A COMPARISON OF LIDOCAINE AND LIDOCAINE METOCLOPRAMIDE COMBINATION IN PREVENTION OF PAIN DURING INJECTION OF PROPOFOL

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ABSTRACT: BACKGROUND: Combination of lidocaine hydrochloride and metoclopramide is most effective for prevention of pain during propofol injection than by lidocaine hydrochloride alone. **METHODS:** Ninety healthy patients of both sex aged between 5–50 years ASA physical status I & II, scheduled for short surgical procedures. Patients in group 1(n=30) were induced with propofol 2-2.5mg/kg i.v, patients in group 2(n=30) were induced with propofol 2-2.5mg/kg i.v and lidocaine hydrochloride 20mg (Preservative free) i.v, and group 3(n=30) patients were induced with propofol 2-2.5mg/kg i.v and lidocaine hydrochloride 20mg (Preservative free) and metoclopramide 10 mg. Pain was assessed at 0, 5 and 10 seconds by verbal pain scale. The mean blood pressure (MBP) and heart rate (HR) were recorded as the base value, before induction and at 0, 5 and 10 seconds respectively. **RESULTS:** Pain after administration of group 1 shows increase as the duration of time elapsed, at the time of administration it is 83.33%, after 5 & 10 secs it had increased to 86.66% and 93.33% respectively. Pain after administration of group 2 cases increased as the time elapsed at the time of administration it is 66.66% and 5 & 10 secs it is 80.00% and 93.33% respectively. Pain after administration of group 3 cases shows decreased incidence of pain as the time lapsed in comparison with group 1 & 2 respectively. **CONCLUSION:** Combination of lidocaine hydrochloride and metoclopramide is most effective for prevention of pain during propofol injection than by lidocaine hydrochloride alone.

KEYWORDS: Cardiovascular system, Drug synergism, Propofol, lidocaine hydrochloride, Metoclopramide.

INTRODUCTION: Pain on injection with propofol is a common problem and can be very distressing to the patient. Incidence of pain varies between 28% and 90% (Mangar D et al)¹ in adults and 25% to 85% in children (Valtonen M et al)^{2,3} The younger the child, the higher is the incidence and severity of propofol injection pain. Factors known to influence the incidence of venous discomfort include: site of I.V cannula, speed of injection, temperature of propofol and pre-treatment with sedatives and opioids.¹

Pain on injection of propofol can be immediate or delayed. Immediate pain probably results from a direct irritant effect whereas delayed pain probably results from an indirect effect via the kinin cascade. Delayed pain has latency of between 10 and 20 secs (Briggs LP et LL).⁴ The sensation produced is usually described as tingling, cold or numbing or at its worst, a severe burning pain proximal to the site of injection.

Doenicke et al⁵ study demonstrated that with addition of lipid there is reduction in pain on injection of propofol. With lipid addition, a higher percentage of propofol is absorbed by the fat

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particles and a smaller concentration of propofol in the aqueous phase of the emulsion hence reduction in pain on injection of propofol.

MATERIAL AND METHODS: The present study entitled "A comparison of lidocaine and lidocaine metoclopramide combination in prevention of pain during injection of propofol" were carried out in the department of anaesthesiology collaboration with pediatric department, G.R Medical college and J. A Group of hospitals, Gwalior. The study was done in 90 healthy patients of both sex, aged between 5-50 years of ASA grade I & II, scheduled for short surgical procedure, after approval from institutional ethical committee. The study was carried out in patients undergoing short surgical procedures like medical termination of pregnancy (MTP), MTP with LTT, MTP with CuT, Plain laparoscopic tubectomy (LTT) diagnostic laparoscopy, Dilatation and curettage, suction and evacuation, incision and drainage and close fracture reduction in (pediatric & adult pts) orthopaedics etc.

Criteria for inclusion of patients:

1. All patients with ASA grade I and II only.
2. Patients without any systemic diseases.
3. All patients of age 5-50 yrs.
4. Pre anaesthetic check-up was done 1 day prior to day of admission.
5. Well informed written consent was taken.

Criteria for Exclusion of Patients:

1. Those taking analgesic and sedative agents.
2. Patients with hypersensitivity to propofol, lidocaine and metoclopramide.
3. Any patient with history of Hypertension and diabetes mellitus or currently under treatment for respiratory diseases.
4. Patient with history of myocardial infarction or cerebral infarction, patients with dementia or any psychiatric illness.
5. Patient under dialysis treatment due to renal failure or patients in whom it is difficult to perform endotracheal intubation, at over Mallampati class 3 or 4.

