Original Article

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Efficacy of Gabapentin versus Combination of Dexamethasone-Ondansetron in Prevention of Postoperative Nausea and Vomiting in Middle Ear Surgery: A Randomised Clinical Study

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ABSTRACT

Introduction: Postoperative Nausea and Vomiting (PONV) is the most common and unpleasant complication with incidence of 30-80% after elective surgery. Dexamethasone and Ondansetron (DO) combination has superior efficacy and is recommended as an ideal choice for prevention of PONV in Middle Ear Surgery (MES). Oral Gabapentin, an anticonvulsant has been introduced as an antiemetic to fast-track bundles and enhanced recovery after surgery.

Aim: To compare the efficacy of DO with gabapentin monotherapy in prevention of PONV in patients undergoing MES.

Materials and Methods: This randomised, double-blind, parallel group clinical study was done at Department of Anaesthesiology, St. John's Medical College, Bengaluru, Karnataka, India from November 2018 to March 2020. Sixty-six of patients were randomised to Group DO (Intravenous Dexamethasone at start and Ondansetron at end of surgery, 100 µg/kg each) and Group G (Oral Gabapentin 300 mg one hour prior to surgery). Postoperatively, incidence and severity of PONV, duration of antiemesis and analgesia, total rescue antiemetics and analgesics, along with side-effects were assessed for 24 hour period. Descriptive statistics was summarised for continuous (mean and standard deviation) and categorical (number with percentages) variables. Inferential statistics were depicted using Fisher's-exact and Student's t-test.

Results: The demographic profile was comparable between the two groups. Incidence of PONV was significantly lesser in Group DO compared to the Group G (12% versus 36%, p-value=0.0129). Duration of antiemesis was four hours in Group DO and two hours in Group G was statistically significant (p-value=0.021). Severity of PONV was significant (p-value=0.033 and 0.009, respectively) at four and six hours between the groups. Duration of analgesia (6.28±5.96 in Group DO versus 5.62±3.63 hours in Group G; p-value=0.252), rescue analgesics and side-effects were comparable between the two groups (p-value >0.05).

Conclusion: In MES, DO combination reduced the incidence and severity of PONV and is better prophylactic antiemetic therapy than gabapentin alone.

Keywords: Analgesia, Antiemetics, Therapy

INTRODUCTION

PONV occurring 24-48 hours after surgery leads to patient distress and dissatisfaction. Various anaesthetic, surgical and predisposing patient risk factors contribute to PONV with incidence of 50-80% in patients undergoing ear surgery without prophylactic antiemetics [1]. MES is a surgical risk factor and requires pharmacotherapy [2]. Apfel risk scoring system includes primary predictors as female gender, history of PONV or motion sickness, non smoking status and postoperative opioid use. Risk increases by 10, 20, 40, 60 or 80%, when 0, 1, 2, 3 and 4 factors are present, respectively [3]. Early PONV is stimulated by serotonin whereas late PONV is induced by dopamine and histamine. Ondansetron, a 5-Hydroxytryptamine 3-receptor antagonist (5-HT3-RA) at a dose of Intravenous (i.v.) 100-150 µg/kg, given at the end of surgery reduces early PONV. Dexamethasone (i.v. 100-150 µg/kg) given at induction benefits in late PONV. Proposed mechanisms of antiemesis by dexamethasone are activation of glucocorticoid receptors in solitary tract nucleus in medulla, interaction with serotonin, tachykinin, Neurokinin (NK) receptors in central nervous system [4]. Gabapentin mitigates tachykinin neurotransmitter activity, reduces calcium signalling in area postrema, reduce perioperative inflammation and opioid consumption. The safety and efficacy, minimal drug interactions, good oral bioavailability and renal elimination favour the clinical use of gabapentin [5,6].

Various studies have investigated the benefits of DO combination [7-10] and gabapentin individually [5,6,11-13]. However, there is paucity in literature exploring the benefits of this combination therapy with comparison to gabapentin monotherapy to prevent PONV in MES [14-16].

The primary objective of this study was to compare the effects of DO combination and gabapentin on the incidence and severity of PONV. The secondary objectives were to compare the duration of antiemetic activity, analgesic requirement and sedation score in the postoperative period.

