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Original Research Article

To Study and Evaluate the Effect of 0.5 % Dilution of Propofol MCT/LCT and Propofol LCT on Pain during Injection of Propofol for Induction of GA in Paediatric Patients

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Conflict of interest: Nil

Abstract:

Introduction: Propofol with its attractive kinetic properties like titratable level of anaesthesia, absence of cumulation, rapid and clear headed recovery and minimal side effects is an ideal agent for induction of anaesthesia.

Materials and Methods: This prospective, randomized controlled study was conducted on 100 children in the age group of 6 to 12 years undergoing elective surgery under GA at VIMS hospital, Ballari during November 2015-November 2016.

Results: Age of children was 8.66±2.26 and 8.68±1.9 years in group LCT and group MCT/LCT respectively. Mean weight of children was 21.58±4.74 and 21.56±4.53 kgs in group LCT and group MCT/LCT respectively. Both the groups were comparable demographically. There was no statistically significant difference between the two groups with respect to age and weight

Conclusion: Intravenous injection of 0.5% dilution of propofol MCT/LCT is associated with significantly less pain than 0.5% dilution of propofol LCT in paediatric patients aged 6-12 years.

Keywords: Propofol, Paediatric

Introduction

Propofol with its attractive kinetic properties like titratable level of anaesthesia, absence of cumulation, rapid and clear headed recovery and minimal side effects is an ideal agent for induction of anaesthesia. [1,2] Kay and Rolly confirmed its potential as an anaesthetic agent and is being used for clinical purpose since 1982. [3] It is known to cause severe, sharp, stinging or burning pain on injection that can be distressing to the patient. This pain is considered to be clinically unacceptable as it can cause agitation and interfere with smooth induction of anaesthesia. Incidence of pain on injection of propofol varies from 3-85% in adults [7,8,9]. The pain on injection of propofol

can be immediate or delayed in nature. The immediate pain probably results from direct irritant effect whereas delayed pain results from indirect effect via the kinin cascade, which occurs 10-20 seconds later. [4] The various suggested methods to alleviate this pain are injection in larger size veins, cooling or warming the propofol solution, pretreatment/preinjection of various drugs like, lignocaine, prilocaine opioids like butorphanol, tramadol, alfentanil, remifentanil, thiopentone sodium, metoclopramide, ketorolac, magnesium sulphate, acetaminophen, clonidine, and ketamine. [2-21] Intravenous lignocaine, local anaesthetic, has been well documented to reduce the incidence and severity of pain on injection of propofol. [2,5,6] It is considered superior to other drugs but cannot reduce the incidence and severity of pain on intravenous injection of propofol, in all situations. Widely available propofol is in long chain triglyceride (LCT) emulsion. Another preparation of propofol is available in a combination of medium chain triglyceride (MCT) and LCT emulsion. Commonly available MCT/LCT propofol has low free propofol content and is expected to reduce pain on injection; the free propofol content is less by 30%–45% compared to LCT propofol. [9] In several other studies, less pain is reported with MCT/LCT preparation compared to LCT preparation. In paediatric group of patients, some studies have found no reduction in POPI while some studies showed a significant reduction in POPI with MCT/LCT preparation. Dilution of propofol to 0.5% in MCT/LCT produced less pain in children between 2 and 6 years, but there was an increase in triglyceride levels in blood [10] .In this study we have compared effect of 0.5% dilution of propofol MCT/LCT with 0.5% dilution of propofol LCT on injection pain during induction in paediatric patients.

Materials and Methods

This prospective, randomized controlled study was conducted on 100 children in the age group of 6 to 12 years undergoing elective surgery under GA at VIMS hospital, Ballari during November 2015-November 2016.

Method of collection of data

The patients were included in the study by applying the following inclusion and exclusion criteria

Inclusion criteria

- Patients of either sex aged between 6-12 years.
- Patients of ASA physical status I and II.
- Patients scheduled to undergo any elective surgical procedure under general anaesthesia (GA).

Exclusion criteria

- History of allergy to propofol
- Significant co-existing systemic diseases
- Any contra-indication to propofol
- Any child in whom 22G IV cannula could not be secured on dorsum of either hand.

