

PROSPECTIVE AND COMPARATIVE STUDY OF THE ANALGESIC EFFECT OF INTRAVENOUS 2% XYLOCARD VERSUS INTRAVENOUS TRAMADOL IN AMELIORATING PROPOFOL INJECTION PAIN

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HOW TO CITE THIS ARTICLE:

T. Jamuna, Y. Nicolas Israel. "Prospective and Comparative Study of the Analgesic Effect of Intravenous 2% Xylocard Versus Intravenous Tramadol in Ameliorating Propofol Injection Pain". Journal of Evidence based Medicine and Healthcare; Volume 2, Issue 24, June 15, 2015; Page: 3529-3539.

ABSTRACT: Intravenous injection of Propofol causes pain at the site of injection. Aim of this study was to compare the analgesic effect of two drugs (Tramadol & 2% Xylocard) in ameliorating Propofol injection pain. The study was randomized and prospective. 100 adult patients of both sexes of ASA status 1 & 2 were randomly assigned into 2 groups of 50 each, where Group 1 received Tramadol intravenously & Group 2 received 2% Xylocard intravenously 1 minute before injection of Propofol. The efficacy of the analgesic effect of Tramadol & 2% Xylocard was compared in ameliorating Propofol injection pain. It was observed that 2% Xylocard has got more potent analgesic action compared to Tramadol (P value < 0.05).

KEYWORDS: Propofol Injection Pain, Analgesic Effect, Tramadol & 2% Xylocard.

INTRODUCTION: Propofol (2, 6-di-isopropyl phenol) introduced clinically in 1977, is an alkyl phenol compound with many characteristics of an ideal anesthetic agent and has been found to be an effective agent for the induction of anesthesia with low incidence of excitatory side effects. Rapid induction and recovery is one of the most advantage of Propofol compared with other drugs used for the same purpose. Although Propofol is widely used as an intravenous anesthetic for induction, pain on injection is major disadvantage with incidence of 28% to 90% in adults. 2% xylocard has been used to alleviate the Propofol induced algesia. Tramadol a centrally acting analgesic also reduces pain due to Propofol. A good number of studies for 2%xylocard and only a few number of studies have been conducted where efficacy for Tramadol in reducing Propofol induced algesia are available. However, studies comparing 2%xylocard with Tramadol in reducing the Propofol induced algesia are scanty. Moreover, Propofol is being used frequently as intravenous anaesthetic agent, making it mandatory to reduce injection pain caused by Propofol. Keeping in view the scanty data available for comparing the efficacy of Tramadol and 2% xylocard in reducing the incidence and severity of pain induced by Propofol, the present study will be carried out.

Intravenous administration of Propofol is associated with a high incidence (3-100%) of pain and discomfort.¹ Various treatments have been tried to alleviate this pain.^{2,3,4} One well accepted therapy is I.V. 2% Xylocard using tourniquet venous occlusion for one minute followed immediately by Propofol injection, renders Propofol injection nearly painless in most cases.^{5,4}

A satisfactory alternative to Xylocard has not yet been found.

Tramadol has been reported to be as effective as Xylocard in reducing Propofol injection pain.⁴ Using venous retention for two minutes, Ketorolac 10mg was also effective in decreasing the incidence of Propofol injection pain.^{6,7}

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Pain on injection is less than or equal to that of Etomidate, equal to that of Methohexital, and greater than after Thiopentone sodium.^{8,9,10}

Pain on injection of propofol is reduced by using a large vein, avoiding veins in dorsum of the hand and adding Xylocard to the Propofol solution.⁸

Propofol produces greater incidence of apnea lasting longer than 30 seconds.^{11,12}

The addition of an Opiate increases the incidence of apnea, especially prolonged apnea.^{11,13}

Addition of an opiate just before induction of anaesthesia appears to augment the decrease in arterial blood pressure.¹⁴

Preceding the Propofol with (using the same injection site as for Propofol) or by prior administration of a potent short acting opioid or 2%Xylocard decreases the incidence of discomfort experienced by the patient.

Changing the composition of the carrier fat emulsion for Propofol to long and medium chain triglycerides decreases the incidence of pain on injection (Doenicke et al., 1997).¹⁵

Accidental intra-arterial injection of Propofol has been described as producing severe pain but no vascular compromise (Holly and Cuthrell, 1990).¹⁶

In this study we designed to compare the peripheral analgesic efficacy of Xylocard and Tramadol in reducing Propofol injection pain.

