



## Comparative Study on the Effectiveness of Granisetron and Metoclopramide for Reducing Propofol Injection Pain

Authors

**Dr Aravind Johnson, Dr Harikrishnan S, Dr Radhika Devi B**

Department of Anaesthesiology, Government Medical College Hospital Thiruvananthapuram, Kerala

### ABSTRACT

**Background:** Propofol is one of the widely used intravenous anaesthetics, although pain on injection still remains a considerable concern for the anaesthesiologists. The aim of my randomized double blinded study was to compare the effectiveness of Granisetron and Metoclopramide in reducing Propofol injection pain. Both these drugs are used as anti emetic drugs. This study also compares the effectiveness of Granisetron and Metoclopramide in reducing post operative nausea and vomiting.

**Methods:** 760 patients, aged 21-50 years, American society of Anaesthesiologists grading (ASA) 1-2, scheduled for various surgeries under general anaesthesia were randomly assigned to one of two groups (380 in each group). One group (Group A) received 2ml Granisetron (1mg/ml) while the other group (Group B) received 2ml Metoclopramide (5mg/ml) and were accompanied by manual venous occlusion for one minute. Then 2ml Propofol was injected through the same cannula. Patients were asked by a blinded anaesthesiologist to score pain on injection of Propofol with a four point scale (VRS-Verbal Rating Scale): 0= no pain, 1= mild pain, 2=moderate pain, 3=severe pain. The Post operative nausea/vomiting was assessed by Visual Analog Scale (0=no symptoms, 10=worst symptoms)

**Results:** 65 patients (17.1%) complained of pain in group pretreated with Granisetron that is 31 patients (8.1%) with mild pain (VRS 1), 20 patients (5.3%) with moderate pain (VRS 2), 14 patients (3.7%) with severe pain (VRS 3). 151 patients (39.7%) complained of pain in group pretreated with Metoclopramide that is 76 patients (20%) with mild Pain (VRS 1), 57 patients (15%) with moderate pain (VRS 2), 18 patients (4.7%) with severe pain (VRS 3). The presence and severity of pain was less in the Granisetron group compared with Metoclopramide group ( $P < 0.05$ ).

In Granisetron group, 41 patients (10.8%) complained of post operative nausea /vomiting that is 38 (10%) had VAS score 1, 2 (0.5%) had VAS score 2, 1 (0.3%) had VAS score 3. In Metoclopramide group, 112 patients (29.5%) complained of post operative nausea /vomiting that is 76 (20%) had VAS score 1, 19 (5%) had VAS score 2, 17 (4.5%) had VAS score 3. The presence and severity of post operative nausea and vomiting was less in the Granisetron group compared with Metoclopramide group ( $P < 0.05$ ).

**Conclusion:** Intravenous Granisetron at a dose of 2mg was more effective than intravenous Metoclopramide at a dose of 10 mg along with manual occlusion for one minute in reducing Propofol injection pain when given before propofol injection. Also, Granisetron was more effective than Metoclopramide in reducing post operative nausea and vomiting.

## Introduction

Anaesthesia can be defined as the provision of insensibility to pain with adequate management of vital functions during various therapeutic and diagnostic procedures. With the decrease in adverse events after surgery, patient satisfaction with perioperative care is assuming more importance.

Ever since its introduction in the clinical scenario in 1977, propofol has attained unmatched popularity as an agent for intravenous (i.v.) induction. It is also used for short duration surgery, sedation and ambulatory surgery. But very often, it has the disadvantage of causing pain or discomfort on injection, especially when given in small veins on the dorsum of hand. This pain may be distressing to the patients and can reduce the acceptability of an otherwise useful agent.<sup>[1]</sup>

Among 33 low morbidity clinical outcomes, considering clinical importance and frequency, pain during injection of propofol was ranked as the seventh most important problem of current clinical anesthesiology.<sup>[2]</sup> Incidence of pain with intravenous propofol varies between 28% and 90% in adults and 28% and 85% in children.<sup>[3][4]</sup> Several techniques were proposed over the years to reduce the incidence and severity of such pain. However, all had variable results.<sup>[4-13]</sup>

Many factors like site of injection, size of vein, speed of injection, buffering effect of blood, temperature of propofol and concomitant use of drugs such as local anaesthetics, opiates, etc., appear to affect the incidence of pain<sup>[14-16]</sup>. A number of both pharmacological (e.g., pre-treatment with lignocaine, ondansetron, ketorolac, 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 with variable results and the research for the ideal agent to decrease pain on propofol injection is still going on. Nausea and vomiting occurs in 20-30% of patients in the postoperative period complaints reported<sup>[24][25][26][27][28][29][30][30]</sup>

