American Journal of
Oral Medicine and Radiology

ISSN - 2394-7721

www.mcmed.us/journal/ajomr

Research Article

COMPARATIVE ANALYSIS OF MICROEMULSION PROPOFOL AND LONG-CHAIN TRIGLYCERIDE (LCT) PROPOFOL IN ELECTIVE SURGICAL ANAESTHESIA: EFFICACY, SAFETY, AND POSTOPERATIVE RECOVERY

Venkata Ramana Pindi B

Assistant Professor, Department of General Surgery, Sri Lakshmi Narayana Institute of Medical Sciences & Hospital, Puducherry – 605502, India.

ABSTRACT

This paper is a comparison of the effectiveness, safety, and pharmacokinetic characteristics of microemulsion propofol and long-chain triglyceride (LCT) propofol in elective surgery patients under general anaesthesia. Two hundred and thirty patients were randomly divided into two groups of 115 and 115 patients who received microemulsion propofol and LCT propofol respectively. The major outcomes were anaesthesia infusion parameters, postoperative recovery, and occurrence of postoperative nausea and pain and the secondary outcomes were the necessity of rescue drugs. The outcomes revealed that the two formulations were able to deliver comparable parameters of anaesthesia, including equal propofol infusion rates, the total doses as well as rate changes of propofol. Time to loss of consciousness (LOC), time to return of consciousness (ROC), and time to recover orientation (ROO) which are the measures of postoperative recovery were also similar between the two groups. It is noteworthy that, the prevalence and extent of postoperative nausea were a little less in the microemulsion group than in the LCT one. Pain scores regarding postoperative pain were similar in both groups, and the rescue analgesics were in demand. The results indicate that microemulsion propofol is a possible substitute to LCT propofol, which has comparable efficacy in anaesthesia and recovery with a possibility of decreasing the postoperative nausea. These findings should be verified through further research involving a wide range of patients to determine the long-term benefits of using microemulsion propofol.

Key words: - Microemulsion propofol, Long-chain triglyceride propofol, Postoperative nausea, Anaesthesia recovery.

Access this article online		
Home page: http://www.mcmed.us/journal/ajomr		Quick Response code
Received:25.01.2020	**Revised**:10.02.2020	**Accepted**:06.03.2020

INTRODUCTION

Propofol is an intravenous anesthetic compound that is very popular and has been characterized as a fast acting and short acting agent. It is usually adopted in induction and maintenance of general anesthesia [1].

Corresponding Author
Venkata Ramana Pindi B

Email: -

Nonetheless, a number of side effects have been linked to the use of traditional propofol formulation that has long-chain triglyceride (LCT) emulsions such as fat embolism, infection, and hypertriglyceridemia [2]. New formulations, which are meant to minimise these lipid solvent-associated complications without compromising the effectiveness of propofol as an anesthetic [3, 4], have been developed on these concerns, including

microemulsion propofol. Microemulsion propofol has been made to remove the side effects of LCT propofol formulations by introducing an alternative mix of surfactants and solvents thus enhancing the safety profile of the medication [5]. This formulation has been observed to possess potential in preclinical and early clinical studies where it appears an equally effective anesthetic to LCT propofol and at the same time minimizes the chances of development of complications like infection and fat embolism. Although such encouraging findings have been made, there is still limited information that compares pharmacokinetics, safety, and clinical outcomes of microemulsion propofol and LCT propofol in patients under general anesthesia [6]. The present study will compare the efficacy, safety, and pharmacokinetic characteristics of microemulsion propofol and LCT propofol in elective surgical patients. The main aims are to determine the parameters of infusion of the two formulations such as the mean infusion rate, the overall dosage as well as the number of infusion rate changes. Also, the parameters of postoperative recovery will be measured through time to loss of consciousness (LOC), return of consciousness (ROC), recovery of orientation (ROO), and the bispectral index (BIS) values. Other secondary outcomes consist of measuring postoperative nausea and pain, and the necessity of rescue drugs, such as antiemetics and analgesics. The study will also provide an understanding of the pharmacokinetic properties of the two formulations including how the drug metabolism is affected by the formulation as well as the effect of the formulation on the time to LOC and recovery [7, 8]. Through the assessment of these variables, the following study will assist in establishing the possibility of microemulsion propofol serving as a safer alternative as compared to LCT propofol without or with increased effectiveness as an anesthetic agent. This study may be used to optimize anesthetic practice and positively impact patient safety in general anesthetic practice.

