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Research Article

Triglyceride Levels in the Blood after Anesthesia with Target-Controlled Infusion of Propofol for Brachial Plexus Surgeries in Adults: A Comparison between Conventional Propofol (LCT Propofol) and Newer Formulation of Propofol (MCT-LCT Propofol)

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ABSTRACT

Background: This study compares the impact of Medium chain-long chain triglyceride (MCT-LCT) Propofol and Long Chain Triglyceride Propofol on blood triglyceride (TG) levels in patients undergoing brachial plexus repair surgery. The study also investigates the effects of these drugs on postoperative recovery and overall patient well-being.

Methods: The study included fifty patients aged 18-60 scheduled for brachial plexus repair between July 2016 and July 2018. Patients were randomly assigned to two sets: Set LP received 1% LCT Propofol, while Set MP was given MCT-LCT Propofol using TCI-pumps. Blood samples for TG level determination were collected before anesthesia induction, after concluding the infusion, 4 hours after stopping infusion and on day 1 post surgery.

Results: Both sets showed a significant increase in TG levels above baseline, with a higher increase observed in the LCT Propofol set (P value = 0.014). After 4th hr of infusion, TG levels significantly decreased only in the MCT-LCT Propofol set (P value= 0.001), with levels lower than those in the LCT Propofol set (P value= 0.021).

Conclusion: Prolonged infusion of LCT and MCT-LCT Propofol (1%) resulted in elevated TG levels. However, the increase in TG levels was lower with MCT-LCT Propofol. No significant ill effects were observed.

Introduction

Hypertriglyceridemia is placed only after first two cause of acute pancreatitis. The first two being gallstones and alcohol [1]. The theory is that when triglyceride levels elevate more than 1,000mg/dl, the low-density fat particles can block the capillaries, leading to necrosis of the pancreatic tissue. This exposes the tissue to pancreatic lipases ultimately causing pancreatitis. The potential occurrence of hypertriglyceridemia after Propofol infusion must be addressed [2]. While slight elevation of triglycerides in the blood after infusion is often an incidental finding,

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levels above 1,000mg/dl can be correlated to pancreatitis [3].

The effects of studied drug on blood lipid levels are still debated. Some literature states that Propofol can cause an increase in triglycerides [4], while others have failed to demonstrate any effect. The outcome depends on a balance between the formation and dissolution of these lipid particles, making it multi-factorial [5]. With the availability of a new formulation of Propofol, it is important to study whether these newer drugs cause a lower rise of triglycerides than their older counterparts.

TCI is a software-mediated delivery system. The algorithm uses the patient details like body weight, height and age as the input data and accurately gets to the target concentrations of drug required for the initial bolus for induction and sets a rate of flow for maintenance of anesthesia and delivers them through the infusion pump. A TCI model is crucial for understanding the drug pharmacology and ensures patient safety [6-7].

To study the effect of prolonged Propofol infusion, we have selected patients undergoing brachial plexus repair surgery at our center. These surgeries often require durations exceeding an hour, which is an inclusion criterion for our study. Furthermore, brachial plexus surgeries necessitate intraoperative neurophysiological monitoring, requiring the avoidance of muscle relaxants. TIVA-Propofol fulfills these requirements without compromising surgical conditions [8].

Methods

This prospective study was approved by the institute's ethical committee. Fifty randomly selected consenting patients aged 18-60 years who were hospitalized at our Center at least one day before the scheduled surgery for brachial plexus repair from July 2016 to July 2018 were included in the study. The patients were within the BMI of 18-30 kg/m2. All selected patients underwent regular baseline basic blood investigations. Patients classified as ASA grade 3 and above were excluded from the study. Additionally, patients with co-morbidities such as cerebral abnormalities (history of brain trauma, seizures), deranged baseline values were excluded. Patients with drug or alcohol abuse, known allergies to study drug, gravid and nursing women, those on psychotropic medications were also not included in the study.

In this observational, randomized, controlled parallel-group prospective study, subjects were randomly assigned into two sets by random number generator application, Jess Tucker, version 1.1.3, 2013. A detailed pre-anesthetic assessment was performed with details of demography, vital signs and blood parameters. Informed consent was obtained from all the study subjects. Patients were advised to fast based on specific guidelines. No sedatives or opioids were administered during premedication.

Set LP received an I.V infusion with 1% LCT Propofol. Set MP received an I.V infusion with 1% MCT-LCT Propofol. Blood samples were collected to document the pre-induction levels of study parameters. Patients received a lactated ringer solution to replenish the fluid deficit due to fasting. No other premedication was administered. The patients then were shifted to the operating room and positioned on the O.T. table in a supine position. Baseline vitals were recorded.