All patients received uniform premedication of inj. glycopyrrolate 0.2mg IM ½ hr before start of anaesthesia.

After the patient was admitted to operation room an electrocardiogram (ECG), non-invasive manometer, pulse oximeter were attached to the patient. All patients were asked to breathe deeply 10l/min oxygen 8 times for one minute.

Patients were Randomly divided into 3 groups of 30 each. The groups were as follows:

Group 1: Patients were induced with propofol 2-2.5mg/kg i.v.

Group 2: Patients in group 2 (n=30) were induced with propofol 2-2.5mg/kg i.v and lidocaine hydrochloride 20 mg (Preservative free) i.v.

Group 3: (n=30) patients were induced with propofol 2-2.5mg/kg i.v and lidocaine hydrochloride 20mg (preservative free) and metoclopramide 10mg.

Various scales are frequently used for measuring the intensity of pain like visual analogue scale (VAS), numeric pain scale (NPS), pain face scale (PFS), verbal pain scale (VPS) etc. in our study

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we have used verbal pain scale (VPS) because it's simple to use, not subjective and appropriate hand eye coordination of the patient is not required as the patient is in altered state of consciousness.

Technique: All the patients were premedicated with injection glycopyrrolate 0.2mg intramuscular half hour before surgery. All patients were explained the technique and well informed written consent was taken. All patients were tested for sensitivity to propofol, lidocaine and metoclopramide. An 18 to 22 gauge cannula was placed in a fresh vein on the dorsum of the hand of the upper limbs. By the intravenous cannula used for administration of study drugs no intravenous fluids was given as it can cause dilution of administered drug. Through the 18 to 22 gauge cannula in the other limb intravenous fluids were administered to the patient. A pneumatic tourniquet was applied on the arm of the limb on which cannula for giving drugs was placed. Pneumatic tourniquet was inflated to 70 mmHg to produce venous occlusion. The inflation of the tourniquet occludes the IV line thereby the study drug stayed in the vein and did not enter systemic circulation to produce any systemic effects as long as the tourniquet was inflated. The study drugs were injected after inflation of the tourniquet. After one minute the tourniquet was deflated and followed by 1/4th of total calculated dose of propofol immediately. All patients were graded for pain felt on verbal pain scale (VPS) at 0, 5 and 10 seconds. All the drugs at the time of use were at room temperature and propofol used in each case was of same formulation. Thereafter, the induction of anaesthesia was continues as per plan. Patients were asked to recall if there was any pain during injection of propofol in the recovery room and incidence of pain was graded as 0-no recall of pain & 1-recall of pain present.

For statistical analysis, the study used SPSS (version 13.0) and all results were indicated as mean $\pm$ standard deviation. inter group comparison by time points was conducted using an unpaired T test and intra group variations of MBP and HR according to time were analysed by using repeated ANOVA measures. If the p value was < 0.05, it was determined to be statistically significant.

RESULTS:

	Group 1	Group 2	Group 3
Gender (M/F)	4/26	9/21	3/27
Age (yrs)	29.27 $\pm$ 5.37	31.77 $\pm$ 7.87	39.33 $\pm$ 6.61
Weight (Kgs)	49.03 $\pm$ 9.44	52.87 $\pm$ 9.16	53.33 $\pm$ 9.95

Table 1: Demographic data (mean $\pm$ SD)

Pre intervention mean heart rate (HR) with standard deviation (SD) in group 1 is 90.13 $\pm$ 7.718, in group 2 is 80.47 $\pm$ 6.776, and in group 3 is 87.47 $\pm$ 13.544. post intervention mean HR with SD in group 1 is 97.17 $\pm$ 7.400, in group 2 is 85.93 $\pm$ 7.017, and in group 3 is 93.03 $\pm$ 13.12.

Pre intervention mean systolic blood pressure with SD in group 1 is 124.87 $\pm$ 4.805, in group 2 is 121.10 $\pm$ 5.803 and in group 3 is 127.40 $\pm$ 6.262. Post intervention MBP with SD in group 1 is 121.93 $\pm$ 5.317, in group 2 is 117.60 $\pm$ 5.882, and in group 3 is 126.33 $\pm$ 6.036.

