An Observational Study of Propofol Mct-Lct Versus Propofol Lct with Lidocaine Pretreatment for Pain During Induction in General Anaesthesia

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Abstract

Aims and Objectives: To compare efficacy between Propofol Medium Chain Triglycerides-Long Chain Triglycerides and Propofol Long Chain Triglycerides with lidocaine pretreatment under venous occlusion on propofol induced pain.

Material and Methods: 50 patients of age 18 to 55 years of either gender of ASA I or II Grade were assigned to two groups of 25 each undergoing elective surgeries under general anaesthesia. Patients in Group M received Propofol MCT-LCT 1% (without any pretreatment with Lidocaine) and Group L received Propofol LCT 1% with Lidocaine pretreatment under venous occlusion. Following propofol injection, patients were asked for any sensation of pain at injection site during propofol injection till patient was unconscious. It was graded as per 4 point verbal pain score, with 0 being No pain to 3 being severe pain.

Anaesthesia was induced by a standard technique of intravenous induction. Endotracheal intubation was done after giving injection succinyl choline (2mg/kg) I V and was maintained on O2, N2O, Isoflurane and Atracurium. Monitoring of heart rate, blood pressure and SPO2 were done during the surgery. After surgery, reversal of neuromuscular blockade was done and extubation was performed. After that patient was transferred to recovery room.

Result and Summary: Both the groups were comparable in term of demographics and ASA grading. It was observed that in the group L a significantly higher proportion (80%) of patients experienced pain while in the Group M only 44% patients experienced pain during propofol administration. (P value-0.0044- highly significant). We observed that the pain intensity score seen in group L was 0, 1, 2 and 3 in 20%, 48%, 20% and 12% of the patients, while in the group M was 0 and 1 in 56% and 44% of the patients, respectively and none of the patients had pain score of 2 and 3. A significantly higher proportion of patients in group M had pain intensity score of 0 (P value<0.01) which was statistically highly significant. Pre and post-operative vitals were comparable in both the groups.

Conclusion: The study concluded that Propofol MCT-LCT is better in view of less incidence and severity of pain on injection during induction of anaesthesia than Propofol LCT with lidocaine pretreatment under venous occlusion.

Keywords: MCT-LCT Propofol, LCT Propofol, Pain, Lidocaine pretreatment, Venous occlusion, General anesthesia.

Introduction

Propofol is a phenolic derivative that is inert chemically and has anaesthetic properties. It is used for induction during general anaesthesia as it as
smooth and rapid recovery, making it favourable to the anaesthesiologists.

Propofol has its drawbacks, in that it causes considerable pain on injection with the incidence varying anywhere between 28% and 90% and the incidence is higher as compared to other IV anaesthetic agents as the pain on induction with thiopentone occurs with incidence of ~7%, and that with methohexitone is 12% to 64%. Gender does not influences injection pain seen with propofol. The factors influencing pain incidence are determined to be injection site, vein size, speed at which the drug is administered, aqueous phase concentration and temperature of propofol and the blood buffering effect. Apart from these factors, other factors impacting pain incidence is concomitantly administered local anaesthetics.

Since many decades now, various methods have been evaluated to reduce pain on injection with propofol. These methods are classified as: non-drug category, drug category and combination of both.

Non-drug techniques: Mechanical interventions methods like infusing the drug at different rates, occlusion of veins, different size of needle and different sites of injections, microfiltration, altering the temperature of the syringe material and changing the bacteriostatic in the formulation. However, the most effective technique was selecting antecubital vein instead of hand vein for administering drug.

Drug techniques: It consists of administering various drugs or drug combination such as antiemetics, local anaesthetics, sedative hypnotics etc along with propofol injection. Various trial have shown that lidocaine-propofol admixture was successful in reducing pain on injection.

Combined drug and non-drug category: This involves combining non-drug and drug techniques. Studies have shown that pretreatment with lidocaine when combined with venous occlusion results in effective pain prevention from propofol injection.

