

Propofol Induced Pain: Comparison of Efficacy of Pre-Treatment with Paracetamol and LidocaineHemani Ahuja¹, Jithin J Cherian²¹Associate Professor, Department of Anaesthesiology and Critical Care, Christian Medical College & Hospital, Ludhiana²Senior Resident, Department of Anaesthesiology and Critical Care, Christian Medical College & Hospital, Ludhiana

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Conflict of interest: Nil

Abstract:

Background and Objectives: Propofol is one of the most commonly used agent for induction of anaesthesia due to its rapid onset, short duration of action and favourable side effects profile.[1-2] But despite these favourable properties, the pain caused during injection of propofol is one of the most excruciating pain that patient recalls during perioperative period. None of the interventions alleviate this pain completely. So we aimed to investigate the effect of i.v Paracetamol pre-treatment on propofol induced pain and to compare it with lidocaine.

Materials and Methods: This Prospective, randomized, double blind study was conducted on 300 patients aged 20-60 years, American Society of Anaesthesiologists (ASA) physical status 1 and 2 undergoing surgeries under general anaesthesia. The patients were allocated to two groups. In Group L- Patients were pre-treated with 0.5mg/kg of lidocaine diluted to 20ml and in Group P- Patients were pre-treated with 2mg/kg of paracetamol diluted to 20ml before administering propofol.

Results: The incidence of pain on injection of propofol in i.v. Paracetamol (Group P) and lidocaine (Group L) groups were 89.3%, 34.7% respectively($p < 0.001$). Group L had better analgesia than Group P for all the VRS values ($p < 0.001$). Chi-square test was used for statistical analysis. Differences were considered to be significant at $p < 0.05$.

Conclusions: We concluded that i.v. Paracetamol is not as effective as lidocaine on propofol associated pain.

Keywords: Propofol, Pain, Lidocaine, Paracetamol.

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Introduction

Propofol causes smooth induction and rapid recovery, so it is one of the most popular induction agent used.[1,2] But pain caused during injection is very distressing for the patient and it happens in 28% to 90% of adults.[3.] The pathophysiology of this pain is attributed to mainly three mechanisms. The first mechanism relates to triggering of local kallikrein-kinin cascade, the second proposed mechanism suggested stimulation of nerve endings in the venous wall and the third cause relates to pain due to pH and concentration of propofol.[4]

So various interventions have been investigated to alleviate this pain which include addition of lidocaine to propofol, cooling or warming the drug, and pretreatment with ephedrine, opioids, ketamine.[4,5,6,]

Among these intravenous injection of lidocaine in conjunction with venous occlusion is the most effective intervention.[7,8,9,] Paracetamol is widely used for pain management. Its clinical

effects mainly arise from central actions. Recent studies have demonstrated its weak peripheral action by blocking impulse generation within bradykinin-sensitive chemoreceptors responsible for generating nociceptive impulses.[10]

As very few studies have explored the use of paracetamol on propofol injection pain, we aimed to compare the effect of i.v. paracetamol with lidocaine for propofol induced pain.

Materials and Methods

After approval from Institutional Ethics Committee and Review Board and after obtaining written informed consent, this Prospective, randomized, double blind study was conducted on 300 patients aged 20-60 years, American Society of Anaesthesiologists (ASA) physical status 1 and 2 undergoing surgeries under general anaesthesia. Patient who had history of hyper sensitivity to Propofol (egg allergy), Paracetamol or Lidocaine

were excluded from the study. The relevant investigations were done after taking a detailed history and patients were kept nil orally for six hours prior to surgery.

These patients were randomly divided into 2 groups of 150 each using block randomization. The drug was freshly prepared by an anesthetist who was not involved in the study. A 20-gauge I.V cannula was inserted into a superficial radial vein and a pneumatic tourniquet (pressure inflated to 70 mmHg) was placed on the upper arm, to occlude the venous drainage. The patients were pretreated over a period of 10 seconds with one of the pretreatment solutions: 0.5mg/kg of lidocaine diluted to 20 ml (Group L), or 2mg/kg of paracetamol (Group P) diluted to 20ml. After 2 min, the occlusion was released and one-fourth of the total calculated dose of propofol (Propofol 1%) was delivered through the i.v. line. After 20 seconds of injection of propofol, a clinician blinded to the group assignment, will evaluate pain using a four- point verbal rating scale (VRS) (none = 0, mild = 1, moderate = 2, and severe = 3) and noticing any behavioural signs associated. Behavioural signs were considered as VRS = 3, when the patient had tears, arm withdrawal, strong

vocal response or responses accompanied with facial grimacing. Thereafter induction of anesthesia was continued.

Statistical analysis was performed using SPSS software version 21.0. Categorical data was expressed as number or percentage. The groups were compared using Chi-square test. The chi square test was used to assess differences between categorical variables. A p value of less than 0.5 was considered significant.

