

# A Randomized Study to Compare the Efficacy of Lignocaine, Dexamethasone, Pethidine, and Placebo in the Prevention of Pain Caused by Propofol Injection

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# ABSTRACT

**Introduction:** Propofol is used in injectable form intravenously by anesthetists for the induction of anesthesia. It is the drug of choice in short or daycare surgical cases. The patients who experience pain, are also able to experience anxiety and fear. In the most severe cases, they can also face myocardial infarction and ischemia.

**Aim:** A comparison of pain-alleviating effects of Lignocaine, Dexamethasone, Pethidine, and placebo in a patient caused by the administration of Propofol for the induction of anesthesia.

**Methodology:** The study included 144 patients who had been given injection Propofol for the induction of anesthesia. The patients were divided into four groups as four types of drugs were administered. The allocation of the participants was done randomly. The age range of the patients was from 18-62 years. All the participants were undergoing upper abdominal surgery. After the administration of 25% Propofol, the patients were asked for the status of pain. A randomized controlled trial. This study was conducted at Chandka Medical College, SMBBMU Larkana, Pakistan from April 2020 to April 2021.

**Results:** The drugs Lignocaine, Dexamethasone, and Pethidine reduced the pain caused by injection Propofol as compared to the placebo. The pain score in these three drug groups was not significantly different. Also, the recall of pain in these groups was not significantly different. However, the difference between the placebo group and the remaining three groups was significant.

**Conclusion:** Lignocaine, Dexamethasone, and Pethidine significantly reduce the pain caused by the Propofol injection as compared to a placebo. There is no significant difference between their efficacies. Nonetheless, the difference between the previously mentioned drugs and placebo is significant.

Key Words: Lignocaine, Dexamethasone, Propofol, Pethidine, Anesthesia, Drawback

# **INTRODUCTION**

Propofol is used in injectable form intravenously by anesthetists for the induction of anesthesia. It is the drug of choice in short or daycare surgical cases. It is also used when a laryngeal mask airway is supposed to be used. It has various benefits, whereas, the most common drawback of the drug is pain. This adverse effect of the Propofol injection is severely distressing for the patient. The incidence of pain is almost 70%.<sup>1</sup> Some studies have shown that the incidence of pain followed by Propofol injection is 28-90%.<sup>2</sup> It has been observed in some studies that the pain due to Propofol injection is also related to the age of the patient. Children experience it more severely as compared to adults.<sup>3</sup> This difference in the experience of pain can be due to the small veins of children in the hand. Other factors which are correlated with the pin of Propofol injection are injection speed, site of the intravenous line, vein size, buffering effect, use of recreational drugs, and temperature of the injection. The patients who experience pain, are also able to experience anxiety and fear. In the most severe cases, they can also



face myocardial infarction and ischemia.<sup>4</sup> The pain can also affect the safety and satisfaction of the patient. Some patients report that the intensity of pain is quite severe. The pain becomes very intense sometimes that the patient can also experience it peri-operatively.<sup>5</sup>

Factors that can reduce the pain of Propofol injection are medium-chain triglycerides, long-chain triglycerides, venous occlusion, emulsified Propofol, injecting in large veins, temperature adjustment of Propofol, injection of lidocaine along with a tourniquet, and small doses of opioids such as butorphanol and sufentanil.<sup>6</sup> Moreover, the use of a  $\beta$ -blocker, midazolam, and magnesium are also useful in this regard.<sup>7</sup> The most effective method of alleviating the pain of Propofol injection out of all these factors is lidocaine. It is a commonly used drug for the induction of local anesthesia. Lidocaine is administered intravenously for the pain of cancer, postoperative pain, refractory complex regional pain syndrome, and neuropathic pain.

The mechanism of alleviating the pain of Propofol injection through lidocaine is not fully understood. It has also been observed that different doses of lidocaine have different mechanisms of action.<sup>8</sup> Other drugs used for the reduction of pain due to Propofol injection are metoclopramide, butorphanol, opioid, thiopentone, and ondansetron.<sup>9</sup> However, all these techniques and drugs are not able to reduce the psychological impact of Propofol injection. A physiological technique called the Valsalva maneuver is used in this regard.<sup>10</sup>

The current study is conducted to compare the pain-alleviating effects of Lignocaine, Dexamethasone, Pethidine, and placebo in a patient caused by the administration of Propofol for the induction of anesthesia.

# **METHODOLOGY**

The study was conducted in the Anesthesiology and critical care department of our hospital. Permission was taken from the ethical review committee of the institute. The study included 144 participants. The ASA physical status of the patients was 1 and 2. The ages of the patients ranged from 18 years to 62 years. All the participants were going to undergo the surgical process in the upper abdomen. Those patients who had hypersensitivity to Propofol, pethidine, or lignocaine were not included in the study. Patients with difficulty in access to the venous line and who had cardiac defects were also excluded from the study. Patients were allocated in four groups. They were allocated randomly. Each group included 36 participants in each group.

All the patients included in the study were given Diazepam 5mg through the oral route. The drug was given on the night before the operation. When the patients were shifted in the Operation Room, a 20 G cannula was inserted in the largest

found vein on the dorsal aspect of the hand. Ringer lactate solution was infused through the intravenous line. This procedure was done without any anesthesia. Identical syringes were prepared by personnel who was not involved in the study.

