Original Article:

Does addition of metoclopramide to lignocaine confer additional advantage on reducing pain on propofol injection?

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ABSTRACT

Background: Intravenous injection of lipid emulsion propofol induces a considerable degree of pain and the most preferred treatment suggested is pretreatment with intravenous lignocaine to alleviate such pain. The present study was designed to evaluate whether addition of metoclopramide to lignocaine offers any advantage over lignocaine alone as a pretreatment in prevention of pain following propofol injection.

Methods: In this prospective, randomized, double-blind controlled study, 60 patients were randomized to receive either lignocaine (group A) or lignocaine with metoclopramide (group B) intravenously as a pretreatment before injection of propofol. Pain due to injection of propofol was assessed with a four point categorical verbal rating pain scale. The incidence and magnitude of pain was compared between the two groups.

Results: There was no statistically significant difference in the perceived intensity of pain between the two groups at different time points after administration of propofol. The incidence of moderate pain was 23.3% in group A and 20% in group B ($p = 0.211$); 26.7% patients in group A and 43.3% patients in group B had no pain during propofol administration ($p = 0.116$).

Conclusions: Addition of metoclopramide to lignocaine does not have additional advantage over lignocaine alone in alleviating the pain of emulsified propofol injection.

Key words: *Lignocaine, Metoclopramide, Propofol, Pain*

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INTRODUCTION

Patient satisfaction with peri-operative care is assuming more importance and the quality of an anaesthetic is judged by any recall of discomfort or pain. Propofol is an intravenous (IV) sedative and hypnotic agent commonly used for anaesthesia induction. However, pain on injection when given intravenously is a common problem with propofol and the incidence varies from 40%-86%.[1] Although the mechanism of pain due to propofol injection is not well understood, many drugs have been studied to alleviate this pain. Among the various drugs, lignocaine pretreatment has been the most favoured one.[2-4] However addition of lignocaine does not assure complete pain free propofol injection and the failure rate is between 13%-32 %.[2,3] Additives to lignocaine may provide better alleviation of pain. Metoclopramide is a dopamine receptor agonist and belongs to benzamide group of drugs, which has local anaesthetic properties similar to those of lignocaine[5] and was shown to exert

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analgesic action at local site. Study of pretreatment with several doses of intravenous metoclopramide suggested that 5 mg of metoclopramide pretreatment reduced the pain of propofol injection effectively.[5] We hypothesized that addition of metoclopramide to lignocaine as a pretreatment will have a better pain relieving effect compared to lignocaine drug alone and undertook the present study.

MATERIAL AND METHODS

Approval from Institutional Ethical Committee was obtained for the study. The reported incidence of pain to propofol injection along with lignocaine pretreatment has been reported to be 35%.[6] Assuming that addition of metoclopramide would further reduce the pain by 85%; and α of 0.05, and a power of 80%, the sample size for each group was calculated to be 30.

After obtaining informed consent, 60 patients of either gender in the age group of 18-58 years belonging to American Association of Anesthesiologists physical status grade I and II,[7] scheduled for elective surgery and requiring general anaesthesia were included in this prospective randomized double-blind controlled study. Patients were allocated into two groups, Group A received 2 mL 2% lignocaine (40 mg) + 1 mL of normal saline; and Group B received 2 mL 2% lignocaine (40 mg) + 1 mL (5 mg) of metoclopramide. The allocation was made according to random numbers generated using online Graphpad software available at http://graphpad.com.