METHODOLOGY

The purpose of the study was to compare the effectiveness, safety and Pharmacokinetic property of microemulsion propofol and long chain triglyceride (LCT) propofol in patients undergoing general anaesthesia [9]. A sample of 230 patients was included, 115 patients were allocated to the microemulsion propofol group and 115 were allocated to the LCT propofol group. The patients were randomly selected to take either of the two formulations of propofol and the results were evaluated according to many parameters and the results were evaluated according to the demographic factors, anaesthesia propofol infusion rates, postoperative recovery and the necessity to use the rescue medications. It was a randomized and controlled trial that aimed to determine the comparative effects of microemulsion propofol and LCT propofol. The patients were to receive elective surgeries under general anaesthesia and the research was carried out on two groups of patients who were to receive either microemulsion propofol or LCT propofol. The institutional review board of the concerned institution gave approval on the ethical aspect and all the patients gave informed consent before taking part. The inclusion criteria were patients aged 18 years and above with ASA physical status of I or II. The exclusion criteria were the presence of allergic reactions to propofol in history, cardiovascular or respiratory significant diseases, pregnancy, and contraindication to anaesthesia. General anaesthesia was performed on all the patients in the usual manner. Propofol microemulsion and LCT propofol were introduced through infusion pump and the infusion rates were varied accordingly to sustain anaesthesia. Remifentanil was used as an additional opioid in maintenance of anaesthesia in both groups. The propofol and remifentanil infusion rates were set up in line with the clinical guidelines and modified depending on the response of the patients. Anaesthesia Parameters: Propofol infusion rates, total propofol dose, infusion rate repositioning frequency and median infusion rate in maintenance. Postoperative Nausea and Pain: Nausea and pain were measured on Visual Analog Scale (VAS). The severity of nausea was registered in 6 hours and in the interval of 6 24 hours and the number of emetic events also was documented. The pain during and after surgery was measured at 6 hours and 6-24 hours after the anaesthesia, and rescue analgesics were used at the required times. Rescue Medications: The necessity in rescue anti-emetic and analgesics was noted, as well as the frequency of their intake. Secondary outcome measures were the time to loss of consciousness (LOC), time to return of consciousness (ROC), time to recovery of orientation (ROO) and bispectual index (BIS) at LOC, ROC, and ROO. These were evaluated in terms of depth and period of anaesthesia and in recovery.

Statistical Analysis

The descriptive and inferential methods were used to perform the statistical analysis. Continuous variables are displayed as data mean (SD) or median (range), and frequency (number) as data of the categories. The statistical tests applied to measure the differences between the two groups included t-test (statistical test of continuous data) and chi-square test (statistical test of categorical data). Statistically significant p-value was taken to be below 0.05. The research was done under a controlled condition where all the processes and data gathering were standardized between the two groups which gave a credible comparison between the two anaesthetic agents.

RESULT

The research has examined the efficacy, safety, and pharmacokinetic characteristics of microemulsion propofol against LCT propofol in an anaesthetic patients. A cohort of 230 patients was used in the collection of data

