

FREQUENCY OF PAIN DUE TO INJECTION OF PROPOFOL WITH IV ADMINISTRATION OF LIGNOCAINE WITH AND WITHOUT METOCLOPRAMIDE

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ABSTRACT

Objective: To determine the frequency of Propofol associated pain in patients undergoing general anaesthesia using lignocaine alone and metoclopramide given prior to lignocaine.

Study Design: Double blind Randomized controlled trial.

Place and Duration of Study: It was conducted in Anaesthesia department, Combined Military Hospital, Rawalpindi; over a period of Six Months from 20-02-2011 to 19-08-2011

Material and Methods: One hundred and twenty Patients were included in the study, and were randomly divided into two groups of 60 each. 20 ml (1% aqueous) Propofol solution was mixed with 2 ml of 2% lignocaine. Propofol dose was calculated as 2 mg/kg. Group A were given intravenous 10mg metoclopramide. One fourth dose of propofol (1% aqueous solution) was then given in the most prominent vein of the hand through cannula at a rate of 1 mL/s. Group B were given intravenous normal saline instead of metoclopramide, and then received 25% the total dose of propofol mixed with lignocaine in the same manner.

Results: Mean age was 31 ± 5.07 and 32.9 ± 6.42 in group- A and B respectively. In group-A, 70%patients and in group-B, 65%patients were male. Pain was present in 4(6.7%) patients in group-A, and in 13 (21.7%) patients in group-B. Significant difference between two groups was found ($p=0.018$).

Conclusion: It is concluded from this study, that intravenous metoclopramide given prior to mixture of lidocaine and propofol is superior to administration of lidocaine mixed with propofol alone to prevent propofol induced pain.

Keywords: Lidocaine, Metoclopramide, Pain on Propofol.

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INTRODUCTION

Propofol is one of the widely used intravenous agents. It is not a water soluble drug but the intravenous solution available in market is 1% aqueous solution (20 mg/20 ml). It is oil-in-water emulsion which contains soybean oil, glycerol and egg lecithin. This formulation is known to cause pain on injection. Its incidence varies from 28% to 90%¹. Pain is severe, sharp, itching or burning in nature that can cause discomfort and distress to the patient.

A number of studies have been performed to find out strategies to reduce the incidence of Propofol associated pain including mixing of

lignocaine or selecting a larger vein or combining these two strategies, combination of intravenous lignocaine and dexamethasone, pretreatment with fentanyl¹, pretreatment with flurbiprofenaxetil and prior injection of certain drugs like ondansetron, ketamine, opioids, magnesium sulfate, ketorolac or tramadol.

Though lignocaine has been found to be effective in reducing the incidence of pain, however, Propofol associated pain may still be there.

Metoclopramide increases gastric emptying, intestinal transit and lower esophageal sphincter pressure. This makes it one of the commonest antiemetic used for prevention of preoperative and postoperative aspiration, and postoperative nausea and vomiting². Importantly, it has local anesthetic properties like lignocaine.

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Statistical data shows that the incidence of Propofol associated pain is 5% when lignocaine (40mg) and metoclopramide (10 mg) are given together as compared to 20% when only lignocaine is given³.

The rationale of the study is to find out strategy to reduce the frequency of pain which occurs on injecting Propofol so that it may be used in other hospital as well. It will benefit patients in terms of recovery and good anesthetic experience.

MATERIAL AND METHODS

This was a Double blind Randomized clinical trial. It was conducted in Main operation theatre, Anaesthesia Department, Combined Military Hospital Rawalpindi. This study was carried out over a period of Six months from 20-02-2011 to 19-08-2011. Patients were included in the study through Non-Probability consecutive sampling. All ASA I and II patients of both gender and 20 to 50 years of age coming for elective surgeries, who require general anaesthesia. Patients who have history of Allergy/ hypersensitivity to Lignocaine and propofol.

- Disoriented patients.
- Patient with carotid artery disease.
- Patient with coronary artery disease.

The study was conducted after approval of the Hospital ethical committee and all the data were recorded after explaining the risk and benefits to the patients and getting informed consent.

The patient and the anesthetist making observations were blind to the drug administered. An intravenous access was secured by 18G intravenous cannula in most prominent vein of right hand of each patient before start of surgery. Randomization was done by computer generated table of random numbers. Patients were monitored in the operating room using non-invasive blood pressure monitoring and pulse oximetry. Rubber tourniquet was used to occlude vein for 1 mintue before administration of drugs.

