### **Original Research Article**

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## A prospective, randomized, double blind study to evaluate and compare the efficacy of lidocaine, ramosetron and tramadol pre-medication, in attenuating the pain caused due to propofol injection

Ifra Zahoor<sup>1</sup>, Aabid Hussain Mir<sup>1\*</sup>, Mohmad Syed Qazi<sup>1</sup>, Zahoor Ahmad Jan<sup>2</sup>, Abida Yousuf<sup>1</sup>, Ajaiz Rasool<sup>1</sup>

<sup>1</sup>Department of Anaesthesiology and Critical Care, SKIMS, Soura, Srinagar-190011, Jammu and Kashmir, India <sup>2</sup>Department of Anaesthesiology, Al-Jabr Eye and ENT hospital, Al-Hofuf, Dammam, Saudi Arabia

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\***Correspondence:** Dr. Aabid Hussain Mir, E-mail: meeraabid111@gmail.com

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#### ABSTRACT

**Background:** Propofol is a popular induction agent, especially for short cases, day care surgeries and when a laryngeal mask is to be used. It produces a good quality of anaesthesia and rapid recovery. Pain on injection of propofol has been reported and is an important limitation of its use. A multitude of interventions: pharmacological as well as non-pharmacological, have been tried for the attenuation of pain caused due to propofol injection. In our study, we evaluated and compared the efficacy of lidocaine, ramosetron and tramadol in attenuating pain on propofol injection.

**Methods:** A total of 180 patients belonging to American Society of Anesthesiologists (ASA) grade I and II, of either sex, aged between 21 to 50 years undergoing elective surgery under general anaesthesia, were taken up for the study and were divided into group A, B and C. Group A received 2ml of 2% (40mg) lidocaine, Group B received 2ml of ramosetron (0.3mg) and Group C received 1mg/kg of tramadol in 0.9% normal saline to make a total solution of 2ml. Venous occlusion was done by compressing forearm with tourniquet to increase the local concentration of drug after establishing an intravenous access. The study drug was injected over 10 seconds and then occlusion was removed after 60 seconds, followed by giving 25% of the total calculated dose (2.5mg/kg) of propofol (1% w/v in lipid base) injected over 20 seconds. This was followed by asking the patient about the severity of pain felt. The intensity of pain was graded using verbal rating scale (McCrirrick and Hunter) and was assessed at 0, 5, 10, 15 and 20 seconds, as after 20 seconds, the patient would be under the influence of propofol.

**Results:** Lidocaine showed the best efficacy in attenuating propofol injection pain amongst the 3 groups recorded at 5 (95%), 10 (91.7%) and 15 seconds (98.3%). In addition to reducing the incidence of pain, it also reduced its severity, with majority of patients experiencing only mild pain. Ramosetron ranked  $2^{nd}$  in the overall reduction of propofol pain, with lowest incidence of propofol pain amongst 3 groups, recorded at 0 (98.3%) and 20 seconds (95%) of propofol injection. However, ramosetron failed in reducing severity of pain, with a significant number of patients experiencing moderate and severe pain. Tramadol ranked  $3^{rd}$  in the overall attenuation of propofol pain and showed lowest incidence of pain at 0 seconds (93%) of propofol injection.

**Conclusions:** All the three study drugs viz lidocaine, ramosetron and tramadol cause a significant decrease in propofol injection pain with lidocaine as the most efficacious drug amongst the 3 drugs followed by ramosetron and tramadol. Lidocaine has an added advantage of decreasing incidence and severity of pain associated with propofol and ramosetron prevents postoperative nausea and vomiting.