AIMS AND OBJECTIVES OF THE STUDY: To compare the analgesic effect of 2%Xylocard and Tramadol in ameliorating Propofol injection pain.

The whole study and the interpretation of results were planned to be conducted under a uniform and standard anaesthetic technique.

METHODOLOGY:

PATIENTS AND METHODS: The study was conducted at Sri Venkateshwara Ramnarayan Ruia Hospital, Tirupati. Study period was between February 2014 to September 2014. One hundred patients with ASA Grade I and Grade II, undergoing elective surgeries under general anaesthesia were included in the study, age of the patients ranged from 15-45 years.

Patients with any major systemic illness or those taking medications for pain were excluded from the study. Patients with difficulty in communication, history of epilepsy, cardiac conduction defects, bronchial asthma, allergy to egg, presence of neurological and psychiatric disease, pregnancy, lactating mothers and patients with disorders of lipid metabolism were not included in the study.

STUDY DESIGN: Prospective Randomised Comparative Study.

SAMPLE SIZE: Minimum number of 100 cases will be studied prospectively.

STUDY SUBJECTS: Patients are randomly allocated into two groups, of 50 each.

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Group A(n=50)	:	Receive injection 2%Xylocard 60mg at the rate of 0.5ml/sec, one minute before the injection of propofol 2.5mg/kg at the rate of 0.5ml/sec.
Group B(n=50)	:	Receive injection Tramadol 50mg at the rate of 0.5ml/sec which is prepared in 3ml volume with addition of distilled water, one minute before the injection of propofol 2.5mg/kg at the rate of 0.5ml/sec.

INCLUSION CRITERIA: Adult patients of age 15-45 years of ASA grade I and II posted for elective surgeries under general anaesthesia.

EXCLUSION CRITERIA:

1. Patients with ASA grade III and IV.
2. Patients with history of drug abuse.
3. Patients undergoing emergency surgeries.
4. Unconscious patients.

STUDY SETTING: S. V. R. R. Govt. General Hospital, Tirupati.

STUDY PERIOD: From February 2014 till November 2014.

STUDY METHODS:

PREANAESTHETIC CHECKUP AND PREOPERATIVE INVESTIGATIONS: An informed consent will be taken from the subjects.

At the preanaesthetic interview, the patients will be familiarized with the Visual analogue scale (VAS).

Patients will be kept on overnight fasting of 8-10hrs. Oral diazepam 0.2mg/kg given the night before the surgery.

1. Preoperative questionnaire will be completed, and demographic data will be noted.
2. On arrival into the pre-operative room, patients will be explained about VAS and thereafter, a 20G i.v cannula will be placed into the antecubital vein and ringer lactate infusion will be started.
3. No premedication will be given. Patients will then be shifted to the operating table.

INTRA-OPERATIVE:

1. In the operation theatre before induction, they will be explained about the possibility of pain on injection of anesthetic agents. The patients will be instructed to inform about the amount of pain, they would experience using a VAS from 0-10, with 0 being no pain and 10 being the most excruciating pain.
2. Patient will be kept in supine position. Thereafter i.v infusion will be stopped and arm with i.v line will be elevated for 15 seconds for drainage of venous blood. A pneumatic tourniquet will be placed on the arm with pressure inflated to 50mmHg to produce venous occlusion.
3. Patients will be randomly allocated into two groups, of 50 each.

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Group A(n=50): Receive injection 2%Xylocard 60mg at the rate of 0.5ml/sec, one minute before the injection of propofol 2.5mg/kg at the rate of 0.5ml/sec.

Group B(n=50): Receive injection Tramadol 50mg at the rate of 0.5ml/sec which is prepared in 3ml volume with addition of distilled water, one minute before the injection of propofol 2.5mg/kg at the rate of 0.5ml/sec.

4. The study drugs will be prepared in 3ml volume with addition of distilled water for tramadol and given at the room temperature. All the injections will be given at the port, immediately proximal to i.v cannula at the rate of 0.5ml/sec.
5. One minute after the injection of drug under study, tourniquet will be deflated, followed immediately by i.v injection of propofol (2.5mg/kg) at the rate of 0.5ml/sec, for induction of anaesthesia.
6. VAS will be assessed before the patient lost consciousness. Absence or presence of erythema or wheal in the arm will be observed and recorded.