Pre intervention mean of diastolic blood pressure (DBP) with standard deviation (SD) in group 1 is 80.93 $\pm$ 5.112, in group 2 80.33 $\pm$ 5.683 and in group 3 is 84.20 $\pm$ 7.618. Post intervention DBP with SD in group 1 is 81.00 $\pm$ 4.948, in group 2 is 80.07 $\pm$ 5.620, and in group 3 is 83.50 $\pm$ 7.138.

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Pain after administration of propofol in group 1 cases show increase as the duration of time elapsed. At the time of administration it is 83.33% after 5 second and 10 seconds it increased to 86.66% and 93.33% respectively. (See Table 2)

Pain after administration of lidocaine hydrochloride 20 mg (Preservative free) in group 2 cases increased as the time elapsed. At the time of administration it is 66.66%, 80% at 5 seconds and 93.33% at 10 seconds respectively. (See Table 3)

Pain after administration of lidocaine hydrochloride 20 mg (Preservative free) and metoclopramide 10 mg combination in group 3 cases decreased incidence of pain as the time elapsed in comparison with group 1 and 2. (See Table 4)

Pain scale	0 secs		5 secs		10 secs	
	no of cases	%	no of cases	%	no of cases	%
No pain(0)	5	16.66	4	13.33	2	6.66
Mild pain (1)	5	16.66	5	16.66	3	10.00
Moderate pain(2)	11	36.66	7	23.33	10	33.33
Severe Pain(3)	9	30.00	14	46.66	15	50.00
1+2+3	25	83.33	26	86.66	28	93.33
total	30	99.99	30	99.99	30	99.99

Table 2: Distribution of pain score in group 1 at 0, 5 and 10 seconds

Pain scale	0 secs		5 secs		10 secs	
	no of cases	%	no of cases	%	no of cases	%
No pain(0)	10	33.33	6	20.00	2	6.66
Mild pain (1)	15	50.00	18	60.00	13	43.33
Moderate pain(2)	5	16.66	5	16.00	13	43.33
Severe Pain(3)	0	0.00	1	3.33	2	6.66
1+2+3	20	66.66	24	80.00	28	93.33
total	30	99.99	30	99.99	30	99.99

Table 3: Distribution of pain score in group 2 at 0, 5 and 10 seconds

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Pain scale	0 secs		5 secs		10 secs	
	no of cases	%	no of cases	%	no of cases	%
No pain(0)	5	16.66	27	90.00	27	90.00
Mild pain (1)	7	23.33	3	10.00	3	10.00
Moderate pain(2)	11	36.66	0	0.00	0	0.00
Severe Pain(3)	7	23.33	0	0.00	0	0.00
1+2+3	25	83.33	3	10.00	3	10.00
total	30	99.98	30	99.99	30	99.99

Table 4: Distribution of pain score in group 3 at 0, 5 and 10 seconds

Group 1	df.	Mean of square	f'-factor	p Value
Group 2	3	3.981	46.583	0.000
Group 3	3	1.919	54.889	0.000

Table 5: One way ANOVA table 0 seconds

Group 1	df.	Mean of square	f'-factor	p Value
Group 2	3	2.756	10.693	0.000
Group 3	3	1.270	11.556	0.000

Table 6: One way ANOVA table 5 seconds

Group 1	df.	Mean of square	f'-factor	p Value
Group 2	3	4.589	68.833	0.000
Group 3	3	2.511	35.612	0.000

Table 7: One way ANOVA table 10 seconds

Comparisons of mean of pain score between group 1, 2, 3 at 0, 5 and 10 seconds found to be significant at p value <0.01, confidence interval 99.00%. On comparing variance of square, incidence of pain in various groups at 0, 5 and 10 seconds is statistically significant (p=0.000) as per one way ANOVA table. The result is statistically validated by 'f'-factor.

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DISCUSSION: Result of this study, it is identified that combination of lidocaine hydrochloride and metoclopramide is most effective for prevention of pain during propofol injection than by lidocaine hydrochloride alone.

Pain was assessed by verbal pain scale grading done as per scale score immediately after administration of drug followed by interval of 0, 5 and 10 seconds. Grading of pain scale is as- GRADE 0: none (negative response to questioning) GRADE 1: mild pain (pain reported only in response to questioning, without any behavioural signs) GRADE 2: moderate pain (pain reported in response to questioning and accompanied by behavioural signs, or pain reported spontaneously without questioning) GRADE 3: severe pain (strong vocal response, or response accompanied by facial grimacing, arm withdrawal or tears).