White<sup>[31]</sup>, *postoperative nausea and vomiting (PONV)* became the more commonly used clinical term; and in 1999, PONV became a medical subject heading in the National Library of Medicine. The term *PONV* will be used throughout this chapter to reflect its current widespread usage to describe the composite postoperative symptoms of nausea and/or vomiting and/or retching. However, the description of these symptoms as “postoperative” should not be construed to suggest that surgery is their most important direct cause, although this is a widely held belief. Several large prospective cohort studies now suggest that the varying incidence of PONV observed after different types of surgeries are largely a reflection of important patient-specific and anaesthesia-related risk factors rather than surgery itself. PONV can be such an unpleasant experience that patients often rate it worse than postoperative pain<sup>[32]</sup>. Prevention of PONV in high-risk patients significantly improves postoperative ratings of well-being and satisfaction.<sup>[33]</sup>

While the experience of PONV is generally self-limited, postoperative vomiting/retching (PONV) can lead to rare but serious medical complications such as aspiration of gastric contents, suture dehiscence, oesophageal rupture, subcutaneous emphysema, or pneumothorax (the actual incidence due to PONV has not been quantified).<sup>[34][35]</sup> PONV may delay patient discharge from post anaesthesia care units (PACUs) and can be the leading cause of unexpected hospital admission after ambulatory anaesthesia.<sup>[36]</sup>

It has been demonstrated that ondansetron, a specific 5-hydroxytryptamine (5HT<sub>3</sub>) receptor antagonist, provided numbness when injected under the skin.<sup>[37]</sup> It has been further demonstrated that ondansetron successfully relieved pain following propofol injection without any adverse effects in a significant number of patients.

Granisetron is a serotonin 5HT<sub>3</sub> receptor antagonist and demonstrates superior efficacy and longer duration to ondansetron.

Metoclopramide shares structural and physicochemical properties with lignocaine and is a weak local anaesthetic<sup>[38][39]</sup>. It has been shown to be as effective as lignocaine in reducing propofol injection pain<sup>[40]</sup>.

This study compares the effectiveness of Granisetron and Metoclopramide in reducing Propofol injection pain and also compares the effectiveness of Granisetron and Metoclopramide in reducing post operative nausea and vomiting.

### Aims and Objectives

The aim of this study is to compare the effectiveness of Granisetron and Metoclopramide for reducing propofol injection pain.

### Objectives

#### Primary objective

- To compare the effectiveness of Granisetron and Metoclopramide for reducing propofol injection pain.

#### Secondary objective

- To compare the effectiveness of Granisetron and Metoclopramide for reducing post operative nausea and vomiting.

### Materials and Methods

**Study Design:** A double blind randomised controlled study

**Study Period:** Twelve months

**Setting of the Study:** Department of Anaesthesiology, Government medical college, Thiruvananthapuram.

**Study Population:** Includes 760 patients coming for elective surgery under general anaesthesia during the study period satisfying the following inclusion and exclusion criteria.

#### Inclusion Criteria

- ASA(PS) 1& 2 patients
- 2Adults in age group 21-50years

#### Exclusion Criteria

- Patient refusal
- Neurological deficit
- History of allergy to propofol and study drugs.

4. History of taking any analgesic before surgery

5. Emergency surgery

### Sample Size

**Reference 1:** Pre-treatment with intravenous Granisetron to alleviate pain on propofol injection: A double –blind randomized, controlled trial (Ahmed et al IJA Mar-Apr 2012-15% complained of pain with Granisetron<sup>[71]</sup>).

**Reference 2:** Pain on injection of propofol: The mitigating influence of Metoclopramide using different techniques (W J Liaw et al Acta anaesthesiologica Scandinavica 1999-23% complained of pain with Metoclopramide<sup>[11]</sup>).

$$N = \frac{2 * (Z_{(1-\alpha/2)} + Z_{(1-\beta)})^2 * P * Q}{D^2}$$

$$P = (23+15)/2 = 19;$$

$$\text{Substituting } P=19; Q(100-P)= 81 ; D=8(23-15) ;$$

$$Z_{(1-\alpha/2)} = 1.96; \quad Z_{(1-\beta)} = 0.842$$

$$N=380 \text{ in each group.}$$

The total sample size is 760 with 380 in each group .

### Methodology

760 Study subjects are selected from patients posted for elective surgery under general anaesthesia after applying inclusion and exclusion criteria. Selected patients are asked about their willingness to participate in the study after explaining the details of the study to them.

