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Comparison of the Two Different Formulations of Propofol I.E. Propofol 1% (Long Chain Triglyceride) With Propofol Lipuro 1% (Medium Chain Triglyceride +Long Chain Triglyceride) As an Induction Agent for Elective Short Surgical Procedures: A Study from Tertiary Care Centre

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KEYWORDS

Different Formulations, Propofol Lipuro

ABSTRACT:

Introduction: The rapid return of psychomotor functions has made propofol an anaesthetic agent of choice for day care surgeries. The more rapid return of consciousness with minimal residual central nervous system effects is one of the most important advantages of propofol compared with alternative drugs administered for the same purpose. The context-sensitivity half time of propofol is very short even with prolonged periods of infusion combined with short effect site equilibration time, which makes this drug an intravenous agent of choice for maintenance of anaesthesia and for intravenous sedation.

Objective: To compare the two different formulations of Propofol i.e. Propofol 1% (long chain triglyceride) with Propofol lipuro 1% (medium chain triglyceride +long chain triglyceride) as an induction agent for elective short surgical procedures.

Results: 62.0% of patients have pain on injection with standard Propofol while 38.0% of patients have pain on injection with Propofol lipuro. By applying chi-square test p value was 0.01 which was statistically significant. Total dose for induction in standard Propofol group was 123.60±20.678 (MEAN±SD) and in Propofol lipuro group was 120.00±14.142 (MEAN±SD) sec. It was not statistically significant.

Conclusion: In this study on hundred healthy subjects, we found that, the new formulation of Propofol (Propofol lipuro 1%- medium chain triglyceride + long chain triglyceride) was well tolerated and generally indistinguishable from standard Propofol 1% (long chain triglyceride). However, we did find a significant decrease in the incidence of pain on injection with new formulation of Propofol.

Conclusion: Propofol 1% (long chain triglyceride) with Propofol lipuro 1% (medium chain triglyceride +long chain triglyceride), elective short surgical procedures

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Introduction

Anesthesia has undergone revolutionary changes from its inception till date. Today it has become a highly safe and skilled branch of medicine. The recent focus on day care surgeries has lead to discovery of newer and safer drugs and techniques in this field. Earlier day care surgeries were performed with anesthesia techniques using nitrous oxide and ether; however, it has been replaced today by safer intravenous drugs like propofol, and short acting opioids like fentanyl, sufentanil, remifentanyl.[1]

Propofol is a novel anesthetic agent introduced in 1977 by Kay & Rolly with rapid induction and excellent recovery profile. The rapid return of psychomotor functions has made propofol an anaesthetic agent of choice for day care surgeries. The more rapid return of consciousness with minimal residual central nervous system effects is one of the most important advantages of propofol compared with alternative drugs administered for the same purpose. For induction of anaesthesia, it is used in the dose of 1.5 to 2.5 mg/kg intravenously. The context-sensitivity half time of propofol is very short even with prolonged periods of infusion combined with short effect site equilibration time, which makes this drug an intravenous agent of choice for maintenance of anaesthesia and for intravenous sedation. Typical conscious sedation dose is 25 to 100 µg/kg/min. Propofol has been administered as sedative during mechanical ventilation in ICU in variety of patients including postoperative patients (cardiac surgery/neurosurgery/and in head injury patients). The incidence of postoperative nausea and vomiting is decreased. [2,3]

The aim of our study is to compare this new formulation of propofol 1% (medium chain triglyceride + long chain triglyceride) with that of standard propofol 1% (long chain triglyceride) as an induction agent with respect to pain on injection, induction time and total dose for induction.

AIMS AND OBJECTIVES

To compare the two different formulations of Propofol i.e. Propofol 1% (long chain triglyceride) with Propofol lipuro 1% (medium chain triglyceride +long chain triglyceride) as an induction agent for elective short surgical procedures with respect to the following:

1. The incidence of pain on injection.

2. The intensity of pain on injection according to four-point pain scale as:

a. No pain

b. Mild pain

c. Moderate pain

d. Severe pain

Materials and methods

After approval from hospital scientific review committee and ethics committee, the study was conducted on hundred healthy consenting patients of ASA grade I and II, undergoing elective short surgical procedures. The aim of the study was to compare the two different formulations of propofol i.e. Propofol 1% (long chain triglyceride) with propofol lipuro1% (medium chain triglyceride + long chain triglyceride) as an induction agent for elective short surgical procedures. Hundred patients were randomly allocated to two groups (n=50 in each group) by a computer-generated randomization list. The preoperative anaesthetic evaluation was done including history, general and systemic examination and routine investigations like Hb, CBC, ECG, X-ray chest and blood urea nitrogen.

