Prevention of Propofol Injection-Induced Pain, Using Lignocaine in Large Volume: A Prospective Randomized Double-Blind Study

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Abstract

Background: Propofol is a common intravenous (IV) anesthetic drug, used for induction of general anesthesia. Pain during bolus injection is a major drawback of propofol. Different methods of propofol formulations and drugs have been used to decrease pain on propofol injection (POPI), but still it remains an unresolved problem. It is assumed that IV administration of diluted lignocaine in a large volume before propofol injection could be more effective in prevention of both immediate and delayed types of pain associated with propofol injection than the most commonly used method of mixing lignocaine with propofol (20 mg lignocaine added to the 20 ml propofol). Objectives: The aim of this study was to compare the effect of lignocaine used in a large volume for prevention of propofol injection pain. Materials and methods: Eighty adult patients undergoing general anesthesia for elective ENT surgery were included in this study. Patients were classified into two groups, Group A (study group), in which 20 mg lignocaine diluted into a total volume of 20 ml using normal saline was given IV after venous occlusion for with BP cuff followed by propofol injection. In group B (control group), 20 mg lignocaine was mixed with propofol and given to the patient as commonly used. Results: This study showed statistically significant reduction in pain on propofol injection (POPI) in the study group compared to control group. Conclusion: Lignocaine when used diluted with normal saline in large volume after venous occlusion has significantly reduced propofol injection pain in adults.

Keywords: Propofol, lignocaine, Pain on propofol injection (POPI)

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Introduction

Propofol is the most widely used intravenous (IV) anesthetic agent for induction and maintenance of anesthesia as well as for sedation inside and outside of operation theatre. It is almost an ideal IV anesthetic agent, but pain on its injection still remains problem. The pain may not be a serious complication, but most patients remember it as one of the unpleasant encounters with anesthesiologists. Pain on propofol injection (POPI) is a common problem in adults, which varies between 30 and 90%.¹ Several strategies have been suggested to prevent or reduce pain at the site of propofol administration. Most previous and recent work in this area has been performed on the adjuvant use of hypnotic, analgesic, anti-inflammatory or local anesthetic drugs, which include adding lignocaine to propofol, cooling or warming propofol, diluting the propofol solution, injection of propofol into a large vein²³ and pretreatment with intravenous injection of lignocaine, ondansetron, opioids,⁷ granisetron,⁸ thiopentone,¹⁰ metoclopramide,¹ ketorolac,¹² dexamethasone,¹³ and magnesium,¹⁴ with or without tourniquet. All these drugs have been tried with variable and sometimes conflicting results.

Propofol belongs to a group of phenol that can irritate the skin, mucous membrane and venous intima. The pathophysiology of this pain is attributed till this moment to one and a combination of more than one of the three proposed mechanisms. The first mechanism relates to the triggering of the local kallikrein-kinin cascade,¹⁷ which explains the decrease in the incidence and severity of non-immediate (delayed) pain resulting from propofol administration when the drug is premixed with lignocaine¹⁸ or a non-steroidal anti-inflammatory agents, which inhibit the
prostaglandins. Another suggested mechanism was the stimulation of the nociceptive receptors at the free nerve endings located between the intima and media layers of venous wall, in which a direct and immediate response is transmitted through the A-delta fibers; drugs like lignocaine, fentanyl, morphine and procaine are effective when administered few seconds before propofol injection. The third proposed mechanism relates the pain to the pH and concentration of propofol; which when lowered by premixing it with lignocaine or 10% intralipids causes less pain.

In this study, it is assumed that IV administration of diluted lignocaine in large volume (20 mg lignocaine diluted in 20 ml of normal saline) before propofol injection could be more effective in prevention of both immediate and delayed types of pain associated with propofol injection than the most commonly used method of mixing lignocaine with propofol (20 mg lignocaine added to 20 ml propofol). Lignocaine diluted in such volume and injected during venous occlusion may give a chance for larger volume of drug to spread over larger surface area to block more pain producing nerve endings, not only within the veins but also by passing to block perivascular nerve endings, which could prevent both immediate and delayed types of pain caused by propofol.

Material and Methods
This prospective randomized double-blind study was conducted on 80 patients of American Society of Anesthesiologists (ASA) physical status I and II, aged 20-55 years of both sexes, at National Institute of ENT, Dhaka from February to April 2018. Written informed consent was obtained from all patients. Patients with known history of allergy to either propofol or lignocaine were excluded. Eligible patients were randomly divided into two groups: Group A (study group) and Group B (control group). All patients were cannulated with a 20 gauge intravenous cannula on the distal part of the forearm. On arrival to the operation room, all patients were monitored with electrocardiogram, pulse oximetry, non-invasive arterial blood pressure, and capnography. Mean arterial blood pressure and heart rate were recorded during and within 1 min after propofol injection (POPI) between two groups. Comparison of age and weight between the two groups was obtained by unpaired t-test. The results were expressed as number or mean ±SD. p value <0.05 was considered to be statistically significant.

Results
There is no significant demographic difference between the groups (Table II). In both groups MAP and HR decreases during pre-intubation and post intubation from basal reading. There is some difference of MAP and HR between the two groups but is not significant (Table III). The incidence of pain in group A (study group) is 5% patients and in group B (control group) is 20% patients, which is statistically significant p<0.05. In both groups we found only mild pain, no moderate or severe pain was recorded (Table IV).