Patients were randomly divided into two groups using random numbers table-1% aqueous solution of Propofol was mixed with 2 ml of 2% lidocaine. Group-A was given 10mg of metoclopramide intravenously. Then dose of propofol was calculated at dose of 2mg/kg, and 25% of this dose was injected into most prominent vein of the hand through cannula at a rate of 1 mL/s. Group-B was injected with normal saline intravenously instead of metoclopramide, then they received 25% the total dose of propofol mixed with lignocaine in the same manner. Pain was assessed as per patient response by the anaesthetist and was recorded.

Statistical analysis

All the data collected through the proforma were entered into the statistical package for social sciences (SPSS) version. Mean and standard deviation (SD) were calculated for quantitative data age, weightwhile frequency and percentage were calculated for qualitative data as gender and pain. Chi Square was used to compare gender and pain response between two treatments. Independent samples t-test was used to compare age. *p*-value of less than 0.05 was taken as significant.

RESULTS

One hundred and twenty patients were included in study, and they were randomly divided in two groups of 60 each. Regarding age distribution, majority of the patients in both groups were between 20-30 Years of age. Mean age was 31 ± 5.07 and 32.9 ± 6.42 in group-A and B respectively (table-1); [*p*= 0.007]. In group-A, 42 patients (70%) and in group-B, 39 patients (65%) were male, while 18 patients (30%) of group-A and 21 patients (35%) of group-B were female (table-2); (*p*= 0.559). Pain was present in 4 patients (6.7%) in group-A and 13 patients (21.7%) in group-B. Frequency of pain was significantly higher in group-B (*p*=0.018) (table-3).

DISCUSSION

The popularity and usage of propofol has increased markedly around globe due to its rapid onset and short duration of action. But, pain

encountered upon its injection, is a major drawback to its use. Different methods have been tested, which had different level of success⁴.

Site of injection and size of vessel are directly related to incidence and severity of pain caused by propofol⁴. For example, pain is less if propofol is injected into antecubital fossa⁴. Clinical factors such as younger age group and female gender seem to increase pain on injection of propofol⁵.

So using larger vein, warming the site of injection or cooling it, mixing lignocaine or

pain may have delayed onset, but may be immediate if it involves direct action on nerve endings.

Many studies have been conducted on efficacy of lignocaine, and they showed its effective role⁹. It may be due to its local anesthetic action or by inhibition of kinin release⁴. Different Concentrations were tested. P. Lee et al compared dose of 40 mg in two concentrations of 1% and 2%; and found good results. Sharon et al on the other hand, used same volume but different concentrations. He took 1 ml of 0.5%, 1% and 2%, thereby using 5 mg, 10 mg, and 20 mg; and

Table-1: Distribution on the basis of age among groups.

Age (Year)	Group-A (Metoclopramide+lignocaine) (n=60)		Group-B (Lignocaine alone) (n = 60)	
	No.	%	No.	%
20-30	39	65.0	38	63.3
31-40	13	21.7	16	26.7
41-50	08	13.3	06	10.0
Mean ± SD	31 ± 5.07		32.9 ± 6.42	
p-value	0.007			

Table-2: Gender distribution of two groups.

Sex	Group-A (Metoclopramide+ lignocaine) (n = 60)		Group-B (Lignocaine alone) (n = 60)	
	No.	%	No.	%
Male	42	70.0	39	65.0
Female	18	30.0	21	35.0
p-value	0.559			

Table-3: Distribution of cases by pain responses.

Pain	Group-A (Metoclopramide+ lignocaine) (n = 60)		Group-B (Lignocaine alone) (n = 60)	
	No.	%	No.	%
Yes	04	06.7	13	21.7
No	56	93.3	47	78.3
p-value	0.018			

pretreatment with different drugs like metoclopramide, ondansetron, ketamine; can reduce this pain⁶. Most common of these is lignocaine but it may not be effective with pain occurring in 13% and 32% patients^{4,7}.

Propofol is an irritant to the skin and even venous intema¹¹. It is speculated that the pain is due to formation of kinins, including bradykinin. Bradykinin is a vasodilator and increases permeability. So it increases contact of propofol with free nerve endings, resulting in pain⁸. This

combined it with propofol (19 ml of 1% aqueous solution). They recommended 20 mg for prevention of propofol induced pain⁴.

In present study administration of intravenous metoclopramide prior to injection of 2 ml of 2% lignocaine plus propofol, reduced propofol-induced pain on injection significantly as compared lignocaine alone for the sake of prevention.

