ORIGINAL ARTICLE

Comparative Study of Pain on Injection of Propofol MCT-LCT with Propofol Nanoemulsion for General Anaesthesia

Shakya S, Vaidya P, Paudel B

ABSTRACT

Introduction: Pain during injection of propofol continues to be a major discomfort for patients. Different propofol formulations have been introduced to reduce the incidence of pain. **Aims**: To know the incidence, severity of pain at induction and post operative amnesic effect of two different formulations of propofol. **Methods:** This double-blinded comparative study involved randomly selected 100 patients undergoing elective surgery under general anesthesia with physical status score I or II (American Society of Anesthesiologists). Out of 100 patients, 50 received medium and long chain triglyceride Propofol (Group A) while another 50 received nanoemulsion Propofol (Group B) intravenously. Parameters measured and compared were the gender, age, weight, physical status score, pain on injection and postoperative recall of pain during injection of propofol. **Results:** Both groups were comparable with regards to age, gender, physical status score, mean duration of surgery. The presence of pain during injection with propofol in group A was 76% (38 patients) while 36% (18 patients) in group B which was statistically significant (p =0.0001). Severity of pain was more in group A which was statistically significant in comparison to group B (p=0.0001). The arm withdrawal during the injection of propofol was found more in Group A than Group B, 24% vs 0% (p=0.0002). Recall of pain after 4 hours postoperatively was found in 5 patients of Group A (10%) and 3 patients of Group B (6%) which came out to be statistically insignificant (p=0.715). There was no significant difference between groups regarding heart rate, mean arterial pressure, respiratory rate and arterial hemoglobin oxygenation at all assessed times (p > 0.05) intraoperatively. **Conclusion**: This study clearly shows the incidence and severity of pain on intravenous administration in nanoemulsion Propofol is significantly less. However, amnestic effect was equally present in both the groups.

Keywords: Incidence, Nanoemulsion, Pain, Propofol

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INTRODUCTION

Propofol is an intravenous sedative hypnotic agent, causes unconsciousness rapidly and reliably.[1] It has advantages like rapid onset and metabolism, early recovery and lesser post-operative nausea and vomiting.[2] Although several formulations of propofol were tested,formulation reducing the incidence of pain after injection has not been found yet. Definite mechanism of pain by propofol is uncertain. Propofol belongs to phenol group that can irritate skin, mucous membrane and venous intima.[3] Propofol also produces indirect action on endothelium, activates the kallikrein-kinin system and releases bradykinin, thereby producing venous dilation and hyper permeability, increases contact between aqueous phase of propofol and free nerve endings within the vein, resulting pain.[4-6]

Conventionally, propofol contains long chain triglycerides (LCT) which is the cause for severe pain on intravenous injection.[7] It is experience by 70% of the adult and 85 % of the children.[8] Solutions with lesser soyabean oil, with short and medium chain fatty acids, albumin emulsions, etc are some of the efforts made to alter the propofol carrier for reduction of pain.[9] Incidence of pain may also be reduced by decreasing the particle size of propofol which in turn lowers the free fraction of propofol.[10] Nanoemulsion propofol, newer formulation with reduce amount of free propofol, more stability, useful lifespan, wider antimicrobial spectrum causes lesser pain.[11] The aim of this study was to compare the incidence, severity of pain on intravenous injection of propofol with Medium and Long Chain Triglycerides (MCT-LCT) versus Nanoemulsion propofol for induction as well as to know the amnesic effect postoperatively.

METHODS

This hospital based prospective, double-blinded comparative study was carried out in the Department of Anaesthesiology, Nepalgunj Medical College and Teaching Hospital, Kohalpur, Nepal from August 2021 to December 2021 after approval from the Institutional Review Committee.

A total of randomly selected 100 patients willing to give written informed consent fitting into the inclusion criteria (age between 18-65 years, all genders, American Society of Anesthesiologists (ASA) I & II) were included in this study scheduled for various elective surgeries under general anaesthesia. These patients were randomly allocated to two groups, each consisting of 50 patients by closed envelope technique. Patients with known allergy to the study drug, pregnancy, neurologic or cardiovascular disorder, abnormal renal and liver function, chronic pain disorder were excluded from the study.

Group allocation as well as the study drug (2mg/kg) for induction to be administered were prepared by the second anaesthesiologist or nurse not involved in the study. Patients in Group A received 25% of Propofol MCT-LCT induction dose while in Group B received 25% of Propofol Nanoemulsion induction dose. The person injecting the study drug and evaluating the effects were blinded to the drug solution.