All patients undergo a detailed preoperative evaluation prior to surgery, including

Detailed history Age and weight

General and systemic examination Airway assessment

Type of surgery

Investigations:

Haemoglobin,

Total and differential count

Renal function test, Serum electrolytes

Platelet count, ECG, Chest X-ray.

Screening markers- for HIV, HBsAg, HCV, VDR.

All patients will be fasted for 8 hrs and will receive ranitidine 150 mg in the evening and on

morning of surgery. Patient will be randomized into two groups using a computer generated random number table into

Group A - those receiving intravenous Granisetron 2ml (1mg/ml). Group B - those receiving intravenous Metoclopramide 2ml (5mg/ml).

All drugs were prepared by an anaesthesiologist (who is not blinded) not included during induction of anaesthesia. The patient as well as anaesthesiologist who induce the patient (who gives the study drugs) will be unaware of nature of test drug. No patient was given any premedication (except ranitidine) before the pretreatment injection.

Standard monitors ECG, pulse oximeter, noninvasive blood pressure (NIBP), and end tidal carbon dioxide were attached and baseline vital parameters of patient were recorded before injecting propofol and at 1 and 3 min after. The intravenous (i.v) access was established with 18G cannula without any local infiltration in suitable vein on dorsum of non dominant hand and intravenous fluid (0.9% normal saline) was infused.

Each patient received 2ml of pretreatment solution for a period of 5s while the venous drainage was occluded manually at mid forearm for 1 minute to increase the local concentration of drug. Then the occlusion was released and anaesthesia was induced with propofol 2.5mg/kg. The initial 2ml bolus was given over 4s; 15 seconds later, the patient was asked to rate immediately any sensation of pain during injection of propofol.

The grading of pain was similar to the method used in previous studies and will be explained to patient at the pre anaesthetic visit as well as before giving propofol injection. Thereafter, induction of anaesthesia will be achieved with propofol and for analgesia, fentanyl 2ug/kg will be given to all patients. The patients will be intubated with appropriate size endotracheal tube after giving vecuronium. Anaesthesia will be maintained with isoflurane and nitrous oxide-oxygen (66-33%).

## Outcome

The pain during injection of propofol will be evaluated using a Verbal

Rating Scale (VRS):

0 - none (negative response to questioning)

1 - mild pain (pain reported only in response to questioning without any behavioural signs)

2 - moderate pain (pain reported in response to questioning and accompanied by behavioural signs or pain reported without questioning)

3 -severe pain (strong vocal response or response accompanied by facial grimacing, arm withdrawal or tears)

The post operative nausea and vomiting (in 24 hr period) will be assessed using Visual Analog Scale (VAS). The patient is asked to rate severity of nausea and vomiting between '0-10' with '0' corresponding to no symptoms and '10' corresponding to worst possible symptoms.

## Observations and Results

### Statistical Interpretation

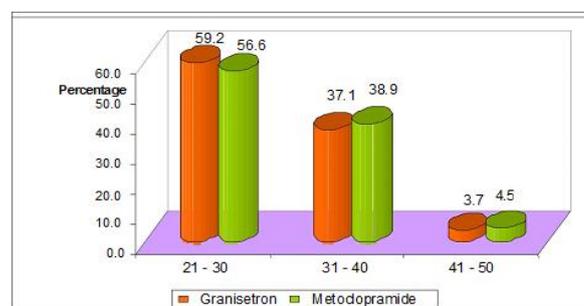
Chi-Square test, Mann Whitney U test were used for analysis.

A 'P' value of less than 0.05 was considered statistically significant.

Table 1 Comparison of Age based on Group

Age in years	Group A		Group B		$\chi^2$	p
	Count	Percent	Count	Percent		
21 - 30	225	59.2	215	56.6	0.69	0.709
31 - 40	141	37.1	148	38.9		
41 - 50	14	3.7	17	4.5		
Mean $\pm$ SD	30.7 $\pm$ 5		30.3 $\pm$ 5.3			

Figure 1 Comparison of Age based on Group

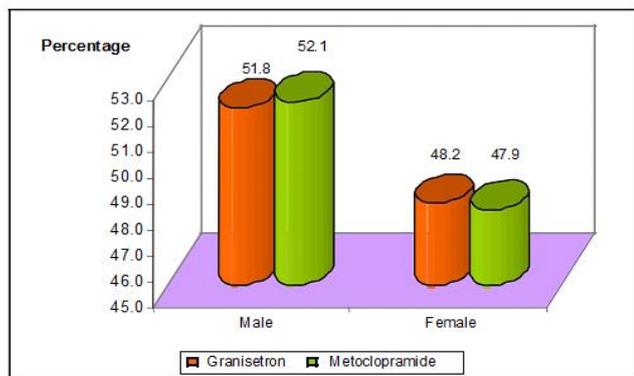


Average age in years were 30.7 and 30.3 respectively for patients selected for Group A and Group B. The Chi square test ( $p > 0.05$ ) shows that there is no statistical difference in age between the two groups.