Intra-operative monitoring: The following parameters will be monitored intra-operatively,

- Pulse rate.
- Blood pressure.
- Continuous O_2 monitoring.
- VAS on propofol injection.
- Monitoring of any allergic reactions to the Study drugs.

The above parameters will be assessed and recorded. The pulse rate and blood pressure will be recorded before and after injection of the propofol and study drugs.

VISUAL ANALOGUE SCALE FOR PAIN ON INJECTION OF PROPOFOL: The intensity of pain on injection of propofol was assessed by the patients using a verbal 10 point scale.

Scale 0 = No pain at all.

Scale 10 = Worst pain imaginable.

STATISTICAL SOFTWARE: Statistical software mainly SPSS 17.00 was used for the analysis of the data and Microsoft Word and excel have been used to generate graphs, table etc.

OBSERVATION AND RESULTS:

PATIENT DATA OF XYLOCARD GROUP:

Sl. No	Demographic characters	Mean $\pm$ S.D
1	Age in years	34.26 $\pm$ 7.94
2	Sex (M:F)	20:30
3	ASA (I:II)	43:7
4	Weight in kgs	50.7 $\pm$ 3.7

Table 1: Demographic Characteristics

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Before injection of propofol		After injection of propofol	
MAP	P.R	MAP	P.R
93.68±6.67	87±9.03	82±6.51	78.54±6.007

Table 2: Hemodynamic Monitoring (Mean±S.D)

After injection of propofol	
Change in MAP	Change in P.R
11.78±4.8	8.3±7.09

Table 3: Changes in map and PR (Mean±S.d)

V.A.S SCORE AFTER PROPOFOL INJECTION: 0.36±0.91.

VAS SCORE	N (%)
0	43 (86%)
More than 0	7 (14%)

Table 4: V.A.S score 0 and more than 0

Sl. No.		n (%)
1	Pain on injection of Xylocard	7 (14%)
2	Redness on injection of Xylocard	0 (0%)

Table 5: Adverse effects with the study drug xylocard

PATIENT DATA OF TRAMADOL GROUP:

Sl. No	Demographic characters	Mean±S.D
1	Age in years	31.66±8.68
2	Sex (M:F)	28:22
3	ASA (I:II)	44:6
4	Weight in kgs	51.2±2.68

Table 1: Demographic characteristics

Before injection of propofol		After injection of propofol	
MAP	P.R	MAP	P.R
94.77±5.51	86±6.21	81.17±5.8	76.4±4.9

Table 2: Hemodynamic monitoring (Mean±S.d)

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After injection of propofol	
Change in MAP	Change in P.R
13.61±7.14	10.46±5.56

Table 3: Changes in map and PR (Mean±S.d)

V.A.S SCORE AFTER PROPOFOL INJECTION: 1.24±1.76.

VAS SCORE	N (%)
0	32 (64%)
More than 0	18 (36%)

Table 4: V.A.S score 0 and more than 0

Sl. No.		N (%)
1	Pain on injection of tramadol	7 (14%)
2	Redness on injection of tramadol	4 (8%)

Table 5: Adverse effects with the study drug tramadol

OBSERVATIONS AND RESULTS:

COMPARISION OF XYLOCARD, TRAMADOL AND PLACEBO GROUPS:

Sl. No	Demographic feature	Group A Xylocard n=50	Group B Tramadol n=50
1	Age in years	34.26±7.94	31.66±8.68
2	Sex (M:F)	20:30	28:22
3	ASA (I:II)	43:7	44:6
4	Weight in kgs	50.7±3.7	51.2±2.68

Table 1: Demographic characters in different groups. (Mean±S.d)

Sl. No	Parameter	Group A Xylocard n=50	Group B Tramadol n=50
1	Change in M.A.P after propofol injection	11.78±4.8	13.61±7.14
2	Change in P.R after propofol injection	8.3±7.09	10.46±5.56

Table 2: Hemodynamic monitoring in different groups. (Mean±S.d)

Sl. No	Groups compared for change in M.A.P after propofol injection	P-value	Remarks
1	Group A VS Group B	>0.05(0.14)	Nil significant

