A Randomized Comparative Study of Metoclopramide, Ketamine and Lignocaine given Intravenously to Attenuate Pain due to Propofol

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ABSTRACT

Introduction: Propofol is one of the preferred intravenous anaesthetic agent because of rapid induction and the rapid recovery of psychomotor functions. Pain during propofol injection is a known entity. Various strategies have been practiced to reduce pain due to propofol like: Choosing a larger vein, cooling propofol solution, dilution of propofol,increasing the speed of injecting propofol,pretreatment with agents like Aspirin and NSAIDS,Thiopentone sodium, Opiods, Lignocaine, Ondansetron, Ketamine and Metoclopramide. Objective: To compare efficacy of lignocaine, ketamine and metoclopramide in decreasing the incidence of pain during propofol injection.

Material and Methods: Study was conducted among 75 patients belonging to ASA grade I and II status undergoing surgery under general anaesthesia. Random allocation of patient was done to three groups with the help of computerized randomization into Group I:25 patients received 2% Lignocaine 40mg Group II:25 patients received 100mcg/ kg Ketamine[18] Group III:25 patients received 10mg metoclopramide. Data was collected by measuring hemodynamic parameters at preinduction, after test drug, after ¼ dose of propofol, after full dose of propofol. Verbal rating scale (VRS) and Visual Analogue scale (VAS) score noted. The investigator was same for all the cases of the study. Data was analyzed using ANOVA test (Windostat Version 8.6 from indostat services, Hyderabad).

Results: The P-value for VRS and VAS between lignocaine, ketamine and metoclopramide group was statistically significant. Lignocaine came to be more efficient.

Conclusion: All the three pretreatment drugs alleviated pain due to propofol injection. Lignocaine has higher efficacy in comparison with ketamine and metoclopramide in alleviating pain.

Keywords: Propofol, pain, lignocaine, ketamine, metoclopramide.

INTRODUCTION

Propofol, a short acting intravenous anaesthetic agent is being used extensively because of its smooth induction and rapid recovery. It is the agent of choice for day care anesthesia, total intravenous anaesthesia, for sedation in intensive care units, and as an agent for maintenance of anaesthesia[1-3] However, pain on intravenous injection is a major drawback of propofol.

Many factors were established as reason for causaing pain on intravenous injection like intrinsic drug property (e.g. osmolarity, emulsion composition, temperature, injection volume and pH of the formulation), Injection procedure itself (speed of administration, concentration the aqueous phase, speed of IV carrier fluid, use of local anesthetics, and the blood's buffering capacity[4-9]).

Klement and Arndt[9] found that pain occurred at 1 osmole / kg during infusion and 3osmole/kg during rapid injection. Solutions with pH values less than 4 and more than 11 cause pain. This theory does not explain the cause of pain on propofol injection as the drug is isotonic and has Ph of 8.5.

When administered in to antecubital fossa[10-14] there was no pain. Contact with the vein wall is minimal when the drug comes in contact with midstream of high concentration of blood. The blood also effectively buffers the drugs. Duration of exposure of the vein wall to propofol injection is also a determining factor for causation of pain.[15-18] Scott et al[6] noticed that slow injection caused more pain than a rapid bolus.Pain alleviation can be due to local anaesthetic action, analgesic effect, dilution of propofol, stabilization of kinin cascade by pretreatment drug.

In present study we compared the efficacy of lignocaine, ketamine and metoclopramide in attenuating pain during propofol injection.

MATERIAL AND METHODS

After approval from scientific and ethical committee and written informed consent, a randomized double blind study was conducted on 75 patients belonging to ASA I and II between the age group of 18-60 yrs undergoing surgery under general anaesthesia. Patients were randomly allocated to any of the three groups with the help of computerized randomization as:

Group I: 25 patients received 2% xylocard 40mg as pretreatment[15]

Group II: 25 patients received 100mcg/ kg Ketamine as pretreatment[18]

Group III: 25 patients received 10mg of metoclopramide as pretreatment[13]

Inclusion criteria

1. Patients posted for elective surgeries under general anaesthesia
2. Age >18 years and <60 years
3. ASA I and II

Exclusion criteria

1. Patients with history of allergy to propofol or its components
2. Patients with neurological disorders or altered sensorium or those on antipsychotic medication

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How to cite this article: Pakhare Vandana Patilbuwa, Surya Prakash Yarramalle. A randomized comparative study of metoclopramide, ketamine and lignocaine given intravenously to attenuate pain due to propofol. International Journal of Contemporary Medical Research 2016;3(9):2746-2749.