In group 1 incidence as well as severity of pain are increasing, this suggests that propofol apart from irritating the nerve endings of intima also cause pain by other mechanism which does not come into play immediately. Incidence of pain varies between 28% and 90% (Mangar D et al)¹ in adults and 25% to 85% in children (Valtonen M et al).^{2,3}

The incidence of pain at 0, 5 and 10 seconds in group 2 were 66.66%, 80.00% and 93.33% respectively. Causes suggest that lidocaine apart from its local action also effect the delayed mechanism of propofol induced pain. As per Eriksson et al⁶ study addition of lidocaine to propofol causes migration of propofol from aqueous phase to lipid phase and this migration causes change in pH. Thereby migration of propofol to lipid phase, change in pH and local anaesthetic action are responsible for propofol injection pain prevention on its addition. Nakane et al⁷ postulated that the lipid solvent for propofol activates the plasma kallikrein-kinin system and produces bradykinin that modifies the injected local vein. This modification of the peripheral vein may increase the contact between the aqueous phase propofol and free nerve endings of the vessels, resulting in aggravation of propofol induced pain.

According to Mangar et al¹ also lidocaine administered after tourniquet inflated to 50 mmHg for 1 min virtually abolishes the pain with intravenous propofol. The incidence of pain and of moderate and severe pain in group 2 in Hansen SH et al.⁸ Study was 32.5% and 5 % respectively. Scott et al,⁹ Johnson et al,¹⁰ Gehan et al,¹¹ Adachi et al¹², Sharpe et al,¹³ Asik et al,¹⁴ Kunitz et al¹⁵ and Schaub et al¹⁶ study also demonstrated that use of lidocaine significantly reduces pain on propofol injection. The incidence of postoperative recall of propofol injection pain in recovery room in lidocaine group was 23.33%. The incidence of postoperative recall of pain is lower in lidocaine group compared to propofol group.

According to Bruton et al¹⁷ the chemical structure of metoclopramide is an analog of the local anaesthetic procaine or anti arrhythmic procainamide, in the current study a possible local anaesthetic action by metoclopramide was further supported. According to Albibi R. and Watcha M.F¹⁸ metoclopramide is a benzamide with both central and peripheral actions enhance the analgesic efficacy of lidocaine for controlling pain during propofol injection. According to Fujii Y and Nakayama M¹⁹ venous occlusion with a rubber tourniquet represents a useful mode for investigating the peripheral actions of study drug in the absence of a central effect, similar to a modified bier block.

Large dose (more than 20 mg) metoclopramide occasionally causes dystonic and extra pyramidal reactions. In this study however, patients received metoclopramide in dose of up to 10mg, and none experienced extra pyramidal disturbance after recovery from anaesthesia.

According to W. J Liaw et al²⁰ I.V retention of metoclopramide with tourniquet is as good as lidocaine and may be be useful alternative for reducing pain on propofol injection.

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Ganta and co workers²¹ studied intervenous injection of metoclopramide 5 mg before the induction of anaesthesia with propofol reduced the incidence of pain on injection ($p=0.001$ compared with saline)

Maroof and Co workers²² have demonstrated the analgesic efficacy of metoclopramide 10mg administered intravenously, using a venous tourniquet for one minute before propofol injection for reducing propofol induced pain on injection.

Fujii and Uemura²³ have demonstrated pre-treatment of a dorsal hand vein with metoclopramide in dose of 5 to 10 mg, with venous occlusion for one minute, effectively decreases the incidence of pain caused by propofol injection.

Thus it is evident that combination of lidocaine hydrochloride and metoclopramide is most effective for prevention of pain during propofol injection followed by lidocaine.

BIBLIOGRAPHY:

1. Mangar D, Holak EJ. Tourniquet at 50 mmHg followed by intravenous lidocaine diminishes hand pain associated with propofol injection. *Anesth Analg* 1992; 74: 250-2.
2. Valtonen M, Iisalo E, Kanto J and Rosenberg P. Propofol as an induction agent in children: pain on injection and pharmacokinetics. *Acta Anaesthesiol Scand* 1989; 33: 152-5.
3. Valtonen M, Iisalo E, Kanto J and Tikkanen J. Comparison between propofol and thiopentone for induction of anaesthesia in children. *Anaesthesia* 1988; 43: 696-9.
4. Briggs LP, Clarke RSJ, Dundee JW, Moore J, Bahar M, Wright PJ. Use of di-isopropyl phenol as main agent for short procedures. *Br J Anesth* 1981; 53: 1197-201.
5. Doenicke AW, Roizen MF, Rau J, Kellermann W, Babl J. reducing pain during propofol injection: the role of solvent. *Anesth Analg* 1996; 82: 472-4.
6. Eriksson M, Engleson S, Niklasson F, Hartvig P. Effect of lidocaine and pH on propofol induced pain. *Br J Anesth* 1997; 78: 502-6.
7. Nakane M and Iwama H. a potential mechanism of propofol- induced pain on injection based on studies using nafamostat mesylate. *Br J Anesth* 1999; 83: 397-404.
8. Hansen SH, Westergaard V, Krogh BL, Svendsen HP. The reduction of pain on injection of propofol: the effect of addition of lidocaine. *Acta Anaesthesiol Scand* 1988; 32: 502-4.
9. Scott RPF, Saunders DA, Normon J. propofol: clinical strategies for preventing pain on injection. *Anaesthesia* 1988; 43: 492-4.
10. Johnson RA, Harper NJN, Chadwick S, Vohra A. pain on injection of propofol. *Anaesthesia* 1990; 45: 439-42.
11. Gehan G, Karoubi P, Quinet F, Leroy A, Rathat C, Pourriat JL. Optimal dose of lidocaine for preventing pain on injection of propofol. *Br J Anesth* 1991; 66: 324-06.
12. Adachi H, Inagaki Y, Harada T, Tsubokura H, Otsuki A, Hirose J, Ishibe Y. effects of concentration and dosage of lidocaine on preventing pain on injection of propofol. *Masui* 2002 Sep; 51 (9): 983-7.
13. Sharpe P, Asif M, Victoria A, Rowbotham DJ. Iontophoretically applied lidocaine and the prevention of pain associated with the injection of propofol: a comparison with intravenous lidocaine. *Eur J Anaesthesiol* 2002 Mar; 19 (3): 170-2.
14. Asik I, Yorukoglu D, Gulay I, Tununay M. Pain on injection of propofol: comparison of metoprolol with lidocaine. *Eur J Anaesthesiol* 2003 Jun; 20 (6): 487-9.

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15. Kunitz O, Losing R, Schulz-Stubner S, Haaf-Von-Below S, Rossaint R, Kuhlen R. Propofol-LCT versus propofol-MCT/LCT with or without lidocaine- a comparison on pain on injection. *Anaesthesiol Anesth Analg Intensivemed Notfallmed Schmerzther* 2004 jan; 39 (1): 10-4.
16. Schaub E, Kern C, Landau R. pain on injection: a double blind comparison of propofol with lidocaine pretreatment versus propofol formulated with long- and medium – chain triglycerides. *Anesth Analg* 2004; 99: 1699-1702.
17. Brunton LL. Agents affecting gastrointestinal water flux and motility; emesis and anti-emesis: bile acids and pancreatic enzymes. In: Hardman JG, Limbird LE, eds. *The pharmacological basis of therapeutics*, 9th ed. New York: McGraw Hill, 1996; 332, 868, 932.
18. Albibi R, McCullum RW. Metoclopramide: Pharmacology and clinical application. *Ann Intern Med* 1983; 98: 86-95.
19. Fujii Y and Nakayama Mashiro. Prevention of pain due to injection of propofol with IV administration of lidocaine 40mg + metoclopramide 2.5mg, 5 or 10 mg or saline: a randomized double blind study in Japanese adult surgical patients. Doi: 10.1016/j Clin. Thera 200.05.019.
20. Liaw WJ, Pang WW, Chang DP, Hwang MH. Pain in injection of propofol: the mitigating influence of metoclopramide using different techniques. *Acta Anaesthesiol Scand* 2005 Feb; 49 (2): 248-51.
21. Ganta R, Fee JPH. Pain on injection of propofol: Comparison of lignocaine with metoclopramide *Br J Anaesth*; 66: 324-06.
22. Maroof M, Khan RM, Khalid A, Siddique MSK, Rahman Z. Pain associated with propofol injection is abolished by pre- treatment with metoclopramide. *Br J Anesth* 1995; 74 (suppl 1): 8A.
23. Fujii Y, Uemura A. Effect of metoclopramide on pain on injection of propofol. *Anaesth Intensive care* 2004 Oct; 32 (5): 653-6.

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