Table 3

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Sl. No	Groups compared for change in P.R after propofol injection	P-value	Remarks
1	Group A VS Group B	>0.05(0.09)	Nil significant

Table 4

V.A.S SCORE AFTER PROPOFOL INJECTION:

Parameter	Group A Xylocard n=50	Group B Tramadol n=50
V.A.S	0.36±0.91	1.24±1.76

Table 5: In different groups Mean±S.d

Sl. No	Groups compared for V.A.S score after propofol injection	P-value	Remarks
1	Group A VS Group B	< 0.05(0.002)	Significant

Table 6

When compared to Tramadol group decrease in the incidence of pain was more and statistically significant in Xylocard group. 14% of the patients in Xylocard group (n=7) and 36% of the patients in tramadol group (n=18) complained of pain on injection of propofol. There was statistically significant difference between Xylocard and tramadol in reducing propofol injection pain. Xylocard could prevent the pain on injection of propofol significantly as compared to Tramadol group.

V.A.S SCORE 0 AND MORE THAN 0:

Parameter	Group A Xylocard n (%)	Group B Tramadol n (%)
V.A.S 0	43 (86%)	32 (64%)
V.A.S >0	7 (14%)	18 (36%)

Table 7: In different groups n (%)

The overall incidence of pain in Xylocard group was 14%(7 patients) when compared to tramadol group with incidence of 36% (18 patients).

The administration of Xylocard could significantly reduce the incidence of pain on injection of propofol 36%in Tramadol group to 14% in Xylocardgroup which is statistically significant. P value<0.05. 0.002by applying Unpaired Student T Test and 0.021 by applying Chi Square Test.

Xylocard is effective than Tramadol in ameliorating the pain on injection of Propofol.

Sl. No	Effect	Group A Xylocard n (%)	Group B Tramadol n (%)
1	Pain on injection of the study drug	7 (14%)	7 (14%)
2	Redness on injection of the study drug	0 (0%)	4 (8%)

Table 8: Adverse effects

The incidence of pain on injection of Xylocard and tramadol is almost the same in both group A and group B, 14%. Redness is observed in only 4 patients in group B on tramadol injection, 8%.

DISCUSSION: Intravenous administration of Propofol is associated with a high incidence (3-100%) of pain and discomfort.¹ Various treatments have been tried to alleviate this pain.^{2,3,4} The incidence ranges from 3-100% and may be recalled as an unpleasant experience by the patient. Many methods have been used to reduce the incidence and severity of this complication with varying success rates.

Propofol (2, 6-di-isopropyl phenol), is an alkyl phenol compound with many characteristics of an ideal oil based intravenous anaesthetic agent and has been found to be an effective agent for the induction of anaesthesia with low incidence of excitatory side effects. Propofol is an emulsion containing 1% (weight/volume) Propofol, 10% Soyabean oil, 2.25% Glycerol and 1.2% purified egg phosphatide. Rapid induction and recovery is one of the most advantage of Propofol compared with other drugs used for the same purpose. Although Propofol is widely used as an intravenous anaesthetic for induction, pain on injection is major disadvantage with incidence of 28% to 90% in adults.

2% xylocard has been used to alleviate the Propofol induced algesia. Tramadol a centrally acting analgesic also reduces pain due to Propofol.

A good number of studies for 2% xylocard and only a few number of studies have been conducted where efficacy for Tramadol in reducing Propofol induced algesia are available. However, studies comparing 2% xylocard with Tramadol in reducing the Propofol induced algesia are scanty. Moreover, Propofol is being used frequently as intravenous anaesthetic agent, making it mandatory to reduce injection pain caused by Propofol. Keeping in view the scanty data available for comparing the efficacy of Tramadol and 2% xylocard in reducing the incidence and severity of pain induced by Propofol, the present study will be carried out.

Intravenous administration of Propofol is associated with a high incidence (3-100%) of pain and discomfort.¹

Various treatments have been tried to alleviate this pain.^{2,3,4} One well accepted therapy is I.V. 2% Xylocard using tourniquet venous occlusion for one minute followed immediately by Propofol injection, renders Propofol injection nearly painless in most cases.^{5,4}

A satisfactory alternative to Xylocard has not yet been found.

