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### RESEARCH ARTICLE

## ONDANSETRON VERSUS LIDOCAINE 2% FOR THE PREVENTION OF PROPOFOL INJECTION INDUCED PAIN.

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#### Abstract

**Background:** The use of Propofol often results in pain upon injection, which is sometimes very distressing for patients. Injection-induced pain during induction of anesthesia can result in patient's discomfort and this study aimed to alleviate this pain and compare between lidocaine and ondansetron as a pretreatment drug.

**Objectives:** This study was performed to evaluate the comparison on pain severity in patients undergoing propofol injection.

**Patients and Methods:** In this double-blind randomized clinical trial, 90 patients with ASA class I and II undergoing anesthesia with propofol injection were selected for the study from 2015 to 2016 in Qassim National Hospital. Patients were randomly assigned to three groups received either 40 mg lidocaine or ondansetron 4 mg and placebo group. The severity of injection pain was assessed using a four-point scale.

**Results:** The pain severity in ondansetron group was significantly lower compared with the lidocaine 2% group ( $p < 0.01$ ).

**Conclusions:** Ondansetron is an effective preinduction drug for pain reduction in patients under propofol injection. Hence, its use for reduction of Propofol injection-induced pain is recommended and more effective than lidocaine.

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#### Introduction:-

Propofol, commonly dubbed as “milk of anesthesia”, is one of the most popular intravenous anesthetic agents in modern medicine. The mechanisms of action on the central nervous system are rather complex with interactions at various neurotransmitter receptors [1]. Propofol is the most widely used intravenous anesthetic drug in induction and maintenance of anesthesia for its rapid onset, short duration and prompt recovery. However, its disadvantage of pain at injection site is unpleasant experience for most patients, especially when a small vein on the dorsum of hand was selected. The pain can be highly sharp, aching, or burning which may decrease the patients' satisfaction with anesthetic care. It is reported that incidence of propofol injection pain varies between 28% and 90% in adults and 28% and 85% in children in the absence of other pretreatments [2]. It has been ranked as the seventh among the top 33 clinical problems of anesthesia in current clinical setting by American anesthesiologists [3].

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Mechanism of the propofol induced pain has been unclear. Yet as reported, one of the potential reasons may be that propofol is insoluble in water and prepared in oil emulsion which consists of long-chain triglyceride solution [4]. These lipid solvents can directly irritate the skin, mucous membranes, and venous intima, and thus stimulate nociceptors and free nerve endings [5]. What's more, propofol can also lead to a delayed pain at about 15 seconds after injection of propofol due to the activation of kallikrein and bradykinin [6]. Various factors, including the site of injection, speed of injection, vein size, aqueous phase propofol concentration, propofol temperature, blood buffering, and the concomitant use of various drugs, appear to influence this pain [7-9]. Many strategies has been proposed to reduce propofol-induced pain with variable results including both pharmacological (e.g. pre-treatment with lidocaine, ondansetron, magnesium sulfate, nafamostat, ketamine or topical nitroglycerine application with propofol, diluting propofol with 5% dextrose or 10% intralipid and using medium and small-chain triglycerides) and non-pharmacological methods have been used [10, 11].

### **Materials and Methods:-**

A randomized, double-blind, placebo-controlled study was designed to evaluate the efficacy and safety of the 2 % lidocaine and ondansetron for prevention of propofol-induced pain as well in hospitalized surgical patients. This study was done in Qassim National Hospital - KSA. Informed consent was obtained from all patients prior to be enrolled in this study.

In our study, a total of 90 patients who were categorized as American Society of Anesthesiologist (ASA) class I and II, aged between 18 to 50 years, randomly assigned to three groups of 30 patients each. No premedication was administered. A 20 gauge cannula was placed into the largest vein on the dorsum of the left hand after placing the routine monitors include lead II electrocardiogram, noninvasive blood pressure and pulse oximeter. Patients received 2 mL pretreatment lidocaine 40 mg (group L), 4 mg ondansetron in the saline (group O), solution saline control group (group C) intravenously for a period of 10 seconds while the venous drainage was occluded by placing an air-filled tourniquet (pressure inflated to 70 mm Hg) on the upper arm by an assistant . A blinded anesthetist prepared the solutions, and the investigator did not know the contents of the solutions. The occlusion was released after 20 seconds. Then 2 mg/kg propofol 1% was injected for a period of 10 seconds. No analgesics or sedatives were administered before propofol. Another clinician, unaware of the group to which the patients had been allocated, assessed the level of pain on injection of propofol. The patients were asked a standard question "Is the injection comfortable?" The verbal response and behavioral signs, such as facial grimacing, arms withdrawal, or tears, were recorded. We used a four point categorical verbal rating scale (VRS-4) with the words "no pain," "mild pain," "moderate pain" and "severe pain". A score of 0 to 3, corresponding to 0=no, 1=mild, 2=moderate, 3= severe pain, was noted.