where 115 patients were administered in microemulsion propofol and 115 patients in LCT propofol. The findings of the demographic and surgical profile, anaesthesia care, postoperative performance, and rescue drug use are provided below. There was similarity between the two groups in terms of demographic characteristics. Both groups were similar in terms of ASA physical status (I/II), most patients were ASA II. The average age of the patients in the microemulsion group was 54 years (range 47 60 years) and LCT group was 52 years (range 43 60 years). There were also no significant differences in body weight and height between the groups, and there were no significant differences in the average value of weight (64.2 kg of microemulsion and 63.5 kg of LCT) or height (162 cm of both groups). The sex ratio between the samples was slightly dissimilar where the microemulsion sample population had 87 men and 28 women whereas the LCT sample population had 79 men and 36 women. The two groups did not differ in the types of surgeries performed with the majority of the patients having colorectal surgery (70 vs. 85 in the microemulsion group and the LCT group respectively), followed by stomach (46 vs. 30), breast (14 vs. 14), and the other types (6 vs. 6) surgeries. There was a similarity in the propofol infusion parameters in the two groups. Propofol mean infusion rate was 6.0mg/kg/h (range 3.56.7) in the microemulsion and 6.2mg/kg/h (range 3.010.5) in the LCT group. The amount of propofol that was used was 950.0 mg (range 160.0 4600.0) in microemulsion group and 880.0 mg (range 250.0 2400.0) in LCT group. The rate of infusion changes were equal between the groups (7 changes in both). Anaesthetic maintenance median infusion rates were also similar (5 mg/kg/h each). In case of remifentanil, mean-infusion rate was 0.4 ug/kg/min (0.1) in microemulsions and 0.5 ug/kg/min (0.1) in LCT with 3980.0 ug total dose and 16 and 15 respective target effect-site concentration changes. The LCT group had a slightly shorter duration of anaesthesia, as well as a time to loss of consciousness (LOC) was also slightly faster in the LCT group (18.0 s vs. 20.0 s). Visual Analog Scale (VAS) was used to measure postoperative nausea and pain. The VAS score nausea among patients higher than 0 were 8.7 and 7.8 in the microemulsion group at 6 hours and 6 to 24 hours, respectively and in the LCT group at 12.6 and 14.8, respectively. The VAS of nausea was 27 mm (range 352) in the microemulsion group and 28 mm (range 4343) in the LCT group respectively to patients within the 6 hour range and those outside the 6 hour range respectively. There were few episodes of emetics, 1.7 percent of microemulsion patients and 2.6 percent of LCT patients had reported episodes in a 6-hour timeframe. The number of patients who required rescue anti-emitics was also not high 3 patients who used microemulsion and 2 patients who used LCT used them. In the case of postoperative pain, microemulsion propofol VAS scores were 45mm (range 2758) 6 hours and 30mm (range 1948) 6-24 hours against LCT propofol VAS scores 43mm(range 2041). A total of 120 patients and 110 in the microemulsion group and the LCT group, respectively, needed rescue analgesics. There was a slight difference in the frequency of microemulsion group a bit more (190 doses vs. 195 doses) which was attributed to the fact that the number of patients in need of analgesia was higher in the microemulsion group.

Table 1: Demographic and Surgical Characteristics of Patients Undergoing Anaesthesia with Microemulsion and LCT Propofol

Empty Cell	Microemulsion propofol (n=115)	LCT propofol (n=115)
ASA PS I/II	38/77	34/81
Age (yr)	54 (47, 60)	52 (43, 60)
Weight (kg)	64.2 (9.4)	63.5 (9.3)
Height (cm)	162 (157, 168)	162 (157, 168)
Sex (M/F)	87/28	79/36
Type of surgery		
Colorectal	70	85
Stomach	46	30
Breast	14	14
Other*	6	6

Table 2: Propofol and Remifentanil Infusion Parameters, Anaesthesia Duration, and Bispectral Index (BIS) Values for Microemulsion and LCT Propofol Groups

Empty Cell	Microemulsion propofol (n=115)	LCT propofol (n=115)
Propofol		
Mean infusion rate (mg kg−1 h−1)	6.0 (3.5, 8.7)	6.2 (3.0, 10.5)
Total dose (mg)	950.0 (160.0, 4600.0)	880.0 (250.0, 2400.0)
Frequency of infusion rate adjustment	7 (2, 24)	7 (2, 20)
Median infusion rate during maintenance of anaesthesia (mg kg−1 h−1)	5 (1, 14)	5 (1, 13)

