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A CLINICAL STUDY – COMPARISON OF ONDANSETRON, DEXAMETHASONE, ONDANSETRON WITH DEXAMETHASONE AND PLACEBO FOR PREVENTION OF POST-OPERATIVE NAUSEA AND VOMITING FOLLOWING GENERAL ANAESTHESIA.

Anaesthesiology

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ABSTRACT

BACKGROUND: pain, nausea and emesis are common distressing symptoms following general anaesthesia in immediate post operative period. Timing of administration of dexamethasone, ondansetron and their combination for an effective prophylaxis against PONV is an important determinant of their antiemetic efficacy.

Aims: This study aims to compare the efficacy of monotherapy ondansetron I.V, dexamethasone i.v with combination therapy on PONV and to study the incidence & risk factors of PONV.

Settings and Design: This was a randomized, prospective, and comparative study

Materials and Methods: In this study, recruited patients were randomly allocated into 4 groups**.** Groups I, II, III and 4 received IV normal saline, IV Ondansetron 4mg, IV dexamethasone 8mg, IV ondansetron and dexamethasone 8mg, respectively. Incidence, risk factors of PONV and antiemetic properties, complications were assessed and compared among groups.

Statistical analysis: Mean and standard deviation were calculated. Test of analysis between groups was done by *Chi square*, then *P* value was calculated.

Results: Incidence of PONV was significantly lower in Group 4 (12%) in comparison to Group I (67%) group II (35%) and Group III (40%).

Conclusion: combination of IV ondanseton & dexamethasone before GA is safe & more effective than monotherapy. Females, combined H/O motion sickness & previous H/O PONV are considered as reliable predictors of PONV.

KEYWORDS

Dexamethasone, Ondensetron, General anaesthesia, PONV

INTRODUCTION

Pain, nausea and emesis are common distressing symptoms following GA in immediate post-operative period[1]. Both incidence & frequency have decreased recently but still occurs with unacceptable frequency (30-70%) and hence described as "big little problem".[2] In day care anaesthesia PONV results in delayed discharge, expanded nursing care and at times readmission – all factors increasing total health care costs[3]. Persistent PONV causes patient discomfort, electrolyte imbalance, venous hypertension, increasing bleeding under skin flaps and tension on suture lines[4]. Older antiemetics produced certain side effects like EPS, dystonia, dryness of mouth[5]. 5HT3 receptor antagonists ondansetron has been gold standard antiemetic because of its safety & efficacy[6]. Dexamethasone was first reported as an effective antiemetic in patients receiving cancer chemotherapy[7], subsequent studies shown its effectiveness in preventing PONV[5]. Timing of administration for an effective prophylaxis against PONV may be an important determinant of their antiemetic efficacy[5,8].

The purpose of the present study was to compare and evaluate the efficacy and safety of monotherapy against that of combination administered IV just before induction are effective in preventing PONV in patients undergoing GA for surgical procedures more prone to develop PONV.

MATERIALS AND METHODS

After approval from the Ethical Committee and taking written consent from the patients, the study was conducted at father muther medical college, mangalore, over a period of 1 year. This prospective study was conducted on 160 adult patients of the American Society of Anesthesiologists physical status Classes I and II, aged 20–60 years scheduled for surgery undergoing laproscopic cholecystectomy, abdominal hysterectomy, stapedectomy, thyroidectomy, Patients were systematically randomized into four groups, consisting forty patients in each group.

Group 1: placebo group – IV normal saline
Group 2: ondansetron group – IV ondansetron 4mg
Group 3: dexamethasone group – IV Dexamethasone 8mg
Group 4: combination group – IV ondansetron 4mg & Dexamethasone 8mg

Exclusion criteria

Patient refusal, patients with GERD, severe liver, renal, endocrine, neurological and cardiac diseases. Preoperative retching and vomiting within 24hours. Patients who have received anti emetic within 24hrs. Pregnant and lactating patients.

During preanaesthetic evaluation, demographic parameters such as age, sex, and weight were noted. History of motion sickness and PONV during previous surgeries was elucidated. Detailed airway, spine, cardiovascular and respiratory examination were done. Laboratory data: haemoglobin, routine urine examination, blood sugar, urea and creatinine, ECG, CXR were evaluated.

Written informed consent obtained. Patients received T.Diazepam 0.1mg/kg and T.Ranitidine 3mg/kg HS and fasted overnight. All the patients premedicated with inj pethidine 1mg/kg and inj atropine 0.01mg/kg IM two hours preoperatively.

In the operation theatre IV access secured, monitors like NIBP, pulse oxymetry and ECG monitoring were fixed. Coded study drugs loaded in 5ml syringes injected IV just before induction of anaesthesia. GA induced with Inj thiopentone 5mg/kg, Inj suxamethonium 2mg/kg used to facilitate endotracheal intubation. Anaesthesia maintained with 34% O2 & 66% N2O, Inj pancuronium 0.08mg/kg was administered as relaxant to facilitate IPPV with bain's circuit. To maintain adequate depth of anaesthesia throughout entire surgical procedure a) halothane 0.5%was used for first 15minutes post intubation & then switched off. B) Soon after switching off halothane, Inj fentanyl 2µgm/kg supplementation done. At the end of surgery patients reversed from neuromuscular block with Inj Neostigmine 0.05mg/kg and Inj Atropine 0.02mg/kg and extubated.