The present study intends to compare the incidence and severity of pain on injection with propofol MCT-LCT against propofol LCT with lidocaine pretreatment under venous occlusion

**Aim**

To compare efficacy between stand alone Propofol Medium Chain Triglycerides-Long Chain Triglycerides and Propofol Long Chain Triglycerides with lidocaine pretreatment under venous occlusion on propofol induced pain.

**Objectives**

1. To find out incidence of propofol induced pain in both groups
2. To find out proportion of patients with propofol induced pain according to Severity in both groups
3. To compare hemodynamics in the form of heart rate and blood pressure in both groups
4. To observe side effects/complications if any

**Materials and Methods**

This observational study was conducted in Department of Anaesthesiology of Dhiraj hospital.

After institutional ethical committee approval the study was conducted on 50 patients undergoing elective surgeries under general anesthesia.

**Study site**: Dhiraj Hospital, S.B.K.S.M.I.R.C, Piparia, Vadodara, Gujarat.

**Study duration**: This study was performed for a period of 18 months.

All the patients were explained clearly about the purpose and nature of the study in their own language. They were included in the study only after obtaining a written informed consent.

For each of the patient data on sociodemographic parameter, haemodynamic variables and levels of perceived pain upon intervention and associated factors if any was collected in predefined performa and analysed.

**Sample size**: Based on literature the incidence of pain on injecting propofol is 80% and assuming a 50% reduction in pain as clinically significant, a sample size of n=25 per group was required to detect significant
difference in the level of pain achieved between the two groups with a power of 90% and a significance level of 5%. A value of P<0.05 was considered statistically significant.

**SAMPLE SIZE** was calculated using formula: 
\[ N = \left( Z_{\alpha/2} + Z_{\beta} \right)^2 \frac{2 \times \sigma^2}{\delta^2} \]

Where \( Z_{\alpha/2} \) is the critical value of normal distribution at \( \alpha/2 \); \( Z_{\beta} \) is the critical value of normal distribution at \( \beta \).

**Study Population:**

**Inclusion Criteria:**

1. Patient willing to participate in the study.
2. Patient willing to sign informed consent.
3. All patients above 18 years and below 55 years of either gender.
4. Patients undergoing elective surgeries under general anaesthesia.
5. Patients belonging to American Society of anesthesiologists physical status I and II.
6. No known history of drug allergy, sensitivity or other form of reaction.

**Exclusion Criteria:**

1. Patients not willing to participate in the study.
2. Patients with known allergy, sensitivity or any other form of reaction to study drug.
3. Patients with ASA III or more.
4. Patients with anticipated difficult airway (Mallampati grade 3 & 4).
5. Patients with renal, hepatic, cardio vascular and respiratory disease.
6. Peripheral vascular disease.
7. Severe trauma and infection of the upper limb.
8. Arteriovenous(AV) fistula in upper limb.

Patients fulfilling the above said inclusion criteria was subjected to the study.

**PRE-OPERATIVE MANAGEMENT**

**Preoperative assessment:**

detailed pre-anaesthetic check-up and routine investigations of all the patients posted for elective surgery undergoing General anaesthesia was done a day prior to surgery to decide the fitness and eligibility of the patients to undergo the said study.

All the patients were kept nil by mouth minimal 10 hours preoperatively before surgery.

**Intra-operative Measures:**

In operation theatre, a 20 gauge venous cannula was inserted into a vein on the dorsum of the patient’s non-dominant hand.

Multipara monitor attached and baseline reading in the form of Heart rate, Blood pressure and oxygen saturation (SPO2), ECG were recorded.

All the patients were premedicated with Inj glycopyrrolate 0.004 mg/kg, Inj ondansetron 0.1mg/kg intravenously in operation theatre prior to induction of anaesthesia. Patients were given drugs according to clinical indication.

Pre oxygenation were carried out with face mask of appropriate size for 5 min with 100% oxygen followed by induction of anaesthesia.

**Induction of Anaesthesia:**

Patients were divided to Group M and Group L.

In Group M received 3ml of bolus of 1% MCT-LCT propofol intravenously directly.