Statistical analysis:

The collected data were entered into an excel sheet. After appropriate data cleaning, the data sheet was transferred and analysed using SPSS for Windows: IBM Corp®, version 20,Armonk, NY, USA. Descriptive statistics were used to describe the study variables of the subjects. Quantitative data were expressed as mean and standard deviation and were analysed using paired t test. Qualitative data were expressed as percentage and were analysed using Chi-square test. P-value <0.05 was considered significant. Sample size was calculated based on pilot study conducted in 20 patients where in 63 % decrease in pain was observed with 0.5% propofol MCT/LCT(mean M& H score 1.2) compared to 0.5% propofol LCT (mean M& H score 1.9) with power

of study being 90 % , two sided confidence interval of 95% and alpha error of 0.05 sample size was calculated to be 42 in each group. Assuming drop outs from the study, the final sample size was set at 100 patients,50 patients in each group

Results

Table 1: Showing age and weight distribution of study subjects in two groups

Basal characteristics	Group LCT	Group MCT/LCT	P value*
	Mean±SD	Mean±SD	
Age(years)	8.66±2.26	8.68±1.9	0.962
weight(kgs)	21.58±4.74	21.56±4.53	0.983

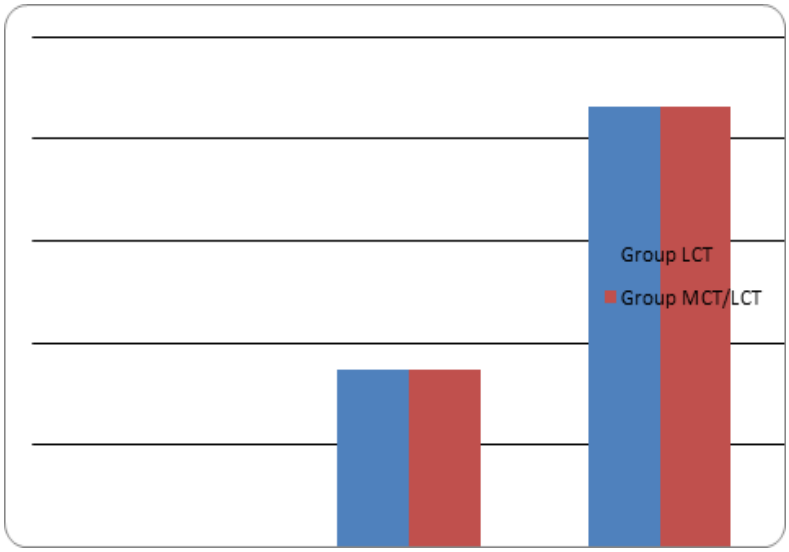

Figure 1: Showing age and weight distribution

Age of children was 8.66±2.26 and 8.68±1.9 years in group LCT and group MCT/LCT respectively. Mean weight of children was 21.58±4.74 and 21.56±4.53 kgs in group LCT and group MCT/LCT respectively. Both the groups were comparable demographically. There was no statistically significant difference between the two groups with respect to age and weight(Table 1 & Graph 1)

Table 2: Comparision of basal vital parameters in the study groups

Parameters (BASAL)	Group LCT(N=50)	Group MCT LCT(N=50)	P value*
	Mean ± SD	Mean ± SD	
PR (beats/min)	108.34 ± 13.9	110.46 ± 13.12	0.44
SBP (mmHg)	115.66 ± 11.1	116.62 ± 12.7	0.69
DBP (mmHg)	75.3 ± 10.67	74.12 ± 10.38	0.58
MAP	86.82 ± 11.01	85.34 ± 11.25	0.51

Basal vital parameters - HR were 108.34 ± 13.9 and 110.46 ± 13.12 bpm, SBP were 115.66 ± 11.1 and 116.62 ± 12.7mm Hg, Mean DBP were 75.3 ± 10.67 and 74.12 ± 10.38 mm Hg, MABP were 86.82 ± 11.01 mm of Hg and 85.34 ± 11.25 mm of Hg in group LCT and group MCT/LCT respectively. (Table 4).