INCLUSION CRITERIA

- Age group: 20-45 years
- ASA Grade: I and II of either sex
- Patients with pre-study laboratory results within normal limits

EXCLUSION CRITERIA

- ASA Grade III and IV
- Drug allergy to commonly known anaesthetic agents or their constituents,

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- Drug allergy to egg lecithin.
- History of significant hepatic / renal / cardiac / hematological / neuropsychiatric / respiratory and endocrine disorders.
- Pregnant and lactating mothers.
- Paediatric age group.
- Anticipated difficult intubation.
- Patients who did not consent to the study.

Methods of data collection

In preanesthetic holding area, the preoperative anaesthetic evaluation was done including history, general and systemic examination and routine investigations like Hb, CBC, serum electrolytes, ECG, X-ray chest PA view and blood urea nitrogen. Nil per oral status for at least 6 hours was confirmed. All patients involved in the study were explained about occurrence of pain on injection of propofol and were asked to report the pain when it occurs. Informed written consent was obtained.

All patients were premedicated with Inj midazolam 0.07mg/kg intramuscularly before shifting to operation room. In the operation theatre all standard monitoring equipment were applied such as electrocardioscope, non-invasive blood pressure monitor, pulse oximeter and end tidal carbon dioxide monitor. An appropriate size intravenous cannula (20G) was inserted into a prominent vein on the forearm or antecubital fossa and crystalloid infusion was commenced. The patients were asked to hold a 20ml syringe in the opposite hand to assess the drop of 20ml syringe from hand on induction. The drug used for the study was prepared by an independent anesthesiologist in a separate room and administered by another anesthesiologist who was blinded to the drug group and who was also not a part of the study.

Before induction all patients received Inj. Glycopyrrolate 4µg/kg intravenously. After preoxygenating with 100% oxygen for 3 minutes the patients were induced with either Inj. Propofol 1% (long chain triglyceride) i.e. GROUP1 or Inj. Propofol 1% (medium chain triglyceride +long chain triglyceride) i.e. GROUP2 according to randomization list at the rate of 10 mg/10 sec with the help of stop watch until the loss of response to verbal command. Time for loss of eyelash reflex and drop of 20ml syringe from hand and time for apnoea was also noted. During induction all patient were continuously asked about pain on injection of the drug. If pain occurred on injection, then the scoring of pain was done according to four-point pain scale as given below.[4]

0	NO PAIN	
1	Mild pain	Pain reported only in response to questioning Without any behavioral signs.
2	Moderate pain	Pain reported only in response to questioning with behavioral signs or pain reported spontaneously
3	Severe pain	Strong vocal response with facial grimacing or arm withdrawal

Supplementary bolus doses of 0.5mg/kg were given if an induction criterion was not met in both the groups. Total dose required for induction was also noted. After induction criteria was achieved all patients received Inj. Vecuronium 0.1mg/kg IV and their lungs ventilated with oxygen, nitrous oxide and inhalation agent (isoflurane) for three minutes. Tracheal intubation was achieved with appropriately sized endotracheal tube. Anaesthesia was maintained with 66% nitrous oxide in oxygen with inhalational agent (isoflurane). Inj Fentanyl 2µg/kg was used as intraoperative analgesic. During induction following parameters were noted:

1. Time for induction: was assessed by

a) Loss of response to verbal command.

2. Time for apnoea

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Results

TABLE 1: Distribution according to age group

AGE IN YEARS	GROUP I	GROUP II
MEAN WEIGHT± SD	44.70±11.562	44.68±11.469

TABLE 2: Distribution according to weight

WEIGHT IN KG	GROUP I	GROUP II
MEAN WEIGHT± SD	56.12±12.545	54.30±10.086

Analysis of demographic data (table 1and 2) showed that two groups included in the study did not differ significantly with regard to age and weight. The average age in years in group 1 was 44.70±11.562 (Mean ± SD) and in group 2 was 44.68±11.469 (Mean ± SD). The average weight in kilograms in group 1 was 56.12±12.545 (Mean ±SD) and in group 2 was 54.30±10.086 (Mean ± SD).

