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Antiemetic Effect Of Propofol Administered At The End Of Surgery

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Abstract : *Post operative nausea and vomiting (PONV) remains one of the most common and distressing complications after surgery resulting in pain, hematoma and wound dehiscence. Furthermore, small dose of propofol was reported to possess direct antiemetic effects. Thus, a study was done to evaluate the antiemetic efficacy of propofol. Group A received Propofol 0.5mg/kg IV, Group B received Propofol 0.75mg/kg IV and Group C received Normal Saline, respectively. Incidence of nausea and vomiting was assessed by VAS score within 24 hours in PACU. We also noted the incidence of rescue antiemetic administered within 24 hours in PACU.At 6 to 24 hrs, among 33.3% of controls nausea was present, while only in 3.3% nausea was present in group 1 and group 2, thereby 33.3% of controls required antiemetics. We concluded that administration of Propofol in the dose of 0.5mg/kg IV and 0.75mg/kg IV at end of surgery reduced PONV.*

Keywords: *Post operative nausea and vomiting, propofol, visual analogue score.*

I. Introduction

Post operative nausea and vomiting (PONV) remains one of the most common and distressing complications after surgery resulting in pain, hematoma and wound dehiscence. To maintain the efficacy and cost-saving benefit of surgery, effective antiemetic administration and prophylaxis for certain patients undergoing surgery would be desirable [1].

Nausea and vomiting are important defense mechanisms against the injection of toxins. The complex act of vomiting involves the co-ordination of respiratory, gastrointestinal and abdominal musculature and is controlled by the emetic centre. This area is situated in the lateral reticular formation close to the tractus solitarius in the brain stem and is thought to be emetic centre. Electrical stimulation of the emetic centre and tractus solitarius will cause immediate vomiting [2].

It is widely believed that propofol based anaesthesia reduces post operative nausea and vomiting (PONV). Furthermore, even a small dose of propofol was reported to possess direct antiemetic effects. Although the precise mechanism of propofol's antiemetic effect has not been elucidated, several mechanisms have been proposed, including a direct depressant effect on the CTZ, the vagal nuclei and other centers implicated in post operative nausea and vomiting (PONV) [3].

II. Objectives

1. To evaluate antiemetic effect of propofol administered at the end of surgery.
2. To evaluate the need for administering rescue antiemetic to patients administered with propofol at the end of surgery.

III. Material And Methods

90 patients admitted for elective surgeries, to be done under general anaesthesia at R.L. Jalappa Hospital and Research centre, Tamaka, Kolar during the period of December 2015 to March 2016 were included in the study. Patients of ASA physical status I and II in the age group of 18 years to 60 years of either sex, posted for elective surgeries under general anesthesia were selected for the study. If there was patient's refusal, history of allergies to any study medications, gastrointestinal disease, Insulin-dependent diabetes mellitus, administration of antiemetic or steroids 24 hours prior to surgery, cardiac diseases, neurological diseases, and impaired hepatic/renal function, were excluded from the study.

SPSS (version18.0) to analyze data (version 18.0), and Sigma-Stat 12.0 is used to decide sample size. Statistical analyses were performed using the Chi-square test and Fisher's exact test for categorical data and one-way ANOVA for continuous data. A P value of < 0.05 was considered significant.
Statistical evaluation of data or parameters were done as follows Sample Size
$2P\bar{Q}(Z\alpha+Z1-\beta)2$

n = ----------
(P1-P2)2
where,
P1=22.5%, P2=2.5%, P =12.5, Q̄ =87.5
Zα=95% confidence interval=1.96
Z1-β=power at 80%=0.842
Thus, the sample size required is 30 per group.

A prospective randomized double blind study was planned. After obtaining approval from the ethical committee and taking informed consent, the patients who met the inclusion criteria were taken for the study. They were randomly allocated into two groups.

- Group A received propofol 0.5mg/kg IV, 15min before the end of surgery.
- Group B received propofol 0.75mg/kg IV, 15min before the end of surgery.