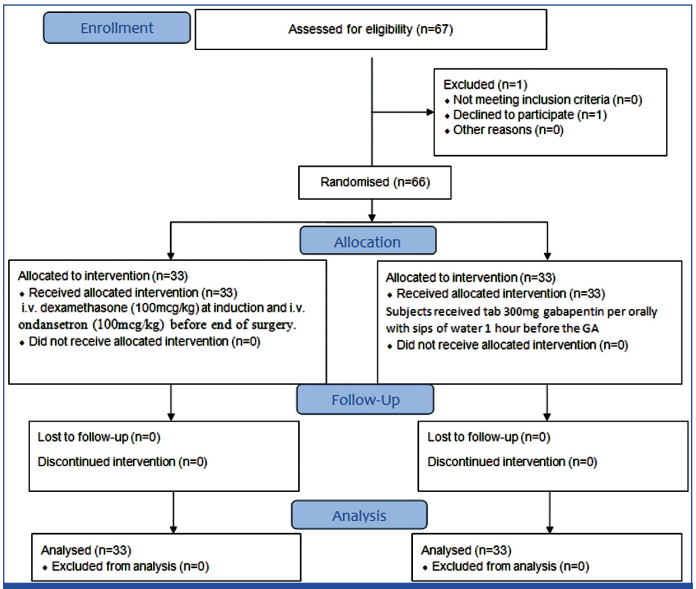
MATERIALS AND METHODS

This study was a randomised, double-blind, parallel group clinical trial conducted at St. John's Medical College and Hospital, Bengaluru, Karnataka, India from November 2018 to March 2020. Institutional Ethical Committee (IEC) clearance (IEC study Ref No.226/2018) and Clinical Trial Registry of India (CTRI/2018/11/016294) registration were obtained. Informed consent was taken from the recruited subjects.

Inclusion criteria: Age group of 18-59 years, either sex, American Society of Anaesthesiologists (ASA) I-II patients undergoing MES under General Anaesthesia (GA) and non smokers were included in the study.

Exclusion criteria: Pregnant and lactating mothers, patients with history of motion sickness, central nervous system disorders, complicated chronic suppurative otitis media and those who refused to participate in the study were excluded from the study.

Sample size estimation: The required sample size was derived based on a pilot study of 10 in each group which estimated the incidence of Group G as 70% compared to Group DO of 30% at two hours postoperatively [12]. With 80% power and 5% level of significance and considering 10% drop out, the sample size was estimated to be 33 patients in each group [Table/Fig-1].



[Table/Fig-1]: Consort flow diagram.

The subjects were then randomised via computer generated table and allocated by opaque sealed envelope method to one of the two groups- Group DO and Group G. Standard preoperative evaluation was done. All the subjects were informed about the score for PONV and Visual Analog Scale (VAS) for postoperative pain on the previous day. All patients were fasted for six hours and premedicated with Tab. Alprazolam 0.5 mg and Tab. Pantoprazole 40 mg on the night prior to surgery and on the morning of surgery respectively. Group DO– Subjects received i.v. Dexamethasone-0.1 mg/kg [17] at induction and i.v. Ondansetron-0.1 mg/kg [18] before end of surgery. Group G- Subjects received Tab Gabapentin 300 mg [14] per orally with sips of water one hour before the induction of anaesthesia in preoperative room. Drugs were prepared by the primary investigator. The participants and the anaesthesiologist assessing the outcome variables were blinded in this study.

Intraoperatively standard monitoring used were electrocardiography, non invasive blood pressure, pulse oximetry and capnography. A venous access (20G) was secured and i.v. fluid started and 0.2 mg of glycopyrrolate and 1 mg of midazolam were given as preinduction drugs. Standard anaesthetic technique was performed in these subjects. Patients were induced after adequate preoxygenation with 100% O_2 with i.v. fentanyl 2 µg/kg and i.v. propofol 1.5 to 2 mg/kg followed by neuromuscular blocking agent i.v. atracurium 0.5 mg/kg. At three min, airway was secured with appropriate sized endotracheal tube. Anaesthesia was maintained with O_2: Air (50:50), inhalational agent (isoflurane 0.8-1% titrated to keep minimum alveolar concentration values between 1.0 to 1.2) and i.v. atracurium 0.1 mg/kg at regular intervals. An i.v. Fentanyl 20 µg/hr was given for analgesia. Postsurgery the neuromuscular blockade was reversed with i.v. neostigmine 0.5 mg/kg and i.v. glycopyrrolate 0.01 mg/kg. Patients were extubated and shifted to the recovery room.