Keywords: Lidocaine, Ramosetron, Pain, Propofol, Tramadol

#### **INTRODUCTION**

Pain during injection is a limiting factor in the use of some anaesthetic drugs like propofol, etomidate and diazepam. Propofol is a popular induction agent, especially for short cases, day care surgeries and when a laryngeal mask is to be used. It produces a good quality of anaesthesia and rapid recovery.<sup>1,5</sup> Chemically, propofol belongs to the group of sterically hindered phenols. Hence, like other phenols propofol irritates the skin, mucous membrane and venous intima. Pain on injection of propofol has been reported and is an important limitation of its use.<sup>1</sup> Overall incidence of pain after propofol injection, in the absence of any pretreatment is around 60% as observed in a meta-analysis done in 2011; the incidence varying from less than 10% in the anticubital fossa, to more than 90% on the back of the hand.<sup>2-</sup> <sup>4</sup> The exact mechanism for the production of pain with propofol injection is yet to be established. However, the activation of pain mediators such as the release of a kininogen from the vein wall triggering a local kinin cascade system during intravenous injection has been suggested.5 The free fraction of propofol has been implicated, which explains a slight delay before pain is experienced.<sup>6</sup> Scott et al speculated that the injection pain is caused by activation of the kallikrein-kinin system either by propofol or by the lipid solvent, thereby generating kinins, probably bradykinin.<sup>7</sup>

A multitude of interventions: pharmacological as well as non-pharmacological, have been tried for the attenuation of pain caused due to propofol injection. In the pharmacological class of interventions, several classes of drugs like alpha2 agonists- dexmeditomidine and clonidine antiemetics- metoclopramide, ondansetron and granisetron, barbiturates, benzodiazipines, cholinesterase inhibitors, kallikrien inhibitor- Nafamostat mesilate, NMDA receptor antagonists ketamine and magnesium sulphate, nitroglycerine, NSAIDS, opiods- tramadol, pethidine, alfentanyl, sufentanyl, remifentanyl, steroidsdexamethasone and hydrocortisone, local anesthestheticsprilocaine and lidocaine have been tried.<sup>8-30</sup>

Non-pharmacological strategies that have been employed include different infusion rates, venous occlusion, different needle sizes, different injection sites, microfiltration, variation in temperature, different speeds of intra venous carrier fluid, and use of saline.<sup>31,39</sup>

Besides these, several drug and non-drug combination strategies have been used with variable results. Despite some of the strategies showing promising results, none of the above-mentioned methods has been fully effective in attenuating the pain due to propofol injection and the research for the ideal agent or intervention, that would make anesthesia administration with propofol a pleasing experience, continues. As lidocaine has both a local anaesthetic effect and a kinin cascade-stabilizing effect, it can be used for injection pain prevention.<sup>33</sup> Of the techniques used to decrease the incidence and intensity of

pain resulting from propofol injection, the most effective method is to inject lidocaine at 0.5mg/kg i.v. while applying venous occlusion before administering propofol.

Recently, 5-HT<sub>3</sub> receptor antagonists, which are used as antiemetics, were found to have characteristics of local anesthetics and effective in the prevention of injection propofol.<sup>12,40,41</sup> caused by Descending pain monoaminergic pathways from brainstem are known to able to influence nociceptive signalling in the dorsal horn of the spinal cord. Such descending influences are both facilitatory and inhibitory in nature. Suzuki and colleagues showed that the descending influences are predominantly facilitatory, and act via spinal 5-HT<sub>3</sub> receptors (expressed on nerve terminals of small diameter afferents), revealing a role for selective 5-HT<sub>3</sub> receptor antagonists like ondansetron and granisetron in relieving pain.42,43

Tramadol is a centrally acting analgesic agent. Initially, it was thought that tramadol produced its antinociceptive and analgesic effects through spinal and supraspinal sites rather than via local anaesthetic action. However, several clinical studies have shown that it might have peripheral local anaesthetic type properties. By direct application to the sciatic nerves in rats, it was proven that tramadol exerts a local anaesthetic type of effect.45 When extracellular sodium decreases, nerve fibres become sensitive to local anaesthetic. Jon et al suggested tramadol affects sensory and motor nerve conduction by similar mechanism to that of lidocaine which acts on voltagegated Na<sup>+</sup> channels leading to axonal blockade.<sup>45</sup> However, Mert et al proposed tramadol might have a mechanism different from that of lidocaine, the presence of a large Ca<sup>++</sup> concentration in the external medium increases tramadol's activity while decreasing lidocaine's activity.7

Various studies have been carried out to test wide range of drugs for attenuating pain on propofol injection. In present study, we evaluated and compared the efficacy of lidocaine, ramosetron and tramadol in attenuating pain on propofol injection.