Table I: Grading of pain

<table>
<thead>
<tr>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No pain</td>
</tr>
<tr>
<td>1</td>
<td>Mild pain (pain reported only in response to questioning without any behavioral signs)</td>
</tr>
<tr>
<td>2</td>
<td>Moderate pain (pain reported in response to questioning and accompanied by a behavioral sign or pain reported spontaneously without questioning)</td>
</tr>
<tr>
<td>3</td>
<td>Severe pain (strong vocal response or response accompanied by facial grimacing, arm withdrawal or tears)</td>
</tr>
</tbody>
</table>

The chi-square test was used to compare pain on propofol injection (POPI) between two groups. Comparison of age and weight between the two groups was obtained by unpaired t-test. The results were expressed as number or mean ±SD. p value <0.05 was considered to be statistically significant.

Table II: Comparison of demographic data between the two groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group A (n=40)</th>
<th>Group B (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (mean±SD)</td>
<td>37.73±7.12</td>
<td>38.53±8.42</td>
</tr>
<tr>
<td>Weight in kg (mean±SD)</td>
<td>65.52±8.64</td>
<td>66.12±6.89</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>21/19</td>
<td>20/20</td>
</tr>
</tbody>
</table>

Table III: Changes of mean arterial pressure and heart rate between two groups

<table>
<thead>
<tr>
<th>Hemodynamic parameter</th>
<th>Basal Group A</th>
<th>Basal Group B</th>
<th>Pre intubation Group A</th>
<th>Pre intubation Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean arterial pressure (MAP) mm Hg</td>
<td>102/104</td>
<td>87/89</td>
<td>94/96</td>
<td>84/86</td>
</tr>
</tbody>
</table>
smooth induction of anesthesia which is associated with patient pretreatment for prevention of this pain become the standard technique in anesthesia practice. Overbaugh et al concluded agitation and enhancement of the stress response, so lignocaine pretreatment because propofol pain may hinder after venous occlusion with tourniquet. They reported that bolus injection before propofol injection. Second was mixing lignocaine with propofol, and the third by giving lignocaine using tourniquet was the most effective method. We studied prevention of propofol injection pain. The first was lignocaine and time effective as it can be used during the period of pre-intubation measurements of mean arterial blood pressure and heart rate in the study group compared to the control one could be explained by attenuation of the stress response as a result of reduction of the propofol injection pain in the study group.

Discussion
In this study it is found that, the incidence and severity of propofol injection induced pain were significantly less in pre treatment lignocaine diluted in large volume with normal saline using tourniquet, than the premixed lignocaine with propofol. It has been suggested that lignocaine is not effective in reducing the pain of propofol injection except when a tourniquet is used. The mechanism of action is possibly the blockade of the nerve fibers responsible for pain transmission resulting from direct irritation of the inner walls of blood vessels by propofol; this direct anesthetic effect of lignocaine is achieved when sufficient time is allowed for the drug to work. However, the results of studies related to the amount of time lignocaine remains in blood vessels when a tourniquet is used are controversial. Local anesthetic activity of lignocaine may be high due to long duration, but in the study of Ewart and Whitwam, lignocaine was most effective at reducing pain when administered immediately before applying propofol. Liaw et al found that IV lignocaine was retained in the veins for 1 minute, and injecting propofol after releasing the rubber tourniquet was found to be effective in reducing pain when compared with the saline group. In a study Picard and Tramer compared three different methods of using lignocaine in prevention of propofol injection pain. The first was lignocaine bolus injection before propofol injection. Second was mixing lignocaine with propofol, and the third by giving lignocaine after venous occlusion with tourniquet. They reported that using the tourniquet was the most effective method. We studied lignocaine pretreatment because propofol pain may hinder smooth induction of anesthesia which is associated with patient agitation and enhancement of the stress response, so pretreatment for prevention of this pain become the standard technique in anesthesia practice. Overbaugh et al concluded that lignocaine more effectively reduces pain on injection of propofol when it is administered as a mixture than when given as a pretreatment before the propofol injection. Our technique is different because of using markedly diluted lignocaine under tourniquet which may explain the different results between our study and Overbaugh et al. The present study was both cost and time effective as it can be used during the period of pre-oxygenation. In this study, the reduction of the pre-intubation and post-intubation measurements of mean arterial blood pressure and heart rate in the study group compared to the control one could be explained by attenuation of the stress response as a result of reduction of the propofol injection pain in the study group.

Table IV: Incidence and severity of pain following propofol injection between two groups

<table>
<thead>
<tr>
<th>Characteristics of pain</th>
<th>Group A (n=40)</th>
<th>Group B (n=40)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pain</td>
<td>38 (95%)</td>
<td>32 (80%)</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Pain</td>
<td>2 (5%)</td>
<td>8 (20%)</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Mild Pain</td>
<td>2 (5%)</td>
<td>8 (20%)</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Moderate Pain</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Severe Pain</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion
Lignocaine pre treatment decreases pain on propofol injection (POPI) using in large volume under venous occlusion significantly than premixed lignocaine with propofol injection in adult patients. This method has no wastage of time, without adding cost and also easy to apply. This method causes reduced pain on propofol injection so it is associated with smooth induction of general anesthesia and attenuation of stress response.

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References


