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The Effectiveness of Ondansetron versus Tramadol as Pretreatment in Alleviating Propofol Injection Pain: A Comparative Study

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Abstract

Introduction: Propofol is widely used for induction of anesthesia, although the pain during its injection remains a concern for all anesthesiologists. A number of techniques have been adopted to minimize propofol-induced pain. Various 5-hydroxytryptamine-3 antagonists have shown to reduce propofol-induced pain. Hence, this placebo-controlled study was conducted to compare the efficacy of ondansetron, ramosetron, and lignocaine in terms of attenuation of propofol-induced pain during induction of anesthesia. *Aim of the Study:* To assess the effectiveness of ondansetron and tramadol as pre-treatment in alleviating propofol injection pain. *Materials and Methods:* 36 patients were randomly allocated into two groups. Group 1 who received up to 2 mL pretreatment with 50 mg tramadol with 1 ml NS while group 2 cases who received 2 mL pretreatment 4 mg ondansetron. The drug is injected into the largest vein on the dorsum of the hand by means of a 20 gauge cannula and the tourniquet being closed to the arm above the cannula and inflated upto 70 mmHg. The tourniquet is deflated after 20 seconds and propofol 2mg/kg injected over 10 seconds and assessment for pain was made. *Results*: Tramadol and ondansetron both reduced the incidence and severity of propofol injection pain but pain reduction with ondansetron was significant compared to tramadol (p=0.0402). Significantly 14 patients in the ondansetron group felt no pain when compared to only 8 patients in the tramadol group. *Conclusion:* In addition,ondansetron had the additional benefit as it controlled postoperative nausea and vomiting.

Keywords: Ondansetron; Tramadol; Propofol; Pain; Intravenous Injection.

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Introduction

Propofol is the medication of choice for induction of general anesthesia in a large number of patients consistently as a result of its rapid onset and short-term of action, easy titration, and favorable side effect profile [1]. Despite these positive qualities, around three out of five patients encounter severe or excruciating pain during the infusion of propofol, which is very distressing to patients. A few patients consider the perioperative period as the worst part of anesthesia induction. It is ranked seventh among thirty-three clinical problems when the frequency of occurrence and clinical significance were considered in clinical practice by American anaesthesiologist [2]. Moreover, 70% of patients encounter pain which is aching or burning and extremely sharp in nature [3]. Although various interventions are been used to alleviate the pain caused by intravenous infusion of propofol, the exact mechanism of how itinduces pain is still unclear [4]. Tramadola centrally acting weak μ receptor agonist promotes the release of serotonin

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there by inhibiting nor-adrenaline re-uptake [5]. Like lidocaine, pre-treatment with tramadol was found to be effective in alleviating pain on propofol infusion by Wong and Cheong [6]. Ondansetron which is a 5-HT receptor antagonist specific which blocks Na channel in rat brain neurons and it is also found to cause numbness, 15 times more than lidocaine when injected under the skin, has shown promising results as analternative to tramadol as described by Ye et al. [7-9]. Further recent studies have documented ondansetron as an established agent in preventing postoperative nausea and vomiting in procedures done for eye surgeries [10-13]. But till date very little published data are available illustrating the efficacy of ondansetron in alleviating pain caused by propofol infusion. Thus, we postulated thatpretreatment with intravenous ondansetron perhaps will reduces pain on propofol infusion. Hence, this study was designed to assess the effectiveness of ondansetron and tramadol as pretreatment for the alleviation of pain on propofol injection.

Materials and Methods

The prospective, comparative, double-blinded study. This study was conducted in the Department of Anaesthesiology, Karpaga Vinayaga Institute of Medical Science, after obtaining approval by the Institutional Ethics Committee. Totally thirty-six patients, eighteen in each group, aged between 18 and 60 years of either sex, scheduled for an elective surgery were considered for this study. Written informed consent was betaken from all the patients.

Inclusion Criteria

1. Patients aged between 18-60 years.
2. Patients scheduled for an elective surgery belonging to American Society of Anaesthesiologists Status I and II.