We injected sedative and opioid after propofol to get the most reliable response to our patients. Anesthetic induction was continued with fentanyl 2 µg/kg. Tracheal intubation was facilitated with 0.5 mg/kg cisatracurium and anesthesia was maintained with isoflurane 1.2%. The patients were extubated after administering muscle relaxation antagonist. Patients were followed up, during first 6 hours and were assessed for pain, swelling or allergic reaction at the injection site of propofol by a blinded anesthesiologist.

Patients with known hypersensitivity to propofol, concomitant analgesic or sedative medication; indications for rapid sequence intubation, thin dorsal veins, and uncooperative patients were excluded.

### **Statistical analysis:-**

The age, sex, weight, and pain severity were the study variables. Data was analyzed using SPSS 18.0 (SPSS Inc, Chicago, Illinois, and the United States). Differences were tested by independent-samples t test, Fisher exact test, and Chi square test and were considered statistically significant at P values < 0.05.

### **Results:-**

A total of 90 patients were randomly allocated into three groups. Demographic data were comparable among the groups and there was no statistical difference between the three studied group as regarding age, weight and sex (Table 1).

**Table 1:-** Demographic variables.

Variables	Control group	Lidocaine group	Ondanetron group
Patient number	30	30	30
Age , y	46.233±19.266	46.233±19.266	47.667±16.953
Weight , kg	69.4±6.63	69.4± 6.33	69.3±6.99
Gender	Male	22	29
	Female	8	4

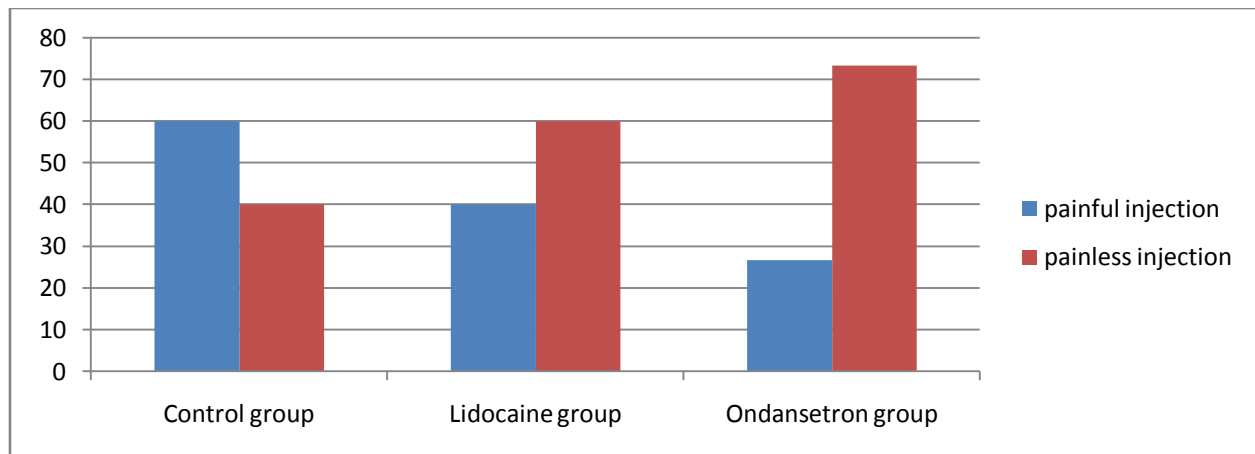
Pain after the application of propofol was present in 38 patients (47.2%) patients. The highest frequency of pain was recorded in the control group (18 patients, 60%), and significantly lower ( $p < 0.01$ ) in the patients who received ondansetron (8 Patients; 26.7%) in comparison with control group (table 2 and figure 1).

As regarding the pain score, the incidence of no pain was significantly reduced ( $P < 0.01$ ) in ondansetron group (22 patients, 73.3%) when compared with control group (Table 2) and the incidence of moderate pain (1patient, 3.4%) and was significantly reduced ( $P < 0.05$ ) in the ondansetron group and also significantly reduced ( $P < 0.05$ ) in the lidocaine group (2 patients, 6.7 %) (Table 3 and figure 2).