In Group L received pretreatment lidocaine 2 % (1 mg/kg). After occlusion of 60 seconds 1%LCT Propofol 3ml administered as bolus intravenously.

Study drug was administered over 3 secs @ 1cc/sec to assess pain on injection site. Following of study drug administration, crystalloids were administered at maximal gravity flow. Remaining dose of Propofol was injected and patient was asked for any sensation of pain.
at injection site during propofol injection till patient was unconscious. It was graded as per 4 point verbal pain score. Pain score were graded as follows:

0 – No pain.
1 – Mild pain (discomfort in the hand or arm which is acceptable to the patient)
2 – Moderate pain (discomfort in hand or arm which is unacceptable)
3 – Severe pain (grimace or limb withdrawal).

Endotracheal intubation was done after giving injection succinylcholine (2mg/kg). Tube was connected to circuit, bilateral air entry was checked, cuff was inflated and tube was fixed and controlled ventilation was started. Inj Midazolam 1 mg I V and Inj Paracetamol 10 mg/kg I V were given. General anaesthesia was maintained with Oxygen: Nitrous oxide(50:50), Isoflurane , loading dose of Inj Atracurium 0.5 mg/kg and maintenance doses of Inj Atracurium 0.1 mg/kg were given intravenously. Intraoperatively patients were monitored for pulse rate, blood pressure and SPO₂.

Heart rate, blood pressure and SPO₂ were noted at 0, 1, 3, 5, 10 ,15, 30, 60 and 90 minutes after propofol bolus. At the end of surgery, neuromuscular blockade was reversed with inj. Neostigmine (0.05mg/kg) and inj. Glycopyrolate (0.008mg/kg) I V after fulfillment of extubation criteria.

Trachea were extubated and patient shifted to recovery room.

- Change in heart rate of +/- 20 beats and 20% rise or fall in blood pressure from the baseline would be considered clinically significant in the study.
- Bradycardia was defined as pulse rate < 60/ minutes and was managed with intravenous (IV) atropine sulfate 0.6mg.
- Hypotension was defined as fall of systolic BP>20% of base level and was treated with IV mephentermine 6mg.

**Postoperative:**

Postoperatively, following were observed for all the patients: Pulse, blood pressure, SPO₂, any complications such as nausea, vomiting, rigor, hypotension, bradycardia, respiratory depression, head ache, local pain at the injection site, thrombosis, phlebitis at 0, 2, 4 and 6 hours postoperatively.

**Observations And Results**

A total of 50 patients with ASA grading I or II undergoing elective surgery under General anaesthesia were enrolled in the present study. They were divided into two groups. 25 patients in Group M and 25 patients in Group L.

**Group M:** Patients received Propofol MCT-LCT 1% (without any pretreatment with Lidocaine)

**Group L:** Patients received Propofol LCT 1% with Lidocaine pretreatment under venous occlusion.

The demographic distribution in terms of age, weight, gender and ASA grading was comparable between two groups. (P value>0.05), statistically not significant.
Graph 1: Graph showing proportion of patients that experienced pain during propofol administration

In Group M 11 (44%) patients experienced pain while in Group L 20 patients (80%) experienced pain during propofol administration. It was observed that in the Group L a significantly higher proportion of patients experienced pain compared to Group M during propofol administration (P value<0.01), statistically highly significant.

Graph 2: Graph showing Severity of Pain during propofol injection
We observed that the pain intensity score seen in Group L was 0, 1, 2 and 3 in 20%, 48%, 20% and 12% of the patients, while in the group M was 0 and 1 in 56% and 44% of the cases, respectively and none of the patients had pain score of 2 and 3. A significantly higher proportion of patients in group M had pain intensity score of 0 (\(P\) value<0.01), which was statistically highly significant.

**Intraoperative Parameters**

Graph 3: Graph showing mean pulse rate in both the groups at various time intervals

The mean pulse in both the groups was comparable at baseline and at various time intervals. (\(P\) value>0.05), statistically not significant.