Exclusion Criteria

1. Patients with known hypersensitivity to propofol or tramadol, concomitant analgesic or sedative medication.
2. Presence of infection on the dorsum of the left hand; indications for rapid sequence intubation; the presence of cardiac conduction defects; epilepsy; and use of anti-arrhythmic medications, thin dorsal veins, and uncooperative patients.In our study, patients were randomly assigned to two groups of 18 patients each. There was no administration ofpre-medication. The largest vein on the dorsum of the left hand was chosen for placing the 20-gauge cannula along with other monitoring instruments like lead II electrocardiogram, pulse oximeter, and noninvasive blood pressure. As pretreatment, group 1 patients received 2ml tramadol 50mg in the saline while group 2 patients received 4mg ondansetron 2ml for a period of 10 seconds while the venous drainage was occluded by placing an air-filled tourniquet on the upper arm by an assistant. The solution was prepared by a blinded anesthetist, while the investigator was not aware of the content of the solution. 1% propofol (2mg/kg) was injected over a period of 10 seconds after the occlusion was released after 20 seconds. The drug was preservative free and was kept at room temperature. No sedative or analgesic was administered before propofol administration. The levels of pain on injection of propofol were assessed by another clinician who was unaware of patients allotment into groups. Patients verbal response, behavior signs which includes facial grimacing, arms withdrawal, or tears were recorded after answering to standard questions regarding any adverse effects after drug administration. A score of 0 to 3 was noted (0=nil, 1=mild, 2=moderate, 3=severe pain). We injected opioid and sedative after propofol for recording the patient's reliable response. Anesthetic induction and tracheal intubation were facilitated accordingly. The patients were extubated after administration of muscle relaxant antagonist and were followed up for the next 6 hours and assessed for any adverse reactions including pain, swelling or any allergic reactions at the propofol injection site by a blinded anesthesiologist.

Statistical Tool Used

Chi-square and t-testwereused.The statistical significance was taken as $p<0.05$ Data were tabulated in Exceland analyzed using SPSS software version 18.

Results

This study involved totally 36 patients who were designated into two groups (the ondansetron group and the tramadol group) of 18 each. The mean age of patients who participated in the study was

44.78±11.11 while for was ondansetron group was 45.22±9.42 (8 males and 10 females) and for tramadol group, it was 44.33 ± 12.84 (9 males and 9 females) respectively.

The incidence of overall pain was found to be 55.5% in tramadol group, while it was only 22.2% among ondansetron group which was found to be significant in this study with a p-value of 0.04 ($p<0.05$). But there was no significant association between pain and age of the patients (Table 1).

Totally 10 patients in the tramadol group experienced pain while the remaining 8 patients were pain-free after propofolinjection.while the number of patients who were pain-free in the ondansetron group was comparatively higher and only 4

Table 1: Comparison between pain and no pain among ondansetron and tramadol groups

Pain level	Tramadol	Ondansetron	Overall	Chi-square test	p-value
No pain	8	14	22	4.2078 (DF=1)	0.0402
Pain	10	4	14		p-value