TABLE 3: PAIN ON INJECTION

	STANDARD PROPOFOL (group1)	**PROPOFOL LIPURO (group2)**	**SIGNIFICANCE p value**
NO PAIN	19 (38.0%)	31 (62.0%)	Chi-square test (0.01)*
PAIN	31 (62.0%)	19 (38.0%)	

***p value <0.05 (significant)**

From above table it was observed that 62.0% of patients have pain on injection with standard Propofol while 38.0% of patients have pain on injection with Propofol lipuro. By applying chi-square test p value was 0.01 which was statistically significant.

Table 4: comparison of induction characteristics

GROUP (MEAN±SD)	STANDARD PROPOFOL	PROPOFOL LIPURO	P VALUE
Total dose	120.00±14.142	120.00±14.142	0.312
Time for loss of eyelash reflex	120.00±14.142	105.10±17.103	0.039*
Time for loss of response to verbal command	97.00±21.293	108.68±16.123	0.041*
Time for drop of 20 ml syringe	100.06+24.553	109.28±15.451	0.035*
Time for apnoea	105.86+26.331	114.54±13.989	0.042*

***P value <0.05 (significant)**

Time for loss of eyelash reflex in standard Propofol group was 97.00 ± 21.293(MEAN±SD) sec while in Propofol lipuro group was105.10 ± 17.103(MEAN±SD) sec which was statistically significant.

Time for loss of response to verbal command in standard Propofol group was 100.06 ± 24.553 (MEAN±SD) sec while in Propofol lipuro group was 108.68 ± 16.123(MEAN±SD) sec which was also statistically significant.

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Time for drop of 20ml syringe in standard Propofol group was100.50+24.548 (MEAN±SD) while in Propofol lipuro group was 109.28±15.451 (MEAN±SD) sec and time for apnoea in standard Propofol group was 105.86±26.331 (MEAN±SD) and in Propofol lipuro group was 114.54±13.989 (MEAN±SD) sec, both these values are statistically significant.

Total dose for induction in standard Propofol group was 123.60±20.678 (MEAN±SD) and in Propofol lipuro group was 120.00±14.142 (MEAN±SD) sec. It was not statistically significant.

Discussion

Propofol is a short acting intravenous anaesthetic agent. It is being used extensively these days because of its smooth induction and rapid recovery profile. It is the anaesthetic agent of choice for day care anaesthesia, total intravenous anaesthesia, for sedation in intensive care units, and as an agent for maintenance of anaesthesia. It also reduces postoperative nausea and vomiting. Propofol is a short acting intravenous anaesthetic agent. It is being used extensively these days because of its smooth induction and rapid recovery profile. It is the anaesthetic agent of choice for day care anaesthesia, total intravenous anaesthesia, for sedation in intensive care units, and as an agent for maintenance of anaesthesia. It also reduces postoperative nausea and vomiting. [5]

Propofol has also been used for laryngeal mark airway insertion and tracheal intubation without the use of neuromuscular blocking agents.

Propofol has many characteristics of an ideal anaesthetic agent as it produces hypnosis in one arm brain circulation time with minimal excitation. It causes less psychomotor disability. An important advantage is that recovery is immediate in terms of return of consciousness and protective airway reflexes and resumption of motor activity. The "home readiness" and "street fitness" are achieved earlier.

However, there are certain disadvantages of Propofol like it causes pain when injected intravenously, myoclonus, apnea, decrease in blood pressure and rarely thrombophlebitis of vein into which Propofol is injected. The quality of an anaesthetic agent as judged by patient is clearly influenced by the pain or discomfort at the time of induction.

It may be distressing to patient and can reduce the acceptability of an otherwise useful agent. Also the pain during induction can affect the haemodynamic and stress response to induction as can be seen, incidence of pain due to propofol injection is very high (28-90%)

The main cause of pain on injection is the concentration of "free propofol" in aqueous phase of standard Propofol containing exclusively long chain triglyceride.

Recently a new formulation of Propofol containing long chain triglyceride as well as medium chain triglyceride as compared to standard propofol which contains only long chain triglyceride has been introduced. In this new formulation the concentration of "free propofol" was reduced to 14 µg/ml as compared to 18.6 µg/ml in standard Propofol.[6]

Due to presence of medium chain triglyceride the oil phase of this new formulation has got increased resolving capacity as compared to long chain triglyceride fat emulsions. The aim of our study is to compare this new formulation of propofol 1% (medium chain triglyceride +long chain triglyceride) with that of standard propofol1% (long chain triglyceride) as an induction agent with respect to pain on injection, Induction time, total dose for induction, haemodynamic changes during induction and any adverse reactions like myoclonus/ yawning/ coughing/rash etc.