**Table 2** Comparison of Sex based on Group

Sex	Group A		Group B		X <sup>2</sup>	p
	Count	Percent	Count	Percent		
Male	197	51.8	198	52.1	0.01	0.942
Female	183	48.2	182	47.9		

**Figure 2** Comparison of Sex based on Group

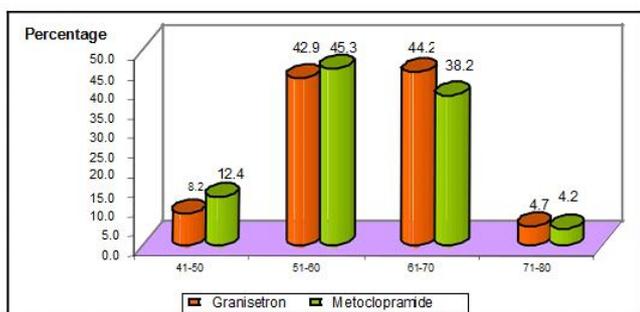


Among 380 cases of Group A 197 were males and 183 were females and among 380 cases of Group B 198 were males and 182 were females. The Chi square test ( $p > 0.05$ ) shows that there is no statistical difference in sex between the two groups.

**Table 3** Comparison of Weight based on Group

Weight in kg	Group A		Group B		X <sup>2</sup>	p
	Count	Percent	Count	Percent		
41-50	31	8.2	47	12.4	5.33	0.149
51-60	163	42.9	172	45.3		
61-70	168	44.2	145	38.2		
71-80	18	4.7	16	4.2		
Mean ± SD	61.3 ± 6.6		60.1 ± 6.7			

**Figure 3** Comparison of Weight based on Group

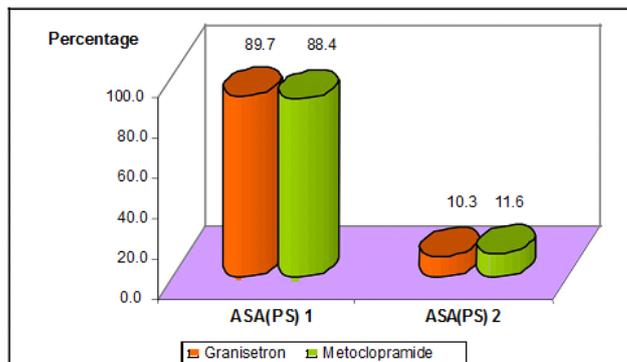


Average weight in kg were 61.3 and 60.1 respectively for patients selected for Group A and Group B. The Chi square test ( $p > 0.05$ ) shows that there is no statistical difference in weight between the two groups.

**Table 4** Comparison of ASA(PS) status based on Group

ASA	Granisetron		Metoclopramide		X <sup>2</sup>	p
	Count	Percent	Count	Percent		
Grade 1	341	89.7	336	88.4	0.3	0.561
Grade 2	39	10.3	44	11.6		

**Figure 4** Comparison of ASA(PS) status based on Group



Among 380 cases of Group A 341(89.7%) were ASA (PS) 1 and 39 (10.3%) were ASA (PS) 2 and among 380 cases of Group B 336 were ASA(PS) 1 and 44 were ASA (PS) 2. The Chi square test ( $p > 0.05$ ) shows that there is no statistical difference in ASA (PS) between the two groups.

