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Prospective Randomized Comparative study between Lidocaine versus Dexamethasone to reduce Propofol Induced Vascular Pain During Laparoscopic Surgeries.

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Abstract: *Pain on injection of propofol was ranked by American anaesthesiologists as seventh most important problem of current clinical anaesthesiology. Various methods both non pharmacological and pharmacological, have been tried for alleviating pain during intravenous injection of propofol. Neither a single agent nor method is found to be satisfactory to relieve the pain till date. The aims and objectives of our study was to compare efficacy of lidocaine and dexamethasone to alleviate intravenous propofol induced pain in patients undergoing laparoscopic surgery. 182 patients were randomly allocated into two study groups(n-91) ,Group-L received 0.5 mg/kg of lidocaine hydrochloride and those in Group-D received 0.25 mg/kg of dexamethasone sodium phosphate intravenously. VAS and VRS scores along with hemodynamic parameters were noted at different time intervals. There was no significant difference in mean VAS at different time intervals of the patients of the two groups (p>0.05) and t-test showed that there was no significant difference in mean VRS also at different time intervals of the two groups (p>0.05). From this study it can be concluded that intravenous dexamethasone can effectively reduce propofol induced vascular pain. There is no significant difference in reduction of propofol induced vascular pain between lidocaine and dexamethasone.*

Key Words: *Pain Propofal Lidocaine dexamethasone.*

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I. Introduction

Propofol (2, 6-diisopropylphenol) is the induction agent of choice in millions of patients every year due to its rapid onset and short duration of action, easy titrability and favourable profile for side effects. Pain on injection of propofol was ranked by American anaesthesiologists as seventh most important problem of current clinical anaesthesiology.[1] The pain on injection of propofol is attributed to direct irritation of the venous adventitia leading to release of mediators such as kininogen from kinin cascade. The release and activity of kininogen is regulated by formation of Nitric Oxide (NO) species.[2] Various methods both non pharmacological and pharmacological, have been tried for alleviating pain during intravenous injection of propofol. Neither a single agent nor method is found to be satisfactory to relieve the pain till date.

Pharmacological methods including pre treatment with several agents have been tried, like lidocaine, alfentanyl, thiopentone, ketamine , esmolol, magnesium etc.[3,4]Among the pharmacological methods lidocaine injection, an amide local anesthetic prior to injection of propofol [4] or as an admixture with propofol is one of the two leading methods for reducing pain on injection [3].The pain has been linked to the release of Nitric Oxide (NO) on the vascular endothelial lining.[5] Dexamethasone has been earlier demonstrated to suppress NO production and release.[6] Dexamethasone is widely used for relief of post operative pain[7] and for the treatment of post operative nausea and vomiting.[8] Therefore its favorable profile along with its widespread use, economic feasibility and easy availability justifies the choice to evaluate its action to alleviate pain on injection of propofol. Our study intended to compare efficacy of Lignocaine and dexamethasone in reducing pain induced by intravenous propofol injection.

Laparoscopic surgeries have been selected for this study as identification of a specific type of surgery excludes confounding factors like different durations of the surgery and difference in demographic profiles.

The aims and objectives of the present study was to compare efficacy of lidocaine and dexamethasone to alleviate intravenous propofol induced pain in patients undergoing laparoscopic surgery.

II. Materials And Methods

The study was a prospective randomized double blinded clinical trial done at a teaching hospital in the city of Kolkata during the period of March 2017 to September 2018. After approval from the institutional ethical

committee and obtaining informed consent from all patients admitted for laparoscopic surgeries under general anaesthesia were recruited for the study.

Study Design: prospective randomized double blinded clinical trial.

Study Location: This study was a teaching hospital based study in the city of Kolkata in the Department of anaesthesiology, Surgery and Obstetrics and Gynaecology.

Study duration: March 2017 to September 2018.

Sample Size: 182 patients.