All subjects were pre-oxygenated with a pre-checked anesthesia work station before anesthesia was induced. Prior to induction, fentanyl 1.5 μg/kg I.V. was infused. For induction, Propofol was infused using the TCI device (EVADROP TCI syringe pump, Schiller, UK). The type of Propofol a patient was given was based on the group to which they belonged. The anesthetist was blinded throughout the case for both groups.

The TCI unit utilized the patient demographics to calculate the rate of infusion required to achieve the set target plasma concentration of 8 μg/ml for bolus, 5-6 μg/ml for intubation and 3μg/ml for anesthesia maintenance. Simultaneously, a constant infusion of fentanyl at a dose of 0.5 μg/kg/min was initiated. The position of the ET tube was confirmed by end-tidal CO2 tracing. In case of difficulty securing the airway, succinylcholine was administered to facilitate intubation.

Mixture of gases with O_2 and N_2O at 33% and 67% allowed a FiO_2 of 40% with low flow closed circuit. The ventilator delivered controlled ventilation with a set tidal volume of 6-8ml/kg and an I: E ratio of 1:2. ETCO2 was maintained around 40mmhg throughout the surgery. Muscle paralysis was avoided. Direct nerve stimulation was done by the surgeon using a bipolar stimulator to observe motor responses as and when required throughout the surgery. TIVA with Propofol facilitated such observations.

We monitored the vitals and temperature every 3rd minute intra-operatively. On completion of surgery, we stopped the drug infusion. Another blood sample was collected for blood triglyceride (0). The patient was extubated on good spontaneous efforts of breathing and shifted to the postoperative recovery room. Study parameters, such as the total study drug injected and surgical duration were recorded. Any hemodynamic instability was treated accordingly. Another measurement of the study parameter was done after 4 hours of stopping the infusion (4), and the final measurement was done on postoperative day 1 (D1). All four measurements were taken while the patients were in their fasting state. We formulated the study hypothesis as follows: Null theory- Both formulations of study drug cause similar elevation of blood triglycerides after anesthesia in adults using TCI.

Alternate theory - Either form of study drug formulation caused a higher rise in the blood triglyceride levels than the other after anesthesia in adults using TCI.

Results

Patient characteristics were evenly distributed in both the sets eliminating the confounding elements (Table 1). The means for blood triglycerides at various intervals in both sets were significantly different, with P value= 0.00 (Table 2) and P value= 0.001(Table 3).

The mean value of blood triglycerides on intra-set comparisons (Table 4,5), at the stopping of drug infusion (TG-0) were substantially more than the mean values at the baseline (TG-BL) in both sets (P value= 00.003) and (P value =00.003), indicating an increase of triglycerides after prolonged administration of Propofol. The mean (S.D.) fell while a subsequent value was taken at 4th hour (TG-4). The value was similar to TG-BL (P value= 00.989 and 00.628), suggesting the fall of blood triglycerides to the pre-operative values in both sets.

Table 1- Patient characteristics and other comparative variables.

	Set LP (n=25) n%	Set MP (n=25) n%	P value
ASA 1	18 72	19 76	1.0*
ASA 2	7 28	6 24	
Sex M	22 88	20 80	0.7*
F	3 12	5 20	
Age (years)	33.08 ± 9.96	33.0 ± 11.1	0.876+
Height (cm)	167.42 ± 8.93	166.9 ± 10.3	0.845+
Weight (kg)	63.3 ± 10.7	60.6 ± 11.6	0.32+
Duration of surgery (min)	262 ± 112	273 ± 108	0.36+
volume of Propofol (ml)	168 ± 72.2	167.6 ± 73.5	0.79+
Awake time (mins)	15.76 ± 5.18	16.28 ± 7.33	0.29+

Set LP- LCT Propofol, Set MP- MCT-LCT Propofol, n-No. of patients, * = parametric data, Fisher's exact test (P value <00.05), + = non-parametric data, Mann Whitney U test (P value <0.05), Values are presented as mean± S.D. number and %. Patient characteristics were comparable between the two groups.