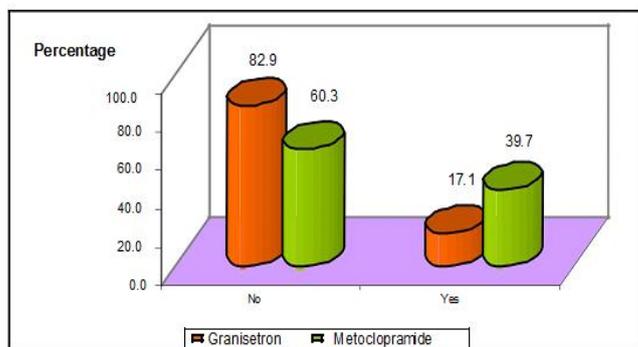
Table 5 Comparison of Presence of Pain based on Group

**Table 5** Comparison of Presence of Pain based on Group

Pain	Group A		Group B		X <sup>2</sup>	p
	Count	Percent	Count	Percent		
No	315	82.9	229	60.3	47.84**	0.000
Yes	65	17.1	151	39.7		

\*\* : - Significant at 0.01 level

**Figure 5** Comparison of Presence of Pain based on Group



Among 380 cases of Group A 315 (82.9%) had no pain (VRS 0) but 65 (17.1%) complained of pain (VRS 1,2,3) and among 380 cases of Group B 229 (60.3%) had no pain (VRS 0) but 151 (39.7%)

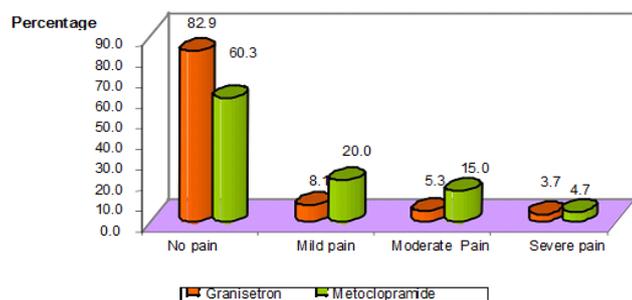
complained of pain (VRS 1,2,3) .The Chi square test (p<0.05) shows that there is statistical difference in presence of pain between the two groups.

**Table 6** Comparison of Severity of Pain based on Group

Pain	Granisetron		Metoclopramide		X <sup>2</sup>	p
	Count	Percent	Count	Percent		
No pain	315	82.9	229	60.3	47.83**	0.000
Mild pain	31	8.2	76	20.0		
Moderate pain	20	5.3	57	15.0		
Severe pain	14	3.7	18	4.7		

\*\*:- Significant at 0.01 level

**Figure 6** Comparison of Severity of Pain based on Group



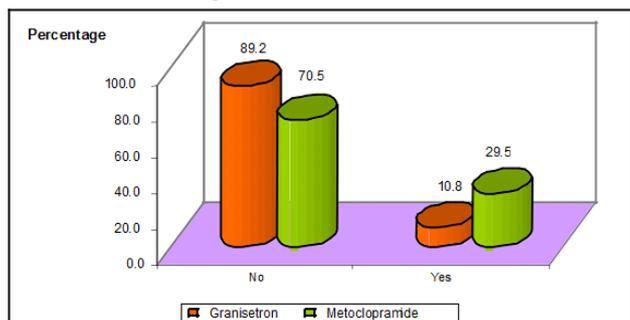
Among 65 cases which complained of pain in Group A, 31 patients had Mild pain VRS 1 (8.1%), 20 had Moderate pain VRS 2 (5.3%), 14 had Severe pain VRS 3 (3.7%) but among 151 cases which complained of pain in Group B, 76 had Mild pain VRS 1 (20%), 57 had Moderate pain VRS 2 (15%), 18 had Severe pain VRS 3 (4.7%) . The Chi square test (p<0.05) shows that there is statistical difference in severity of pain between the two groups.

**Table 7** Comparison of Presence of Nausea & Vomiting based on Group

Nausea & Vomiting	Group A		Group B		χ <sup>2</sup>	p
	Count	Percent	Count	Percent		
No	339	89.2	268	70.5	41.25**	0.000
Yes	41	10.8	112	29.5		

\*\*:- Significant at 0.01 level

**Figure 7** Comparison of Presence of Nausea & Vomiting based on Group



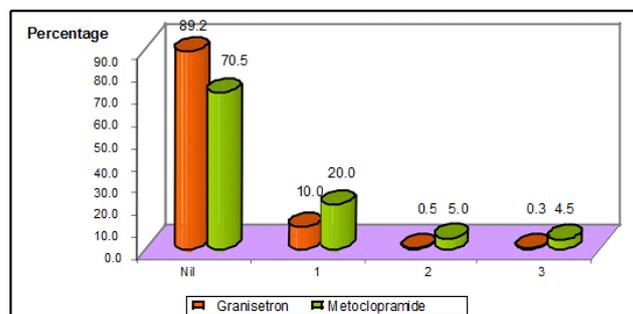
Among 380 cases in Group A, 41 patients (10.8%) had nausea/vomiting but in Group B which had 380 patients, 112 patients (29.5%) complained of nausea/vomiting. The Chi square test (p<0.05) shows that there is statistical difference in presence of nausea/vomiting between the two groups.