Sample Size calculation: The sample size was calculated by Kelsey's method by using the available data of earlier study by Tan CH and Onsong MK.[9] The power of the study was taken to be 70% and the two sided confidence interval of the study to be 80%. Equal number of participants for both the groups receiving lidocaine (Group-L) and dexamethasone (Group-D) respectively were selected. the total number of participants was calculated to be 182. They were randomly divided in groups of 91 each(n-91) for the two drugs. The final number was achieved after recruited participants adjusted for dropouts (three).

Subjects and selection method: The study population was recruited from consecutive patients admitted in the Departments of Surgery and Obstetrics and Gynaecology for laporoscopic surgeries in a medical college in the city of Kolkata, India.

Inclusion criteria:

1. Patients admitted for laparoscopic surgeries
2. Either sex
3. Aged between 18 to 50 years,
4. American Society of Anaesthesiologists Physical Status I & II ,
5. Consenting to participate in the study.

Exclusion criteria:

1. Patients having hypersensitivity to propofol, soy bean oil, glycerol, egg lecithin, or sodium oleate
2. Patients having small calibre veins on the dorsum of the hands
3. Patients requiring intravenous drug administration prior to induction of anaesthesia
4. Patients requiring a rapid sequence induction of anaesthesia ,
5. Pregnant or lactating mothers and those with a history of chronic pain, with neurologic, psychiatric, significant cardiac, renal, or liver disease
6. Taking sedatives or analgesics preoperatively.

Procedure methodology: After obtaining Institutional ethical committee approval and informed consent, 182 patients were randomly allocated into two study groups(n-91) by computerized randomization tables. The patients were counseled about the terminology pain on injection of propofol and were familiarized with the scoring scale prior to the scheduled surgery. The patients allocated in Group-L received 0.5 mg/kg of lidocaine hydrochloride and those in Group-D received 0.25 mg/kg of dexamethasone sodium phosphate intravenously, both diluted upto 5 ml with normal saline in identical syringes prior to administering 0.5 mg/kg (i.e. approximately one fourth dose of induction) LCT- propofol (long chain triglyceride) by intravenous route. The necessary injection propofol for induction of anaesthesia (2 – 4 mg/kg) was administered after obtaining the pain score.

All patients were kept in fasting state in respect to solid foods for≥ 6 hours. All patients were pre medicated with tab. Alprazolam (0.5 mg) and tab. Ranitidine (150mg) the night before. Prior to the transfer to the operating room, an 18-gauge intravenous cannula was inserted into the largest vein on the dorsum of the non dominant hand, and an infusion of Lactated Ringer's solution was started at a rate of 3-4ml/kg/hr. In addition, an appropriately sized sphygmomanometer cuff was placed on the upper arm above the cannulation site. Patients were asked to rate the severity of pain experienced on insertion of the IV cannula using a visual analogue scale (VAS) and a verbal rating score (VRS) for pain. VAS scoring is done using a 10 point graded scale with 0 being no pain and 10 being unbearable or severe pain. In the Verbal Rating Score, score is assigned from 0 to 3. Score '0' is equivalent to 'no pain'. Score '1' is equivalent to 'mild pain. Score '2 'is equivalent to' moderate pains and score '3' is equivalent to 'severe pain. No other drugs were administered through the IV cannula prior to the administration of the study drugs.

Before starting the procedure , standard monitors were attached and all the baseline parameters such as heart rate(HR), non invasive blood pressure (NIBP), oxygen saturation(SPO_2),electrocardiography(ECG), capillary blood glucose(CBG) were recorded. The fluid infusion was stopped, and the arm was elevated for 15 seconds. The blood pressure cuff was manually inflated to bring about venous stasis. The pretreatment study drug was injected over five seconds (5s) into the injection port closest to the cannulation site. The study medication was prepared by a single anaesthesiologist,who was not involved in the study. The anaesthesiologist