#### **METHODS**

After approval of the study protocol by the Ethical Committee of the Institute, a total of 180 patients belonging to American Society of Anesthesiologists (ASA) grade I and II, of either sex, aged between 21 to 50 years undergoing elective surgery under general anaesthesia, were taken up for the study. A written, well informed consent was taken from all the patients. Patients with age <21 years and >51 years, ASA III and IV, any previous history of systemic illness, history of allergy to study drugs, pregnant women, morbidly obese patients, patients scheduled for emergency surgery, patients with neurological and psychiatric disorders were excluded from study. Patients were randomly allocated, for receiving the study drug, into 3 groups of 60 patients each. Randomization was done using a sealed envelope. Group A received 2ml of 2% (40mg) lidocaine, Group B received 2ml of ramosetron (0.3mg) and Group C received 1mg/kg of tramadol in 0.9% normal saline to make a total solution of 2ml. Drug solutions were prepared by co-supervisor and given to the observer who would dispense 2ml of the study drug. This way the observer was blindfolded to the drug given to the patient.

Prior to the surgery, all the patients underwent routine pre-anaesthetic checkup. The patients (aged 21-50 years and scheduled for elective surgery) were visited a day before surgery and explained the procedure. The patients were kept fasting for 6-8 hours. On the day of surgery, intravenous access with 20G cannula, with no local anaesthetic infiltration on the dorsum of non-dominant hand, was done and intravenous fluid (Ringer lactate) was infused at rate of 100ml/hr.

After 2 minutes, lactated ringer's infusion was stopped and arm with intravenous access was elevated for 15 seconds for gravity drainage of venous blood. Heart rate, NIBP, SPO2 and ETCO2, ECG were monitored. The procedure was again explained to the patients. No analgesic drug was given to the patient before injecting propofol. Venous occlusion was done by compressing forearm with tourniquet to increase the local concentration of drug. The study drug was injected over 10 seconds and then occlusion was removed after 60 seconds, followed by giving 25% of the total calculated dose (2.5mg/kg) of propofol (1% w/v in lipid base) injected over 20 seconds. This was followed by asking the patient about the severity of pain felt. The intensity of pain was graded using Verbal Rating Scale (McCrirrick and Hunter)8 and was assessed at 0, 5, 10, 15 and 20 seconds, as after 20 seconds, the patient would be under the influence of propofol.

For the assessment of pain, 4 point verbal rating scale (McCrirrick and Hunter) was used. None (No pain/no response to questioning, 0 points), mild pain (pain reported only in response to question with-out any behavioral sign, 1 point), moderate pain (pain reported only in response to question and accompanied by behavioral sign, 2 points) and severe pain (strong vocal response/response accompanied by facial grimacing, arm withdrawal or tears, 3 points).

Thereafter, the induction of anaesthesia was continued with the rest of the calculated propofol dose and for analgesia, fentanyl 2ug/kg was given to all the patients. The patients were intubated with appropriate sized ETT after giving vecuronium and then anaesthesia was maintained with isoflurane and nitrous oxide + oxygen (66% + 33%). NIBP, ECG, heart rate, SPO<sub>2</sub> and end tidal carbon dioxide were monitored throughout the surgery. All the study drugs were kept at room temperature and were used within 30 minutes of preparation.