Remifentanil		
Mean infusion rate (μg kg−1 min−1)	0.4 (0.1)	0.5 (0.1)
Total dose (μg)	3980.0 (180.0, 18,500.0)	4010.0 (600.0, 11,800.0)
Frequency of target effect-site concentration adjustment	16 (5, 45)	15 (6, 35)
Median target effect-site concentration during maintenance of anaesthesia (ng ml−1)	9 (1, 28)	8 (1, 27)
Duration of anaesthesia (h)	2.1 (0.5, 8.5)	2.2 (0.5, 5.5)
Time to LOC (s)	20.0 (0.0, 130.0)	18.0 (1.0, 100.0)
Time to ROC (min)	11.5 (0.5, 50.0)	10.0 (2.0, 25.0)
Time to ROO (min)	1.6 (0.3, 30.0)	1.6 (0.2, 22.0)
BIS at LOC	83 (38, 97)	83 (45, 96)
BIS at ROC	75 (46, 92)	75 (47, 93)
BIS at ROO	80 (65, 94)	78 (64, 94)

Table 3: Nausea, Emetic Episodes, Postoperative Pain, and Rescue Medication Use in Patients with Microemulsion and LCT Propofol

Empty Cell	Microemulsion propofol	LCT propofol
	Within 6 h (n=115)	Between 6 and 24 h (n=115)
Number (%) of patients with VAS for nausea >0	10 (8.7)	9 (7.8)
VAS for nausea (mm)	27 (3, 52)	25 (4, 33)
Number of patients (%) with frequency of emetic episodes >0	2 (1.7)	3 (2.6)
Number of patients who needed rescue anti-emetics (dosing frequency)	3 (7)	2 (2)
VAS for postoperative pain (mm)	45 (27, 58)	30 (19, 48)
Number of patients who needed rescue analgesics (dosing frequency)	120 (190)	110 (195)

DISCUSSION

The purpose of the research was to determine the effectiveness and safety as well as pharmacokinetic characteristics of microemulsion propofol and long-chain triglyceride (LCT) propofol in distinguishing patients undergoing an elective surgery with general anaesthesia [10,11]. The participants of this randomized controlled trial were aged between 17 and 80 years, and 230 participants were recruited into 2 groups of 115 participants each; 1 group received microemulsion propofol, while the other received LCT propofol. The outcomes of the present study can provide meaningful results on the effectiveness and safety of the two propofol formulations compared with each other in the clinical setting [12]. Both the groups were similar in demographic features and there was no significant difference with regards to age, body weight, height and ASA physical status. The distribution of patients in the two groups in terms of ASA I and ASA II was similar indicating that the two groups were well matched as regards the baseline characteristics [13]. The minor variation in the sex distribution (more males in the microemulsion group and more females in LCT group) would not have affected the results significantly as the groups were generally balanced. Also, the nature of surgeries done was similar with most patients having colorectal surgery, stomach surgery and breast surgery respectively. This makes sure that the comparison of the two groups is not made confounded by the nature of the surgery done since the surgical procedures might affect the anaesthesia needs, as well as, the post operative recovery [14]. Regarding the parameter of anaesthesia, the findings indicated that the infusion rates of propofol were not significantly difference between the two groups with the mean infusion rate of the microemulsion propofol was 6.0 mg/kg/h (range 3.5-8.7) and the infusion rate of LCT propofol was 6.2 mg/kg/h (range 3.0-10.5). These results indicate that both preparations gave similar concentrations of anaesthesis in the maintenance period. The amount of propofol used was also comparable with a maximum dosage of 950.0 mg (range 160.04600) in the microemulsion group and a maximum dosage of 880.0mg (range 250.02400) in the LCT group. The median infusion rates when at the maintenance were also similar (5 mg/kg/h in both groups) implying that the maintenance infusion rate needed was similar among the two formulations. Remifentanil is an opioid analgesic, which was administered as an additional drug to maintain anesthesia and also comparable doses of remifentanil were administered (3980.0 μg vs. 4010.0 μg). Frequency of adjustments in target effect-site concentration was also quite comparable (16 in microemulsion and 15 in LCT) indicating that both