who administered the study drug was blinded to the study group. The patient was then asked to rate the discomfort associated with the injection using VAS scale and VRS score. The investigator was also made accustomed to the use of a VAS and VRS scale. Blood pressure, Heart rate, SPO_2 was noted and recorded . Two minutes following the study drug administration, the blood pressure cuff was deflated manually, and the intravenous infusion restarted by releasing the roller clamp. Blood pressure, Heart rate, SPO_2 were noted and recorded. Then approximately one fourth of induction dose i.e. 0.5 mg/kg propofol was injected through the same injection port over 5 seconds. A spontaneous complaint of pain by the patient was noted. Hand withdrawal from the injection was regarded as a VAS score of 10 and VRS of 3. If there were none, 15 seconds following the injection the patient was asked to rate the discomfort associated with the propofol injection. Behavioral signs were also recorded. Blood pressure, heart rate, SPO_2 was noted and recorded as values '15'. VAS and VRS scores were again noted at 30 seconds from injection of the test dose of propofol. Blood pressure, heart rate, SPO_2 were noted and recorded as values '30'. Anaesthesia was induced in the standard manner with the remaining dose of propofol and anesthetic management was at the discretion of the anaesthesiologist. Following recovery from anaesthesia capillary blood glucose was measured and noted. Patients were visited 24 hours following surgery and questioned about pain, swelling or rashes at the injection site. The time of rescue analgesic first dose administered post operatively was collected from the medicine records. Capillary blood glucose was also checked with aseptic precautions and noted after 24 hours in the post operative period. The anaesthesiologist who is unaware of the study groups recorded the visual responses at the designated intervals. The same personnel also recorded and reported adverse events if any.All data were manually collected and then tabulated using Microsoft Excel ^{TM} 2013.

Statistical analysis: Statistical Analysis was performed with help of Epi Info™ 7.2.2.2 which is a public domain epidemiology software developed by the Centers for Disease Control and Prevention (CDC). Using this software, basic cross-tabulation and frequency distributions were prepared. χ^2 test was used to test the association between different study variables under study. Corrected χ^2 test was used in case of any one of cell frequency was found less than 5 in the bivariate frequency distribution. Test of proportion (Z-test) was used to test the significant difference between two proportions. t-test was used to test the significant difference between means. $P \leq 0.05$ was considered statistically significant.

III. Result

Demographic profile was comparable in both groups as shown in table no1 ,there was no significant difference in gender, mean age, weight and ASA Grade of the patients of the two groups ($p>0.05$).

Table no1: Demographic Parameters of two groups.

Demographic Parameters	Group-L (n=91)	Group-D (n=91)	Test Statistics	p-value
Male : Female	39:52	35 : 56	χ^2 =0.36	0.546
Age (in years)	38.45±7.55	40.16±7.36	t_{180}=1.551	0.123
Weight (in kg)	57.09±6.13	58.62±8.92	t_{180}=1.346	0.180
ASA Grade (I : II)	41:50	41:50	χ^2 = 0.01	0.999

Table no 2 showed that there was no significant difference in mean heart rate at different time intervals except after tourniquet release and at 0 minute of the patients of the two groups ($p>0.05$).

Table no 2: Comparison of HR at different time of the two groups.

HR	HR baseline	HR study drug	HR after tourniquet release	HR-0	HR-15	HR-30
Group-L	73.37±2.75	73.41±2.71	78.04±5.22	83.30±3.70	83.47±3.33	84.02±3.33
Group-D	73.88±4.76	73.88±4.76	76.79±6.08	81.95±3.76	83.66±3.46	82.52±4.40
t- test (t_{180})	1.491	0.878	2.66	2.447	0.371	1.604
P-value	0.138	0.381	0.009	0.015	0.711	0.101

Table no 3 showed that there was no significant difference in mean SBP of the patients of the two groups at different time intervals (p>0.05). And t-test showed that difference in mean DBP was only significant at 30 minute after propofol injection(P ≤0.001).