It was a double blind study and the anaesthesiologist was not aware of the drug used. Patients were randomly allocated to 2 groups using a computerized randomization table: those who received 0.5 mg/kg of propofol (propofol 0.5 group, n = 45) and those who received 0.75 mg/kg of propofol (propofol 0.75 group, n = 45). For induction of anesthesia, intravenous propofol 2 mg/kg and intravenous scoline 2 mg/kg was administrated to facilitate endotracheal intubation. After induction, anesthesia was maintained with 0.8-1.2 vol% isoflurane and 50% nitrous oxide in oxygen. Ventilation was mechanically controlled and adjusted to maintain an end-tidal CO2 concentration of 35-40 mmHg. For appropriate muscle relaxation, vecuronium was administered as required.

Fifteen minutes before the end of surgery, patients received propofol at 2 different doses, 0.5 mg/kg IV or 0.75mg/kg IV. Injected drugs were prepared in identically shaped syringes covered with black transparent plastic by persons not involved in the study. Isoflurane was discontinued at the completion of surgery. Glycopyrrolate (0.2 mg) and neostigmine (2.5 mg) were administered intravenously to facilitate the reversal of muscle relaxation. The endotracheal tube was removed when the patient was spontaneously breathing and was able to open eyes on command.

Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit, and vomiting was defined as the forceful expulsion of gastric contents from the mouth.[1] For the evaluation of the severity of nausea, a visual analog score (VAS) was used. Ondansetron (4 mg) was administered intravenously when a patient complained of persistent nausea (VAS for nausea >4), developed vomiting (>1 episode) or needed another rescue antiemetic in the PACU. To avoid delay in treatment of PONV, there was a detailed description of rescue antiemetic at a preanaesthetic visit. All PONV episodes were recorded through direct interviews by a single anesthesiologist who was blinded to patient groups during the postoperative 0-2, 2-6 and 6-24 hours, visits.

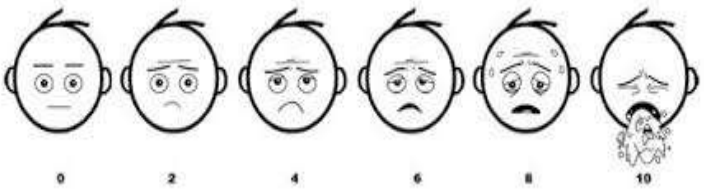

Fig 1: Visual Analogue Score For Nausea

IV. Results

There was no significant difference in age and gender distribution between two groups.

Table 1: Age distribution of subjects

	Group						P value
	Propofol 0.5 mg		Propofol 0.75 mg		Control		
	Mean	SD	Mean	SD	Mean	SD	
Age	41.5	16.8	39.3	15.3	37.5	14.7	0.612

There was no significant difference in mean age between three groups.

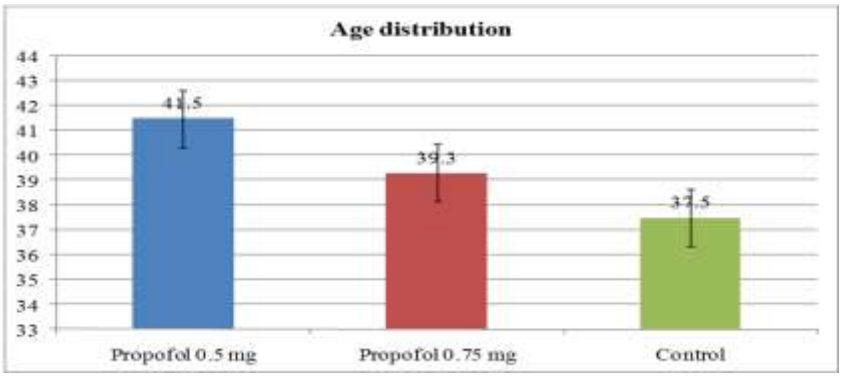

Fig 2: Bar diagram showing Age distribution of subjects.

Table 2: Gender distribution of subjects

		Group						P value
		Propofol 0.5 mg		Propofol 0.75 mg		Control		
		Count	%	Count	%	Count	%	
Gender	Female	15	50.0%	18	60.0%	16	53.3%	0.731
	Male	15	50.0%	12	40.0%	14	46.7%	

In the study majority of subjects were female. No significant difference was observed in gender distribution between two groups.

