Original Research Article

Hemodynamics and Pain on injection, a comparison observational study between Propofol MCT_LCT and Propofol LCT preparations

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Abstract

Introduction- Propofol is an intravenous induction agent popular for induction, maintanence and smooth recovery from anaesthesia in both adults and children. It has gained popularity due to its intravenous sedative – hypnotic property producing rapid unconsciousness. The conventional preparation of Propofol contains a higher percentage of aqueous phase which contains free propofol responsible for pain on injection. **Objectives –** To compare the injection pain on induction with 1% Propofol LCT and 1% Propofol MCT / LCT preparations. To compare intraoperative hemodynamic changes between the two preparations. **Methods-** The current study is an observational study done in Fifty patients aged 20-60 years of American Society of Anaesthesiologists (ASA) Physical status I and II undergoing surgery under General Anaesthesia in Pushpagiri Institute of Medical Science and Research Centre. Patients were recruited by consecutive sampling technique, grouped into two with each group having 25 each. Group MCT – received Propofol MCT / LCT (2mg/kg), Group LCT – received Propofol LCT (2mg/kg). The pain was assessed by a second anaesthesiologist using the 4 point scale. **Results -** The incidence of pain was more with Group LCT. The incidence of pain score 0 with no pain were 0% in Group LCT whereas 16% in Group MCT. The incidence of pain score 1 was highest in Group MCT with 76% whereas 4% with Group LCT. The incidence of pain score 2 was highest in Group LCT with 60% *vs* 8% in Group MCT. **Conclusion-** Propofol Medium Chain triglyceride / Long Chain triglyceride used for intravenous injection did not eliminate pain completely but definitively had less pain on injection compared to Propofol Long Chain Triglyceride preparation. There were no significant hemodynamic changes for both the groups other than heart rate variability.

Keywords - Propofol Medium Chain Triglyceride / Long Chain Triglyceride, Propofol Long Chain Triglyceride, Lipid Emulsion, Four point scale.

Introduction

Propofol is an intravenous induction agent popular for induction, maintanence and smooth recovery from anaesthesia in both adults and children[1]. It has gained popularity due to its intravenous sedative – hypnotic property producing rapid unconsciousness at a dose of 1.5 – 2.5 mg /kg in 30 seconds and awakening being rapid and full when compared to the other intravenous anaesthetics making it even more popular especially in Day Care Anaesthesia[2]. Propofol being an insoluble drug requires a lipid vehicle for emulsification. The current formulation use soybean oil as the oil phase and egg lecithin as the emulsifying agent. The standard preparation is a 1% aqueous solution of 10% soybean oil, 2.25% glycerol and 1.2% purified egg yolk lecithin phosphatide. As Propofol is a lipid emulsion the most common side effect is pain on injection especially in awake patients and increased plasma triglyceride concentrations in prolonged intravenous infusions[3]. The empirical formula contains C12H18O with two isopropyl groups positioned on each side of a hydroxyl group in ortho position on a phenol ring. The conventional preparation of Propofol contains a higher percentage of aqueous phase which contains free propofol responsible for pain on injection and several methods were used to reduce this[4]. Popular method used in reducing pain was by using lidocaine prior to propofol injection but the mixture resulted in coalescence of oil droplets and resulted in pulmonary embolism and changes the concentration of aqueous propofol. Since 1995 1%Propofol MCT / LCT with MCT (50%) and LCT (50%) (Propofol Lipuro) preparation has been reported to reduce pain on injection due to low free Propofolv(14mcg / ml) content[5]. The current study was done to compare the incidence of pain on injection between the two preprations, Propofol MCT/LCT and Propofol LCT. Also to compare the hemodynamic changes and local site reactions between the two preparations.

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Materials and Methods

It was a Observational Study with Comparison Groups. Study was formulated after obtaining approval from the Institutional Research and Ethical committee and Written Informed consent from the patient. Patients were secured from Pushpagiri Institute of Medical Science and Research centre, Tiruvalla. March 2016- March 2017. The study was designed in a way that 2 groups would receive,

➢GRP LCT receive Propofol LCT 1% (2mg/kg)
➢GRP MCT – receive Propofol MCT/LCT 1%(2mg/kg)

Sample size

$$N = \frac{2pq\,(Z_{\alpha}+Z_{\beta})^2}{P_1 - P2}$$

$$= \frac{2 * 0.7 * 0.3 (1.96+2.84)^2}{0.7 - 0.3}$$

N= 25 Total : 50 patients (25 in each group) Assuming a significance level of 5 %, power of 80 % and prevalence of pain[6] on injection to be 70% among Propofol LCT alone 30% among MCT/LCT the sample size was calculated to be 25. Hence 25 patients in each group. Consecutive sampling with those patients satisfying, inclusion and exclusion criteria with written informed consent was formulated till the desired sample size were achieved.

Inclusion criteria

50 patients, Aged 20-60years, ASA I and II (American Society of Anaesthesiologists), undergoing General Anaesthesia.