All patients admitted to the hospital before surgery underwent complete pre-anaesthetic evaluation including detailed history taking, physical examination and routine pre-operative investigations. All the patients kept fasting for 6 hours were received and identified in the Operation Theater. An intravenous line was established with an 18G intravenous cannula in a large vein on the dorsum of the hand or forearm. All patients were attached with standard monitors with heart rate(HR), non-invasive blood pressure(NIBP), respiratory rate(RR), arterial hemoglobin oxygenation by pulse oximeter(SPO2) and electrocardiography (ECG) before the procedure was started and recorded. Patient was preoxygenated and 25% of the induction dose of study drug was givenover 3 seconds by other staffs not involved in study according to the envelop code.[7] The patients were asked with a standard question, "Is the injection comfortable?" The data of verbal response and behavioral signs, such as facial grimacing, arm withdrawal, or tears, were recorded. A score of 0 to 3, corresponding to absent, mild, moderate, or severe pain, respectively was followed for recording system.[12,13] (Table I)

Pain score	Degree Of pain	Response
0	Absent	Negative response to questioning
1	Mild	Pain reported in response to questioning only, without any behavioral sign
2	Moderate	Pain reported in response to questioning and accompanied by a behavioral sign, or pain reported simultaneously without questioning
3	Severe	Severe Strong vocal response or response accompanied by facial grimacing, arm withdrawal, or tears

Table I: Assessment and severity of Pain During Injection of Propofol

This was the end point of this study for incidence and severity of pain. Four hours after the postoperative period, the patient was asked if S/He felt pain during injection and recorded.

Statistical Analysis

Data thus recorded and collected were analyzed by standard statistical tests such as Chi square test and Students unpaired t-test with SPSS version 20. The p value < 0.05 were considered statistically significant.

RESULTS

Both groups were comparable with regards to age, gender, ASA physical status, mean duration of surgery. There was no statistically significant difference between groups (p > 0.05). (Table II)

Variables	Group A	Group B	p-value
Age(yrs)	42.18 ± 14.70	42.22 ± 13.86	0.741
Gender			
Male	12 (24)	8 (16)	0.454
Female	38 (76)	42 (84)	
Weight(Kg)	55.48 ±6.99	58.02±9.56	0.06
Physical Status			
ASA I	34 (68)	37 (74)	0.660
ASA II	16 (32)	13 (26)	
Duration of Surgery(min)	80 ±19.79	77.40±17.36	0.661

Table II: Study population demographic data

The presence of verbal response of pain during injection with propofol in group A was 76% (38 patients) while 36% (18 patients) in group B with p value of 0.0001. 24% (12 patients) in group A had arm withdrawal during the injection of propofol while none had arm withdrawal in group B(p=0.0002). Severity of pain was statistically significant in group A in comparison to group B with p value of 0.0001. There was no significant difference between the two groups (p = 0.715) in recall of pain that was assessed at 4 hours postoperatively. (Table III)

	Group A	Group B	p-value
Pain during injection(Verbal Response)			
Yes	38 (76)	18 (36)	X^2 =16.234
No	12 (24)	32 (64)	0.0001*
Arm withdrawal during injection			
Yes	12 (24)	0	X^2 =13.636
No	38 (76)	50 (100)	0.0002*
Severity of pain during injection			
Absent	12 (24)	31 (62)	
Mild	22 (44)	18 (36)	X^2 =22.045
Moderate	15 (30)	1 (2)	0.0001*
Severe	1 (2)	0	
Postoperative pain recall after 4hrs			
Yes	5 (10)	3 (6)	X2 =0.543
No	45 (90)	47 (94)	0.715

Table III: Distribution of patients regarding presence and severity of pain, arm withdrawal during propofol injection and postoperative pain recall of pain after 4 hrs

There was no significant difference between groups regarding HR, MAP, RR and SpO2 at all assessed times (p > 0.05) intraoperatively. (Fig. 1, 2 and 3)

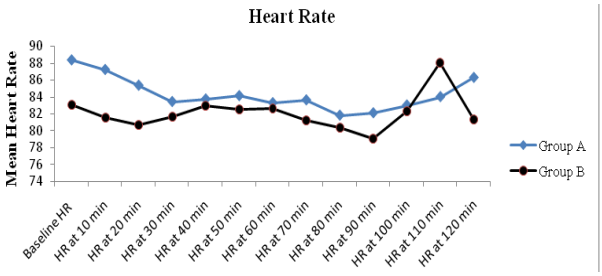

Figure 1: Mean Heart Rates (beats per min) of the two study groups at different time intervals