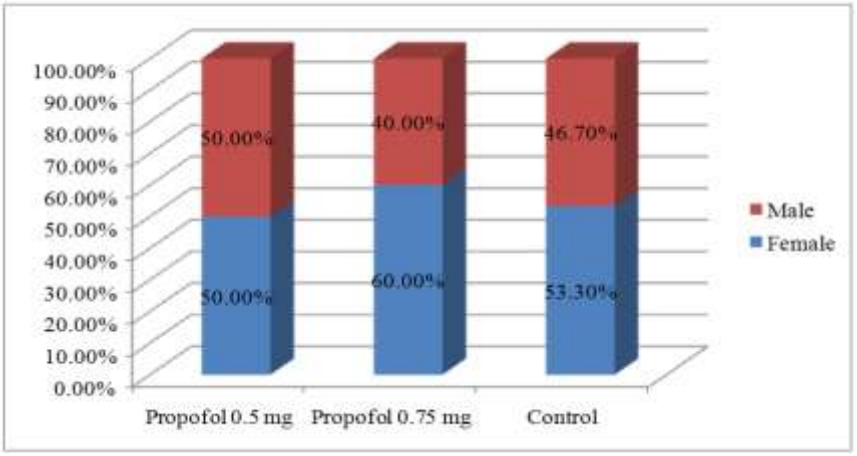

Fig 3: Gender distribution of subjects

Table 3: Nausea among subjects in three groups

	Group						P value
	Propofol 0.5 mg (n = 30)		Propofol 0.75 mg (n = 30)		Control (n = 30)		
	Count	%	Count	%	Count	%	
2 hrs	3	10.0%	2	6.7%	2	6.7%	0.856
2 to 6 hrs	6	20.0%	5	16.7%	4	13.3%	0.787
6 to 24 hrs	1	3.3%	1	3.3%	10	33.3%	<0.001*

In the study no significant difference was observed in Nausea between three groups at 2 hrs and 2 to 6 hrs. Were as at 6 to 24 hrs, among 33.3% of controls nausea of present, were as only in 3.3% nausea was present in group 1 and group 2.

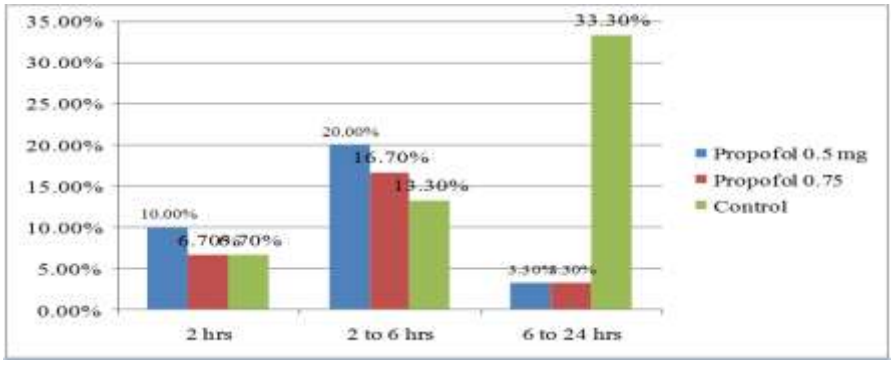

Fig 4: Bar diagram showing Nausea among subjects in three groups

Table 4: Vomiting among subjects in three groups

		Group						P value
		Propofol 0.5 mg		Propofol 0.75 mg		Control		
		Count	%	Count	%	Count	%	
2 hrs	Present	1	3.3%	1	3.3%	3	10.0%	0.429
2 to 6 hrs	Present	3	10.0%	2	6.7%	7	23.3%	0.133
6 to 24 hrs	Present	0		0		0		

There was no significant difference in incidence of vomiting between three groups at 2 hrs, 2 to 6 hrs and 6 to 24 hrs.