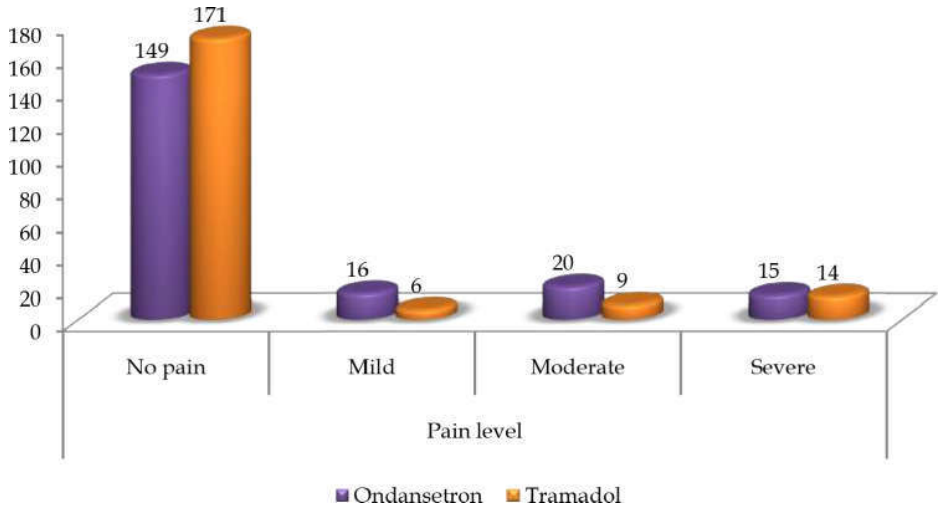

Fig. 1: Comparison of pain levels between ondansetron and tramadol groups

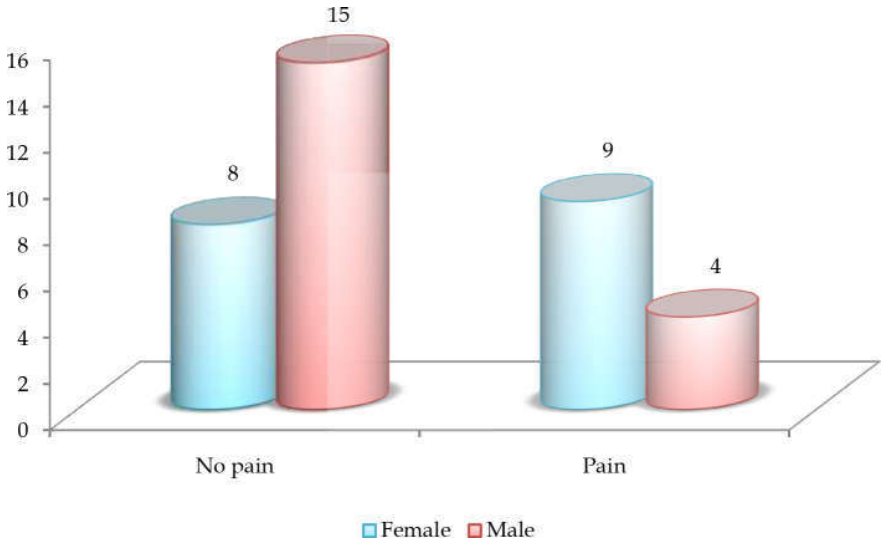

Fig. 2: Comparison between gender and pain among patients

patients experienced some sort of pain (Table 2).

Discussion

Propofol has always been a problem for clinicians for over a decade as it causes pain on injection. Studies reveal incidence around 28% to 90% in adults while in children, the incidence rate is around 85% [14,15]. Propofol which is commonly used for induction and maintenance of anesthesia causes distress to patients on infusion. While the uncertainty remains over the mechanism of causation of pain. Propofol irritates skin, mucous membrane and venous intima and has the tendency to stimulate nociceptors and free nerve endings [8]. Yull et al. described the cause of propofol infusion pain was due to release of local kininogens and they also stated that nonsteroidal anti-inflammatory drugs can certainly reduce the incidence of pain (eg – ketorolac) [16]. Propofol, when administered through small veins at the dorsum of the hand, causes pain which accounts for 45% -75% of patients [17,18]. Various methods to minimize this pain have been proposed, which includes utilizing bigger veins [19], preparations containing lidocaine, an opioid or midazolam before the injection of propofol [17, 18, 20-22], decreasing the concentration of propofol with 5% glucose or 10% intralipid [20], infusing cool saline with the propofol or discontinuing fluid during the injection [23], or administering 5-hydroxytryptamine-3 antagonist [24]. Bradykinin which is released by the activation of the kallikrein-kinin system is speculated as the root cause of pain as described by Scott et al.[17]. Bradykinin by increasing the contact between the nerve endings and aqueous phase propofol results in pain on propofol injection [25]. We have used venous retention with a tourniquet in our study as it is the procedure frequently utilized for pretreatment of propofol infusion pain [26-28]. Ondansetron is considered an antiemetic drug and a widely used 5-hydroxytryptamine-3 antagonist [29]. Ye et al. [7] havepreviously exhibited that ondansetron may be considered for novel type local anesthetics as it blocks sodium channel neurons in the rat brain. Like local anestheticsondansetron can block sodium channels; 5-hydroxytryptamine-3 receptors are additionally associated with nociceptive pathways and have demonstrated binding at opioid μ receptors showing agonist activity, subsequently bringing about a peripheral antinociceptive effect [7,30]. Ondansetron additionally attaches to opioid μ receptors with agonist action and might be useful in counteracting infusion pain caused by medications, for example, propofol [30] Ondansetron, when given at 2 ml, was found to be satisfactory in preventing injection site pain which was demonstrated by Ambush et al.[8]. In our investigation, we utilized the same dosage of ondansetron as Ambush et al. which diminishes the pain, however, did not completely prevent it. Tramadol is a centrally acting analgesics that delivers a pain relieving effect by preventing the norepinephrine take-up and release without activating the all of the opioid receptors [31]. Pang et al.[31,32] demonstrated that 25 mg of tramadol IM infusion provided an anesthetic effect and in addition demonstrated that 50 mg of tramadol IV prevented injected site pain after propofol infusion when compared with lidocaine but still did not eliminate the pain totally. In our study, 44% of patients did not experience the pain when treated with tramadol compared to 77% of patients treated with ondansetron. A study done by Zahedi et al demonstrated that the percentage of patients around 82.2% had pain or discomfort which significantly reduced to around 24.4% after ondansetron pretreatment [14].

Conculsion

Taking everything into account, ondansetron pretreatment provides a safe and simple procedure for lessening propofol infusion pain with the added benefit of preventing postoperative nausea and vomiting and thereby preventing the usage of undesired medicationswhich could be bothersome in specific conditions.

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Conflict of Interest: None

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