Graph 4: Graph showing mean systolic blood pressure in both the groups at various time intervals
The mean systolic blood pressure in both the groups was comparable and there was no statistically significant difference between the two groups. \((P \text{ value}>0.05)\)

The mean diastolic blood pressure in both the groups was comparable and there was no statistically significant difference between the two groups. \((P \text{ value}>0.05)\)

The mean oxygen saturation at various time intervals was comparable in both groups. There was no statistical difference observed in terms of oxygen saturation. \((P \text{ value}>0.05)\)

**Post-Operative Vitals**

The vitals in both the groups were compared in the post-operative period, it was observed that mean pulse rate, mean systolic blood pressure, mean diastolic blood pressure and mean oxygen saturation \((\text{SPO}_2)\) was comparable between two groups. \((P \text{ value}>0.05), \text{statistically not significant.}\)

No complication was observed in Group M and Group L during intraoperative as well as postoperative period.

**Discussion**

Propofol, dubbed as “milk of anesthesia”, is used for induction of anaesthesia in millions of patients round the year because of its favorable properties.

However ~60% patients experience pain on injection of propofol, and 20% experience severe or excruciating pain. The pain experienced is unpleasant to the patient.\(^2\)

The pain that occurs following propofol injection can be immediate or delayed. Immediate pain may be due to direct irritant effect of the drug on the endothelium of veins. Delayed pain that occurs with a latency of 10 to 20 seconds may be via the kinin cascade.\(^4\)

Some patients even recall the pain caused by propofol as the most painful part of the perioperative period. Due to these several interventions have been carried out to alleviate the pain associated with propofol injection.

Hence we have compared Propofol LCT 1% with lidocaine pretreatment under venous occlusion and Propofol MCT-LCT in 50 patients aged between 18 and 55 years, ASA □ or □ scheduled for elective surgeries under General anaesthesia.

In our study, experience of pain was \textbf{statistically highly significant} in LCT group as compared to MCT-LCT group. \((p=0.0044)\)

The findings were also observed in studies conducted by \textit{Rau J, et al}\(^5\) (2001), \textit{Yamakage M, et al}\(^5\) for LCT and MCT-LCT groups.

In our study, moderate to severe pain observed in group L while none of the patients had pain in group M.


The cause of pain on injecting propofol is unknown and several mechanisms for explaining the same have been proposed. Some authors had postulated that pain might be due to unphysiological osmolality or pH of the formulations and the pain severity can be decreased with increasing osmolality, acidity and alkalinity. 2

Others had opined that the pain might had its origin in the neural elements within the venous walls, especially from the free afferent nerve endings that are present between media and intima. It was also suggested by some that degree of pain depends on the injected volume, injection rate, blood flow through vein and size of vein, this opinion comes from the fact that pain was reduced when propofol was injected into a large vein in the antecubital fossa and as a rapid bolus, since the drug was cleared rapidly from the vein and was taken to systemic circulation. 12

Some authors believed that the pain might be due to release of inflammatory mediators rather than it being a direct irritant effect of propofol. Propofol emulsion on coming into contact with vascular endothelium, it caused kininogen release that stimulated painful nerve endings resulted in delayed sensation of pain. However, immediate pain sensation might be due to direct effect. 1

Propofol MCT-LCT has combination of medium chain triglycerides and long chain triglycerides, this change in the structural configuration, reduces the amount of free propofol in the emulsion thereby causing less pain on injection site than Propofol LCT.

The usage of lidocaine to avoid propofol injection pain is the most broadly learnt technique and is being generally used in clinical practice. It is used either before propofol injection with or without a tourniquet or added to the propofol emulsion as a premixture. The mechanism of pain relief is that lignocaine acts as a stabilizer in the kinin cascade. 13

Venous occlusion by applying tourniquet is done to ensure that lidocaine gets enough time to blocking Aδ fibres, as these fibres are responsible for pain transmission in vessel walls. 14

Conclusion

It is concluded that Propofol MCT-LCT is better in view of less incidence and severity of pain on injection during induction of anaesthesia than Propofol LCT with lidocaine pretreatment under venous occlusion.

Conflict of Interest: Nil

Source of Fund: Self

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