**Table 2:-** Presence of pain reaction after propofol

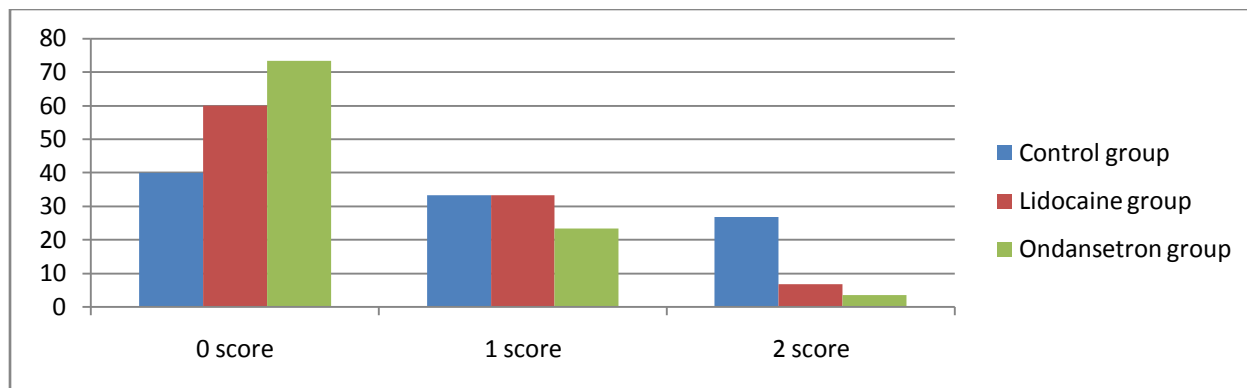
Groups	Painful injection	Painless injection
Control group	18 (60.0%)	12 (40.0%)
Lidocaine group	12 (40.0%)	18 (60.0%)
Ondansetron group	8 (26.7%) * *	22 (73.3%)
Total	38 (42.2%)	52 (57.8%)

\*  $p < 0.05$ ; \*\*  $p < 0.01$  – compared with control group (Pearson  $\chi^2$  test)

**Figure 1:-** . Percentage of pain reaction after propofol injection**Table 3:-** Pain intensity after administration of propofol

Groups	Verbal rating scale		
	0	1	2
Control group	12 (40.0%)	10 (33.3%)	8 (26.7%)
Lidocaine group	18 (60.0%)	10 (33.3%)	2 (6.7%) *
Ondansetron group	22 (73.3%) *	7 (23.3%)	1 (3.4%) **

\*  $p < 0.05$ ; \*\*  $p < 0.01$  – compared with control group (Pearson  $\chi^2$  test)



**Figure 2:-** Percentage of Pain intensity after propofol injection

### Discussion:-

Propofol is one of the common drugs in anesthesia induction and maintenance, but it induces pain and can cause extreme distress among patients [12]. Mechanism of pain induction by propofol in patients is not unclear. Some investigators believe that propofol as a member of phenol group can irritate the skin; mucus membrane and venous intima immediately stimulate nociceptors and free nerve endings [13]. Some other investigators found that propofol might increase the contact between aqueous phases of propofol and free nerve endings, resulting in delayed pain within half a minute [14].

Yull *et al.*, in their study reported that propofol induced pain might be related to the release of local kininogens and nonsteroidal anti-inflammatory drugs may have a role in pain reduction [15]. Although injection pain of propofol has been reported formerly, this could not cause a limitation and physicians try to solve this discomfort. Some interventions such as injecting lidocaine or other drugs prior to propofol injection had been assessed in randomized clinical trials [16].

Ondansetron has blocking ability for sodium channels. Peripheral 5-HT<sub>3</sub> receptors involve nociceptive pathways. Ondansetron binds to the opioid receptors in humans and exhibits agonist activity. As a result of its multifaceted actions as a Na channel blocker also, ondansetron may potentially be used to alleviate pain induced by a drug such as propofol [17].

This study aimed to evaluate and compare the effects of ondansetron and lidocaine on propofol injection pain during anesthetic inductions. The results of this study showed that pain caused by propofol had a significant difference when compared with the control group and the number of patients with painless injection was reduced in patients pretreated with ondansetron than the patients pretreated with lidocaine. The number of patients without pain was 18 in lidocaine patient group (60%), 22 in ondansetron group (73.3%).

Ondansetron is commonly used as an antiemetic drug [18]. In animal study, demonstrated that ondansetron administered intrathecally reduces the nociceptive responses of dorsal horn neurons [19].

Ye *et al.*, showed that ondansetron is about 15 times more potent as local anesthetic than lidocaine, and this property probably contributes to its antiemetic action. Ondansetron also results in numbness when injected under the skin [20]. Ondansetron has the ability to block sodium channels. Peripheral 5-HT<sub>3</sub> receptors involve nociceptive pathways [20]. Ondansetron binds to the opioid  $\mu$  receptors in humans and exhibits agonist activity [21].

