

Pain on Injection: Comparison between Propofol LCT vs Propofol MCT-LCT

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Abstract

Background and Aims: Propofol is widely used for induction and maintenance of anaesthesia. It has the disadvantage of causing sharp pain on injection which can interfere with smooth induction of anaesthesia. The aim of the study was to compare the incidence and intensity of injection pain with medium chain triglyceride/ long chain triglyceride (MCT-LCT) propofol and long chain triglyceride (LCT) propofol during intravenous induction of anaesthesia. **Methods and Material:** Two hundred adult patients belonging to ASA physical status I or II, scheduled for elective surgeries under general anaesthesia were selected and randomly allocated to two groups L and M. Group L received 3 cc of LCT propofol and Group M received 3 cc of MCT-LCT propofol. Patients were observed and questioned after 30 sec of injection and pain was scored on a 4 point scale. Pain recall was done on the same 4 point scale 30 minutes postoperatively. **Statistical Analysis:** Data was collected and analysed using Fisher's exact test and unpaired t test. Statistical significance was taken as $p < 0.05$. **Results:** Both the incidence and intensity of pain was greater in group L compared with group M ($p = 0.0002$). The mean pain score was also higher in group L (2.71) when compared with group M (1.08). The difference between two groups with regard to recollection of pain on injection of propofol was statistically significant ($p = 0.0001$). **Conclusion:** Propofol MCT-LCT reduces both intensity and incidence of pain on injection.

Keywords: Pain on Injection; MCT Propofol; MCT-LCT Propofol.

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Introduction

Ever since Kay and Rolly introduced propofol in 1977, it is widely used for induction and maintenance of anaesthesia. Propofol because of its titratable level of anaesthesia, rapid recovery and minimal side effects is considered as an ideal induction agent [1]. Pain on injection is one of the disadvantages of propofol.

Propofol induced injection pain can cause agitation and interfere with smooth induction.

Various mechanisms are responsible for this including venous irritation and activation of kallikrein and bradykinin [2]. Incidence of propofol injection pain has been estimated between 28 - 90% in adults [3]. Considering its clinical importance and frequency propofol induced pain was ranked seventh among 33 clinical concerns [4].

Various pharmacological methods (e.g., pre-treatment with lignocaine, fentanyl, tramadol, ketamine, ondansetron, garnisetron) [5,6,7,8,9] and non-pharmacological methods (e.g., injecting into larger veins, cooling, or warming) [10,11] have been

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used with varying results. A new formulation of propofol consisting of long-chain triglycerides (LCT) and medium-chain triglycerides (MCT) emulsion has been advocated to reduce injection pain compared with propofol LCT in adults and teenagers [12].

This prospective, double-blind, randomized study was conducted to compare the incidence and intensity of injection pain and recall of injection pain postoperatively with different formulations of propofol, propofol LCT with propofol MCT-LCT in adult patients undergoing elective surgery requiring general anaesthesia.

Materials and Methods

After obtaining approval from hospital ethics committee and informed consent from the patients, 200 patients belonging to American Society of Anaesthesiology (ASA) physical status I and II, of either sex, aged between 18 and 60 years, undergoing elective surgery under general anaesthesia, were studied. Patients less than 18 years or more than 60 years, patients with IHD, psychiatric or neurological disorders, patients belonging to ASA physical status III or IV, patients undergoing emergency surgery, morbidly obese patients, patients who were receiving analgesics before surgery, patients with history of hypersensitivity to the study drug were excluded from study. A thorough pre-anaesthetic evaluation with general physical and systemic examination was done the evening before the proposed surgery. Patients were kept fasting 6 h for solids and 2 h for clear liquids prior to surgery. The anaesthetic technique used and verbal rating scale was explained to the patient.

All the patients falling under inclusion criteria were numbered and every nth patient was selected by Systematic Random Sampling Procedure. The patients were randomly allocated into 2 groups of 100 patients each, LCT propofol group (Group L) or MCT-LCT propofol group (Group M) using computer generated random numbers and sealed envelope which were opened just before shifting the patient to the operation theatre.

On arrival of patient to the operating room, 18G intravenous cannula was inserted into cephalic vein of the non-dominant hand. Heart rate, non-invasive blood pressure (NIBP), electrocardiograph (ECG), peripheral oxygen saturation (SpO₂) was monitored and baseline values were noted. Verbal rating scale

was again explained to the patient. Anaesthetic drugs were prepared by the same person who opened the envelope but was not involved in the intraoperative management or post-operative assessment of the patients. No analgesic drug was given to the patient before injecting propofol.

Induction of anaesthesia was done with either 1% LCT propofol (2mg/kg)(Group L) or 1% MCT-LCT propofol (2mg/kg) (Group M). 3 ml of study drug was injected (LCT/MCT-LCT propofol) was injected over 15 seconds. Then, patients were asked to rate the severity of injection pain. Pain was assessed using verbal rating scale and was assessed 15 seconds following injection.

Pain Score	Description
0	No pain
1	Mild pain
2	Moderate pain
3	Severe pain
4	Extreme pain

Following this, induction of anaesthesia was continued with the rest of the calculated propofol dose and fentanyl 12µg/kg was given to all patients. Patients were then intubated with appropriate size endotracheal tube after giving vecuronium. Anaesthesia was maintained with isoflurane, oxygen-nitrous oxide (50:50). ECG, heart rate, NIBP, SpO₂, and end-tidal carbon dioxide was monitored throughout. After the completion of operating procedure patient was extubated and shifted to Post anaesthesia care unit and asked to recall propofol injection pain on complete regain of consciousness. Recall of injection pain was scored using same pain score.

