



## Original Research Article

## Injection with long chain triglyceride or long chain triglyceride/medium chain triglyceride propofol: Which is less painful?

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## ABSTRACT

**Introduction:** Long chain triglyceride/Medium chain triglyceride (LCT/MCT) Propofol 1% suspension is a new formulation having 10% fat emulsion consisting of long chain triglycerides (LCT) and medium-chain triglycerides (MCT). The pharmacokinetics and efficacy are similar to the standard Propofol LCT.

**Objective:** To compare incidence, intensity of pain on injection and hemodynamic stability with both 1% Propofol -LCT and 1% Propofol-LCT/MCT in patients undergoing surgery with general anaesthesia.

**Materials and Methods:** This was a comparative study conducted in Shri M.P. Shah Medical College and Guru Gobind Hospital, Jamnagar. After due ethical clearances, 60 patients were divided into L group and L/M group by using random number table after taking written informed consent. The L-Group received 1% propofol-LCT while the L/M group received 1% propofol-LCT/MCT. After induction, pain was assessed using Verbal Rating Score for incidence and intensity of pain.

**Results:** In L-group, 29 (96.67%) patients complained of pain, while in L/M-group 24 (80%) patients perceived pain. Ten (33.3%) patients in L group and 18 (60%) in L/M group had none to mild pain, but moderate to severe pain was perceived by 20 (66.67%) patients in L group compared to 12(40%) in L/M group. The incidence of pain and intensity of pain on injection was greater in group L (p=0.04 and 0.03 respectively).

**Conclusions:** Propofol-LCT/MCT may be considered in place of propofol-LCT as an anaesthetic agent since it reduces pain of injection.

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### 1. Introduction

Long Chain Triglyceride-LCT Propofol is widely used as an intravenous anaesthesia induction agent. It is well known for its safety and efficacy in terms of rapid induction, shorter action and fast recovery. Propofol is commonly used for both in induction as well as maintenance of anaesthesia. It is preferred for short and ambulatory surgery. However, it is commonly reported to induce pain in 60-90% of patients when given intravenously.<sup>1,2</sup> This increased patient discomfort, including discontent with the anaesthesia and

behaviour of patients which leads irritation of patients and responsible for many complications. Pain on injection is largely due to higher concentration of free propofol in the aqueous phase.<sup>3</sup> Common factors which contribute for high incidence for pain are properties of propofol, site of administration, speed of administration and also concentration in aqueous phase.<sup>4</sup>

A new formulation of Propofol LCT/MCT with 10% fat emulsion consisting of long chain triglycerides (LCT) and medium-chain triglycerides (MCT) is now available. Its pharmacokinetics and efficacy are similar to the standard propofol-LCT. Studies have shown that these

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newer Propofol-LCT/MCT formulations reduce injection pain.<sup>2,4-6</sup> The studies, however, have limitations such as lack of control over site, speed of injection, propofol temperature, premedication, anesthetic technique, patient variability and gender.

This comparative clinical study was conducted to compare the incidence and intensity of injection pain with 1% Propofol-LCT with 1% Propofol- LCT/MCT in 60 patients of either gender of ASA grade I and II, weighing between 40-80 kgs undergoing general anesthesia for surgical procedures lasting for 45-90 mins.

## 2. Materials and Methods

This comparative clinical study was conducted to compare the incidence and intensity of injection pain with 1% propofol LCT and 1% propofol LCT/MCT in tertiary care hospital of saurashtra region, Gujarat state which is attached with Shri M.P. Shah Medical College, Jamnagar. Ethical clearance was taken from ethical committee of institute. Sixty adult patients were randomly selected from routine surgical list being operated under general anesthesia. Written informed consent was obtained from the patients after explaining the objectives of the study and pre-anaesthetic assessment was done before the day of surgery.

L-group- patients received inj.propofol LCT 1% at the dose of 2mg/kg.

L/M-group- patients received inj.propofol LCT/MCT 1% at the dose of 2mg/kg

### 2.1. Inclusion criteria/exclusion criteria

Patient's age: 18 to 60 years, belonging to ASA grade I and II, weight in range of 40 to 80 kg and duration of surgery between 60–90 minutes under general anaesthesia were included in the study.