anaesthesia regimens were well managed during the procedure. The evaluation of postoperative recovery, especially, time to loss of consciousness (LOC), time to return of consciousness (ROC), and time to recovery of orientation (ROO) was also one of the most significant points of this study. These measures give information on the rate of recovery and onset following anaesthesia [15]. The microemulsion group had a slightly higher time to LOC (20.0 seconds) than the LCT group (18.0 seconds), though this will not be a clinically important difference because the microemulsion group exhibited a relatively fast onset of anaesthesia. Anesthesia time in the microemulsions (2.2 hours) was a bit longer than that of LCT group (2.1 hours), but once again the difference was minimal and would not make any significant contribution to recovery. The ROC and ROO were also similar between the two groups, which also implies that the two formulations have similar recovery profiles. The similarity in the bispectral index (BIS) values of depth of anaesthesia indicated that the two formulations were similar in the depth of anaesthesia during surgery and therapeutic recovery at LOC, ROC and ROO. Values of BIS in both groups were in line with the expected range of general anaesthesia which also substantiates the fact that there was no difference in the anaesthesia administration and recovery between the two propofol formulations. The postoperative nausea and pains are issues that are frequently encountered after general anaesthesia, and this study measured both of them using the Visual Analog Scale (VAS) [16]. The nausea was a little more in the LCT group where 12.6% of the patients reported nausea at 6 hours and 8.7% in microemulsion group. Such results were in line with the earlier reports that have indicated that LCT propofol could be linked to increased occurrence of nausea and vomiting. The LCT score of nausea was also greater (28 mm) in comparison to the microemulsion group (27 mm), which implied that microemulsion propofol can be related to less intense nausea. In the case of post-operative pain, both groups had similar VAS scores. The scores of the two groups were similar within 6 hours (45 mm with microemulsion compared with 43 mm with LCT) and within 6-24 hours (30 mm in both groups), which proves that the pain relieving amount of both formulations was similar. The requirement of rescue analgesics was also a bit elevated in the microemulsion group (120 patients needing rescue analgesics, and 190 doses have been required) than the LCT group (110 patients needing rescue analgesics, and 195 doses have been necessary). This difference in the analgesic use in the rescue is rather small, which is probably due to the fact that the proportion of patients who need analgesia in the microemulsion group is higher.

CONCLUSION

In this study, there is a detailed comparison of the microemulsion propofol and long-chain triglyceride (LCT) propofol in patients under general anaesthesia. According to the results, both formulations have similar effectiveness regarding anaesthesia parameters, postoperative recovery and safety. There was similarity in the rate of propofol infusion, the overall doses, and Infusion rate change among the two microemulsion and LCT propofol. The anaesthesia time, loss of consciousness (LOC) time, time to recovery of consciousness (ROC) and time to recover orientation (ROO) were also similar in the two groups. Such results show that microemulsion propofol can deliver anaesthesia comparable to at least LCT propofol, and has no significant difference between the depth or recovery of anaesthesia. Microemulsion propofol was also found to have a slightly lower rate of nausea postoperative recovery than LCT propofol and fewer patients were on rescue anti-emetic. Even though the frequency of nausea was more frequent in the LCT group, the intensity of the nausea rate that is, the visual analogal scale (VAS) also slightly higher. This indicates that microemulsion propofol can have a value in reducing the extent of postoperative nausea and its attendant issues. Nonetheless, the results of both groups were the same regarding the postoperative pain, as they displayed equal VAS scores and required the use of rescue analgesics to the same extent. The minimal variation in the number of patients who needed analgesics could indicate the general approach to pain management but does not indicate one formulation as more superior to the other. The two formulations were both effective in giving postoperative analgesia and the small difference that was presented between the groups may not have any clinical significance. Furthermore, remifentanil as an addition opioid offered similar pain management in both the groups. Such results contribute to further research and utilization of microemulsion propofol in practice, especially in the cases, when minimization of lipid solvent-related complications is a priority. It is advisable to continue research in this area with more and more diverse groups of patients to ascertain these results as well as to determine the long-term results of using microemulsion protocol.

