
51-60	12 (20.0)	10 (16.7)

χ^2=1.206, df=3, P=0.752

Table 2: Sex distribution comparison between two groups

Gender	Group, count (%)	
	Group A	Group B
Male	33 (55.0)	31 (51.7)
Female	27 (45.0)	29 (48.3)

χ^2=0.134, df=1, P=0.714

Table 3: Body mass index distribution comparison between two groups

BMI	Group, count (%)	
	Group A	Group B
Normal	6 (10.0)	14 (23.3)
Overweight	25 (41.7)	28 (46.7)
Obese	27 (45.0)	18 (30.0)
Morbid obesity	2 (3.3)	0

χ^2=7.170, df=3, P=0.067. BMI: Body mass index

Table 4: Comparison of vital signs before and after administering propofol

	HR 1 (bpm)		HR 2 (bpm)		*P*
	Mean	SD	Mean	SD	
Group A	83.68	15.62	84.95	14.19	0.4631
Group B	81.50	12.10	83.22	11.83	0.8630
	SBP 1 (mmHg)		SBP 2 (mmHg)		
Group A	126.57	13.13	122.22	12.90	0.8925
Group B	124.82	9.68	121.45	9.50	0.8858
	DBP 1 (mmHg)		DBP 2 (mmHg)		
Group A	80.27	8.45	77.57	8.39	0.9565
Group B	75.23	7.89	74.38	7.60	0.7746
	MAP 1 (mmHg)		MAP 2 (mmHg)		
Group A	95.70	9.13	92.45	9.15	0.9866
Group B	91.76	7.35	90.12	6.97	0.6848
	RR 1 (per min)		RR 2 (per min)		
Group A	14.73	1.66	14.90	1.61	0.8151
Group B	13.27	1.29	13.22	1.24	0.7856

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HR: Heart rate, MAP: Mean arterial pressure

Table 5: Comparison of Verbal Rating Scale between the two groups

VRS	Group, count (%)	
	Group A	Group B
0	43 (71.7)	52 (86.7)
1	16 (26.7)	8 (13.3)
2	1 (1.7)	0

χ^2=4.093, df=1, *P*=0.02154. VRS: Verbal Rating Scale

We found in our study an incidence of pain in 28.4% and 13.3% in propofol LCT and propofol MCT/LCT both premixed with lignocaine 40 mg, with a profound fall in the intensity of pain where only one patient had moderate pain in the LCT with lignocaine group and none in MCT/LCT with lignocaine group.

A study was done by Schaub *et al*. compared propofol MCT/LCT and standard propofol formulation with lignocaine pretreatment. They found the incidence of pain with MCT/LCT formulation to be 47% whereas standard propofol with lignocaine to be 24%.[9] These findings were in accordance with our study, where we got an incidence of 28.4% in the LCT propofol with lignocaine group.

Another study by Röhm *et al*. showed that the incidence of pain in propofol MCT/LCT and standard propofol with lignocaine 40 mg pretreatment to be 16% and 31%, respectively.[23] These are similar to the results found in our study, 13.3% and 28.4%.

Sethi *et al*. found a 15% and 24% incidence of pain in MCT/LCT with lignocaine and LCT with lignocaine groups, respectively, which are similar incidences in our study.[22] In addition, we can observe that they had seen the similar incidence of pain, using 20 mg of lignocaine as opposed to 40 mg in our study. Hence, proving that 20 mg and 40 mg are equally efficacious in bringing down the incidence of propofol-induced pain but the intensity is much reduced with 40 mg.

Further, studies are advised with the large study population to find the minimal and equally efficacious dose in reducing both incidence and intensity of lignocaine to prevent propofol-induced pain.

Conclusion

Premixing lignocaine with MCT/LCT propofol significantly reduces both incidence and intensity of pain as compared to LCT propofol with lignocaine.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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