Table 3: Comparision of heart rates in the study groups

Time interval	HEARTRATE		
	Group LCT(N=50)	Group MCT LCT(N=50)	P value*
	Mean ± SD	Mean ± SD	
BASAL	108.34 ± 13.9	110.46 ± 13.12	0.44
15SECONDS	110.4 ± 15.63	110.64 ± 15.33	0.94
30SECONDS	109.8 ± 12.98	109.5 ± 15.7	0.92
ONE MINUTE	112.2 ± 15.098	107.74 ± 15.07	0.14

Basal heart rate was 108.34 ± 13.9 and 110.46 ± 13.12 bpm in group LCT and group MCT/LCT respectively. At 15 seconds heart rates were 110.4 ± 15.63 and 110.64 ± 15.33 bpm in group LCT and group MCT/LCT respectively ,at 30 seconds heart rates were 109.8 ± 12.98and 109.5 ± 15.7 bpm in group LCT and group MCT/LCT respectively and at 1 minute interval heart rates were 112.2± 15.098 and 107.74± 15.07 bpm in group LCT and group MCT/LCT respectively following induction . There was no statistically significant difference between the two groups when heart rates were compared. (Table 3 and graph 2)

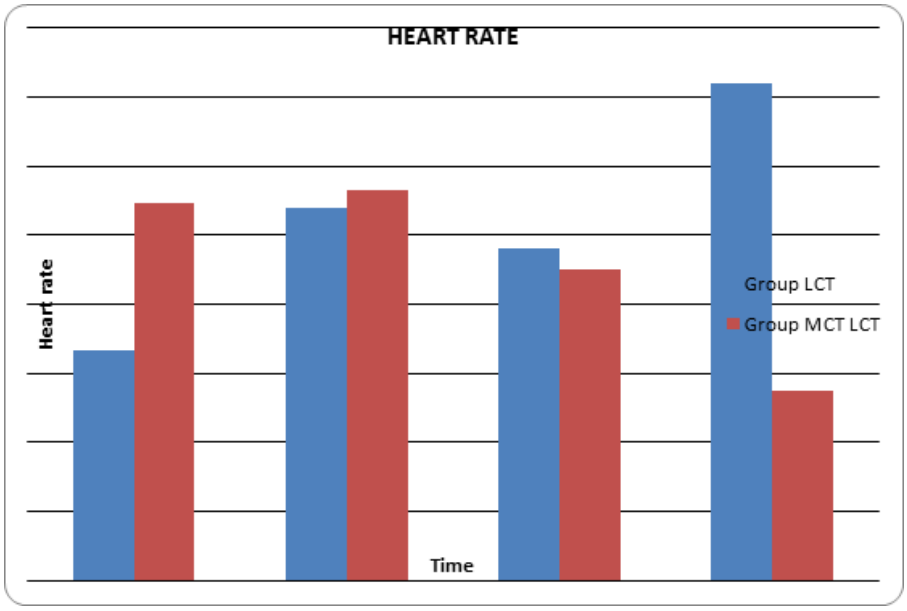

Figure 2: Comparision of heart rate in the study groups

Table 4: Comparision of sbp in the study groups

Time interval	SYSTOLIC BP		
	Group LCT(N=50)	Group MCT LCT(N=50)	P value*
	Mean ± SD	Mean ± SD	
BASAL	115.66 ± 11.1	116.62 ± 12.7	0.69
DURING INDUCTION			
15SECONDS	113.2 ± 11.03	114.3 ± 14.06	0.66
30SECONDS	112.12 ± 11.73	111.3 ± 13.58	0.74
ONE MINUTE	105.78 ± 12.17	101.26 ± 10.41	0.05

Basal SBP was 115.66± 11.1 and 116.62 ± 12.7 mm of Hg, at 15 secs 113.2 ± 11.03 and 114.3 ± 14.06 mm of Hg ,at 30 secs 112.12± 11.73 and 111.3 ± 13.58 mm of Hg and at one

minute 105.78 ± 12.17 and 101.26 ± 10.41 mm of Hg in group LCT and group MCT/LCT respectively. SBP was found to be statistically significant at one minute with P value 0.05 (Table 4 and graph 3)