**Table 8** Comparison of Severity of Nausea & Vomiting based on Group

Nausea & Vomiting	Group A		Group B		Z#	p
	Count	Percent	Count	Percent		
Nil	339	89.2	268	70.5	6.66**	0.000
1	38	10.0	76	20.0		
2	2	0.5	19	5.0		
3	1	0.3	17	4.5		

# Mann-Whitney U Test \*\*: - Significant at 0.01 level

**Figure 8** Comparison of Severity of Nausea & Vomiting based on Group



Among 41 patients of Group A which complained of Nausea/Vomiting, 38 had VAS (Visual analog score) score 1, 2 had VAS score 2, 1 had VAS score 1 but among 112 patients of Group B, 76 had VAS score 1, 19 had VAS score 2, 17 had VAS score 3 . The Mann Whitney U test (p<0.05) shows that there is statistical difference in severity of nausea/vomiting between the two groups.

**Discussion**

Nowadays anaesthesiologists are expected to provide their services with safe, uncomplicated accepted technique of anaesthesia to patient. The incidence and severity of pain on injection may be more when intravenous cannulation is performed in small veins. Hypertonic drugs, size of needle, site of injection, speed of injection and many other factors are important to produce pain on injection.

Again pain on injection is considerably more at extremes of age. In paediatric patients many times un cooperation may result in multiple pricks and more incidence of pain. In geriatric patients overall pain threshold is decreased giving rise to more incidence of pain.

Propofol (2,6, di isopropyl phenol) was introduced in practice of anaesthesia as an induction agent in early 1970's. It gained popularity due to its rapid induction and rapid recovery .

Overall pain on injection of propofol ranges from 25 to 100% at vein on dorsum of hand (Stark R.D. et al 1986<sup>[41]</sup>, Scott R.P.F. et al 1988<sup>[16]</sup>, Johnson R.A. et al 1999<sup>[19]</sup>) and 3 to 26% only when injected into proximal veins.

Gehan et al 1991<sup>[81]</sup> quoted that pain on injection of propofol was attributed to the stabilizing agent Cremophor EL but persisted even though replaced by soybean oil (Brooker J et al 1985<sup>[82]</sup> and McCulloch M.J. et al 1985<sup>[7]</sup>).

To overcome this pain on injection, McCulloch M.J. et al 1985<sup>[7]</sup> suggested injection in large veins. Hiller S.C. et al 1996<sup>[85]</sup> suggested decreasing speed of injection, dilution in 5% dextrose or 10% intralipid or pretreatment with narcotics or thiopentone before propofol administration.

However, pain on injection of propofol, which has been reported to occur in 28%-90% of patients, is a major drawback to its use. Various methods of minimizing pain on injection have been proposed. Based on proposed mechanisms and factors associated with propofol injection pain, several methods for prevention of pain have been tried with varying degrees of success.

Propofol belong to group of phenol that can irritate the skin, mucous membrane, and venous intima (<sup>[8]</sup>Ambesh SP et al 1999). Scott et al <sup>[54]</sup> speculated that the injection pain is caused by activation of the kallikrein-kinin system either by propofol or the lipid solvent, there by generating kinins, probably bradykinin. Bradykinin, by producing local vasodilation and hyper permeability, may increase the contact between the aqueous phase propofol and the free nerve

ending resulting in pain on injection (<sup>[83]</sup>Coderre TJ et al 1993). This pain has a 10-20s delayed onset. But immediate pain may be caused by direct irritation of afferent nerve endings in the veins.

The use of pretreatment to reduce the pain of injection of propofol has become a standard practice. The pain of injection at the induction of anaesthesia can cause agitation and hinder the smooth induction of anaesthesia and thus an effective method of prevention would be beneficial.

This study attempts to compare the effectiveness of Granisetron and Metoclopramide on reducing propofol injection pain. Granisetron and Metoclopramide are used commonly as antiemetic drugs.

In the present study, I evaluated the statistical difference in age, sex, weight, ASA(PS) among the two groups .There was no statistical difference in these. This result was similar to study conducted by Ahmed et al <sup>[71]</sup> 2012. They also did not get any statistical difference in age, weight, ASA physical status.