3. Patients with cardiac abnormalities
4. Patients taking analgesics e.g NSAIDS, opiates etc.
5. Patients with history of epilepsy or extrapyramidal disorders
6. Patients with venous thrombosis

All the test drugs were prepared in a 2 cc syringes by a separate anaesthesiologist. Propofol vials were removed 30 minute prior to procedure and were kept at room temperature (28°C). IV access was established with 18 G angiocath on dorsum of left upper limb and a Ringer lactate infusion was started at a constant infusion rate of 200 ml/hr. All patients were monitored with electrocardiography, pulse oximeter, and non-invasive blood pressure measurement, respiratory gas monitor.

Procedure was carried out by an independent anaesthesiologist who was not aware of the group to which patient belong. While the venous drainage was occluded by tourniquet to arm, the test drug (either lignocaine or Ketamine or metoclopramide), loaded in 2cc syringe, was given over 5 sec. The compression was released after exactly 1 minute and one-fourth the calculated induction dose of propofol (2mg/kg) was given slowly over 5 sec. Data was collected by measuring hemodynamic parameters preoperatively, after administration of test drug, after administration of ¼ dose of propofol and after administration of full dose of propofol. Patients were also interviewed about the pain by using VAS scores and VRS scores. VRS (verbal rating scale)[19-21] patients were asked to rate pain intensity on a numerical scale from 0 to 10, with the zero as no pain and the 10 as the worst pain. Visual Analogue scale VAS [20,21] has 10-cm line with two extremes of pain. Patients were asked to mark on the line that represented their intensity of pain.

STATISTICAL ANALYSIS

Data was analyzed using ANOVA test (Windostat Version 8.6 from indostat services, Hyderabad).

RESULTS

Demographic data (age, sex and weight) were comparable between all three group (P-value>0.5) (table-1).

The P-value for Verbal Rating Scale (table-2) between the lignocaine, ketamine is < 0.05 which means there is significant difference thus lignocaine is better than ketamine in decreasing pain due to propofol injection, similarly P-value between the lignocaine, metoclopramide is < 0.001 which implies lignocaine is better than metoclopramide in decreasing pain due to propofol injection and and P-value between the ketamine, metoclopramide is < 0.01 which means ketamine is better than metoclopramide in decreasing pain due to propofol injection.

There is significant difference of VRS between the lignocaine, ketamine and metoclopramide groups (P-value < 0.000) thus lignocaine is more efficient among the three drugs.

There is significant difference of VAS between the lignocaine, ketamine (P-value < 0.01) which implies lignocaine is better than ketamine in decreasing pain due to propofol injection similarly P-value between the lignocaine, metoclopramide is< 0.001which implies lignocaine is better than metoclopramide in decreasing pain due to propofol injection and between the ketamine, metoclopramide P-value is < 0.05 which means ketamine is better than metoclopramide in decreasing pain due to propofol injection

There is significant difference of VAS between the lignocaine, ketamine and metoclopramide groups (P-value < 0.000) thus lignocaine is more efficient among the three drugs.

From table-3 there is no statistically significant difference in Pulse rate between Lignocaine, Ketamine and propofol group at pre-induction(P-0.13111), after test drug(p-0.13111), after ¼ dose of propofol (0.29509) after full dose of propofol(0.19001).

From table-4 there is no statistically significant difference in Mean blood pressure between lignocaine,ketamine and metoclopramide group at pre-induction(P-0.138), after test drug(p-0.098), after ¼ dose of propofol (0.134) after full dose of propofol(0.300).

DISCUSSION

Propofol is most extensively used intravenous anaesthetic agent. The major drawback of propofol injection is pain on intravenous injection. Various studies have been done to determine the cause of pain during administration of propofol and evaluate different modalities to alleviate pain like choosing bigger vein, increasing speed of injection, diluting propofol, pretreatment with drugs eg ketamine, lignocaine, ondensetron, metoclopramide, aspirin.