Patients with allergies to any of the study drugs, patients premedicated with sedatives or analgesics 24 hours prior to the surgery, those with renal, hepatic, cardiac problems, neurological deficits or psychiatric disorders, pregnant and lactating mothers were excluded from the study.Two hours before induction of anaesthesia, an 18 gauge IV cannula was secured on the dorsum of hand and a maintenance IV fluid (0.9% normal saline) was started. All patients were informed about the study procedure and were requested to report the pain intensity on propofol injection to the investigator injecting the propofol. A rubber tourniquet was applied at mid forearm to occlude the vein before administration of study drugs. All patients received an equal volume of drugs injected from a premixed syringe containing lignocaine 2% (2 mL) along with either normal saline (1 mL) i.e., Group A or metoclopramide (5 mg,1 mL) Group B as per randomization and tourniquet retained for 1 min after the administration of study drug. Twenty five per cent of the total calculated dose of propofol (2 mg/kg) was injected at a rate of 1 mL/sec. The blinded investigator recorded the severity of pain on a categorical verbal rating scale (VRS)[8] every 5 seconds during injection of propofol in accordance to numeric rating scale from 0 to 10, with zero representing, no pain and 10 representing, the worst pain possible. The pain severity was categorized into four distinct groups as related to pain interference: 0 no pain experienced; 1-3, mild pain or soreness; 4-6, moderate pain, and 7-10, severe pain associated with grimacing, withdrawal movement of forearm or both. The remaining induction dose of propofol was administered subsequently after two minutes. The heart rate, blood pressure were recorded at baseline, before administering pretreatment solution and at first, second and third minutes after anaesthesia induction with propofol. Following anaesthesia induction, tracheal intubation was facilitated with an intubating dose of vecuronium bromide and a standard general anaesthesia technique was followed. Patients with unanticipated difficult intubation, and those who had anaphylactic reactions were excluded post randomization. The study concluded after noting the haemodynamic parameters at third minute after induction of anaesthesia and remaining aneasthetic management continued according to the

treating anaesthesiologist. Hypotension was defined as an absolute fall in systolic blood pressure below 90 mm Hg or a 20% decrease in either systolic blood pressure (SBP), diastolic blood pressure (DBP) or mean blood pressure (MBP). Bradycardia was defined as an absolute decrease in heart rate below 55 beats per minute.

Data are expressed as mean (± standard deviation) and frequency. Categorical variables were compared between the groups using Chi-square test or Fisher's Exact test where applicable. Continuous variables were compared between two groups using independent sample t-test. Continuous haemodynamic variables within the groups are compared with baseline value using one-way analysis of variance (ANOVA), and a posthoc Duncan test was run to find out significance with base line preoperative value as control. A p-value < 0.05 was considered significant. Statistical analysis was performed using SPSS version 13 (SPSS Inc., Chicago, USA).

RESULTS

Demographic data of the two groups were comparable (Table 1). The baseline haemodynamic data were comparable between the groups. There was no significant change in the heart rate from the baseline in both the groups. The change in SBP was statistically significant ($p = 0.02$) in between the groups (Table 2).

We did not find any statistically significant difference between the reported pain intensity measured on a VRS. However more number of patients from lignocaine pretreatment group (group A) reported mild to moderate intensity of pain in comparison to metoclopramide pretreated group (group B) at all time points of assessment (Table 3). None of the patients reported severe pain to propofol injection.

We did not find any change in heart rate compared to baseline value in either group. The SBP, DBP and MBP declined significantly by third minute after induction of anaesthesia in both the groups (Table 2). However, none of the patients had developed hypotension.

DISCUSSION

Pain on injection of propofol is still a limitation of this otherwise excellent IV anaesthetic agent. Chemically, propofol belongs to the group of sterically hindered phenols.[9] Hence, like the phenols, it irritates the skin, mucous membrane and venous intima and can cause injection pain. The pain on injection of propofol is not considered as a serious complication, but it is a common problem with an incidence between 40%-86%.[1] It interferes with the patient satisfaction. Efforts are underway to reduce the severity of the pain or discomfort. Although the aetiology of this pain remains obscure, several adjuvants have been used to attenuate this pain like addition of lignocaine, [2-4] cooling[10,11] or warming[12] of the drug, diluting propofol solution.[13,14] However, literature reports the failure rate between 13%-32%.[2,3] Pretreatment with ondansetron,[15] opioids[16] and

Table 1: Demographic data

	Group A	Group B	p-value
Age (years)	40.9 ± 12.5	40.1 ± 12.1	0.819
Weight (Kg)	62.9 ± 9.9	59.9 ± 7.2	0.193
Gender (%)			
Male	43.3	26.6	
Female	56.6	73.3	0.139