Exclusion criteria
Known Hypersensitivity to egg or any study drugs.
Impaired Cognition.
Pre existing neurological disorders.
BMI>25
Pregnancy
Emergency surgeries
Unwilling patient

Methodology
Study was formulated after obtaining approval from the Institutional Research and Ethical Committee. Informed written consent were secured from patients satisfying the inclusion and exclusion criteria. Data safety norms were followed to preserve privacy of patient**.** All patients of ASA I and II undergoing surgery under General Anaesthesia in Pushpagiri Institute of Medical Science and Research Centre were included in the study till sample size was reached.
Patients were assigned into two different groups. Preanaesthetic checkup was done the day before surgery pre induction serum Triglyceride levels were estimated. Routine NPO Protocols were followed and Antiaspiration prophylaxis was given with T. Ranitidine 150mg and T. Metoclopramide 10mg HS and 6am on the morning of surgery. 20G Cannula placed on the largest vein on the dorsum of hand. Before induction the patient was reminded that he or she would receive a medication which may or may not cause pain on injection on fore arm. Routine baseline Hemodynamic parameters and oxygen saturation were recorded after administration of Inj Ondansetron 4mg
GRP MCT – received Propofol MCT/LCT (2mg/kg), GRP LCT – received Propofol LCT (2mg/kg)
All injections were given at 0.5ml/sec in full running drip
After 30% of induction dose the patient was asked question regarding pain. The pain was assessed by a second anaesthesiologist using the four point scale
0 – pain not perceived
1 – pain reported only when asked . No facial or behavioural signs
2- Moderate pain when reported spontaneously in response to pain or a behavioural sign
3- Severe pain, strong vocal response accompanied by facial grimacing. All patients post induction received General Anaesthesia Standardized with Morphine 0.1mg/kg, Vecuronium for adequate muscle relaxation and Sevoflurane as maintanence inhalational agent. Routine intraoperative monitoring protocols with hemodynamic monitoring with Heart Rate, Blood Pressure and Oxygen Saturation recorded at 1min, 3 min 5 min, 10 min, 20 min and 30 minutes post induction. All patients were reversed from General Anaesthesia using Neostigmine 2.5mg and Glycopyrrolate 0.4mg. Serum triglyceride levels were taken 4 hours post induction in all patients irrespective of the duration of surgery.

Statistical Analysis
Data was entered using Microsoft Excel software and Analysed using SPSS (Statistical Package for Social Sciences) Software 20.0. Baseline clinical and demographic correlates were tabulated and frequency/percentage were found out. Comparison of pain on injection was analysed using Chi Square Test Comparison of hemodynamic parameters (HR , SBP, DBP , Spo2) were analysed using test of means / proportions whichever was applicable . P value pf < 0.05 was taken statistically significant.

Results

Table 1- Demographic details of the study participants

Patient Characteristics	Group MCT (n=25)	Group LCT (n=25)
AGE	41.44± 12.197	37.72±10.667
SEX (MALE : FEMALE)	5/20	6/19
ASA (I/ II)	11/14	17/8

As per table 1 In Group MCT 80% were females compared to 76 % in Group LCT. In Group MCT 20% were males compared to 24% in Group LCT. Age distribution with a mean of 41.44±12.197 for Group MCTand 37.72±10.667 for Group LCT. Among the 50 patients 56% were ASA I and 44% were ASA II.

Table 2- Frequency of PainScore – Group MCT Vs Group LCT WithPercentage

Pain score	Group MCT(%) (n=25)	GroupLCT(%) (n=25)	Total (%)	P value
0	4 (16%)	0 (0%)	4 (8%)	<0.001
1	19 (76%)	1 (4%)	20 (40%)	<0.001
2	2 (8%)	15 (60%)	17 (34%)	<0.001
3	0 (0%)	9 (36%)	9 (18%)	<0.001
TOTAL	25	25	50 (100%)	<0.001

As per table 2 In Group MCT incidence of no pain with pain score of was 16% compared to 0% in Group LCT. GROUP MCT had the maximum incidence of pain 76 % for mild pain with pain score of 1 in vs 4 % in GROUP LCT . GROUP MCT had incidence of 8% with moderate pain with pain score of 2 vs 60% in Group LCT. None in Group MCT experienced severe pain with incidence of 0 where as 36% experienced severe pain with a pain score of 3 in Group LCT.
All are statistically significant with a P value of < 0.05

Table 3- Comparison of Hemodynamic Parameters of Group MCT VsGroup LCT

	GROUP MCT(N=25)		GROUP LCT(N=25)		PVALUE
Parameters	Mean	Std Dev	Mean	Std Dev	
SPO2_avg	100.00	0.000	100.00	0.000	1.000
HR_avg	70.12	5.622	75.08	6.639	**0.006**
SBP_avg	127.56	11.303	129.84	7.636	0.580
DBP_avg	72.96	5.734	74.80	5.930	0.496

As per table 3 Hemodynamic variability were comparable in SBP, DBP and SpO2 except in Heart rate which was not comparable with a p value of 0.006. There is significant Heart rate variability between Group MCT and Group LCT at 1 min with a p value of 0.000, at 3 min with a p value of 0.002 and at 5 min with a p value of.002 . In Group MCT the heart rate showed a decrease at 1, 3 and 5 minutes when compared with the baseline when compared to the GRP LCT.