A tourniquet was applied for one minute on the forearm of the patient to create venous occlusion. The study drug was then injected over a duration of 10 seconds. Propofol 2.5mg/ kg was then injected intravenously after releasing the occlusion that was generated previously. The patient was instructed to describe the pain during 10 seconds followed by 25% administration of the calculated dose of the Propofol. The pain intensity was graded by a verbal rating scale. According to the scale: Zero means the absence of pain, 1 means mild pain (pain is only reported upon asking), 2 means moderate pain (pain is reported on questioning and behavior of the patient also shows the presence of pain) and 3 means Severe pain (pain is evident from the actions and behavior of the patient without even questioning)

After taking a record of verbal pain score, the remaining Propofol dose was given. The patients were intubated after the administration of suxamethonium. For strong analgesic, morphine was used. The level of oxygen, halothane, atracurium, and nitrous oxide was maintained in the patients. To wake up the patient and reverse muscle relaxation in these patients, extubation was done after the administration of atropine and neostigmine. The patients were kept in the post-operative recovery area for 2 hours. The patients were requested to recall the level of pain after giving Propofol and the pain was recorded based on the verbal pain score.

#### RESULTS

A total of 144 patients were included in the present study. They were divided into 4 equal groups. There were 36 participants in each group. The differences between the ages, weights and genders of the patients were not significantly different. The class of ASA was also comparable in all the groups. The baseline values of heart rate, systolic blood pressure, diastolic blood pressure, and oxygen saturation were also comparable in the groups. Hemodynamic variables of none of the patients were changed significantly after giving Propofol. The statistical difference between group 1 and other groups was not significant. It was also minor when group 2 was compared with group 3. However, when groups 1, 2, and 3 were compared with group 4, there was a difference in statistics. These differences have been shown in Table 2. Table 1 shows different regimens used in all the groups. Table 3 gives a comparison of recalling of the pain after Propofol injection as described by the patients.

#### Table 1: Drug regimen used in different groups

Groups	Drug used
Group 1	25 mg/5ml of Pethidine
Group 2	20 mg/5 ml of Lignocaine
Group 3	4 mg/5 ml Dexamethasone
Group 4	0.9% 5ml normal saline

#### Table 2: Comparison of pain score in all the four groups

Pain Score	Group 1 n=36 number (percentage)	Group 2 n=36 number (percentage)	Group 3 n=36 number (percentage)	Group 4 n=36 number (percentage)	
0	13 (36.11%)	11 (30.56%)	12 (33.33%)	5 (13.89%)	
1	11 (30.56%)	9 (25%)	7 (19.44%)	3 (8.33%)	
2	6 (16.67%)	8 (22.22%)	7 (19.44%)	12 (33.33%)	
3	6 (16.67%)	8 (22.22%)	10 (27.78%)	16 (44.44%)	
P value	0.001				

# Table 3: Comparison of recall of pain in all the groups

Recall of pain	Group 1 n=36 number (percentage)	Group 2 n=36 number (percentage)	Group 3 n=36 number (percentage)	Group 4 n=36 number (percentage)	
No recall	31 (86.11%)	30 (83.33%)	28 (77.78%)	16 (44.44%)	
Recall	5 (13.89%)	6 (16.67%)	8 (22.22%)	20 (55.56%)	
Total	36	36	36	36	
p-value	0.001				

# DISCUSSION

Propofol is thought to be the drug of choice by most anesthetists, especially when rapid awakening is required such as in daycare surgical procedures. It is a commonly used drug agent in the induction of anesthesia for outpatient procedures. It had rapid recovery and have minimal adverse effects. However, pain is a very stressful adverse effect of Propofol. The pain of Propofol injection can either be immediate or delayed. Immediate pain is usually seen after direct irritation. Delayed pain is seen as a result of an indirect effect such as in kinin cascades. The latency of delayed pain is around 10-20 seconds.<sup>11</sup>

The study of Sapate et al included patients who had been induced with Propofol injection. The pain caused by the drug was prevented by lidocaine and dexmedetomidine administration. They found that there was not a significant difference between both groups. Hence, it was proven that lidocaine is an effective drug in the prevention as well as management of the pain caused by Propofol injection. Lidocaine also did not show any kind of adverse effects such as pain, wheal response, or edema.<sup>12</sup> Takubo et al. conducted a study to evaluate the effect of lidocaine for the prevention of Propofol injection pain. They also included the method of cooling of Propofol before injection. The study included 226 participants. They found that the lidocaine group showed 16% effectiveness in the management of the pain. They concluded that the pretreatment of patients induced with Propofol with lidocaine had less incidence of pain.<sup>13</sup>

Another similar study was conducted by Kwak et al for the comparison of the use of lidocaine and remifentanil for the reduction of pain caused by the Propofol injection. The study included 141 participants and they were divided into two groups. The effectiveness of both the drugs was similar. A combination of both the therapies had shown more effectiveness. Hence, they concluded that combination therapy was more reliable for the reduction of pain after a Propofol injection.<sup>14</sup> Euasobhon et al. also conducted a study in which the effectivity of lidocaine was evaluated for the reduction of Propofol injection pain. It was a meta-analysis of 85 studies. The author concluded that lidocaine is an effective pretreatment for the reduction of pain.<sup>15</sup>

Niazi et al. studied the combined treatment of nitrous oxide in oxygen and lidocaine for Propofol injection pain. The study was conducted on a total of 102 adults. The adults were allocated into four groups. Individual treatment and combination treatment was compared. It was observed that the incidence of pain reduction in the group treated with combination therapy was lesser compared to other groups.<sup>16</sup>

# CONCLUSION

The analysis of the data showed that Pethidine, Dexamethasone, and lignocaine can significantly decrease Propofol injection pain. The placebo is not effective in most cases. Moreover, the difference between the effectiveness of the aforementioned drugs is not significant.

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#### **Conflict of interest**

The present study did not have any kind of conflicts of interest

#### Permission

Permission was asked and taken from the ethical committee of the institute

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