Table 2- Assessment of variance between the mean values of blood triglyceride in Set MP (MCT)

Factor	N	Mean	SD	95% CI	P value	S	R-sq (adj)
TG-BL	25	129.00	35.46	(107.69, 150.31)	0.00	53.62	19.05%
TG-0	25	183.6	77.0	(162.3, 204.9)			
TG-4	25	124.2	54.7	(102.9, 145.5)			
TG-D1	25	111.88	36.64	(90.57, 133.19)			

The mean and standard deviation of blood triglyceride are in mg/dl. The mean readings are assessed for difference with ANOVA (P value <00.05). TG= blood triglyceride, TG-BL= baseline TG, TG-0=TG at stopping the study drug, TG-4= TG at 4th hour of stopping drug, TG-D1= TG on post op day-1 of surgery. In Set MP (MCT), the difference in the mean value of triglyceride at different times was noted (P value =0.00).

There was a statistically significant difference in the fall rate from TG-0 to TG-4 only in the MCT-LCT group (P value= 00.001). This indicates that the fall of triglyceride levels in four hours was only obvious for MCT-LCT group. The difference between the TGs on postoperative day-1 (TG-D1) and TG-BL (P value= 0.673 and 0.985) was not statistically remarkable. This suggests that the rise in triglyceride levels never persisted till the second day in either of the sets.

The distribution of study subjects with baseline TGs of over 200mg/dl was similar between the two sets P value= 0.189 (Table 6). The collation of study subjects with blood triglycerides in excess of 200mg/dl at various intervals between the two sets revealed statistical importance at TG-0, TG-4, and TG-D1 (P value= 00.01, 00.003, and 00.004).

We collated the value of mean triglyceride levels at different study periods in the two sets (inter-set comparison, (Table 7). Although the increase and decrease trend were similar in the two sets, the value of TGs-4 remained lower in the MCT-LCT set than in the LCT set (P value= 00.014), refuting our null theory. The two sets on post-op-day one remained similar (TG-D1) (P value= 00.072).

Table 3- Assessment of variance between the mean values of blood triglyceride in Set LP (LCT)

Factor	N	Mean	SD	95% CI	P value
TG-BL	25	153.3	93.9	(102.6, 204.0)	0.001
TG-0	25	282.4	178.3	(231.7, 333.1)	
TG-4	25	196.6	140.9	(145.9, 247.3)	
TG-D1	25	140.6	68.9	(89.9, 191.3)	

The mean and standard deviation of blood triglyceride are in mg/dl. The mean readings are assessed for difference with ANOVA (P value <00.05). In Set MP (MCT), the difference in the mean value of triglyceride at different times was noted (P value=0.00).

Table 4- Assessment of difference in mean value at time intervals for triglycerides in Set MP (MCT).

Time intervals	Difference in mean value	Standard Error	95% CI	Adjusted P value
TG-0 - TG-BL	54.6	15.2	(14.9, 94.3)	0.003
TG-4 - TG-BL	-4.8	15.2	(-44.5, 34.9)	0.989
TG-D1-TG BL	-17.1	15.2	(-56.8, 22.6)	0.673
TG-4 - TG-0	-59.4	15.2	(-99.1, -19.7)	0.001
TG-D1 - TG-0	-71.7	15.2	(-111.4, -32.0)	0.000
TG-D1 - TG-4	-12.3	15.2	(-52.0, 27.4)	0.849

Tukey simultaneous comparisons (P value <00.05) is used to assess the difference in the mean value of triglyceride at various time intervals. Statistical relevance were seen in the values at the baseline and at the stop of infusion (P value=00.003)

Table 5- Assessment of difference in the mean value at time intervals for triglycerides in Set LP (LCT).

Difference of Levels	Difference of Means	Standard error of Difference	Adjusted P value
TG-0 - TG-BL	129.1	36.1	0.003
TG-4 - TG-BL	43.4	36.1	0.628
TG-D1 - TG-BL	-12.6	36.1	0.985
TG-4- TG-0	-85.7	36.1	0.089
TG-D1 - TG-0	-141.7	36.1	0.001
TG-D1 - TG-4	-56.0	36.1	0.412

Tukey simultaneous comparisons (P value<00.05) is used to assess the difference in the mean value of triglyceride at various time intervals. Statistical relevance were seen in the values at the baseline and at the stop of infusion (P value =00.003)

Table 6- Comparison of triglyceride value above 200mg/dl at different time intervals between the two Sets

	Set LP	Set MP	P value∞
No. of patients with triglyceride (TG) >200mgL/dl at various intervals	TG-BL 5	TG-BL 1	0.189
	TG-0 17	TG-0 7	0.01
	TG-4 12	TG-4 2	0.0036
	TG-D1 8	TG-D1 0	0.004

Set LP- LCT, Set MP- MCT-LCT, ∞= parametric data, assessed with Fisher's exact test (P value <00.05). Set LP-LCT, had more study subjects with triglyceride reading crossing 200mg/dl when compared to Set MP, MCT-LCT, on three intervals, TG-0, 4, and D1.