The use of lignocaine pretreatment to reduce pain on propofol injection has become a standard

practice. In a systematic review, Picard and Tramer found that lignocaine had the best effect for minimizing pain. They also concluded that retention of lignocaine with tourniquet similar to Bier's block was most useful method rather than mixing lignocaine with propofol or giving IV lignocaine before propofol injection¹⁰.

On the other hand, metoclopramide has been shown to be effective for reducing the incidence of pain on injection of propofol, probably because of its local anesthetic action¹¹. Liaw and coworkers have compared different techniques that included intravenous metoclopramide after venous occlusion by using tourniquet. They concluded that this was the most useful method for reducing propofol induced pain on injection¹². In the first report by Ganta et al¹³, intravenous injection of metoclopramide 5mg before the induction of anesthesia with propofol, reduced the incidence of pain on injection. Similarly, a mixture of propofol to which metoclopramide 20mg is added was effective for reducing the incidence of injection pain. Maroof et al¹⁴ have demonstrated the analgesic efficacy of metoclopramide 10mg administered intravenously, using a venous tourniquet for one minute before propofol injection for reducing propofol-induced pain on injection¹⁴. A comparative study has been reported that intravenous retention of metoclopramide with a tourniquet is the most useful method for reducing the incidence of pain on injection of propofol¹². In a study Fujii and coworkers have shown that intravenous metoclopramide reduces pain effectively if 5 or 10 mg is given, and vein is occluded for 01 minute¹¹. Also, Fujii et al tried different doses of intravenous lignocaine and metoclopramide. They used lignocaine 40 mg, but dose of metoclopramide was different. They tested 5 mg, 10 mg, and 2.5 mg. They concluded that using 5 or 10 mg of metoclopramide decreases the incidence of pain; but mean intensity scores are not reduced in comparison to 2.5 mg of metoclopramide or placebo (normal saline)¹⁵.

Various studies were undertaken to find out other drugs which could be as effective as lignocaine in decreasing pain on injection. Alfentanil was tested against lignocaine, and combination of both was tested as well. And it was found that combination is better than either of these used alone, however, prevention was better by alfentanil than lignocaine when used alone (30% and 38.5%)¹⁶. Fentanyl has also been counted in those opioids which can prevent propofol induced pain¹⁷. Another study reported that pretreatment with 100 micro gram fentanyl provided reduction in propofol induced pain which was not statistically different than that with lignocaine¹⁸. Other opioids like remifentanyl are as good as lignocaine in relieving propofol induced pain¹⁹.

One report suggests that combination of prilocaine with propofol reduces pain to same extent as with lignocaine²⁰. Saadawy et al tried various drugs like ketamine, thiopentone, meperidine and lignocaine. And they recommended that ketamine pretreatment at dose of 0.4 mg/kg, with occlusion of vein for 1 minute²¹.

Yoshikawa examined the analgesic effect of clonidine and found that pain on injection of propofol was lower in group receiving clonidine²².

Another report suggested that pretreatment with magnesium sulfate 2.48 mmol can be used as an alternative for reduction of pain on propofol injection as it is a calcium channel blocker and antagonist of NMDA receptor ion channel²³. However they noticed minimal pain on injection of magnesium. Two recent studies with IV paracetamol pre treatment showed that it is effective in reducing pain but not as good as 40mg lignocaine²⁰.

Ondansetron is a widely used anti emetic drug. Ye et al²⁴ tested ondansetron (OND) in rats, and found it more potent local anesthetic than lidocaine²⁴. It was found that numbness is caused when OND is injected subcutaneously. OND has multiple actions like it is μ opioid agonist,

sodium channel blocker, apart from being 5HT₃ receptor antagonist. So it may be used to prevent propofol induced pain. In a double blinded study conducted, ondansetron 0.1 mg kg⁻¹ was proved to alleviate pain on injection of propofol upto 50%. Of course its anti-emetic effect is bonus too in general anesthesia¹¹. Recently Zahedi et al²⁵ recommended its use for prophylaxis of propofol induced pain.

CONCLUSION

It is concluded from this study, injecting metoclopramide prior to administration of lignocaine mixed in propofol is superior to administration of lignocaine mixed with propofol alone, for the sake of reducing propofol induced pain. Administration of intravenous metoclopramide then 25% of the total calculated dose of propofol (2 mg/kg) mixed with 2 ml of 2% lignocaine provided the optimal dose and timing to reduce propofol-induced pain on injection significantly as compared to 25% the total dose of propofol mixed with lignocaine in the same manner, without metoclopramide before injecting Propofol and lignocaine.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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