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0. Statistical software SPSS (version 20.0) and Microsoft Excel were used to carry out statistical analysis of data. Continuous variables were summarized in the form of means and standard deviations and categorical variables were summarized as percentages. Analysis of variance (ANOVA) was employed for inter group analysis of data. Chi-square test or Fisher's exact test, whichever appropriate, was used for comparison of categorical variables. Graphically, the data was presented by bar and line diagrams. A p-value of less than 0.05 was considered statistically significant. All p-values were two tailed.

#### RESULTS

The subject characteristics such as age, weight, ASA status and sex were similar in both groups (Table 1). At 0 seconds of injecting propofol (Table 2), 78.3% of patients (n=47) experienced no pain in the lidocaine group while in the ramosetron and tramadol groups, 98.3% (n=59) and 93% (n=57) patients respectively experienced no pain. In our trial, study of pain at 0 seconds of propofol injection (Table 3) showed statistically significant results in all three groups (p<0.001). Intergroup comparison showed highly significant statistical difference between lidocaine and ramosetron groups (p=0.002) and lidocaine and tramadol groups (p=0.016). However there was no significant difference in pain attenuation between ramosetron and tramadol groups (p=0.619), both of which caused attenuation of propofol injection pain. Out of the 21.7% patients experiencing pain in lidocaine group (group A), 16.7% had mild pain, only 5% had moderate pain while none of the patients had severe pain (Table 2).

Patient characteristics	Group A (n=60)	Group B (n=60)	Group C (n=60)	P-value
Age (years)	33.9±8.63	$34.5 \pm 8.48$	36.2±8.54	0.303
Sex (Male/Female)	33/27	37/23	32/28	0.622
Body weight (Kgs)	55.80±5.24	55.00±6.11	57.33±5.13	0.078
ASA-PS (I/II)	47/13	44/16	46/14	0.807

Value expressed as mean±SD, ASA-PS: American society of anesthesiologists physical status, SD: standard deviation.

Group	Interval	Pain score			
		0	1	2	3
Group A n (%)	0 sec	47 (78.3)	10 (16.6)	3 (5)	0
	5 sec	57 (95)	3 (5)	0	0
	10 sec	55 (91.6)	5 (8.3)	0	0
	15 sec	59 (98.3)	1 (1.6)	0	0
	20 sec	55 (91.6)	5 (8.3)	0	0
Group B n (%)	0 sec	59 (98.3)	1 (1.6)	0	0
	5 sec	56 (93.3)	1 (1.6)	3 (5)	0
	10 sec	50 (83.3)	4 (6.6)	3 (5)	3 (5)
	15 sec	56 (93.3)	2 (3.3)	1 (1.6)	1 (1.6)
	20 sec	57 (93)	0	2 (3.3)	1 (1.6)
Group C n (%)	0 sec	57 (93)	2 (3.3)	1 (1.6)	0
	5 sec	49 (81.6)	10 (16.6)	1 (1.6)	0
	10 sec	42 (70)	10 (16.6)	8 (13.3)	0
	15 sec	38 (63.3)	17 (28.3)	5 (8.3)	0
	20 sec	45 (75)	11 (18.3)	4 (6.6)	0

#### Table 2: Assessment of pain scores at different intervals of time.

Group A= Lidocaine, Group B=Ramosetron, Group C=Tramadol. P-value<0.05=significant, n= no. of patients experiencing different pain score at different time intervals, sec=seconds (time), %= percentage of patients in particular group having particular pain score.

At 5 seconds of propofol injection (Table 2), 95% patient (n=57) in lidocaine group, 93.3% patients (n=56) in ramosetron group and 81.7% patients (n=49) in tramadol group experienced no pain. The study of pain at 5 seconds (Table 3) showed statistically significant results in all the three groups (p=0.029).