RESULTS

Table 1: OVERALL INCIDENCE OF POSTOPERATIVE NAUSEA AND VOMITING (PONV) – (Drug wise) of entire study of 160 patients

	Placebo (n=40)	Ondansetron (n=40)	Dexamethasone (n=40)	Dexamethasone And Ondansetron (n=40)
Total PONV	67%	35%	40%	12%
Nausea only	7.5%	5%	7.5%	2.5%

Early emesis (0-3 hours)	30%	2.5%	22.5%	5%
Late emesis (3-24 hours)	10%	25%	5%	2.5%
Both Early and late emesis	20%	2.5%	5%	2.5%

Table 2: COMPLETE RESPONSE – (No PONV for 24hrs)

	Placebo (n=40)	Dexamethasone (n=40)	Ondansetron (n=40)	Dexamethasone And Ondansetron (n=40)
Total incidence PONV	67%	40%	35%	12%
Complete response	33%	60%	65%	88%

Table 3: RESCUE ANTI-EMETIC

	Placebo	Ondensetron	Dexamethasone	Dexa+ondensetron	Total
Required	52.5%	10%	22.5%	2.5%	21.9%
Not required	47.5%	90%	77.5%	97.5%	78.1%

Table 4: SIDE EFFECTS

	Group				
	Placebo	Ondansetron	Dexamethasone	Dexamethasone And Ondansetron	Total
Giddiness Count %	2.5%	0%	0%	0%	0.6%
Headache Count %	12.5%	7.5%	10.0%	7.5%	9.4%
No side effects Count %	100%	100%	100%	100%	100%

DISCUSSION

PONV is a common sequelae of surgery under GA. Incidence of PONV has decreased of recent due to use of newer I.V and volatile anaesthetic agents, short acting opioids, potent antiemetics and minimal invasive surgical techniques. But PONV still occurs with an unacceptable frequency (30-70%). In day care procedures PONV causes prolonged hospital stay, expanded medical care and increased costeffectiveness. Ponv also increases post-op complications like, electrolyte imbalance, dehydration, aspiration pneumonia, tension on sutures, bleeding at operative site.

Etiology of PONV is probably multifactorial, various studies have been done to control PONV following one type of surgical procedures. Surgical procedures like lap cholecystectomy, stapedectomy, abdominal hysterectomy and thyroidectomyare more likely to predispose to PONV. So we conducted a prospective, randomized, placebo controlled, double blind study, which involves above mentioned surgical procedures under GA.

I.V Ondensetron4mg, a 5HT3 receptor antagonist has been shown to be effective in preventing PONV. Dexamethasone was used initially to treat the emesis induced due to chemotherapy and subsequently found to be effective in preventing PONV by various authors.

The timing of prophylactic antiemetic administration is very important. Ondensetron 4mg is more effective, if administered just before induction (peak onset of action 1-2hours). Probably coinciding with the time of extubation in our study.

Dexamethasone (peak onset of action 1-2hours) is more effective when administered just before induction than at the end of anaesthesia.

In our study 67% of patients in placebo group had PONV, which is comparable with the incidence of PONV in study by Biswas and Rudra[9]. There was a reduction in PONV incidence in ondensetron group (35%), dexamethasone group (40%) and 12% in combination group. Thus combination of ondensetron 4mg and Dexamethasone 8mg appear to be most effective compared to monotherapy to prevent PONV. (Table 1)

Complete response that is no PONV for next 24hrs in placebo, ondensetron 4mg, Dexamethasone 8mg and combination group were 33%, 65%, 60% and 88% respectively. All the observations are in accordance with the study by Biswas and Rudra[9]. Thus maximum complete response was seen in combination group (Table 2)

When emetic episode was >2 Inj Granisetron 40µgm/kg was used as a rescue antiemetic. Rescue antiemetic requirement in placebo, ondensetron and dexamethasone group were 52.5%, 10% and 22.5% respectively and all observations are comparable to study by Honkavara et al[10]. A significant reduction 2.5% was seen in combination group. (Table 3)

Incidence of side effects is statistically insignificant in all the study groups (Table 4) thus ondensetron, dexamethasoneand their combination are safe for PONV prophylaxis.

CONCLUSION

We conclude that combination of ondensetron 4mg with Dexamethasone 8mg given I.V just before induction of general anaesthesia is safe and more effective in preventing PONV than monotherapy with Ondensetron 4mg or Dexamethasone 8mg. Females and combined H/o motion sickness and PONV during previous surgeries are considered as reliable predictors of PONV.

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