The parameters monitored and recorded were the incidence (Early PONV at 0 min, 15 mins, 30 mins, 1 hr, 2 hrs and late PONV at 4 hrs, 6 hrs, 12 hrs, 18 hrs and 24 hrs) and severity of PONV (DO0 DO1,DO2,DO3,G0,G1,G2,G3: Grade 0=no nausea and vomiting, Grade 1=mild nausea not requiring treatment, Grade 2=moderate nausea, mild vomiting and requiring treatment, Grade 3=severe vomiting) in the postoperative period [11]. The duration of antiemetic effect was calculated from the immediate postoperative period to the first time of occurrence of PONV. Total number of rescue antiemetic doses given in 24-hour period was also recorded. Postoperative pain scores were assessed with VAS at 0 min, 15 mins, 30 mins, 1 hr, 2 hrs, 4 hrs, 6 hrs, 12 hr, 18 hrs and 24 hrs. Any side-effects such as headache, light headedness, dry mouth, dizziness, and somnolence were noted. The incidence of postoperative sedation (Ramsay sedation scale) was recorded [19].

Intramuscular Prochlorperazine 5 mg was administered as the rescue antiemetic when PONV ≥2 and i.v. Paracetamol 1gm was administered as the rescue analgesic when VAS ≥3. The i.v. Tramadol 1 mg/kg was the rescue analgesic to be administered if VAS ≥6. The data collected was compiled in an excel sheet and tabulated.

STATISTICAL ANALYSIS

Statistical analysis was performed using R statistical software version 4.2.1 (R CORE TEAM, 2022, Vienna Austria [20]. Descriptive statistics was summarised for continuous (mean and standard deviation) and categorical (number with percentages) variables. Student's t-test was used to compare the quantitative data between the two groups. The incidence and severity of PONV between groups were analysed by Fisher's-exact test. The p-value <0.05 was considered statistically significant.

RESULTS

The demographic profile including age and sex, ASA grading and duration of surgery were comparable between the two groups [Table/Fig-2]. Incidence of PONV was 12% in the Group DO compared to 36% in the Group G which showed statistical significance (p-value=0.0129). Duration of antiemesis was four hours in Group DO and 2 hours in Group G which was statistically significant (p-value=0.021) as shown in [Table/Fig-3]. Only two patients from Group DO had moderate PONV (Grade-2) compared to 12 patients in Group G and 3 patients from Group G had severe PONV (Grade-3) during the 24 hour period [Table/Fig-4]. No patient from the Group DO had severe nausea or vomiting. Severity of PONV was significant (p-value=0.033 and 0.009, respectively) at four and six hours between the groups [Table/Fig-5].

Parameters		Group DO (n=33)	Group G (n=33)	p-value
Age (years)#		38.45±12.87	35.94±11.29	0.402
Sex (M/F)	F	18 (54.5%)	18 (54.5%)	1.0
	M	15 (45.5%)	15 (45.5%)	
ASA grade$	I	19 (576%)	24 (72.7%)	0.301
	II	14 (42.4%)	9 (27.3%)	
Duration of surgery (min)#		177.36±54.41	188.64±51.56	0.391

[Table/Fig-2]: Demographics.
#Student t-test; $Fisher's-exact; p <0.05*- statistically significant

Parameter- PONV	Group DO	Group G	p-value
Incidence of PONV$	12%	36%	0.0129*
Time of rescue antiemetic (hours)	4.00±1.15	2.06±2.11	0.021*
Total number of rescue antiemetics over 24 hours	1.5±0.58	1.5±0.67	0.501

[Table/Fig-3]: Incidence of PONV, number of doses and time of rescue doses.
$Fisher's-exact test; Student t-test; p<0.05*- statistically significant