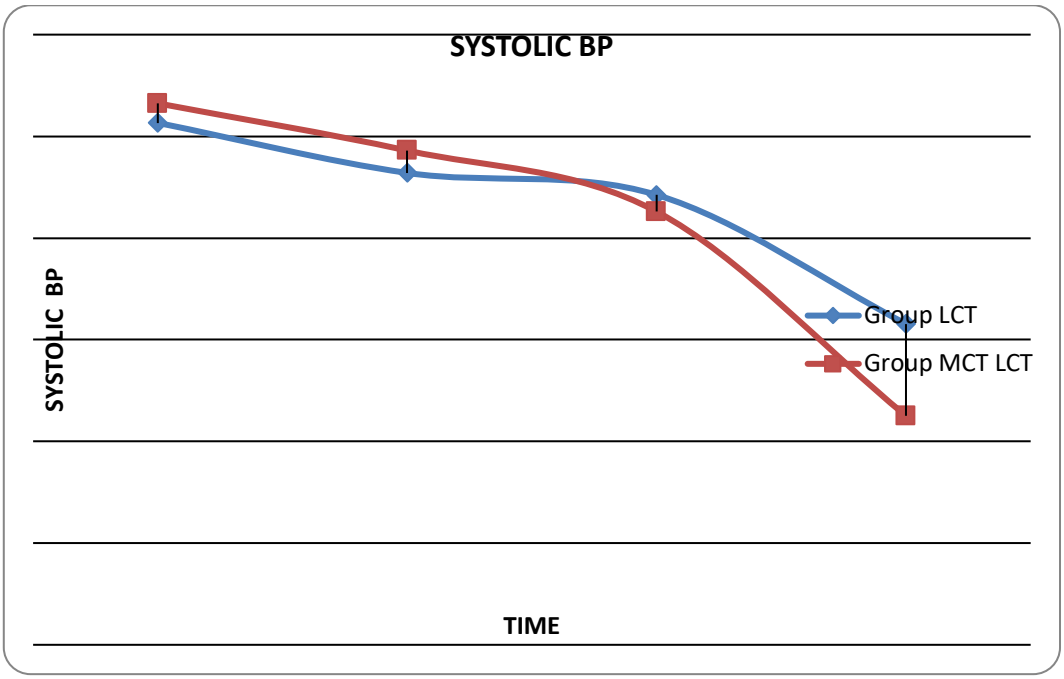

Figure 3: Comparision of sbp in the study groups

Table 5: Comparision of diastolic bp in the study groups

Time interval	DIASTOLIC BP		
	Group LCT(N=50)	Group MCT LCT(N=50)	P value*
	Mean ± SD	Mean ± SD	
BASAL	75.3 ± 10.67	74.12 ± 10.38	0.58
DURING INDUCTION			
15SECONDS	71.38 ± 11.47	70.02 ± 12.83	0.58
30SECONDS	70.22 ± 11.9	68.3 ± 12.8	0.44
ONE MINUTE	65.9 ± 11.97	60.42 ± 10.68	0.02

Table 5: Basal DBP was 75.3± 10.67 and 74.12± 10.38 mm of Hg, at 15 secs 71.38± 11.47 and 70.02 ± 12.83 mm of Hg ,at 30 secs 70.22 ± 11.9 and 68.3± 12.8 mm of Hg and at one minute 65.9 ± 11.97 and 60.42 ± 10.68 mm of Hg in group LCT and group MCT/LCT respectively. DBP was found to be statistically significant at one minute with P value 0.02 (Table 5 and graph 4)