The intergroup comparisons showed statistically significant difference between the lidocaine and tramadol groups (p=0.043), lidocaine proving to be superior to tramadol in attenuation of pain caused due to propofol injection. Although higher percentage of patients in ramosetron group (93.3%) remained pain free, as compared to tramadol group (81.7%), the comparison of efficacies of ramosetron and tramadol groups showed statistically non-significant results (p=0.095). Comparison of lidocaine and ramosetron groups revealed a non-significant co-relation (p=1.000), both being equally effective in attenuating the pain caused due to propofol injection at 5 seconds (Table 3). Important thing to be noted is that all the patients experiencing pain in tramadol group 16.7%, had mild pain and only 1.7% had moderate pain while all the patients experiencing pain in the lidocaine group (5%), had only mild pain. Patients in ramosetron group (5%) experienced moderate degree of pain at 5 seconds.

At 10 seconds of propofol injection (Table 2), 91.7% patients (n=55) in lidocaine group, 83.3% patients (n=50) in ramosetron group and 70% patients (n=42) in tramadol group experienced no pain. The study of pain at 10 seconds (Table 3) showed statistically significant results in all the 3 groups (p=0.008). The intergroup statistical comparisons showed highly significant difference between the lidocaine and tramadol groups (p=0.005),

lidocaine proving to be far superior to tramadol in attenuation of pain caused due to propofol injection at 10 seconds.

# Table 3: Intergroup comparisons of pain scores at different time intervals.

Time (sec)	Intergroup comparison	p-value	Overall p-value	
	Lidocaine v/s ramosetron	0.002*		
0	Lidocaine v/s tramadol	0.016*	< 0.001*	
	Ramosetron v/s tramadol	0.619	<0.001	
	Lidocaine v/s ramosetron	1.00		
5	Lidocaine v/s tramadol	0.043*	0.029*	
	Ramosetron v/s tramadol	0.095		
	Lidocaine v/s ramosetron	0.557		
10	Lidocaine v/s tramadol	0.005*	$0.008^{*}$	
	Ramosetron v/s tramadol	0.084		
	Lidocaine v/s ramosetron	0.364		
15	Lidocaine v/s tramadol	< 0.001*	< 0.001*	
	Ramosetron v/s tramadol	< 0.001*	<0.001	
	Lidocaine v/s ramosetron	0.717		
20	Lidocaine v/s tramadol	0.028*	$0.002^{*}$	
	Ramosetron v/s tramadol	0.005*	0.002	

p-value<0.05=statistically significant, \*=statistically significant, lidocaine= Group A, ramosetron= Group B, tramadol= Group c.

The comparison of lidocaine and ramosetron groups showed statistically non-significant results (p=0.557), both being equally effective in attenuating propofol pain at 10 seconds of injection. Comparison of ramosetron and tramadol groups, revealed a comparable but statistically non-significant relation between their efficacies in attenuating propofol pain at 10 seconds (p=0.084), even though ramosetron showed better results than tramadol as per the percentage of patients feeling propofol pain (16.7%) in ramosetron group v/s (30%) in tramadol group. Although the incidence of pain in lidocaine and ramosetron groups was comparable but the severity of pain differed greatly in all the 3 groups, with patients in lidocaine group who experienced pain (8.3%), had only mild pain, patients in tramadol group who experienced pain (30%), had both mild (16.7%) and moderate pain (13.3%) while patients in ramosetron group who experienced pain (16.7%) had severe pain (5%) in addition to mild (5%) and moderate pain (5%).

At 15 seconds of propofol injection (Table 2), 98.3% of lidocaine group, 93.3% in ramosetron group and 63.3% in tramadol group experienced no pain. The study of pain at 15 seconds (Table 3) showed statistically significant results in all three groups (p<0.001). The intergroup statistical comparisons showed highly significant difference between the results of lidocaine and tramadol groups and between ramosetron and tramadol groups (p<0.001), both lidocaine and ramosetron proving to be far superior than tramadol in attenuation of propofol injection pain at 15 seconds. The comparison of lidocaine and ramosetron groups showed statistically insignificant results (p=0.364).