Twenty-five patients in Group DO and 29 in Group G had VAS scores of 2-3 and required treatment for the mild pain with i.v. 1 gm Paracetamol [Table/Fig-6]. None of the patients had VAS scores >6

Time	Grade of PONV	Group DO n (%)	Group G n (%)	p-value
0 min	1	1 (3.0)	3 (9.1)	0.292
15 mins	1	0	3 (9.1)	0.052
	2	0	1 (3.0)	
30 mins	1	4 (12.1)	4 (12.1)	0.135
	2	0	2 (6.1)	
	3	0	1 (3.0)	
1 hour	1	11 (33.3)	7 (21.2)	0.136
	2	0	6 (18.2)	
2 hours	1	10 (30.3)	6 (18.2)	0.662
	2	0	3 (9.1)	
4 hours	1	10 (30.3)	9 (27.3)	0.033*
	2	0	4 (12.1)	
	3	0	2 (6.1)	
6 hours	1	2 (6.1)	7 (21.2)	0.009*
	2	2 (6.1)	4 (12.1)	
	3	0	3 (9.1)	
12 hours	1	2 (6.1)	1 (3.0)	0.353
	2	0	2 (6.1)	
24 hours	1	2 (6.1)	1 (3.0)	0.555

[Table/Fig-4]: Incidence of PONV at specific time intervals.
Fisher's-exact test, p<0.05*-significant

DISCUSSION

The PONV is an unpleasant symptom for patients after surgery and general anaesthesia. MES stimulates the vestibular labyrinth resulting in PONV which lasts for upto 24 hours in the postoperative period. Due to the increased incidence of PONV after MES, prophylactic antiemetics are definitely warranted [7,21].

The aetiology of PONV in GA is multifactorial. The anaesthesiologist should use an anaesthetic agent that would result in a minimal intratympanic pressure [22]. The anaesthetic management was standardised as per institutional protocol with midazolam and propofol induction, intraoperative use of fentanyl 2 µg/kg at induction and supplement bolus by 20 µg per hour, use of air- isoflurane mixture and judicious dose of neostigmine to antagonise atracurium [23]. The demographic profile and the duration of surgery were comparable between the two groups in this study. Therefore, the difference in the incidence of PONV is attributed to the study drugs alone.

Perioperative pharmacological methods for PONV include Corticosteroids, 5-HT3-RA, NK-1 receptor antagonists, butyrophenones, metoclopramide, phenothiazine, prochlorperazine, antihistamines and anticholinergics [3]. Amongst the available antiemetics, highest effectiveness to prevent PONV was seen for the NK1 receptor antagonist aprepitant (relative risk, RR 0.26), followed by ramosetron (RR 0.44), granisetron (RR 0.45), dexamethasone (RR 0.51) and ondansetron (RR 0.55). The combinations of different antiemetics were more effective than single prophylaxis [3,24,25]. In

Time	Grades of PONV							
	DO0	DO1	DO2	G0	G1	G2	G3	p-value
0 min	97%	3%	0	90.90%	9.10%	0	0	0.306
15 mins	100%	0	0	87.90%	9.10%	3%	0	0.054
30 mins	87.90%	12.10%	0	78.80%	12.10%	6.10%	3%	0.135
1 hour	66.70%	33.30%	0	60.60%	21.20%	18.1%	0	0.136
2 hours	69.70%	30.30%	0	72.70%	18.20%	9.10%	0	0.662
4 hours	69.70%	30.30%	0	54.50%	27.30%	12.10%	6.10%	0.033*
6 hours	87.90%	6.10%	6.10%	57.60%	21.20%	12.10%	9%	0.009*
12 hours	93.90%	6.10%	0	90.10%	3%	6.10%	0	0.353
18 hours	93.90%	0	6.10%	93.90%	3%	3%	0	0.777
24 hours	93.90%	116.10%	0	97%	3%	0	0	0.558

