

The Effect of Dilution of Propofol on Propofol Induced Injection Pain A Randomized Controlled Study

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Abstract

Background and Objectives: Propofol is commonly used induction agent for general anesthesia as well as for sedation in and outside operation room. Pain on injection is one of the major disadvantages with an incidence upto 90%. Various modalities have been tried in the past and in the present to obtund the pain on injection of propofol but the search for the ideal modality continue. This study has been designed to assess the effect of dilution of propofol with 5% dextrose on the pain at the injection site.

Methods: Double blind randomized study was conducted in 150 patients of both genders belonging to ASA I and II posted for elective surgeries under general anaesthesia divided into 3 groups namely A, B and C. Patients in group A, B and C were given 1% propofol 2 ml, 0.5% propofol 4 ml and 0.33% propofol 6ml over 4 seconds and pain at the injection site assessed.

Results: There was statistically significant reduction in pain on injection in group B as compared to group A (p-0.000), also there was significant reduction in pain on injection in group C (triple diluted) as compared to group B (p-0.000) as well as group A (p-0.000).

Conclusion: Double as well as triple dilution of propofol is associated with significant reduction in incidence and severity of pain at the injection site.

Key words:- Dilution, injection, pain, propofol.

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I. Introduction

In the lookout for an ideal anaesthetic agent in clinical practice, Kay and Rolly introduced propofol in 1977. Its advantage in short surgical procedure is attributed to its rapid elimination from blood (half life 1-3 hours due to high hepatic clearance) leading to rapid recovery of cognitive and psychomotor function with a very low incidence of PONV.

Propofol, (chemically, 2, 6 di- isopropyl phenol) is a rapidly acting induction agent and has many characteristics of an ideal anaesthetic agent with low incidence of excitatory side effects¹.

Evidence reveal that among the low morbidity outcomes of current clinical anaesthesiology (with regard to clinical importance and frequency of occurrence) pain during injection of Propofol ranks as the 7th most important problem².

The reported incidence of pain on Propofol injection varies between 28-90% in adults and 28-85% in children in the absence of any pretreatments³. Various modalities have been tried to reduce the incidence and severity of propofol induced pain by using lignocaine, ondansetron, metoclopramide, ketamine, ephedrine, microbiological filter, cooling the solution of propofol, etc.^{4,5} Other physical methods like microfiltration, double line intravenous set, warming the propofol to 37°C, cooling of propofol to 4°C, and reducing the pH of propofol injection have also been tried.⁶⁻¹⁰ However, some investigators have shown that the addition of lidocaine to propofol resulted in a coalescence of oil droplets, and it is thought that the concentration of free propofol in the aqueous phase can be changed.¹¹ Search for an ideal technique for relief of propofol-induced pain on injection still continues as none of the aforesaid techniques to reduce pain on propofol injection have proved to be foolproof.

In the present study, we assessed the effect of double and triple dilution of 1% propofol emulsion with 5% dextrose on pain at injection site.

Objectives: To compare the pain on injection of three different dilutions of propofol -1%, 0.5% and 0.33% at the injection site in 150 ASA- I and II patients in the age group of years admitted for elective surgery under general anaesthesia.

Materials and methods: A Double blind randomized control study conducted after obtaining ethical committee approval, between July 2017- July 2018 Conducted at department of anaesthesiology, Gitam institute of medical sciences and research, Visakhapatnam. Patients of either sex, aged 20-60 years, belonging to ASA-PS 1 and 11 scheduled for elective surgeries under general anaesthesia were divided into three groups GROUP A will receive 1% propofol, GROUP B will receive 0.5% propofol and GROUP C will receive 0.33% propofol.

Inclusion Criteria is patients ASA grade I and II, Age between 20 and 60 and Posted for elective surgeries under general anesthesia. Patient who refused surgery, Allergy to any component of propofol- egg, soya, ASA III & IV, Patients with cardiac, respiratory, renal or hepatic diseases and age less than 20 years or more than 60 years were excluded from study. Sample size was calculated from study of Sourabh Agarwal¹⁷ with α at 95% , confidence interval of 1.96, β at 80% power and considering dropout sample size was estimated as 50 in each group. Sampling method is by block randomization and allocation concealment by sealed envelope.

Severity of pain is assessed by 4 Point categorical pain scale 0-No pain (negative response to questioning) ,1-Mild pain (pain reported only in response to questioning without any behavioural signs), 2-Moderate pain (pain reported in response to questioning and accompanied by behavioural sign or pain reported spontaneously without questioning) and 3- Severe pain (strong vocal response or response accompanied by facial grimacing, arm withdrawal or tears).

All the patients included in the study underwent a detailed pre anaesthetic checkup. Patient and nearest relatives were given a detailed explanation of the procedure and an informed written consent was taken. Basic laboratory investigations like Hb, RBS, Serum creatinine and ECG was taken in all patient. The patient was fasted for 8 hours and no sedative premedication was given on the night prior to surgery.

The study drugs were prepared at operating room temperature by an anaesthesiologist not involved in the induction of anaesthesia. The patient and investigator were blind regarding the contents of the solution. Drugs and equipments necessary for resuscitation and general anaesthesia were kept ready. On arrival to the operation theatre, a 20 G cannula was inserted on the dorsum of the patient's hand and an intravenous fluid drip was started. Standard monitoring of vital signs was instituted which included Pulse oximetry, Non invasive blood pressure , Heart rate , Respiratory rate and ECG. No patient was given any premedication before the injection. The patients in group A will receive 1% propofol 2 ml over 4 sec. The patients in group B will receive 0.5% propofol 4 ml over 4 sec. The patients in group C will receive 0.33% propofol 6 ml over 4 sec. The diluent used is 5% dextrose. Patient was asked to score the pain on a 4 point categorical pain scale.