At 20 seconds of propofol injection (Table 2), 91.7% patients (n=55) of lidocaine group, 95% patients (n=57) of ramosetron group and 75% patients (n=45) of tramadol group experienced no pain on injection of propofol. The study of pain at 20 seconds showed statistically significant results in all 3 groups (p=0.002). The intergroup comparisons (Table 3) showed statistically significant difference between lidocaine and tramadol groups (p=0.028) and between ramosetron and tramadol groups (p=0.005). The comparison between lidocaine and ramosetron groups was statistically insignificant (p=0.717). Both lidocaine and ramosetron being superior to tramadol in reducing propofol injection induced pain at 20 seconds. However, all the patients who experienced pain in lidocaine group (8.3%), had mild pain only while patients in ramosetron group experienced moderate (3.3%) and severe pain (1.7%). Out of the 25% patients who experienced pain in tramadol group 18.3% had mild pain, 6.7% had moderate pain and 0% had severe pain. Order of efficacy of the study drugs on the basis of decrease in the incidence of propofol pain at different time intervals.

- 00 seconds- ramosetron (98.3%) >tramadol (93%) >lidocaine (78.3%)
- 05 seconds- lidocaine (95%) >ramosetron (93.3%) >tramadol (81.7%)
- 10 seconds- lidocaine (91.7%) >ramosetron (83.3%) >tramadol (70%)
- 15 seconds- lidocaine (98.3%) >ramosetron (93.3%) >tramadol (63.3%)
- 20 seconds- ramosetron (95%) >lidocaine (91.7%) >tramadol (75%)

The highest incidence of pain was observed at 10 seconds of propofol injection. Overall, lidocaine showed the best efficacy in attenuating propofol injection pain amongst the 3 groups recorded at 5, 10 and 15 seconds. In addition to reducing the incidence of pain, it also reduced its severity, with majority of patients experiencing only mild pain. Ramosetron ranked 2<sup>nd</sup> in the overall reduction of propofol pain, with lowest incidence of propofol pain amongst 3 groups, recorded at 0 and 20 seconds of propofol injection. However, ramosetron failed in reducing severity of pain, with a significant number of patients experiencing moderate and severe pain. Tramadol ranked 3<sup>rd</sup> in the overall attenuation of propofol pain, with lowest incidence of pain at 0 seconds of propofol injection.

#### DISCUSSION

The quest for an ideal anaesthetic drug that would guarantee both safety and comfort of the patients, led to the discovery of propofol, an intravenous anaesthetic agent. Propofol soon became popular because of its amazing qualities of quick, smooth induction and rapid recovery without any residual effects of anesthesia. Besides, its high safety profile, minimal side-effects, propofol has almost taken over all the other anaesthetic drugs for the induction as well as maintenance of anesthesia and is currently the most popular intravenous anaesthetic agent among anaesthetists all over the world. In spite of all these advantages, there are a few factors that have limited the usefulness of this wonderful drug. These include hypotension and pain on injection of propofol. Pain on injection is the most common and troublesome side effect of propofol, associated with high recall rates even in the post-op period.<sup>46</sup> With the decrease in morbid adverse effects during and after surgery, patient satisfaction with peri-operative care is assuming more importance. Also considering the extensive use of propofol in clinical practice, the pain frequently reported on induction of anesthesia cannot be neglected. Macario and colleagues concluded that among 33 low morbidity outcomes, propofol injection pain ranked as the 7th most important problem of current clinical anesthesiology, thus defeating the very purpose of giving anesthesia i.e. relief from pain.47