R.Ganta and J.P.H.Fee[13] in their randomized control study to compare efficacy of metoclopramide and lignocaine with saline as control group in reducing pain on propofol injection concluded that both the drugs significantly minimized pain. In

Parameter	Statistics	Group I lignocaine	Group II ketamine	Group III metoclopramide	p-value	Significance
Age	Mean	40.280	36.880	38.720	0.51965	Not significant
	Standard Deviation	10.601	10.329	10.478		
Sex	Mean	1.520	1.600	1.480	0.69641	Not significant
	Standard deviation	0.510	0.500	0.510		
Weight	Mean	68.800	66.240	65.640	0.37752	Not significant
	Standard deviation	6.364	7.096	11.094		

Table-1: Summary of demographics in treatment group

Parameter	Statistics	Group I lignocaine	Group II ketamine	Group III metoclopramide	p-value	Significance
Verbal Rating Score	Mean	0.680	1.120	1.680	0.000	**Significant**
	Standard deviation	0.690	0.735	0.748		
Visual Analogue Scale	Mean	1.560	2.320	3.120	0.000	**Significant**
	Standard deviation	0.712	0.945	1.166		

Table-2: Summary of Verbal Rating Score and Visual Analogue Scale

Group	Statistics	Pre induction	After test drug	After ¼ dose of propofol	After full dose of propofol
Group I lignocaine	Mean	86.720	85.120	80.840	76.080
	Standard deviation	6.674	6.260	6.135	6.006
Group II ketamine	Mean	82.320	81.520	78.960	72.920
	Standard deviation	7.087	7.200	7.191	6.467
Group III metoclopramide	Mean	80.960	81.880	82.080	75.280
	Standard deviation	7.300	7.073	7.729	6.420
p-value		0.11328	0.13111	0.29509	0.19001
Significance		Not significant	Not significant	Not significant	Not significant

Table-3: Summary of Pulse rate (PR) /minute in treatment group

Group	Statistics	Pre induction	After test drug	After ¼ dose of propofol	After full dose of propofol
Group I lignocaine	Mean	88.373	87.720	84.893	80.787
	Standard deviation	5.757	5.443	5.179	4.851
Group II ketamine	Mean	89.280	88.453	85.626	81.920
	Standard deviation	6.354	6.307	6.560	5.915
Group III metoclopramide	Mean	89.174	88.427	85.801	81.973
	Standard deviation	7.761	7.985	7.762	7.322
p-value		0.138	0.098	0.134	0.300
Significance		Not significant	Not significant	Not significant	Not significant

Table-4: Summary of Mean arterial pressure (MAP) in mm of Hg

saline group 20 patients reported as severe pain on subsequent propofol injection while only 5 patient in lignocaine and 6 patient in metoclopramide group complained of severe pain on propofol injection(P <0.001).

Barbi et al[19] performed a prospective, randomized, double-blind trial in a paediatric sedation unit to evaluate ketamine as pretreatment for reducing propofol injection pain. In ketamine group 8% patient complained of pain compared to 37% in placebo group (P value= 0.0001). They concluded Ketamine 0.5mg/kg as pretreatment effectively minimizes pain on propofol injection.

Gangur Basappa[22] et al conducted comparative study to evaluate attenuation of propofol injection pain by lignocaine,ramosetron and ondansetron. In their study incidence of mild to moderate pain in lignocaine group was 20%, in ramosetron group 26% and in ondansetron group 56% while incidence of no pain was 76%, 72% and 34% respectively with P value <0.001. They concluded lignocaine and ramosetron are equally effective in minimizing pain due to propofol injection and both were better compared to ondansetron pretreatment.

In our study in lignocaine group (table-2) 12 patients had no pain, 11 rated it as 2 on VRS, 2 patient rated it as 4 while in ketamine group (table 2) 6 patient had no pain, 11 rated it as 2 and 8 patient rated pain as 4 on VRS and in metoclopramide group (table 2) only 1 patient had no pain, 10 rated it to be 2 on VRS, 11 patient rated pain as 4 and 3 patient reported pain as 6 on VRS. The mean VRS (table 2) in lignocaine, ketamine and metoclopramide group was 0.680, 1.12 and 0.680 while the mean VAS was 1.560, 2.320 and 3.120 respectively. P-value for VRS and VAS (table 2) between lignocaine, ketamine and metoclopramide group was 0.000 which implies lignocaine is more efficient among the three drugs in alleviating pain on propofol injection.

Lignocaine alleviates pain due to propofol injection by its local anaesthetic action and stabilization of kinin cascade. Analgesic effect of ketamine is due to its potent analgesic and local anaesthetic action while metoclopramide act as weak local anaesthetic as it shares structural and physiochemical properties with lignocaine.

CONCLUSION

We concluded that all the three pretreatment drugs i.e.lignocaine, ketamine and metoclopramide alleviate pain on propofol injection. Lignocaine is more efficient among the three drugs in alleviating pain on propofol injection.

ACKNOWLEDGEMENT

We thank the department of anaesthesiology, operation theatre staff for giving support and valuable time to conduct the study. No funding was provided for this study.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 02-08-2016; **Published online**: 16-09-2016