Data are represented as mean ± standard deviation or percentage

Table 2: Comparison of haemodynamic changes during propofol injection

Variable	Baseline		1 min		2 min		3 min		p-value (within group) comparison		p-value (between groups comparison)
	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B	Group A	Group B	
HR	75.2 ± 2.0	79.9 ± 4.7	76.8 ± 2.3	80.2 ± 13.5	75.4 ± 1.5	79.7 ± 2.4	74.9 ± 1.3	79.0 ± 2.5	0.124	0.135	0.305
SBP	138 ± 1.3	129 ± 4.9	131 ± 8.7	125 ± 15.0	127 ± 5.6	118 ± 2.0	124 ± 4.8	113 ± 1.7	0.044	0.039	0.02
DBP	82 ± 11.3	81 ± 9.6	78 ± 13.1	77 ± 10.2	77 ± 10.1	76 ± 11.7	74 ± 9.2	70 ± 10.8	0.048	0.031	0.656
MBP	100 ± 13.4	97 ± 11.4	95 ± 13.3	93 ± 11.0	93 ± 10.8	90 ± 10.1	90 ± 10.2	84 ± 9.5	0.042	0.029	0.189

Data are presented as mean ± standard deviation
Group A = lignocaine; Group B = lignocaine with metoclopramide; HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; MBP = mean blood pressure (mm Hg)

Table 3: Comparison of pain score during injection of propofol

Time	Group A No. (%)	Group B No (%)	p-value
5 Seconds			
No pain	19 (63.3)	25 (83.3)	
Mild pain	10 (33.3)	4 (13.3)	
Moderate pain	1 (3.3)	1 (3.3)	
Severe pain	0 (0)	0 (0)	0.184
10 Seconds			
No pain	15 (50.0)	16 (53.3)	
Mild pain	14 (46.7)	12 (40.0)	
Moderate pain	1 (3.3)	2 (6.7)	
Severe pain	0 (0)	0 (0)	0.771
15 Seconds			
No pain	14 (46.7)	18 (60.0)	
Mild pain	14 (46.7)	9 (30.0)	
Moderate pain	2 (6.7)	3 (10.0)	
Severe pain	0 (0)	0 (0)	0.409
20 Seconds			
No pain	14 (46.7)	18 (60.0)	
Mild pain	12 (40.0)	6 (20.0)	
Moderate pain	4 (13.3)	6 (20.0)	
Severe pain	0 (0)	0 (0)	0.235

Group A = lignocaine; Group B = lignocaine with metoclopramide

thiopentone[17] have been tried with varying success.

In contrast, our study showed that there was no statistically significant difference in pain scores between the groups. The incidence of moderate pain was similar in both the groups. None of the patients in either group complained of severe pain. It is possible that the small sample size would have resulted in type II error. There was no statistically significant difference in the haemodynamic parameters among the two groups. Metoclopramide 5 mg pretreatment along with lignocaine decreased incidence of mild pain but did not decrease the incidence of moderate pain which causes discomfort. Hence, our observations suggest that addition of metoclopramide as an adjuvant to lignocaine may not improve the acceptability of propofol as compared to lignocaine alone.

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JCSR, with the intention of encouraging the contributors, is presenting ''Best Paper Awards'', one each under "Original Article" and "Case Report" Categories. The articles published in the year 2014 (Volume 3 Issues 1-4) were examined by three experts for each category and the Best Paper under each of the categories were identified. The ''Best Papers'' for the year 2014 are listed below:

Under **"Original Article"** Category

Dumpala S, Kondagunta N, Malhotra VM, Venna GP, Jothula KY. An outbreak investigation of suspected Chikungunya fever in Nalgonda District of Telangana state. J Clin Sci Res 2014;3:219-23. DOI: http://dx.doi.org/10.15380/2277-5706.JCSR.14.043.

Under **"Case Report"** Category

Das P, Gunaseelan K, Basu D, Ananthakrishnan R, Reddy KS. A rare case of primary vaginal Ewing's sarcoma/primitive neuroectodermal tumour: diagnostic and treatment challenges. J Clin Sci Res 2014;3:145-9. DOI: http://dx.doi.org/10.15380/2277-5706.JCSR.13.033.

The authors shall be issued a merit certificate SVIMS Anniversary day, 26th February 2015. Hope this will stimulate the contributors to send their best work to our journal.

B. Vengamma
Hon. Editor-in-Chief