Results

Three hundred patients were screened for this study and no one was excluded. There was no significant difference in demographic data between the groups (Table 1). The results for incidence of pain during injection of propofol in two groups are shown in Figure 1. 89.3% patients in Group P complained pain whereas this number was only 34.7% in Group L ($p < 0.001$). The data on severity of pain is shown in Table 2 and Figure 2. In Group L, only 33.3% patients had mild pain whereas this number is 66% in Group P. 1.3% patients experienced moderate pain and no one had severe pain in Group L whereas 22.7% patients had moderate pain and 0.7% had severe pain in Group P ($p < 0.001$).

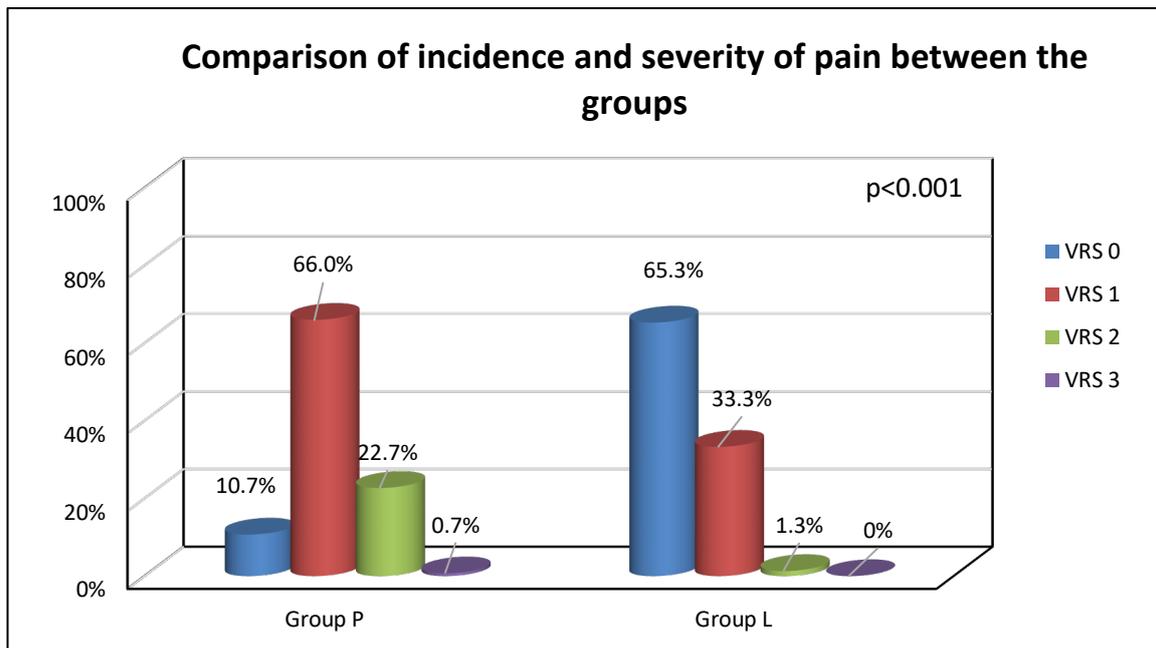


Figure 2: Comparison of incidence and severity of pain between the groups

Discussion

This study was aimed to evaluate and compare the effects of paracetamol and lignocaine pretreatment on propofol injection pain during anesthesia induction. The results of our study showed that there is significant difference in pain caused by propofol between two groups. The number of patients who were pain free in Group L was 65.3% while this number was only 10.7% in Group P. In

a systematic study on 56 studies by Picard et al, including 6264 patients and 12 various drugs, showed that intravenous lidocaine (0.5 mg/kg), through the ligation of a tourniquet on the forearm, 30 to 120 seconds before propofol injection, is able to reduce the pain in up to 60% of patients [14].

Similarly, the results of Radaideh's study in 2007 on 200 patients, indicated that 4 cc of lidocaine 1% reduces the pain of propofol injection by 68 % [15].

The results of these studies are consistent with our findings that lidocaine can reduce pain due to propofol injection upto 65.3%. But majority of the patients who had pain had only mild pain (33.3%), only 1.3% had moderate pain and no patient complained severe pain. Paracetamol is a centrally acting analgesic derived from p-aminophenol. It is widely used for management of pain. Its analgesic effect is most likely due to its effect on central nervous system, although it has shown some peripheral effects. Recent studies have discovered a cyclogenase-2 enzyme that is sensitive to paracetamol.