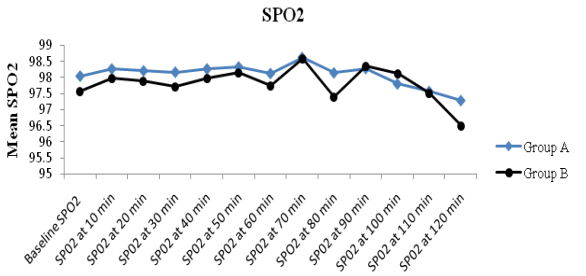

Figure 2: Mean SPO2 of the two study groups at different time intervals

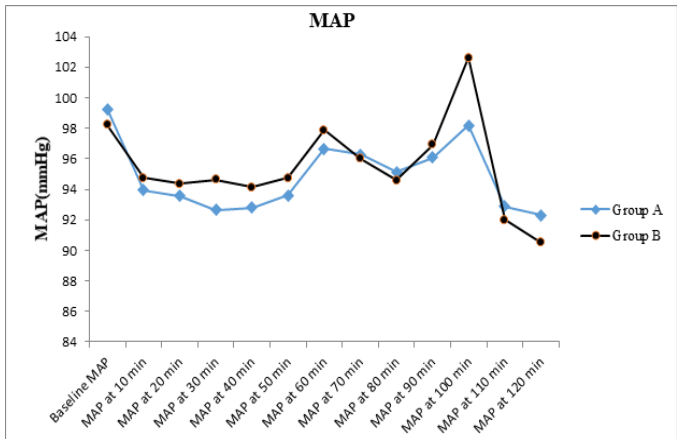

Figure 3: MAP (mmHg) of the two study groups at different time intervals

DISCUSSION

It is worth mentioning that there are not many studies about clinical use of propofol Nanoemulsion.[9,11,14] The comparative study related to Propofol MCT-LCT and Propofol Nanoemulsion isn't readily available in our setting till date. Hence, Propofol Nanoemulsion and MCT-LCT Propofol formulations were compared in 100 patients undergoing elective surgery under general anaesthesia to see the incidence and severity of pain on injection.

In this study, patients receiving Propofol Nanoemulsion had a lower incidence of pain on injection than patients receiving Propofol MCT-LCT (p < 0.05),with statistical relevance (36% vs. 76%). Study done by Rodrigues TA, Alexandrino RA, Kanczuk ME, et al[9] in 2012 distributed patients undergoing upper digestive endoscopy randomly into two groups: the control group (n = 75) with lipid emulsion propofol and the propofol Nanoemulsion group (n = 75). They concluded that the incidence of pain on injection with propofol Nanoemulsion was lower than lipid emulsion propofol (53.3% vs. 82.7%). The difference between the groups was statistically significant (p < 0.001) which came out to be similar with this study.

Krobbuaban B, Diregpoke S, Kumkeaw S et al[15] in 2005 administered two different particle size formulations of propofol (Anepol and standard propofol: average particle size 140.5 nm and 193.3 nm) with or without lidocaine in 388 non-premedicated adult patients. Group I received 2 ml NaCl 0.9% and Propofol (n=97), group II received 2 ml lidocaine 2% and Propofol (n=96), group III received 2 ml NaCl 0.9% and Anepol (n=97) and group IV received 2 ml lidocaine 2% and Anepol (n=97) into a dorsal vein of the hand. Pain during propofol injection was evaluated over 5-10 seconds, until loss of consciousness, using a 4 point scale. 67 patients (69.1%) complained of pain in group I, as compared with 40 patients (41.2%) in group III. Patients receiving Anepol (smaller size particle) had a lower incidence of pain on injection than patients receiving standard Propofol (larger particle) (p < 0.05). The authors concluded that the smaller particle size of propofol was associated with less incidence of pain on injection than the standard propofol which was similar to this study. Regarding

arm withdrawal during propofol injection, it was observed in 12 patients (24%) in group A while none in group B which came out to be statistically significant (p=0.0002 patients).

In this study, severity of pain on injection: mild, moderate and severe pain were found more in Group A being statistically significant in comparison to group B (p=0.0001).

Rittes JC, Cagno G, Perez MV, et al[11] in 2012 did the comparative evaluation of propofol in Nanoemulsion with solutol and soy lecithin for general anesthesia in 50 patients undergoing gynecological procedures. They concluded with the result that Nanoemulsion formulation elicited less intense pain on intravenous injection which was statistically significant. Our results were similar to study done by Rittes JC et al showing more severe pain in the conventional propofol (p=0.01) than Nanoemulsion propofol. In the same study done by Rittes JC et al arm withdrawal frequency during propofol injection, was found statistically not significant (p=0.09). However, it was clinically significant.[11]

Krobbuaban B, Diregpoke S, Kumkeaw S et al[15] in 2005 also did the study to find the severity of pain on injection. The severity of pain on injection was not significantly different between the groups. However, 4 patients (4.1%) had severe pain on injection of standard propofol group while none in small particle propofol group. The findings were similar to this study.

In this study, 5 patients (10%) had recall of pain that was assessed at 4 hours postoperatively in Group A while 3 patients (6%) in Group B. However, there was no statistically significant difference between the two groups (p = 0.715). This may be due to amnestic effect of propofol in both the groups.[16,17]

Our results were compared with the study done by Schaub E, Kern C, Landau R et al. who also observed that at a significant percent of women demonstrating obvious signs of pain during propofol injection had no recall of pain after surgery.[18]

LIMITATIONS

This study could not find the exact particle size of both the propofol formulations. The compositions and the particle size of the Nanoemulsion propofol should be further evaluated to confirm the cause of less pain on injection. As only few studies exist in the literatures related to this study, multicentric study with larger randomized sample can be carried out in future.

CONCLUSION

This study showed that the incidence and severity of pain is lower with Nanoemulsion propofol compare to MCT-LCT propofol. Therefore, this study concludes Nanoemulsion formulation is advantageous to use in anaesthesia practice as far as incidence of pain and severity on injection is concerned. However, amnestic effect was equally present in both the groups.

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