Average age in years for group A and group B were 30.7 and 30.3 respectively. In 21-30 year old age, group A has 225 (59.2%) , group B has 215 (56.6%) while in 31-40 year old age , group A has 141 (37.1%) ,group B has 148 (38.9%) while in 41-50 year old age , group A has 14 (3.7%) , group B has 17 (4.5%). The p value was 0.709. The Chi square test ( $p>0.05$ ) shows that there is no statistical difference in age between the two groups.

Among 380 cases of Group A 197 (51.8%) were males and 183 (48.2%) were females and among 380 cases of Group B 198 (52.1%) were males and 182 (47.9%) were females. Males are predominant in my study. The p value was 0.942. The Chi square test ( $p>0.05$ ) shows that there is no statistical difference in sex between the two groups.

Average weight for group A and group B were 61.3 kg and 60.1 kg respectively. In group A 31 (8.2%) patients had weight between 41-50 kg while in group B it was 47 (12.4%). In Group A 163(42.9%) had weight between 51-60 kg while in

Group B it was 172(45.3%). In group A 168 (44.2%) had weight between 61-70 kg while in Group B it was 145 (38.2%). In Group A 18 (4.7%) patients had weight between 71-80 kg while in Group B it was 16 (4.2%).The p value was 0.149. The Chi square test ( $p>0.05$ ) shows that there is no statistical difference in weight between the two groups.

Among 380 cases of Group A 341 (89.7%) were ASA(PS) 1 and 39 (10.3%) were ASA(PS) 2 and among 380 cases of Group B 336 (88.4%) were ASA(PS) 1 and 44 (11.6%) were ASA(PS) 2. The p value was 0.561. The Chi square test ( $p>0.05$ ) shows that there is no statistical difference in ASA(PS) between the two groups.

In my study, the test drugs were given as pretreatment in 2ml solution over 5 seconds followed by venous occlusion of arm for 1 minute. This was similar to the way the study conducted by to R.A.

Johnson et al 1990<sup>[19]</sup>, S.P. Ambesh et al 1999<sup>[8]</sup>, Ahmed etal<sup>[71]</sup>.

According to Hiller S.C.et al 1992<sup>[59]</sup> speed of injection directly correlates with pain on injection that is why speed of test drug and propofol were kept constant as 4 seconds.

No premedication was given to patients except ranitidine because it might interfere with perception of pain of propofol injection . Best way of measuring pain in the clinical setting is by verbal response or its derivatives, the visual analogue scale (VAS) (Ohnhaus EE et al 1975<sup>[84]</sup>). The VAS appears to be more sensitive than the categorical scales at measuring smaller changes. A four- point verbal categorical scoring system (VRS) was chosen in this study rather than VAS as it was very simple to use by the patient and as appropriate hand eye coordination required for a VAS might not be present in all patients during the rapidly changing state of consciousness of anaesthesia induction.

Group A patients pretreated with Granisetron has less incidence of pain than in group B patients which were pretreated with Metoclopramide. Among 380 cases of Group A 315 patients

(82.9%) had no pain (VRS 0) but 65 patients (17.1%) complained of pain (VRS 1,2,3) and among 380 cases of Group B 229 patients (60.3%) had no pain (VRS 0) but 151 patients (39.7%) complained of pain (VRS 1,2,3). The p value was 0.000. The Chi square test ( $p<0.05$ ) shows that there is statistical difference in presence of pain between the two groups.

In the study by Ahmed etal 2012<sup>[71]</sup>, 15% complained of pain when Granisetron given as pretreatment before propofol injection. In the study by Liaw WJ etal 1999<sup>[11]</sup>, 23% complained of pain when metoclopramide was given as pretreatment before propofol injection.

Group A patients pretreated with Granisetron has less severity of pain than in group B patients which were pretreated with Metoclopramide. Among 65 cases with complaints of pain in Group A, 31 patients (8.1%) had mild pain (VRS 1), 20 (5.3%) had moderate pain (VRS 2), 14 (3.7%) had severe pain (VRS 3) but among 151 cases which complained of pain in Group B, 76 (20%) had mild pain (VRS 1), 57 (15%) had moderate pain (VRS 2), 18 (4.7%) had severe pain (VRS 3). The p value was 0.000. The Chi square test ( $p<0.05$ ) shows that there is statistical difference between the two groups.

Ye Jh *et al*<sup>[37]</sup> suggested the dual mechanism of action of ondansetron as a sodium channel blocker and 5HT3 receptor antagonist (peripheral 5HT3 receptors involve nociceptive pathways). The exact mechanism of alleviation of propofol injection pain by Granisetron is not known. This may have been the result of a peripheral local anesthetic action, which attenuated the afferent pain pathway rather than a central analgesic effect, similar to the mechanism of ondansetron (i.e., blockage of sodium channel and antagonism of 5HT3 receptor).