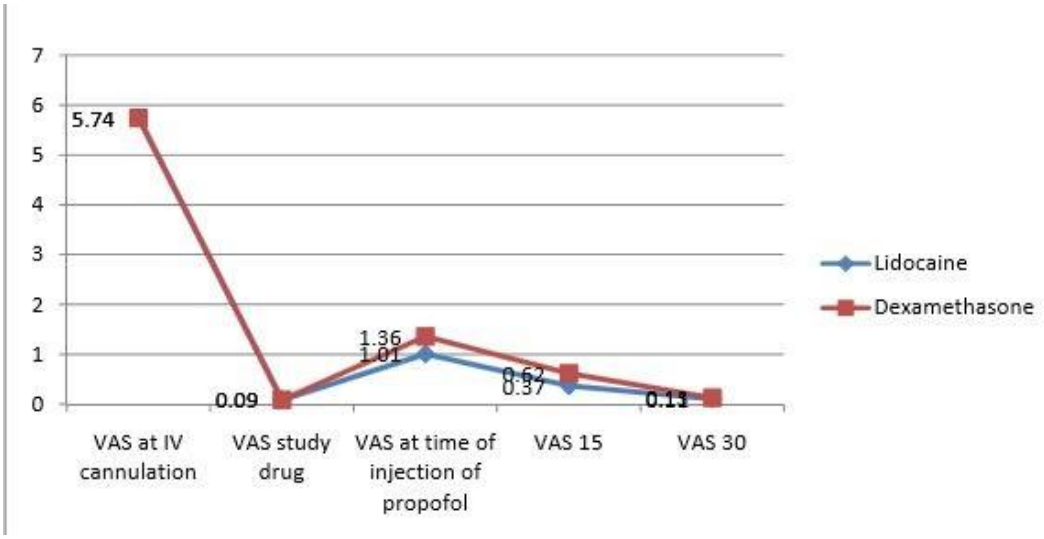
Table no 3: Comparison of Systolic and Diastolic blood pressure of two groups.

		At baseline	At study drug	After tourniquet release	At 30 seconds
SBP	Group-L	121.93±3.81	121.96±3.92	122.40±4.02	131.08±4.47
	Group-D	122.13±±4.76	122.07±3.96	122.88±4.30	131.23±4.65
	P-value	0.435	0.757	0.851	0.820
DBP	Group-L	76.99±4.37	76.88±4.34	76.77±4.44	77.10±4.45
	Group-D	76.46±4.83	76.67±4.44	76.77±4.44	73.65±4.36
	P-value	0.990	0.440	0.749	≤0.001

As shown in table no 4 there was no significant difference in mean VAS at different time intervals of the patients of the two groups (p>0.05). Again t-test showed that there was no significant difference in mean VRS also at different time intervals(table no 4) of the two groups (p>0.05).

Table no 4: Comparison of VAS and VRS of the two groups.

		At IV cannulation	At study drug	At time of injection propofol	At 15 seconds	At 30 seconds
VAS	Group-L	5.74±1.20	0.09±0.41	1.01±1.53	0.37±0.94	0.11±0.46
	Group-D	5.74±1.20	0.09±0.41	1.36±1.76	0.62±1.14	0.13±0.50
	t-test(t_{180})	0.01	0.01	1.438	1.559	0.309
	P-value	0.99	0.99	0.152	0.121	0.757
VRS	Group-L	2.76±0.43	0.07±0.25	0.43±0.62	0.14±0.35	0.05±0.23
	Group-D	2.77±0.42	0.07±0.25	0.58±0.78	0.25±0.46	0.05±0.23
	t-test(t_{180})	0.174	0.01	1.481	1.806	0.01
	P-value	0.862	0.999	0.140	0.073	0.999