When paracetamol was used for propofol induced pain in study done by Radaideh, 54% of paracetamol group(with 50 patients) had no pain [15]. Similarly Borazan et al. in 2010 investigated and compared the effects of three different doses of paramol (0.5mg,1mg,2mg/kg) with lignocaine (0.5mg/kg) and group C(control group) on the reduction of propofol injection pain. The study was done on 250 patients with each group having 50 patients. The pain was 76% in control group, 26% in lidocaine group, 40% in P 0.5 group, 24% in P 1 group, 8% in P 2 group [16]. In 2008, Canbay O et al. did research to see the effects of 40 mg lidocaine and 50 mg of acetaminophen on propofol injection pain. The results showed pain 64% in control group, 22% in paracetamol group,8% in lidocaine group. It was concluded that acetaminophen reduces propofol injection pain but not as much as lidocaine [17]. In a similar study conducted by Alipour M et al.in 2014 concluded that number of patients who were pain free in lidocaine group was 69.64% and in paracetamol group was 28.57% [18]. Similarly in our study also lidocaine was effective in 65.3% cases while in paracetamol only 10.7% patients. Some difference in numbers can be due to the fact that we took 150 patients in each group. So lidocaine in dose of 0.5mg/kg is superior to 2mg/kg of paracetamol in reducing pain associated with propofol administration.

The strength of this study is that it is a randomized, double-blind controlled study. Moreover, it was therapeutic also in which patient benefitted. Also a large sample size also added further support to our findings.

Conclusions

We conclude that administration of iv lidocaine for pretreatment before propofol injection is a superior method to paracetamol pretreatment.

References

1. Hamd MAE. The Clinical Pharmacology of Propofol: A Brief Review. *Open J Anesthesiol.* 2013 Oct 14; 3(8):367–73.

2. Cockshott ID. Propofol ('Diprivan') pharmacokinetics and metabolism- an overview. *Postgrad Med J.* 1985;61 Suppl 3:45–50.
3. Tan CH, Onsiong MK. Pain on injection of propofol. *Anaesthesia.* 1998;53(5):468–76.
4. Kim K, Kim YS, Lee D-K, Lim B-G, Kim H-Z, Kong M-H, et al. Reducing the Pain of Microemulsion Propofol Injections: A Double-Blind, Randomized Study of Three Methods of Tourniquet and Lidocaine. *Clin Ther.* 2013; 35(11):1734–43.
5. Jalota, L., Kalira, V., George, V.E., Shi, Y.Y., Hornuss, C., Radke, O., Pace, N.L. and Apfel, C. Prevention of Pain on Injection of Propofol: Systematic Review and Meta-Analysis. *British Medical Journal,* 2011;342: d1110.
6. Lee, S.K. Pain on Injection with Propofol. *Korean Journal of Anesthesiology,* 2010;59: 297-29
7. Madenoglu, H., Yildiz, K., Dogru, K. and Boyaci, A. Efficacy of Different Doses of Lidocaine in the Prevention of Pain Due to Propofol Injection: A Randomized, Open-Label Trial in 120 Patients. *Current Therapeutic Research,* 2003;64: 310-316.
8. Kaya, S., Turhanoglu, S., Karaman, H., Ozgiin, S. and Basak, N. Lidocaine for Prevention of Propofol Injection-Induced Pain: A Prospective, Randomized, Double-Blind, Controlled Study of the Effect of Duration of Venous Occlusion with a Tourniquet in Adults. *Current Therapeutic Research,* 2008;69: 29-35.
9. Borazan, H., Erdem, T.B., Kececioglu, M. and Otelcioglu, S. Prevention of Pain on Injection of Propofol: A Comparison of Lidocaine with Different Doses of Paracetamol. *European Journal of Anaesthesiology,* 2010;27: 253-257.
10. Anderson, B.J. Paracetamol (Acetaminophen): Mechanisms of Action. *Pediatric Anesthesia,* 2008;18: 915-921.
11. Macario, A., Weinger, M., Carney, S. and Kim, A. Which Clinical Anesthesia Outcomes Are Important to Avoid? The Perspective of Patients. *Anesthesia and Analgesia,* 1999; 89: 652-658.
12. Sim, J.Y., Lee, S.H., Park, D.Y., Jung, J.A., Ki, K.H., Lee, D.H. and Noh, G.J. Pain on Injection with Microemulsion Propofol. *British Journal of Clinical Pharmacology,* 2009; 67: 316-325.
13. Picard P, Tramèr MR. Prevention of Pain on Injection with Propofol: A Quantitative Systematic Review. *Anesthesia & Analgesia.* 2000; 90: 963-969.
14. El-Radaideh KM. Effect of pretreatment with lidocaine, intravenous paracetamol and lidocaine-fentanyl on propofol injection pain. Comparative study. *Rev Bras Anesthesiol.* 2007; 57(1):32–8.

15. Borazan H, Erdem TB, Kececioglu M, Otelcioglu S. Prevention of pain on injection of propofol: a comparison of lidocaine with different doses of paracetamol. *Eur J Anaesthesiol.* 2010; 27(3):253–7.
16. Canbay O, Celebi N, Arun O, Karagoz AH, Saricaoglu F, Ozgen S. Efficacy of intravenous acetaminophen and lidocaine on propofol injection pain. *Br J Anaesth.* 2008; 100(1):95–8.
17. Alipour M, Tabari M, Alipour M. Paracetamol, Ondansetron, Granisetron, Magnesium Sulfate and Lidocaine and Reduced Propofol Injection Pain. *Iran Red Crescent Med J.* 2014; 16(3): e16086.