As a result of its multifaceted actions as a Na channel blocker, a 5-HT<sub>3</sub> receptor antagonist, and  $\mu$ -opioid agonist, ondansetron may potentially be used to alleviate pain produced by a drug similar to propofol. Ondansetron is used at the time of induction of anesthesia for the prevention of post operative nausea and vomiting (22). The usual dose of ondansetron in adults is 4 mg [22].

The use of forearm veins decreases the incidence of pain up to 2.5% (23). Lidocaine pretreatment reduces the incidence of pain to 17.5% (28) and 19.5% [24] while in our study lidocaine decreased pain by 60%.

Other study has shown that mixed propofol and 1% lidocaine reduces the incidence of pain on injection significantly [25]. Hamid et al, demonstrated that the high incidence of pain or discomfort in 82.2% of cases, which was decreased to 24.4% after ondansetron pretreatment which was agreed with our results ( pain decreased from 60 % to 26.7 % in ondansetron group) [26] .

Sumalatha et al. concluded that Pre-treatment with IV ramosetron 0.3 mg is equally effective as 0.5 mg/kg of 2% lignocaine in preventing propofol-induced pain and both were better than ondansetron. The overall incidence and intensity of pain were significantly less in Groups L and R compared to Group O ( $P \leq 0.001$ ). The incidence of mild to moderate pain in Groups O, R and L was 56%, 26% and 20%, respectively. The incidence of score '0' (no pain) was significantly higher in Group L (76%) and Group R (72%) than Group O (34%) ( $P < 0.001$ ) [27] Which is not agreed with our study.

Singh et al. showed that granisetron, nitroglycerine, and magnesium sulfate were consecutively the most effective drugs in attenuating pain of intravenously injected propofol [28]. The results of Zahedi et al. showed that ondansetron reduced the aforementioned pain in 57.8% of the patients [29], which is approximately near to our results (73.3%)

Alipour et al studied five drugs to reduce propofol injection induced pain (Paracetamol, Ondansetron, Granisetron, Magnesium Sulfate and Lidocaine) the results of this study indicated that all of five drugs had almost similar effects in reducing the propofol injection pain compared with the control group. The effects of lidocaine and granisetron are similar (69.64%) and higher than the other groups. The effects of magnesium sulfate (51.78%), ondansetron (39.28%) and paracetamol (28.57%) are less than the lidocaine and granisetron, therefore, these results were not matched with our results [30].

**Conclusions:** Ondansetron is an effective preinduction drug for pain reduction in patients under propofol injection hence, its use for reduction of protocol injection-induced pain is recommended and more effective than lidocaine.

### References:-

1. Trapani G, Altomare C, Liso G, Sanna E, Biggio G. Propofol in anesthesia. Mechanism of action, structure-activity relationships, and drug delivery. *Current medicinal chemistry*. 2000; 7(2):249–71. [PubMed: 10637364]
2. Stark R, Binks S, Dutka V, O'Connor K, Arnstein M and Glen J. A review of the safety and tolerance of propofol ('Diprivan'). *Postgrad Med J* 1984; 61: 152-6.
3. Macario A, Weinger M, Truong P and Lee M. Which clinical anesthesia outcomes are both common and important to avoid? The perspective of a panel of expert anesthesiologists. *Anesth Analg* 1999; 88: 1085-91.
4. Devlin JW, Lau AK and Taniot MA. Propofol-Associated Hypertriglyceridemia and Pancreatitis in the Intensive Care Unit: An Analysis of Frequency and Risk Factors. *Pharmacotherapy* 2005; 25: 1348-52.
5. Ambesh SP, Dubey PK and Sinha PK. Ondansetron pretreatment to alleviate pain on propofol injection: a randomized, controlled, double-blinded study. *Anesth Analg* 1999; 89: 197-9.
6. Scott R, Saunders D and Norman J. Propofol: clinical strategies for preventing the pain of injection. *Anaesthesia* 1988; 43: 492-4.
7. Jalota L, Kalira V, George E, Shi YY, Hornuss C, Radke O, Pace NL and Apfel CC. Prevention of pain on injection of propofol: systematic review and meta-analysis. *BMJ* 2011; 342: d1110.
8. Picard P and Tramer MR. Prevention of pain on injection with propofol: a quantitative systematic review. *Anesth Analg* 2000; 90: 963-9.
9. Tan C and Onsiang M. Pain on injection of propofol. *Anaesthesia* 1998; 53: 468-76.
10. Mattila M and Koski E. Venous sequelae after intravenous propofol ('Diprivan')--a comparison with methohexitone in short anaesthesia. *Postgrad Med J* 1984; 61: 162-4.
11. King SY, Davis MF, Wells EJ, Murchison DJ and Pryor PJ. Lidocaine for the prevention of pain due to injection of propofol. *Anesth Analg* 1992; 74: 246-9.
12. Klement W, Arndt JO. Pain on injection of propofol: Effects of concentration and diluent. *Br J Anaesth* 1991;67:281-4.
13. Ambesh SP, Dubey PK, Sinha PK. Ondansetron pretreatment to alleviate pain on propofol injection: A randomized, controlled, double-blinded study. *Anesth Analg* 1999;89:197-9.
14. Scott RP, Saunders DA, Norman J. Propofol: Clinical strategies for preventing the pain of injection. *Anaesthesia* 1988;43:492-4.