Table 7- Interest collation of blood triglycerides at different times between Set LP (LCT) and Set MP(MCT).

		Set LP(LCT)		Set MP(MCT)		P value
Samples		Mean, SD	Median	Mean, SD	Median	
TG	BL	153.3,93.9	143, (94-175.5)	129,35.46	135, (96-151)	0.238
	0	282.4, 178.3	214, (140-384)	183.6,77.01	172, (134-223)	0.014
	4	196.6, 140.9	140, (89-268)	124.2,54.72	120, (90.5-150)	0.021
	D-1	140.6, 68.93	130, (85-200)	111.9,36.64	102, (88-137)	0.072

The parametric data was assessed with the independent *t*-test (P value < 00.05), and non-parametric data was assessed with the Mann-Whitney U test. (P value <00.05). A statistical relevance was noted for TG-0 and TG-4 between the two sets.

Discussion

The observation examines the impact of prolonged infusion of the drug in the study on blood triglyceride levels. We compared the conventional Propofol (Set-LP) with the relatively newer Propofol (Set-MP). Previous articles have shown a direct link between prolonged Propofol infusion and increased blood triglycerides (TG). However, only few had compared similar increases among different Propofol preparations.

Eddleston J M and Shelly M P observed the effect of Propofol infusion on blood lipid concentration in ICU patients, reporting a significant increase in TG levels and blood cholesterol and a reduction in HDL [9]. Our study found a 00.84-times uprise in the Set LP for TGs compared to a 00.4-times rise in the Set MP.

Our study used TCI-Propofol for anesthesia, which offers the advantage of achieving more steady plasma concentrations. This is especially relevant when studying the outcome of prolonged Propofol infusion on blood triglycerides and in their assessment of safety profile.

Another observation by Devlin J W, Lau K et al. analyzed the effects of Propofol sedation on TG in ICU patients. 18% developed hypertriglyceridemia, and 21% had TGs of more than 1000mg/dl [10]. In contrast, our

study focused on patients undergoing anesthesia with TCI- Propofol for a shorter time frame

Theilen H J et al. collated Propofol in both set of emulsions [11], with our study showing a similar trend and comparability. We demonstrated a less increase in TGs in Set-MP compared to Set-LP, rejecting our null theory.

Overall, these studies highlight the importance of considering the type of Propofol formulation and duration of infusion when assessing its effects on lipid parameters.

We conducted a correlation study to identify co-factors that could impact our analysis. We used Pearson's correlation to analyze variables such as surgery duration, Propofol volume, time required to wake up, and patient specifics. We considered a P value of < 00.1 as relevant. Our findings showed that age, patient weight, surgery duration, Propofol amount, and awake time all influenced the increase in STGs, while height and ASA status did not have an impact (Table 8).

An article by Öztürk et al. Studied the impact of long term infusion of propofol and the possibility of propofol infusion syndrome [12]. They found propofol to be a safe drug. In our study 18 patients in the Set LP showed no side effects, and similarly 21 patients in the Set MP did not exhibit any side effects. Among the Set-LP, three patients had lab values indicating lipemia, one experienced fall in blood pressure and another demonstrated chyle in urine. In the Set-MP, one patient had low heart rate, slow recovery. An incident of pneumothorax was related to the nature of the surgery and not the type of infusion which had an uneventful recovery on day 3rd of placement of ICD. Couple of patients in the Set-LP complained of pain upon injection, while one patient had the same experience in Set-MP. It is important to note that no side effects can be generalized into larger prospects, as their occurrence was too infrequent to be statistically significant.

Limitations

Our study had a few limitations. Since we only included ASA type 1 and 2 patients, the results may not be applicable for patients having dyslipidemias. Those with old age and systemic disorders may exhibit another pattern than these results. Bhukal I et al. [13] and Gottschling S et al. [14] have studied the effects of propofol formulations in pediatric population. While the former study showed similar results to our study in pediatric patients, the latter one showed the LCT-propofol to cause raise in serum triglycerides and pancreatic enzymes in children. More research should explore the possibility of extrapolating the same outcome in different age groups and ASA type. Additionally, larger sample sizes are needed to confirm if the results hold true.