Patient below 18 or above 60 years of age, allergy or seizure history, chronic pain condition, renal insufficiency (creatinine >1.5mg/dl), with Hypovolemia, body weight > 80kg, Systemic illness, Psychiatric illness, acute infections and history of previous reaction to Propofol were excluded.

Premedication was given with inj.Ondansetron (80µg/kg) and inj Glycopyrrolate (4µg/kg) intravenously slowly to all patients.

Patients were randomly allocated to receive either 1% propofol- (Group L) or 1% propofol-LCT/MCT (Group L/M) by means of random number table. All vials were stored at room temperature for 20 minutes before injection. On arrival at the operating room routine monitoring was applied, followed by 18 G cannula insertion on both forearms on the volar aspect. Premedication was given with inj. Ondansetron (80µg/kg) and inj Glycopyrrolate (4µg/kg) intravenously.

Intra operative monitoring of Pulse/SPO2 with EMCO monitor, noninvasive Blood Pressure monitoring, Res-

piratory system/ Cardiovascular system with pre-cordial stethoscope, Electrocardiography with Schillers cardiogram was continuously done.

Propofol 2mg/kg was manually injected at 0.5ml/sec. About 15 sec after propofol injection was completed, the patients were asked about pain of injection via VRS Verbal Rating Score (VRS). The verbal rating score (VRS 0-10) was recorded on pain of injection. VRS > 4 indicates severe or worst pain.

The following parameters were documented:

1. Incidence of pain on IV cannulation.
2. Incidence of pain on injecting propofol.
3. Intensity of pain on injecting propofol.

The pain verbal rating score (VRS) 0-10 with

1. 0 = no pain
2. 1-4 = mild pain
3. 5-7= moderate pain
4. 8-10 = severe or the worst pain imaginable.

### 2.2. Statistical analysis

Data entry was done in MS Excel and analysis was conducted using MedCalc trial version. Results were expressed as proportions for the number of patients in each group. Summary statistics have been reported as mean + SD or Median (IQR) depending on the normalcy of data. Difference in the proportions of patients perceiving pain and score of pain in the two groups have been reported as Chi-square and Mann Whitney U tests respectively. Value of  $p < 0.05$  was considered statistically significant.

## 3. Results

Thirty patients were included in each of groups, one in whom Propofol L and the other in which Propofol L/M was given. The Mean (SD) age in group L was 25.1(10.1) years and in group L/M was 26.5(7.5) years. There was no significant difference in the proportion of patients complaining of pain on insertion of cannula in both the groups ( $P=0.54$ ).

In group L on intravenous injection with propofol one patient did not have pain and remaining 29 (96.6%) patients reported pain while in group L/M 24(80%) patient reported pain. The proportion of patients reporting pain was statistically significant and more in group L Compared to group L/ M ( $P=0.04$ ) (Table 1).

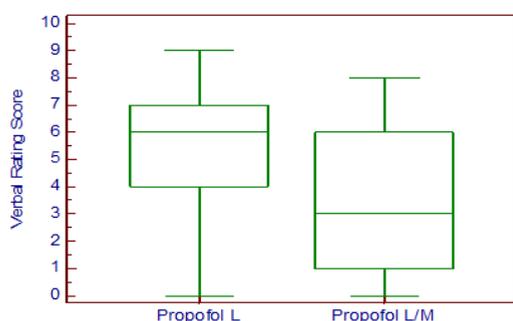
Proportion of patients suffering from moderate to severe pain was more in group L 20 (66.7%) compared to group L/M 12 (40%), the difference was statistically significant ( $P=0.03$ ) (Table 1)

Ten (33.3%) patients in L group and 18 (60%) in L/M group had none to mild pain, but moderate to severe pain was perceived by 20 (66.67%) patients in L group compared

to 12(40%) in L/M group. There was a significantly greater incidence and intensity of injection pain in group L compared with group L/M ( $p < 0.04$  and  $p = 0.03$  respectively).

