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

Pakhare Vandana Patilbuwa¹, Surya Prakash Yarramalle²

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, Opioids, 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 Group III: 25 patients received 10mg metoclopramide. Data was collected by measuring hemodynamic parameters at preinduction, after test drug, after ¾ 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 anaesthesia, total intravenous anaesthesia, for sedation in intensive care units, and as an agent for maintenance of anaesthesia. However, pain on intravenous injection is a major drawback of propofol.

Many factors were established as reason for causing 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).

Klement and Arndt 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 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. Scott et al 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
Group II: 25 patients received 100mcg/kg Ketamine as pretreatment
Group III: 25 patients received 10mg of metoclopramide as pretreatment

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 NSAI DS, 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) 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 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 between the ketamine, metoclopramide P-value is < 0.05 which means ketamine is better than metoclopramide in decreasing pain due to propofol injection.

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, ondasetron, metoclopramide, aspirin. R.Ganta and J.P.H.Fee 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
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 al19 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 Basappa22 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.

**REFERENCES**


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

<table>
<thead>
<tr>
<th>Group</th>
<th>Statistics</th>
<th>Pre induction</th>
<th>After test drug</th>
<th>After ¼ dose of propofol</th>
<th>After full dose of propofol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I lignocaine</td>
<td>Mean</td>
<td>86.720</td>
<td>85.120</td>
<td>80.840</td>
<td>76.080</td>
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<td>Group II ketamine</td>
<td>Mean</td>
<td>82.320</td>
<td>81.520</td>
<td>78.960</td>
<td>72.920</td>
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<tr>
<td></td>
<td>Standard deviation</td>
<td>7.087</td>
<td>7.200</td>
<td>7.191</td>
<td>6.467</td>
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<tr>
<td>Group III metoclopramide</td>
<td>Mean</td>
<td>80.960</td>
<td>81.880</td>
<td>82.080</td>
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<tr>
<td></td>
<td>Standard deviation</td>
<td>7.300</td>
<td>7.073</td>
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<td>p-value</td>
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**Table-4:** Summary of Mean arterial pressure (MAP) in mm of Hg

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<tr>
<th>Group</th>
<th>Statistics</th>
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<th>After test drug</th>
<th>After ¼ dose of propofol</th>
<th>After full dose of propofol</th>
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<td>Group I lignocaine</td>
<td>Mean</td>
<td>88.373</td>
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<td>Mean</td>
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<td>Group III metoclopramide</td>
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<td>Standard deviation</td>
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<td>p-value</td>
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<td>0.098</td>
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<tr>
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Source of Support: Nil; Conflict of Interest: None
Submitted: 02-08-2016; Published online: 16-09-2016