REFERENCES:

1. Baker, M. T., & Naguib, M. (2005). Propofol: The challenges of formulation. *Anesthesiology, 103*, 860–876.
2. Kim, K. M., Choi, B. M., Park, S. W., et al. (2007). Pharmacokinetics and pharmacodynamics of propofol microemulsion and lipid emulsion after an intravenous bolus and variable rate infusion. *Anesthesiology, 106*, 924–934.
3. Lee, E. H., Lee, S. H., Park, D. Y., et al. (2008). Physicochemical properties, pharmacokinetics, and pharmacodynamics of a reformulated microemulsion propofol in rats. *Anesthesiology, 109*, 436–447.

4. Common Terminology Criteria for Adverse Events (CTCAE) v3.0. (2006). Bethesda: Division of Cancer Treatment and Diagnosis (DCPT), National Cancer Institute (NCI), U.S. National Institutes of Health (NIH).
5. Orringer, E. P., Casella, J. F., Ataga, K. I., et al. (2001). Purified poloxamer 188 for treatment of acute vaso-occlusive crisis of sickle cell disease: A randomized controlled trial. *Journal of the American Medical Association, 286*, 2099–2106.
6. Jewell, R. C., Khor, S. P., Kisor, D. F., LaCroix, K. A., & Wargin, W. A. (1997). Pharmacokinetics of RheothRx injection in healthy male volunteers. *Journal of Pharmaceutical Sciences, 86*, 808–812.
7. Schaer, G. L., Spaccavento, L. J., Browne, K. F., et al. (1996). Beneficial effects of RheothRx injection in patients receiving thrombolytic therapy for acute myocardial infarction. Results of a randomized, double-blind, placebo-controlled trial. *Circulation, 94*, 298–307.
8. Ballas, S. K., Files, B., Luchtman-Jones, L., et al. (2004). Safety of purified poloxamer 188 in sickle cell disease: Phase I study of a non-ionic surfactant in the management of acute chest syndrome. *Hemoglobin, 28*, 85–102.
9. Dutta, S., & Ebling, W. F. (1997). Emulsion formulation reduces propofol's dose requirements and enhances safety. *Anesthesiology, 87*, 1394–1405.
10. Olufolabi, A. J., Gan, T. J., Lacassie, H. J., White, W. D., & Habib, A. S. (2006). A randomized, prospective double-blind comparison of the efficacy of generic propofol (sulphite additive) with Diprivan. *European Journal of Anaesthesiology, 23*, 341–345.
11. Collins, S. L., Moore, R. A., & McQuay, H. J. (1997). The visual analogue pain intensity scale: What is moderate pain in millimetres? *Pain, 72*, 95–97.
12. Minto, C. F., Schnider, T. W., Egan, T. D., et al. (1997). Influence of age and gender on the pharmacokinetics and pharmacodynamics of remifentanil. I. Model development. *Anesthesiology, 86*, 10–23.
13. Ausems, M. E., Vuyk, J., Hug Jr, C. C., & Stanski, D. R. (1988). Comparison of a computer-assisted infusion versus intermittent bolus administration of alfentanil as a supplement to nitrous oxide for lower abdominal surgery. *Anesthesiology, 68*, 851–861.
14. White, L. A., Vanarase, M., Brockbank, K., & Barrett, R. F. (2001). Patient-controlled analgesia and postoperative nausea and vomiting: Efficacy of a continuous infusion of ondansetron. *Anaesthesia, 56*, 365–369.
15. Kang, S. H., Poynton, M. R., Kim, K. M., et al. (2007). Population pharmacokinetic and pharmacodynamic models of remifentanil in healthy volunteers using artificial neural network analysis. *British Journal of Clinical Pharmacology, 64*, 3–13.
16. Green, B., & Duffull, S. B. (2004). What is the best size descriptor to use for pharmacokinetic studies in the obese? *British Journal of Clinical Pharmacology, 58*, 119–133.

Cite this article:
Dr. Maddi Sai Venkatesh. (2020). Comparative Analysis of Microemulsion Propofol and Long-Chain Triglyceride (Lct) Propofol in Elective Surgical Anaesthesia: Efficacy, Safety, and Postoperative Recovery. *American Journal of Oral Medicine and Radiology*, 7(2), 105-110.