Propofol (2-6 di-isopropyl phenol) is an ideal intra-venous induction and maintenance agent for day care surgery as it produces rapid and smooth induction with rapid recovery and minimal post-operative nausea and vomiting.⁸

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One of the most common side effects of propofol is pain during intravenous injection,¹ which is usually distressing to the patients. Minimizing pain on injection of propofol enhances the patient's perception of quality and acceptability of anaesthesia.

Xylocard, a local anaesthetic, reversibly blocks peripheral pathways through action on excitable membrane, and its effectiveness in reducing propofol injection pain has been reported in various studies.

Tramadol is a centrally acting weak μ -receptor agonist and inhibits noradrenaline re-uptake as well as promotes serotonin release. Tramadol is a single entity centrally acting analgesic. Its centrally mediated analgesia is only partially reduced by naloxone, suggesting an important non-opioid mechanism of action. Tramadol produces local sensory block of short duration.¹⁷ This local anaesthetic activity of tramadol might account for its analgesic effect in reducing pain on injection of propofol.

In our study, the incidence of pain on propofol injection after Xylocard (60 mg) was 14% with VAS of 0.36 ± 0.91 , while the incidence of side effects due to injection of Xylocard was 14%.

A comparable incidence of pain on injection of propofol 36% with mean VAS of 1.24 ± 1.76 on a ten point rating scale, after pre-treatment with tramadol 50mg, was found in our study. The incidence of side effects of tramadol injection in our study was 22% out of which 14% patients complained of pain and 8% showed local redness. However, the pain on injection of tramadol was mild and subsided after one minute.

Statistically significant reduction in both the incidence and intensity of pain following i.v injection of propofol was evident in group A, when compared to the group B. The statistical significance among both groups in reducing the incidence of pain on injection of Propofol suggests that Xylocard is effective than Tramadol.

The results of present study provide information which could be of value in a meaningful discussion on the mechanism of action of the peripheral analgesic effects of these frequently used drugs.

It is reasonable to assume that pain on injection of propofol involves only the terminal nerve endings. The inflated tourniquet isolated the arm veins from central circulation, minimizing the central analgesic effect of study drugs in our study, thus presenting a useful model for studying the local action of the drug, similar to modified Biers block.

In the present study the overall incidence of pain on propofol injection is consistent with the incidences found in the previous studies and reaffirms that pain on propofol injection is of significant concern in patients undergoing general anaesthesia. In this study it is observed that 60mg intravenous Xylocard significantly reduced the pain on Propofol injection compared to 50mg intravenous tramadol one minute prior to propofol injection with venous retention of pretreatment without any significant adverse effects. Thus Xylocard is effective than Tramadol in reducing propofol injection pain, which is statistically significant when compared with each other.

SUMMARY: This study was undertaken to compare the analgesic effect of Xylocard and Tramadol in ameliorating Propofol injection pain in patients undergoing general anaesthesia.

In this prospective and comparative study the analgesic effects of intra-venous Xylocard 60mg (3ml) and intravenous tramadol 50mg (3ml) were compared. 100 patients of ASA grade I

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and II between the ages of 15-45years undergoing general anaesthesia were randomly allocated into two equal groups. Group A (n=50) received 60mg Xylocard (3ml) 1 minute prior to the injection of propofol. Group B (n=50) received 50mg (3ml) tramadol 1 minute prior to the injection of propofol. Pain on propofol injection was recorded and compared in different study groups. Results were analysed by Chi Square Test and Unpaired Student T Test. P value <0.05 was considered to be significant.

Incidence of pain was 14% in group A and 36% in group B. The difference in the incidence of pain in group A (Xylocard group) and in group B (tramadol group) was statistically significant P value <0.05 by Chi Square test and Unpaired Student T Test. Xylocard effectively reduced the incidence of pain on Propofol injection when compared to Tramadol group.

CONCLUSION: In conclusion the present study suggests that there is statistically significant difference between Xylocard and tramadol as regards to their efficacy in reducing propofol injection pain.

Xylocard 60mg given one minute prior to Propofol injection could effectively prevent the pain on Propofol injection compared to 50mg of Tramadol given one minute prior to Propofol injection in patients undergoing general anaesthesia.

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Date of Submission: 31/05/2015.
Date of Peer Review: 01/06/2015.
Date of Acceptance: 09/06/2015.
Date of Publishing: 11/06/2015.