Median (IQR) Verbal rating score (VRS) for pain on i.v cannula insertion in group L and group L/M was 4(2-6) and 3.5(2-5). Median (IQR) pain score on injection propofol in group L was 3(1-6), while it was 6(4-7) in group L/M. This difference was statistically significant ( $p=0.009$ ) (Table 2 Figure 1)

Hemodynamic stability was measured in terms of heart rate, Systolic blood pressure and diastolic blood pressure monitored for both L group and L/M group, the difference was statistically not significant for all vitals monitored. (Figures 2 and 3)



**Fig. 1:** Box and whisker plot for median Verbal rating score (VRS) in Propofol L and Propofol L/M group

#### 4. Discussion

Pain following injection of propofol is a common problem and one important source of patient dissatisfaction. It may be distressing for the patient and interfere with the smooth induction of general anaesthesia.<sup>3,4</sup> Based on the proposed mechanisms and factors associated with propofol injection pain, several methods for the prevention of pain have been tried with varying degrees of success. The incidence and intensity of the pain are affected by many factors including cannula size and site of injection, volume, speed of injection, and the use of local anesthetics, dilution of propofol, different temperature and premedication.<sup>7,8</sup>

The use of lidocaine to prevent propofol injection pain is the most extensively studied technique and is the most common method used in clinical practice.<sup>7-10</sup> However, the availability of plain lidocaine without preservative is still lacking in many countries. Moreover, the mixing of propofol emulsion with any other drug is not recommended by the manufactures because emulsions are thermodynamically unstable despite the use of stabilizing agent the addition of lidocaine 20 or 40 mg to propofol 200 mg results in coalescence of oil droplets, which finally proceeds to a visible separate layer, indicating physico-

chemical incompatibility.<sup>3,11</sup> These methods also have the disadvantage of requiring additional manipulation, which may or may not alter pharmacokinetics, pharmacodynamics and makes delivery of anesthesia less efficient.<sup>12</sup> There is also the potential of introducing contaminants into the emulsion, because LCT fat emulsion can serve as excellent growth media.<sup>11-13</sup>

Propofol-LCT/MCT formulations have been reported to reduce injection pain, incidence of pain with propofol LCT is more compare to propofol LCT/MCT. Kumar A et al (2019), Sundarathi P et al (2007) also observed higher incidence of pain (85% vs. 38%) and (90.9 vs. 94.5%) with propofol LCT vs. propofol LCT/MCT respectively.<sup>14,15</sup> In our study incidence of pain on injection propofol is 29 (96.6%) in L group which is much higher compare to L/M group, it is 24 (80%). Sundarathi P al (2007) observed that pain on injection with propofol is more with Propofol LCT (98.2%) compare to propofol LCT/MCT (74.5%) and concluded incidence of pain is less with propofol LCT/MCT.<sup>15</sup>

The present results found that the incidence of pain on needle insertion was comparable between the groups. Reflecting that anxiety status of the studied populations was not different. The incidence of pain on injection with propofol-LCT (96.6%) was greater than propofol-LCT/MCT (80%). The authors considered VRS  $> 4$  (moderate to severe pain) indicating the pain intensity.<sup>15-17</sup> In propofol L-group 29 (96.67%) patients complain of pain, VRS $>0$  which indicates none to mild pain, while in propofol L/M-group 24 (80%) patients VRS score  $>0$ . Sundarathi P et al (2007), Sarkar M S et al (2016) and Bechmann M et al (2011) also found that incidence of pain is more common in propofol LCT compared to propofol LCT/MCT.<sup>15,16,18</sup> There was a significantly greater incidence and intensity of injection pain in group L compared with group L/M.

Bechmann et al (2011), Sundarathi P (2007) in their study observed that 60% patients reported moderate to severe pain in propofol LCT group compared to 36.4% in propofol LCT/MCT group and Kumar A et al (2019) in their study also found higher intensity of pain with propofol LCT as compared to propofol LCT/ MCT.<sup>15,16,18-20</sup>

The patients were not over sedated to answer about the pain intensity during induction or suffered from amnesic effect of the studied drugs. Almost 20 years after the advent of propofol, the injection of this anesthetic medication still causes a high incidence of pain, and the mechanisms of that pain are still obscure. It is hypothesized that the concentration of free propofol in the aqueous phase of the emulsion is responsible for the pain on injection. The lesser pain on injection by Propofol-LCT/MCT is most likely attributed to a decreased concentration of propofol in the aqueous phase.<sup>16,18,21</sup>