Table 8- Blood triglycerides against different study variables: Pearson's correlation

Variables	TG-BL	TG-0	TG-4	TG-D1
Age	00.268	00.366	00.320	00.326
	00.060	00.009	00.023	00.021
Weight	00.293	00.310	00.290	00.114
	00.039	00.029	0.041	00.431
Height	00.107	00.127	00.198	00.111
	00.458	00.380	0.167	00.445
Surgical time	00.100	00.234	00.156	00.096
	00.488	00.101	00.281	00.508
Amount of Propofol	00.248	00.516	00.404	00.232
	00.082	00.000	00.004	00.104
Awake- time	00.045	-00.172	-00.158	-00.242
	00.756	00.232	00.272	00.091
ASA type	00.061	00.070	-00.204	00.228
	00.675	00.676	00.234	00.112

Green value indicate correlation; reds indicate no correlation.

Conclusion

Blood triglyceride values taken at various intervals compared the rise and fall between the two sets. Triglyceride levels elevated significantly above the baseline in both the sets but the rise was significantly higher in the LCT set. After four hours of stopping propofol infusion, the mean values dropped significantly only in MCT set and these levels were lower than the levels in LCT set. Hemodynamics was found to be stable in both the groups.

A few side effects caught our attention, but none were of any statistical significance

More research with bigger samples and broader demographic inclusions are required to extrapolate our results to the population at large

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References

[1] Yadav D, Pitchumoni CS. Issues in hyperlipidemic pancreatitis. J Clin Gastroenterol. 2003; 36(1):54-62.
[2] Leisure GS, O'Flaherty J, Green L, Jones DR. Propofol and postoperative pancreatitis. Anesthesiology. 1996; 84(1):224-7.
[3] Geneeskd N. Acute pancreatitis after administration of Propofol. 2014; 158: A7115.
[4] Carrasco G, Molina R, Costa J, Soler JM, Cabre L. Propofol and midazolam in short-, medium-, and long-term sedation of critically ill patients. Chest. 1993; 103:557-64.
[5] Llop J, Sabin P, Garau M, Burgos R, Pérez M, Masso J, et al. The importance of clinical factors in parenteral nutrition-associated hypertriglyceridemia. Clin Nutr. 2003; 22:577-83.
[6] Bienert A, Wiczling P, Grześkowiak E, Cywiński JB, Kusza K. Potential pitfalls of Propofol target controlled infusion delivery related to pharmacokinetics and pharmacodynamics. Pharmacol Rep. 2012; 64:782-95.
[7] Russell D, Wilkes MP, Hunter SC, Glen JB, Hutton P, Kenny GN, et al. Manual compared with a target-controlled infusion of Propofol. Br J Anaesth. 1995; 75:562-6
[8] Mousa SA, Alsobky HA. Efficacy and effect of TIVA with Propofol or dexmedetomidine versus sevoflurane without muscle relaxant during brachial plexus repair. Egyptian J Anesth. 2013; 29(1):31-40.
[9] Eddleston JM, Shelly MP. The effect on serum lipid concentrations of a prolonged infusion of Propofol: hypertriglyceridaemia associated with Propofol administration. Intensive Care Med. 1991; 17(7):424-6.
[10] Devlin JW, Lau AK, Tanios MA. Propofol-associated hypertriglyceridemia and pancreatitis in the intensive care unit: an analysis of frequency and risk factors. Pharmacotherapy. 2005; 25(10):1348-52.
[11] Theilen HJ, Adam S, Albrecht MD, Ragaller M. Propofol in a medium- and long-chain triglyceride emulsion: pharmacological characteristics and potential beneficial effects. Anesth Analg. 2002; 95(4):923-9.
[12] Öztürk I, Serin S, Gürses E. Biochemical markers in total intravenous anesthesia and Propofol infusion syndrome: a preliminary study. Eur Rev Med Pharmacol Sci. 2013; 17(24):3385-90.
[13] Bhukal I, Thimmarayan G, Bala I, Solanki SL, Samra T. Comparison of serum triglyceride levels with Propofol in long chain triglyceride and Propofol in medium and long chain triglyceride after short term anesthesia in pediatric patients. Saudi J Anaesth. 2014; 8:53-6.
[14] Gottschling S, Meyer S, Krenn T, Kleinschmidt S, Reinhard H, Graf N, et al. Effects of short-term Propofol administration on pancreatic enzymes and triglyceride levels in children. Anaesthesia. 2005; 60(7):660-3.