In this study the efficacy of both the drugs in preventing severe pain (severe pain has been postulated as VRS 3 and VAS 7 or above, or any active withdrawal of hand or crying) was 100% as none of the patients either in Group D or Group L complained of severe pain at the time of injection or at an interval of 15 and 30 seconds (table no 4). Less than 5% patients in both groups complained of moderate pain spontaneously at the time of injection of propofol which subsided in both groups at 15 and 30 seconds from the time of injection. Hence it was demonstrated that both drugs were competent in preventing any late pain of injection propofol. Patients in both groups complained of mild pain at the point of injection, incidence of which was around 20-30% in both groups, however, p values (0.15, 0.14) were not statistically significant. The highest VAS score recorded in both groups was 5 and the mean score was less than 3.0 in both groups for study time 0 as well as 15 and 30 seconds.

The mean time to rescue analgesia of Group-D (5.34±0.99 hours) was higher than that of Group-L (4.53±1.15 hours) with significant P-value ($p<0.001$). In this study, however 24 hr glucose levels were not increased to a statistically significant level(P-value being 0.092). In addition proportion of sore throat at post-operative 1 hour of the patients treated with lidocaine(68.1%) was significantly higher than that of the patients treated with dexamethasone (30.7%) , P-value ≤ 0.0001.

III. Discussion

Various techniques have been adopted in an effort to reduce the incidence of propofol injection induced pain. Lidocaine has been studied to be the most effective pharmacological agent to prevent propofol induced pain [4]In studies conducted by Jalota et al, in which they performed a meta analysis of data from 177 randomized controlled trials to enumerate the best intervention to prevent pain on injection of propofol; it was found that pre treatment with lidocaine after venous occlusion was the most effective pharmacological method to prevent this pain[3] Tourniquet is applied during application of the test drug to prevent the drug from spreading into the circulation and ensuring maximum concentration at the injection site, as pain on injection of propofol is highly localized to the point of injection due to higher concentration at that site and not get distributed immediately into systemic circulation.[10]The time of tourniquet application was limited to 2 minutes for both study groups following administration of test drugs. The time of application of tourniquet in different studies have varied from 1 minute [11] to 2 minutes [12]. The dose of dexamethasone in this study is 0.25 mg/kg which is higher than the dose used by Kwak et al in their study(i.e. 6 mg was given to each patient)[13] or Karbasi et al (0.15mg/kg).[14] However S Ahmad et al in their study has used same dose of dexamethasone without any adverse reactions. [12] The VAS and VRS scores at the time of release of tourniquet as well as at the time of injection of propofol and after 15 seconds and 30 seconds did not have any significant difference. This is in concurrence to study conducted by Ahmad S et al.[12]

In this study we have tried to assess the time of rescue analgesia by opioids in both groups. This difference is statistically significant (p value<0.001) and dexamethasone can reduce the post operative requirement of analgesics. This finding is similar to the findings elicited by Waldron et al. in their study. [15] There was significant reduction in sore throat at post-operative 1 hour among those patients who received dexamethasone, and this finding corroborates with the study of Bagchi et al.[16]

This study has some limitations also. Pain is a subjective personal experience which has high inter personal variability. We have tried to eliminate this by looking at the VAS and VRS at the time of IV cannulation which is a universally accepted painful stimulus. However injection of propofol through antecubital vein has an effect in reduction of pain comparable to pre treatment with lidocaine. In this study we have not selected the antecubital vein for IV cannulation, as cannula is difficult to maintain at this site which is overlying elbow joint. We have not administered Inj. fentanyl or any other analgesics prior to administration of propofol for excluding confounding effect.The plasma level of drugs were not monitored due to economic and infrastructural constraints. Placebo was not used in the course of the study as pain on injection of propofol can be very distressing to the patient and denying preventive measures was considered unethical.

IV. Conclusion

Intravenous dexamethasone can effectively reduce propofol induced vascular pain. There is no significant difference in reduction of propofol induced vascular pain between lidocaine and dexamethasone. Dexamethasone and propofol combination in the intravenous route do not produce significant adverse haemodynamic effect. .