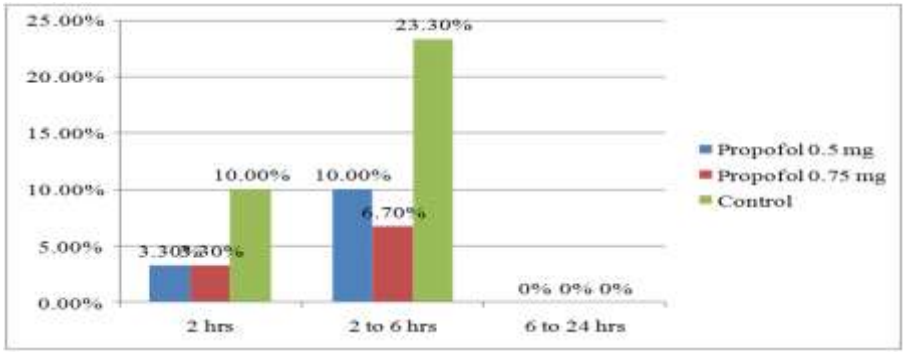

Fig 5: Bar diagram showing Vomiting among subjects in three groups

Table 5: Antiemetic used among subjects in three groups

		Group						P value
		Propofol 0.5 mg		Propofol 0.75 mg		Control		
		Count	%	Count	%	Count	%	
2 hrs	Given	4	13.3%	3	10.0%	5	16.7%	0.749
2 to 6 hrs	Given	9	30.0%	7	23.3%	11	36.7%	0.530
6 to 24 hrs	Given	1	3.3%	1	3.3%	10	33.3%	<0.001*

In the study there was no significant difference in Antiemetic usage between three groups at 2 hrs and 2 to 6 hrs. Were as at 6 to 24 hrs 33.3% of controls required antiemetics. This difference was statistically significant.

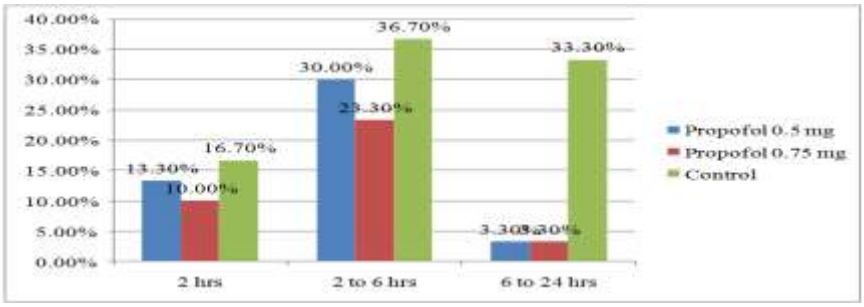

Fig 6: Bar diagram showing Antiemetic used among subjects in three groups..

V. Discussion And Conclusion

Propofol was introduced into clinical practice in 1989. It has been widely used universally since then. Apart from being an induction and maintenance agent, it is also known for its unique antiemetic properties. There are various theories proposed for the antiemetic property of propofol. Ostman et al found that the antiemetic effect of propofol was not due to lipid emulsion used to dissolve the drug [5]. Also, Borgeat et al found that propofol does not have vagolytic properties. Moreover, in a study by Hammas et al, they found that on oral intake of ipecacuanha syrup [6], there was retching because of acids such as glutamate and aspartate, which may be related to its antiemetic activity due to release of 5-hydroxy-tryptamine. On giving propofol to such individuals retching was reduced. Thereby, they concluded that propofol may have anti-serotonin effect. In a case report by Collins C G, it has been reported that propofol decreased synaptic transmission in the olfactory cortex in an animal study, suggesting a decrease in the release of excitatory amino acids [7].

But the dosage of propofol that needs to be administered to have antiemetic effect has always been a challenge. Various studies have tried to identify appropriate doses for the antiemetic effect of propofol. Borgeat et al reported use of 17ug/kg/min propofol infusion in a group of patients receiving cisplatinum chemotherapy [8]. A case report by Schulman et al indicates that the plasma concentration of propofol to treat refractory PONV is 197ng/ml [9]. Moreover, Borgeat et al administered a bolus of propofol in the dose of 10-20mg, for the treatment of PONV [8]. Erdem et al found that intraoperatively, infusion of 20ug/kg/min had a prophylactic antiemetic effect [10]. In another study, Kim et al found that 0.5mg/kg of propofol combined with

In our study we found a significantly lower incidence of nausea and number of rescue antiemetics administered in the propofol 0.5 and propofol 0.75 groups than in the control group. There was no significant difference in mean age and gender distribution between three groups. Also there was no significant difference in nausea and administration of rescue antiemetics between 3 groups at 2hour and 2-6hours postoperatively. But, at 6-24hours, 33.3% of controls and 3.3% of propofol 0.5 and propofol 0.75 developed nausea and rescue antiemetic was administered which is statistically significant.

In our study propofol administered in the dose of 0.5mg/kg IV and 0.75mg/kg IV was effective in reducing PONV.

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