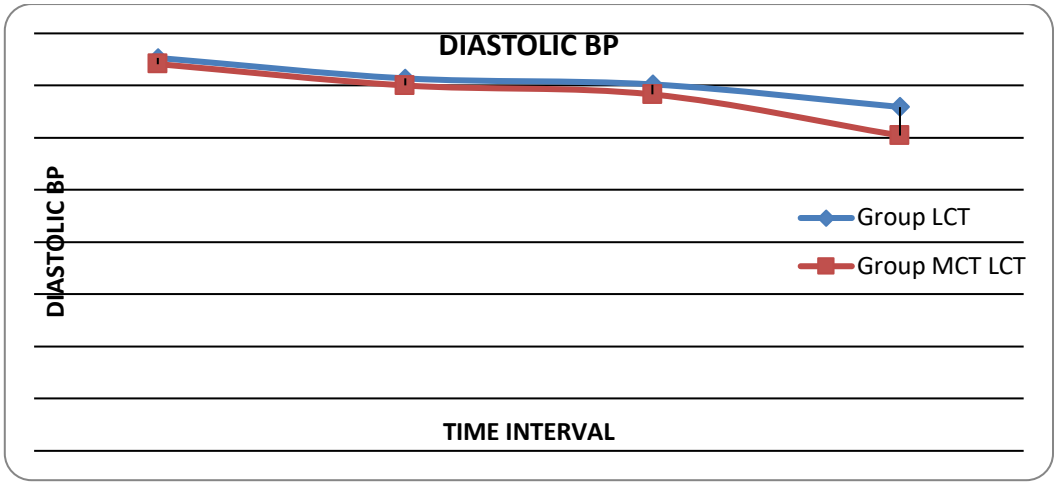

Figure 4: Comparision of diastolic bp in the study groups

Discussion

Propofol is a fast acting iv induction agent and its action wears off quickly making it useful for day care procedures.[1]At sub hypnotic doses, it provides excellent sedation, amnesia, anxiolysis and a state of general well-being. It has antiemetic action which adds to its advantage. It suppresses the upper airway reflexes in response to laryngoscopy and intubation, which is of great help in patients with hypertension, epilepsy or hyperactive airway. It attenuates stress response to intubation. Propofol has got tremendous popularity in day-care surgery, paediatric, cardiac, neuro anaesthesia and ICU sedation for its attractive profile. But it is also associated with side effects such as pain on injection, myoclonus, apnoea and hypotension. The most worrying side effect which has been most extensively studied is pain on injection of propofol. The incidence of pain varies from 30-90% of patients. Various techniques have been tried to decrease propofol injection pain, including choosing larger size veins for injections [11], cooling [12], or warming [13] propofol solution, pre-treatment/ pre injection of various drugs like lignocaine, prilocaine opioids like butorphanol, tramadol, alfentanil, remifentanyl, thiopentone sodium, metoclopramide, ketorolac, magnesium sulphate, acetaminophen, clonidine and ketamine [5,14]. It is demonstrated by several investigators that increased concentration of propofol in aqueous phase increases pain [11]. Doenicke et al noticed that propofol concentration in aqueous phase in regular LCT preparation of propofol is relatively high indicating that it is not completely dissolved in lipid vehicle .They demonstrated that by increasing lipid content of propofol, pain could be reduced mainly due to decreased concentration of propofol in aqueous phase [15,16]. In the propofol emulsion, the drug will be distributed differently in two phases with outer aqueous phase and inner lipid phase. In a bolus injection, the outer aqueous phase comes into contact with venous endothelium causing pain [15]. It has been suggested that dilution of propofol with 5% dextrose or lipid emulsion reduces the concentration of free propofol in the aqueous phase and decreases pain on injection [17]. Various studies have proved that 1 % propofol (MCT/LCT) is associated with less pain on injection compared to 1% propofol (LCT) [18 ,15,8,9] and it has also been proved that 0.5% propofol (MCT/LCT) is less painful on injection compared to 1% propofol (MCT/LCT)10. [20] However, no study comparing 0.5% dilution of propofol (MCT/LCT) with 0.5% dilution of propofol (LCT) for reducing pain on injection is available in the literature and hence the present study was undertaken to

study the same in patients undergoing surgeries under general anaesthesia. Stefan soltez et al conducted a prospective, double-blind study which showed a significant reduction of pain intensity in children aged 2–6 yr after intravenous injection of propofol diluted with a 10% MCT/LCT emulsion to a final concentration of 0.5% compared with the standard formulation of 1% propofol in a similar 10% MCT/LCT emulsion. The incidence of pain on injection of propofol decreased threefold with the 0.5% formulation, from 70% with a 1% MCT/LCT emulsion of propofol to 23% with a 0.5% concentration. Though the study sample size was small, cumulative doses up to 4–5 mg/kg propofol led to moderate increase in triglyceride levels [10]. Hence we have used 5% dextrose as diluent in our study. Very few studies on pain on injection of propofol have been conducted in children. As the incidence of POPI is higher in children as compared to adults, there is a great need for various such measures to reduce pain on propofol injection in children. Hence, we have included children belonging to age group 6-12 years in our study. The best way to assess pain in clinical setting is by verbal response or its derivative, VAS and some of the previous studies were conducted using VAS score.19In our study we chose four point verbal categorical scoring system as advocated by Mccrirrick and Hunter [12] as it is simple, and readily understood by children (6-12yrs). Many previous studies reporting pain on injection of propofol have used either all or none or categorical scoring systems, thus allowing easier comparison with literature. The appropriate hand eye co -ordination required for interpretation of VAS pain score might not be present during the rapidly changing state of consciousness of anaesthesia during administration of bolus dose of propofol such as during iv induction in contrast to infusion of propofol used for sedation in many of the earlier studies. Therefore, we chose four point verbal rating scale for pain assessment in our study.

Conclusion

Intravenous injection of 0.5% dilution of propofol MCT/LCT is associated with significantly less pain than 0.5% dilution of propofol LCT in paediatric patients aged 6-12 years.This reduction in pain intensity was not associated with any clinically significant changes in haemodynamic parameters.

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