Table 4- Changes In Saturation Between Group MCT and Group LCT

SPO2	Group MCT		Group LCT		P Value
	Mean	Std Dev	Mean	Std Dev	
SPO2 0	100	0	99.96	0.2	0.317
SPO2 1 min	99.8	0.5	99.92	0.277	0.371
SPO2 3 min	99.76	0.597	100	0	0.039
SPO2 5 min	99.92	0.277	100	0	0.153
SPO2 10 min	99.88	0.44	100	0	0.153
SPO2 20 min	99.96	0.2	100	0	0.317
SPO2 30 min	99.96	0.2	100	0	0.317
TOTAL	100	0.000	100	0.0	1.00

As per table 4 There was no significant difference in Saturation in both Group MCT And Group LCT.

Discussion

Propofol is the most commonly used intravenous induction agent despite its pain on injection. Various methods were introduced to decrease its pain on injection and one popular method was to increase the lipid formulation and forming Propofol MCT/ LCT preparation. The sex distribution in the study were males 11 (22%) and females 39 (78%). In Group MCT the number of males were 5(20%) and females 20 (80%). In Group LCT the males were 6 (24%) and females were 19 (76%). Even though male to female ratio is not equal but it is statistically insignificant since in both control and study groups male to female ratio is comparable. There were no significant differences in other demographic variables between the two groups. No common clinical technique was used to reduce pain (e.g., mixing with lidocaine). The incidence of pain was more with Group LCT. The incidence of pain score 0 with no pain was 0 in Group LCT vs 16% in Group MCT. The incidence of pain score 1 was highest in Group MCT with 76% vs 4% with Group LCT. The incidence of pain score 2 was highest in Group LCT with 60% vs 8% in Group MCT. The incidence of pain score of 3 was highest in Group LCT with 36% vs 0% in Group MCT. Hence the incidence of pain is not comparable, pain on injection is statistically significant with a P value of 0.000. Incidence and pain is significantly more and higher in Group LCT.

Dubey et al compared lipid free propofol with the Propofol MCT-LCT preparation in in 130 adults pain on injection by infusing over 5s the induction agents over 5 seconds and pain was found to be less in Propofol MCT- LCT (40%) when compared to standard preparation (89%)[7]

Larsen et al compared Propofol pain on injection in 184 adult ASA I and II, who underwent elective surgical procedures under TIVA with Propofol – Lipuro (MCT-LCT) Propofol standard preparation and showed pain was more with standard (64%) than with Propofol Lipuro 37%[8]. Also hemodynamically both were stable. Larsen etal in a prospective, randomised, double-blind study comparing the incidence and intensity of pain on injection of, Propofol-MCT/LCT 1% with conventional Propofol-LCT 1% in 40 children, aged 7-14 years. After premedication with diazepam, 20% of induction dose of Propofol was injected and pain was elicited. More children reported pain with propofol-LCT compared to Propofol - MCT/LCT (25% vs, 10%) with arm retraction during injection of propofol - LCT and propofol MCT- LCT (40% vs. 10%)[8,9]. Bachmann-Mennenga et al studied pain on injection of propofol comparing Propofol MCT LCT and Propofol LCT in 1375 adult patients and concluded that the incidence of pain with Propofol MCT was 28.4% with 16.7% of the patients reporting mild pain[10]. Heart rates: in Group MCT was 70.12 ±5.622 and in Group LCT 75.08±6.639 were not comparable and were statistically significant with a P value of 0.006. This showed that heart rate increased with the administration of Propofol LCT. In Group MCT, the heart rate showed a decrease at 1, 3 and 5 minutes when compared with the baseline. At 1 min for the MCT group mean was 70.32±8.36 vs 86.16± 9.564 for Group LCT. At 3 min MCT mean was 67.08±8.524 vs 75.48±8.856 for LCT. At 5 min MCT mean was 64.2±7.303 vs 71.36±7.599 for LCT. There was significant Heart rate variability in Group MCT and Group LCT at 1 min, 3min and 5 min with a p value of 0.000, 0.002 and 0.002 respectively[9,10,11].

Deutschman et al proposed that propofol anaesthesia decreases parasympathetic tone to a lesser extent than sympathetic tone and this predisposed the patients to bradycardia in response to a noxious stimuli[11].

Conclusion

Propofol Medium Chain Long Chain triglyceride used for intravenous injection did not abolish pain completely but definitively had less pain on injection compared to Propofol Long Chain Triglyceride preparation. Hence 1% Propofol MCT_LCT preparation is a better choice for the induction of anaesthesia with regard to Pain on injection.

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