15. Yull DN, Barkshire KF, Dexter T. Pretreatment with ketorolac and venous occlusion to reduce pain on injection of propofol. *Anaesthesia* 2000;55:284-7.
16. Agarwal A, Ansari MF, Gupta D, Pandey R, Raza M, Singh PK, *et al.* Pretreatment with thiopental for prevention of pain associated with propofol injection. *Anesth Analg* 2004;98:683-6.
17. Nam M, Yoon H. Effect of ondansetron combined with dexamethasone on postoperative nausea and vomiting and pain of patients with laparoscopic hysterectomy. *J Korean Acad Nurs* 2009;39:44-52.
18. Lee EH, Lee SH, Park DY, Ki KH, Lee EK, Lee DH, Noh GJ. Physicochemical properties, pharmacokinetics, and pharmacodynamics of a reformulated microemulsion propofol in rats. *Anesthesiology* 2008;109(3):436-47.
19. Ali Z, Wu G, Kozlov A, Barasi S. The role of 5HT<sub>3</sub> in nociceptive processing in the rat spinal cord: results from behavioural and electrophysiological studies. *Neurosci Lett* 1996;208(3):203-7.
20. Ye JH, Mui WC, Ren J, Hunt TE, Wu WH, Zbuzek VK. Ondansetron exhibits the properties of a local anesthetic. *Anesth Analg* 1997;85(5):1116-21.
21. Gregory RE, Ettinger DS. 5-HT<sub>3</sub> receptor antagonists for the prevention of chemotherapy-induced nausea and vomiting. A comparison of their pharmacology and clinical efficacy. *Drugs* 1998;55(2):173-89.
22. Ebrahim Soltani A, Mohammadinasab H, Goudarzi M, Arbabi S, Mohtaram R, Afkham K, Momenzadeh S, Darabi ME. Acupressure using ondansetron versus metoclopramide on reduction of postoperative nausea and vomiting after strabismus surgery. *Arch Iran Med* 2010;13(4):288-93.
23. MJ, Lees NW. Assessment and modification of pain on induction with propofol (Diprivan). *Anaesthesia* 1985;40(11):1117-20.
24. Johnson RA, Harper NJ, Chadwick S, Vohra A. Pain on injection of propofol. Methods of alleviation. *Anaesthesia* 1990;45(6):439-42.
25. Brooker J, Hull CJ, Stafford M. Effect of lignocaine on pain caused by propofol injection. *Anaesthesia*. 1985;40(1):91-2.
26. Hamid Zahedi, Anahid Maleki, and Gholamreza Rostami .Ondansetron Pretreatment Reduces Pain on Injection of Propofol *Acta Medica Iranica*, Vol. 50, No. 4 (2012)
27. Sumalatha GB<sup>1</sup>, Dodawad RR<sup>1</sup>, Pandarpurkar S<sup>1</sup>, Jajee PR<sup>1</sup>. A comparative study of attenuation of propofol induced pain by lignocaine, ondansetron, and ramosetron. *Indian J Anaesth.* 2016 Jan;60(1):25-9. doi: 10.4103/0019-5049.174810.
28. Singh DK, Jindal P, Singh G. Comparative study of attenuation of the pain caused by propofol intravenous injection, by granisetron, magnesium sulfate and nitroglycerine. *Saudi J Anaesth.* 2011;5(1):50–4.
29. Zahedi H, Maleki A, Rostami G. Ondansetron pretreatment reduces pain on injection of propofol. *Acta Med Iran.* 2012;50(4):239–43.
30. Mohammad Alipour , Masoomeh Tabari , Masoomeh Alipour Paracetamol, Ondansetron, Granisetron, Magnesium Sulfate and Lidocaine and Reduced Propofol Injection Pain *Iran Red Crescent Med J.* 2014 March; 16(3): e16086.