References

[1]. Marcario A, Weinger M , Truong P, Lee M. Which clinical anaesthesia outcomes are both common and important to avoid? The perspective of a panel expert anaesthesiologist AnesthAnalg 1999; 88:1085-91.
[2]. Tan CH, Onsong MK. Pain on injection of propofol. Anaesthesia. 1998, May; 53(5):468-76.
[3]. Jalota L, Kalira Vicki, George E, Shi Y, Hornuss C, Radke O et al. Prevention of pain of injection of Propofol: Systematic Review and meta analysis, BMJ 2011;342:d1110.
[4]. Vuyk J, Sitsen E, Reekers M. Intravenous Anesthetics. In: Miller RD ed. Millers's Anaesthesia, 8th edition. Philadelphia: Elsevier, W.B. Saunders, 2015;821-863.
[5]. Kindgen-Milles D, Arndt JO, Nitric oxide as a chemical link in the generation of pain from veins in humans, Pain 1996; 64: 139–142.
[6]. Huo Y, Rangarajan P, Ling EA, Dheen ST. Dexamethasone inhibits the NOXdependent ROS production via suppression of MKP-1-dependent MAPK pathways in activated microglia, BMC Neuroscience 2011;12: 49.
[7]. Waldron NH, Jones CA, Gan TJ, Allen TK, Habib AS. Impact of perioperative dexamethasone on postoperative analgesia and side-effects: systematic review and meta analysis. BJA 2012;110(2):191-200.
[8]. Oliveira GS Jr, Castro-Alves LJ, Ahmed S, Kendall MC, McCarthy RJ. Dexamethasone to prevent post operative nausea and vomiting: An updated metaanalysis of randomized controlled trials, Anesth Analg 2013;116:58-74.
[9]. Tan CH, Onsong MK. Pain on injection of propofol. Anaesthesia. 1998, May; 53(5):468-76.

[10]. Stokes DN, Robson N, Hutton P. Effect of diluting propofol on the incidence of pain on injection and venous sequelae. Br J Anaesth 1989;62:202-3.
[11]. Shivanna S, Priye S, Singh D, Jagannath S, Mudassar S, Reddy DP. Efficacy of methylprednisolone and lignocaine on propofol injection pain: A randomised, double-blind, prospective study in adult cardiac surgical patients. Indian J Anaesth 2016;60:848-51
[12]. Ahmad S, De Oliveira GS Jr, Fitzgerald PC, McCarthy RJ. The effect of intravenous dexamethasone and lidocaine on propofol-induced vascular pain: a randomized double-blinded placebo-controlled trial. Pain Res Treat. 2013; 2013:734531. doi : 10.1155/2013/734531.
[13]. Kwak H, Ha J, Kim Y, Jeon Y. Efficacy of combination intravenous lidocaine and dexamethasone on propofol injection pain: a randomized, double blind, prospective study in adult Korean Surgical patients. Clin Ther.2008 Jun; 30(6), 1113-9.
[14]. Seyyed Hassan Karbasi, Pooya Derakhshan, Hossein Hashemi.The Effect of Dexamethasone in Reducing Propofol Injection Pain in 6 to 13-Year-Old Children Undergoing Adenotonsillectomy Surgery: A Double-Blind Clinical Trial: Journal of Surgery and Trauma 2016; 4(3-4): 33-37.
[15]. Kay B, Rolly G. ICI.35868, a new intravenous induction agent. Acta Anaesthesiol Belg 1977; 28:303-16.
[16]. Bagchi D, Mandal MC, Das S, Sahoo T, Basu SR, Sarkar S. Efficacy of intravenous dexamethasone to reduce incidence of postoperative sore throat. A prospective randomized controlled trial. J Anaesthesiol Clin Pharmacol, 2012 Oct; 28(4): 477-80.

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