Adverse effects like dizziness, weakness allergic reaction if any were noted. Intravenous premedication was given after assessment of pain and haemodynamic parameters. Anaesthesia induction was achieved with Propofol in a dose of 2.5mg/kg. Subsequent muscle relaxation and intubation was accomplished with Suxamethonium 2mg/kg intravenously and anaesthesia was maintained with N2O and O2 and Isoflurane. Injection Vecuronium was used as muscle relaxant intra operatively.

All the data were tabulated and comparison drawn between the groups. Data was entered into MS Excel and analysed using SPSS version 16.0 software.

II. Observation And Results

The data was collected using a prestructural proforma.

Table-1 Comparison of demographic variables

	Undiluted propofol	Propofol 0.5%	propofol 0.3%
Age(mean+S.D)	42.7±12.1	42.3±10.5	44±10.1
Weight(mean+S.D)	60.2±6.6	59.9±6.2	58.5±4.2
Sex	36%(M)	34%(M)	32%(M)
	64%(F)	66%(F)	68%(F)

The mean age of patients in group A is 42.7, those in group b is 42.3, in group C is 44.

P value is 0.578- all the 3 groups are comparable for weight.

The mean weight of patients in group A – is 60.2 while those in group B is 59.9 and in group C is 58.5. P value is 0.286 – all the 3 groups are comparable for weight.

Table 2:- comparison of pain based on group

Pain	Undiluted Propofol		Propofol 0.5%		Propofol 0.33%		X ²	P value
	Count	Percent	count	percent	count	Percent		
No pain	0	0.0	0	0.0	46	92.0	129.97	0.00
Mild pain	0	0.0	9	18	4	8%		
Moderate pain	14	28.0	0	0.0	0	0.0		
Severe pain	36	72	0	0.0	0	0.0		

Undiluted propofol versus propofol 0.5% dilution $Z=7.49, p=0.00$

Undiluted propofol versus propofol 0.33% dilution $Z=9.33, p=0.000$

Propofol 0.5% dilution versus propofol 0.33% dilution $Z=9.31, p=0.000$

The overall incidence of pain among 150 subjects was 69.3%, 100% in group A, 100% IN GROUO b AND 8% IN GROUP c. In the group of 50 who received undiluted propofol, 36(72%) reported severe pain, 14(28%) reported moderated pain, In the group which received 0.5% propofol, 41(82%) reported moderate pain while 9(18%) experienced mild pain. The group which received 0.33% propofol, 4(8%) experienced mild pain while 46(92%) reported no pain.

III. Discussion

Clinically propofol belongs to the sterically hindered phenols. This structure is associated with chemical stability and less toxicity than phenols. However, like the phenols, propofol irritates the skin, mucous membrane and intima.

Pain at the site of injection of propofol is well documented in the literature with the incidence up to 90%. Its severity ranges from mild to severe and sometimes associated with limb retraction. The pain by propofol has an onset latency of between 10 and 20 s and is probably an indirect effect mediated via the kinin cascade. Propofol belongs to the group of phenols that irritate the skin, mucous membranes, and venous intima. Propofol, by its indirect action on the endothelium, activates the kallikrein-kinin system and releases bradykinin, thus producing venous dilation and hyperpermeability. It increases the contact between the aqueous phase of propofol and the free nerve endings, thus producing the sensation of pain. Propofol, when drawn up in a disposable syringe, may lead to formation of irritants and may result in producing pain sensation. It has been confirmed that propofol strips the silicone lubricant from the inside barrel of plastic syringes. Pain on injection is obviously not important enough to negate its pharmacokinetic and pharmacodynamic advantages over other drugs that have led to this popularity. It is, however, troublesome and unpleasant, particularly during sedation. Various modalities have been tried to reduce the incidence and severity of propofol induced pain.⁴⁻¹¹ In the present study effect of dilution of propofol on propofol induced injection pain at injection site is compared among the 3 groups, Group A receiving 1% propofol, Group B receiving 0.5% propofol and Group C receiving 0.33% propofol.

In the present study, considering the socio demographic data there was no significant difference between the three groups with regard to age, sex and weight. Among the clinical variables the three groups were comparable with respect to ASA physical status and Hemodynamic parameters ($p>0.01$).

36 people (72%) felt severe pain among the 50 who received undiluted propofol and 14 people (28%) felt moderate pain. Of the 50 patients who received propofol 0.5%, 41 (82%) felt moderate pain while 9 patients (18%) felt mild pain. Of the 50 patients who received 0.33% propofol 46 (92%) felt no pain while 4 (8%) felt mild pain.

In a study by Sourabh Aggarwal¹² no pain in 20% of patients receiving triple dilution propofol and severity was reduced in others compared to 1% and 0.5% propofol.

In our study comparing the pain on injection between the undiluted propofol group the half diluted group (0.5%), the reduction in pain was statistically significant in the half diluted group ($p=0.000$).

Comparing half diluted (0.5%) propofol group with triple diluted group, pain was significantly less in triple (0.33%) group ($p=0.000$) opofol.

IV. Limitation Of The Study

None of the study subjects received any premedication prior to the surgery in the current study. Hence there is possibility of apprehension among the subjects prior to the surgery. This may bias their pain interpretation

Conclusion: The study was conducted to evaluate the effect of dilution on propofol induced injection at the injection site. In this study, dilution of propofol to 0.5% significantly reduced the incidence as well as severity of pain as compared to undiluted propofol. Dilution of propofol to 0.33% (one third dilution) significantly reduced the incidence and severity of pain on injection compared to undiluted propofol as well as 0.5% dilution of propofol.

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