The primary outcomes of the study were incidence and severity of injection pain and postoperative recall of propofol injection pain. The secondary outcomes were haemodynamic changes and adverse events if any.

Data was collected and statistical analysis was performed using SPSS version 20. Descriptive statistics such as range, mean, standard deviation (SD) were used to summarize the baseline clinical and demographic profile of the patients. Categorical data were analysed using Fisher's exact tests, and unpaired t test. Statistical significance was taken as p < 0.05

Statistical Analysis:

Table 1 shows the demographic distribution in the study. There was no significant difference in demographic profile of the patients in both groups. Females (57%) were majority in both the groups. Majority of patients in both the groups belonged to ASA grade 1.

Table 2 shows comparison of pain score on propofol injection in 2 groups. All patients complained of pain in Group L. Most patients complained of moderate to severe pain, 8 patients complained of extreme pain. 13 patients in group M had no pain on injection, majority of patients in group M complained of mild pain.

Fischers exact test was used to determine the incidence of pain in two groups. The difference between two groups with regard to incidence of pain on injection of propofol was statistically significant ($p = 0.0002$).

The mean pain score with respect to injection of propofol in group M was 1.08 and in group L was 2.71. The difference between two groups with regard to intensity of pain on injection of propofol was statistically significant ($p=0.0001$).

Table 3 shows comparison of recollection of propofol injection pain in 2 groups. 18 patients in group M had no memory of pain on injection of propofol. All patients were able to recall pain on injection of propofol in group L. Mean pain score of 0.98 was recorded in group M as compared 1.75 in group L. The difference between two groups with regard to recollection of pain on injection of propofol was statistically significant $p=0.0001$.

There were no significant changes in heart rate and blood pressure in both the groups. No adverse events were noted in both the groups.

Discussion

Propofol due to its unique properties like smooth induction, rapid recovery, low incidence of nausea and vomiting, attenuation of upper airway reflexes is the preferred intravenous anaesthetic agent used for induction and maintenance of anaesthesia [13]. Propofol is extensively used in day care surgery, paediatrics, cardiac and neuroanaesthesia. Pain on injection, hypotension, and myoclonus are few of the major side effects associated with propofol [14].

Table 1: Demographic profile

Patient characteristics	Group M (n=100)	Group L (n=100)
Age (years)	36.62±11.84	38.8±11.34
Body Weight (kg)	56.36± 10.38	57.18±9.60
Sex (male/female)	41/59	45/55
ASA PS (1/2)	69/31	68/32

Values expressed as mean±SD. ASA PS - American Society of Anaesthesiologist Physical Status; SD - standard deviation; n- number of patients

Table 2: Pain score of patients on propofol injection

Pain score	Group M (n)	Group L (n)
0	13	0
1	69	5
2	15	27
3	3	60
4	0	8

M- MCT-LCT propofol group; L- LCT propofol group; n- Number of patients

Table 3: Comparison of recollection pain

Pain score	Group M(n)	Group L(n)
0	18	0
1	66	33
2	16	59
3	0	8
4	0	0

M- MCT-LCT propofol group; L- LCT propofol group; n- Number of patients

Several mechanisms including activation of pain mediators, endothelial irritation, osmolality differences have been proposed for causation of injection pain with propofol [15]. Several mechanisms of pain on injection have been suggested, but investigators have shown that the free concentration of propofol in the aqueous phase may be the most important factor [16]. Several methods comprising of both non pharmacological and pharmacological have been tried with varying degree of success for prevention of injection pain. 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 and potential of introducing contaminants into the emulsion, because LCT fat emulsion can serve as excellent growth media [17]. Different preparations of propofol have been tried in various clinical studies to decrease pain on injection. Propofol MCT-LCT formulations have been reported to reduce injection pain in various studies.

In a study conducted by Kinoshita et al., to compare the incidence and intensity of pain on intravenous injection of propofol using long chain and long chain/medium chain propofol emulsion showed pain of LCT propofol injection was stronger than MCT-LCT propofol. As incidence of pain on propofol injection, VAS on MCT-LCT propofol and LCT propofol gave score as 0 and 23.5 ($p=0.0019$). They concluded that propofol with emulsion of long and medium-chain triglyceride appears to reduce the injection pain than with emulsion of only long-chain triglycerides [18].

In our study in both MCT-LCT and LCT propofol groups, the age distribution ranged from 18-60 years with a mean age for MCT-LCT propofol group being 36.62 and for LCT propofol group being 38.80. The difference in age between both groups was not statistically significant. In children, younger the age, higher is the incidence and severity of pain on propofol injection attributable to the smaller size of vein in younger children [19].

We excluded the patients who received benzodiazepine premedication because it may reduce recall of unpleasant or painful injection during induction. The incidence of pain on injection of propofol in MCT-LCT group was 87% which was less than LCT propofol group which was 100%. The difference in two groups were statistically significant ($p=0.0002$). The difference between two groups with regard to intensity of pain on injection of propofol was statistically significant ($p=0.0001$).

18 patients in MCT-LCT propofol group had no memory of pain on injection of propofol. All patients were able to recall pain on injection of propofol in

LCT propofol group. Mean pain score of 0.98 was recorded in MCT-LCT group as compared to 1.75 in LCT propofol group. The difference between two groups with regard to recollection of pain on injection of propofol was statistically significant ($p=0.0001$).

Our study had few limitations. We could have used tourniquet for occlusion at mid forearm, and also drug could have been injected using syringe pump thereby time required for injection of study drug would have been more precise.

Conclusion

Propofol MCT-LCT significantly reduces the incidence as well as the severity of injection pain. It also reduces recall of injection pain when compared with LCT propofol.

Conflicts of Interest: There are no conflicts of interest.

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