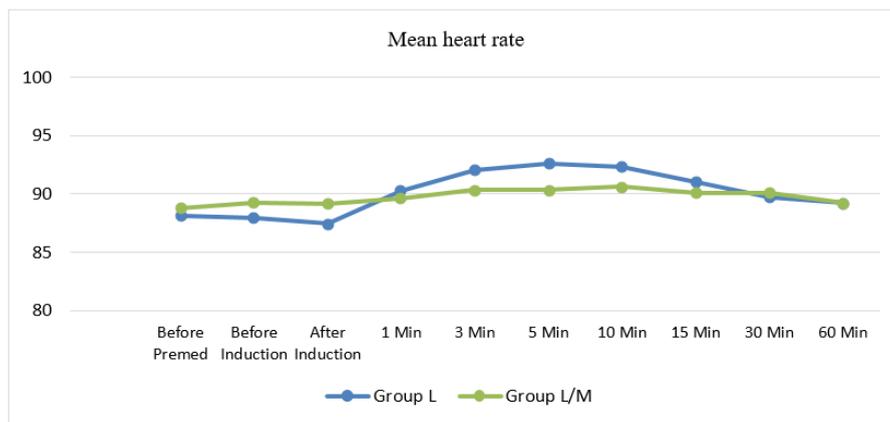
**Table 1:** Incidence and intensity of pain in the groups given Propofol L and Propofol L/M

	Group L (n = 30)	Group L/M (n=30)	p value
Incidence of pain on i.v cannula insertion in L group and L/M group			
No pain (VRS=0)	4(13.33%)	3(10%)	0.540
Pain (VRS>0)	26(86.6%)	27(90%)	
Incidence of pain on injection of propofol in L group and L/M group			
No pain (VRS=0)	1 (3.33%)	6 (20%)	0.04
Pain (VRS >0)	29 (96.6%)	24 (80%)	
Intensity of pain on injection of propofol in L and L/M group			
None to mild pain (VRS 0-4)	10(33.33%)	18(60%)	0.03
Moderate to severe pain(VRS 5-10)	20(66.66%)	12(40%)	

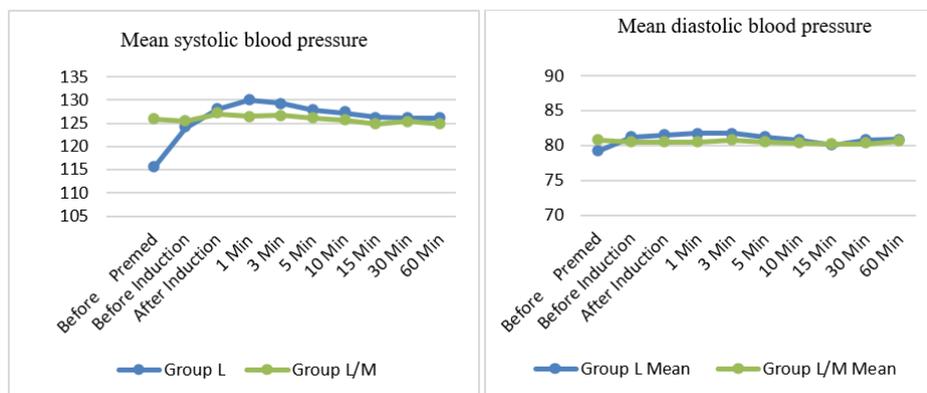
**Table 2:** Median score of pain in the groups given Propofol L and Propofol L/M

	Group L (n = 30)	Group L/M (n=30)	p value*
Median (IQR)			
Pain score on i.v cannula insertion	4 (2-6)	3.5 (2-5)	0.53
Pain score on injection of propofol	3(1-6)	6(4-7)	0.009

\*Mann Whitney U test



**Fig. 2:** Comparison of mean heart rate



**Fig. 3:** Comparison of Mean systolic and diastolic blood pressure

Many methods have been tried, with varying success, to reduce the incidence and severity of propofol injection pain. Currently, another choice would be to use propofol-LCT/MCT in combination with other methods such as a mixture with lidocaine in order to decrease the incidence and intensity of pain on injection.

## 5. Conclusion

1. Incidence and intensity of pain on injection was significantly lower in patients receiving propofol-LCT/MCT compared to propofol LCT (P = 0.006) in patients undergoing general anaesthesia for surgical procedures lasting 45-90 minutes.
2. Thus propofol-LCT/MCT is superior to propofol-LCT on pain of injection especially when the addition of lidocaine is undesirable.
3. Hemodynamically patients stable throughout the procedure for both propofol LCT and propofol LCT/MCT group.

## 6. Source of funding

None.

## 7. Conflict of interest

None.

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