PAIN ON INJECTION:

In **our study**, we noted that 62% patients had pain on injection in standard propofol group while 38% patients in propofol lipuro group had pain on injection. This difference was clinically as well as statistically significant (p=0.01). When we subdivided the pain on injection into mild, moderate and severe. The results were not statistically significant. The main factor responsible for pain on injection was probably the free propofol concentration in the aqueous phase. Pain on injection can be immediate or delayed. The immediate pain results from direct irritant effect to vein while delayed pain results from an indirect effect via kinin cascade. The concentration of free propofol was

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18.6mu*g / m * l in standard propofol which was reduced to 14 mu*g / m * l in propofol lipuro 1% i.e. reduction of 25 % of free propofol concentration. Therefore, probably this new formulation of propofol causes less pain on injection as compared to standard propofol.

In **earlier studies Alfred W. Doenicke et al, [1,2] Bachmann Mennenga B. et al, Larsen et al[7]** it was observed that a higher percentage of patients in standard propofol group had pain on injection as compared to propofol lipuro.

Total dose required for induction

In **our study**, the total dose required for induction of anaesthesia in standard propofol group was 123.6 plus/minus 20.678 mg while in propofol lipuro group was 120 plus/minus 14 mg which was not statistically significant.

In a study conducted by Jens Rau et al[8] and R. Larsen et al[7] they also showed that the mean induction dose required in both groups was equal. Our results were consistent with the results of these earlier studies.

INDUCTION CRITERIA:

The induction criteria were assessed by time for loss of response to verbal command and time for drop of 20 ml syringe from hand. The time for loss of eyelash reflex was also noted.

The time required for induction of anaesthesia was same in both the groups in the study by **Jens Rau et al, [7] Alfred W Doenicke. [1]**

In **our study** we observed that time required for induction of anaesthesia was less in standard propofol group as compared to lipuro group i.e. induction was faster with standard propofol. The cause of slower induction of propofol lipuro again probably due to decreased concentration of free propofol in aqueous phase.

Conclusion

In this study on hundred healthy subjects, we found that, the new formulation of Propofol (Propofol lipuro 1%- medium chain triglyceride + long chain triglyceride) was well tolerated and generally indistinguishable from standard Propofol 1% (long chain triglyceride). However, we did find a significant decrease in the incidence of pain on injection with new formulation of Propofol.

References

1. Alfred W Doenicke, Michael F Roizen, Jens Rau, et al Reducing pain during propofol injection: the role of solvent. Anesth Analg 1996: 82:472- 474
2. Alfred W Doenicke, Michael F Roizen, Jens Rau, et al. Pharmacokinetics and pharmacodynamics of propofol in a new solvent. Anesth Analgesia 1997, 85:1399-40.
3. Anil Agarwal, Sanjay Dhiraj, Mehdi Raza. Vein pretreatment with magnesium sulfate to prevent pain on injection of propofol is not justified: Canadian journal of anaesthesia 2004: 51:133-134.
4. Bachmann-Mennnegab, Ohimera, Heesen M. Incidence of pain after intravenous injection of medium/long chain triglyceride emulsion of Propofol: An observational study in 1375 patients. Arzneimittelforchung 2003; 53(9): 621-626.
5. Auerswald K, Pfeiffer F. Behrends K. Burkhardt U, Olthoff D. Pain on injection with propofol Can J Anaesth 2005 Jun; 52(6): 595-9.
6. Eugene H Cox, Catherine A J, Knibbe Victorine S Koster. Influence of different fat emulsion based intravenous formulations on pharmacodynamics and pharmacokinetics of Propofol. Pharmaceutical research 1998; vol 15 no 3.
7. R Larsen, U Beerhalter, R Erdkonig. B Larsen. Propofol in a new formulation (PROPOFOL MCT/LCT) effect on injection pain in children. Anesthetist 2001, 50. 676-678
8. Jens Rau, Michael F Roizen, Alfred W Doenicke Propofol in an emulsion of long and medium chain triglyceride: The effect on pain. Anesth Analg 2001; 93: 382-384. 15. Jens Rau, Michael F Roizen, Alfred W Doenicke Propofol in an emulsion of long and medium chain triglyceride: The effect on pain. Anesth Analg 2001; 93: 382-384.