To resolve this issue of propofol pain, several studies have been done to find out a possible measure to prevent this pain. In the current study we evaluated and compared the efficacy of lidocaine, ramosetron and tramadol premedication in attenuating the pain caused due to propofol injection and we found that all the three drugs showed statistically significant results causing pain attenuation at 0, 5, 10, 15, 20 seconds of propofol injection. The maximum incidence of pain in all the 3 groups was seen at 10 seconds (Table 2) of propofol injection and the efficacy of the 3 drugs in attenuating pain injection pain showed different trends at different time intervals. At 0 seconds of propofol injection, the order of efficacy of the 3 drugs was: ramosetron >tramadol >lidocaine on the basis of reduction in the incidence and severity of pain by the study drugs. At 5 seconds, the order of efficacy of the 3 drugs was: lidocaine >ramosetron >tramadol. At the 10 seconds, the order of efficacy of the 3 drugs was: lidocaine >ramosetron >tramadol. At the 15 seconds, the order of efficacy of the 3 drugs was: lidocaine >ramosetron >tramadol and at the 20 seconds, the order of the efficacy of the 3 drugs was: ramosetron >lidocaine >tramadol on the basis of reduction in the incidence and severity of pain. The overall order of efficacy of the 3 drugs on the basis of reduction in the severity of propofol injection pain was: lidocaine >ramosetron >tramadol.

Present study correlates with Kaya S and colleagues who in their study done on 100 women concluded that administration of lidocaine with venous occlusion for 60 seconds significantly reduced the incidence and severity of pain during the injection of propofol as compared to normal saline without tourniquet.<sup>48</sup> In another study done by Johnson RA and collegues, it was seen that pain was reduced significantly in all the groups in which lidocaine was used and the degree of pain alleviation was in direct proportion to the dose of lidocaine given.<sup>46</sup> Present result is consistent with the study done by Basappa G and collegues, who studied the effect of lignocaine, ondansetron and ramosetron on attenuation of propofol injection induced pain.49 The study concluded that pretreatment with i.v. ramosetron 0.3mg is equally effective as 0.5mg/kg of 2% lignocaine in preventing propofol induced pain and both were better than ondansetron. In other study done by Singh D and collegues that compared the incidence of pain with propofol injection in patients pre-treated with ramosetron with those pre-treated with lidocaine.<sup>50</sup> The study concluded that pre-treatment with ramosetron 0.3mg and lidocaine 40mg are equally effective in preventing pain from propofol injection which is again consistent with the results of present study. However, our observations varied from Lee HY and collegues who investigated the effect of ramosetron on pain induced by microemulsion propofol injection on 200 ASA I and II patients undergoing general anesthesia.<sup>51</sup> They found that incidence of pain was 96%, 76%, 60% and 38% in patients receiving normal saline, lidocaine 20mg, ramosetron 0.3mg and lidocaine 20mg plus ramosetron 0.3mg respectively (p<0.008). The study concluded that pretreatment with ramosetron 0.3mg with or without lidocaine 20mg with a tourniquet on the forearm 30 seconds before the injection of microemulsion propofol is more effective than lidocaine 20mg or normal saline in preventing pain from a microemulsion propofol injection.

Our observations co-relate with Pang WW et al, who in their study "the peripheral analgesic effect of tramadol in reducing propofol injection pain: a comparison with lidocaine" investigated the local anesthetic effect of tramadol in reducing pain on propofol injection.<sup>52</sup> The study showed that both tramadol and lidocaine significantly reduced the incidence and intensity of propofol injection pain when compared with normal saline. Our observations correlate with Borazan H et al who in their study on 120 ASA I and II patients found that pretreatment with tramadol 60 seconds before propofol injection and propofol-lidocaine mixture significantly reduced propofol injection pain when compared to placebo in children.<sup>53</sup>

So present study revealed that all the three drugs can be used as premedication for attenuation of pain by propofol injection with lidocaine being the most efficient drug followed by ramosetron and tramadol being the least effective. However, the choice of agent should, therefore, be individualised with due consideration to the cost-effectiveness and benefit to the patient.

#### CONCLUSION

All the three study drugs viz lidocaine, ramosetron and tramadol cause a significant decrease in propofol injection pain. Pre-treatment with IV lidocaine 40mg is the most effective followed by ramosetron 0.3mg and tramadol 1mg/kg is least effective. Ramosetron has the added advantage of preventing post-operative nausea and vomiting (PONV) in patients receiving this drug.

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