Among 380 patients in group A, 339 patients had no nausea/vomiting (89.2%) but 41 patients (10.8%) had nausea/vomiting while in group B, 268 patients (70.5%) had no nausea/vomiting but 112 patients (29.5%) complained of nausea/vomiting. The p value is 0.000. The Chi square

test ( $p < 0.05$ ) shows that there is statistical difference between the two groups. Thus Granisetron has less incidence of nausea/vomiting than Metoclopramide.

Among 41 (10.8%) patients of group A which complained of nausea/vomiting, 38 (10%) had VAS score 1, 2 (0.5%) had VAS score 2, 1 (0.3%) had VAS score 1 but among 112 patients (29.5%) of Group B, 76 (20%) had VAS score 1, 19 (5%) had VAS score 2, 17 (4.5%) had VAS score 3. The p value is 0.000. The Mann Whitney U test ( $p < 0.05$ ) shows that there is statistical difference between the two groups. Thus Granisetron has less severity of nausea/vomiting than Metoclopramide. A Wadaskar et al [86] The incidence of nausea and vomiting over a period of 24 hour were found in 20% of patients who had received Granisetron, 45% of patients who had received ondansetron and 77.5% of patients who had received placebo. Granisetron is more effective than ondansetron and placebo in controlling postoperative nausea & vomiting after laparoscopic gynecological surgery. Sabina Yeasmeen et al 2006 Intravenous Granisetron,

Ondansetron and Metoclopramide in the Prevention and Treatment of Post Operative Nausea and Vomiting after Laparoscopic Cholecystectomy - A Comparative Study. The incidence of emesis free (no nausea) was significantly higher in patients who received Granisetron (90.0%, 27/30) than in those who received Ondansetron [(66.7%, 20/30),  $p = 0.028$ ] or Metoclopramide [(40.0%, 12/30),  $p = 0.000$ ]. The incidence of vomiting free (no vomiting) was significantly higher in patients who received Granisetron (93.3%, 28/30) than in those who received Ondansetron [73.3%, 22/30),  $p = 0.037$ ] or Metoclopramide [46.7%, 14/30),  $p = 0.000$ ]. Granisetron was associated with greater patients' satisfaction than Ondansetron and Metoclopramide 40%, 20% and 10% of patients respectively. No need for another rescue antiemetic medication was achieved in 86.7% of patients with Granisetron, 70.60% with Ondansetron and 53.3% with Metoclopramide.

My study had few limitations. Occlusion at mid forearm was done manually, which will vary from person to person, this could have been overcome by using tourniquet with constant pressure. Also drug could have been injected using syringe pump instead of injecting manually.

The incidence of adverse reaction were negligible in my study may be attributed to selection of patients of ASA grade I and II only.

### Summary

760 patients selected for study have no statistical difference in age, sex, weight and ASA(PS) status. 380 of them were given Granisetron (group A) and 380 were given Metoclopramide (group B) before Propofol injection. 65 patients (17.1%) complained of pain in group A that is 31 patients (8.1%) with mild pain (VRS 1), 20 patients (5.3%) with moderate pain (VRS 2), 14 patients (3.7%) with severe pain (VRS 3). 151 patients (39.7%) complained of pain in group B that is 76 patients (20%) with mild Pain (VRS 1), 57 patients (15%) with moderate pain (VRS 2), 18 patients (4.7%) with severe pain (VRS 3). The Chi square test  $P < 0.05$  shows that Granisetron is superior to Metoclopramide in reducing propofol injection pain.

In group A 41 patients (10.8%) complained of post operative nausea /vomiting that is 38 (10%) had VAS score 1, 2 (0.5%) had VAS score 2, 1 (0.3%) had VAS score 1. In group B 112 patients (29.5%) complained of post operative nausea /vomiting that is 76 (20%) had VAS score 1, 19 (5%) had VAS score 2, 17 (4.5%) had VAS score 3. The Mann Whitney U test  $P < 0.05$  shows that Granisetron is superior to Metoclopramide in reducing post operative nausea/ vomiting.

### Conclusion

Intravenous Granisetron at a dose of 2mg was more effective than intravenous Metoclopramide at a dose of 10 mg along with manual occlusion for one minute in reducing Propofol injection pain when given before Propofol injection. Also, Granisetron was more effective than Metoclopr-

amide in reducing post operative nausea and vomiting . No significant adverse effects were noted with either drugs.

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