[Table/Fig-5]: Severity of PONV.
Fisher's-exact test, p<0.05*- significant

Time	Group DO (n=33)	Group G (n=33)	p-value
0	1.42±1.41	0.91±1.26	0.123
15 mins	1.52±1.46	1.18±1.29	0.329
30 mins	1.70±1.38	1.36±1.34	0.324
1 hour	1.822±1.26	1.55±1.62	0.449
2 hours	2.21±1.58	1.91±1.63	0.445
4 hours	2.55±1.94	2.45±1.72	0.841
6 hours	2.45±1.62	2.55±1.72	0.826
12 hours	2.24±1.50	2.33±1.34	0.796
18 hours	2.03±1.61	2.15±1.44	0.748
24 hours	1.79±1.36	1.73±1.36	0.86

[Table/Fig-6]: VAS score.
Student t-test; p<0.05*- significant

and hence did not require i.v. tramadol during the postoperative period. Duration of analgesia (6.28±5.96 in Group DO versus 5.62±3.63 hours in Group G; p=0.252) and rescue analgesics were comparable between the two groups [Table/Fig-7]. Sedation score was also comparable (p>0.05) [Table/Fig-8] and no other side-effects were noted in the two groups.

Parameter-Analgesia	Group DO	Group G	p-value
Time of rescue analgesic (hours)	6.28±5.96	5.62±3.63	0.252
Total no of rescue analgesic (over 24 h)	1.96±0.79	2.03±0.78	0.366

[Table/Fig-7]: Postoperative rescue analgesic.
Student t-test; p<0.05 *- significant

Time	Group DO (n=33)	Group G (n=33)	p-value
0 min	2.82±0.85	2.79±1.24	0.908
15 mins	2.30±0.68	2.48±0.97	0.383
30 mins	2.18±0.39	2.45±0.71	0.059
1 hour	2.12±0.33	2.2±0.65	0.478
2 hours	2.12±0.33	2.21±0.7	0.502
4 hours	2.09±0.46	2.12±0.65	0.828
6 hours	2.03±0.39	2.09±0.63	0.642
12 hours	2.06±0.35	2.18±0.46	0.235
18 hours	2.03±0.39	2.15±0.36	0.199
24 hours	2.00±0.50	2.15±0.36	0.165

[Table/Fig-8]: Sedation score.
Student t-test, p<0.05*-significant

this randomised, double-blind, clinical trial of prophylactic antiemetic therapy in MES, Dexamethasone combined with Ondansetron reduced the incidence and severity of PONV compared with gabapentin alone.

The current study showed that combination of DO was superior to gabapentin monotherapy in reducing the overall incidence of PONV (12% vs 36%, p-value=0.0129) with significant duration of antiemetic effects (time of first rescue antiemetic: four hours in Group DO and two hours in Group G; p-value=0.021) [Table/Fig-3]. Significant studies which have compared dexamethasone ondansetron combination and gabapentin individually with other drugs have been described in [Table/Fig-9] [7-9,12-13].

Study	Population (n)	Intervention	Outcome
Present study India, 2023	Middle ear (66)	1) i.v. dexamethasone (0.1 mg/kg)+ i.v. ondansetron (0.1 mg/kg) 2) Po gabapentin (300 mg)	Incidence of PONV was significantly lesser in Group DO compared to the Group G (12% versus 36%, p-value=0.0129). Duration of antiemesis: 4 hours in Group DO and 2 hours in Group G was statistically significant (p-value=0.021) Severity of PONV was significant (p-value=0.033 and 0.009, respectively) at 4 and 6 hours between the groups. Duration of analgesia, rescue analgesics and side-effects were comparable between the two groups (p-value >0.05)
Srivastava VK et al., [7] India, 2020	Middle Ear Surgery (MES) (64)	1) i.v. Palonosetron 0.075 mg-dexamethasone 8 mg (P) 2) i.v. Ondansetron 8 mg -dexamethasone 8 mg (O)	Incidence of Postoperative Nausea and Vomiting (PONV) (0-24 hours postoperatively) was 37.5% in group O and 9.4% in group P (p-value=0.016) Frequency of rescue medication was more common in group O than in group P patients (p-value=0.026)
Shivakumar KP et al., [8] India, 2019	Middle Ear Surgery (MES) (74)	1) i.v. ondansetron 4 mg and dexamethasone 8 mg (OD) 2) i.v. ramosetron 0.3 mg and dexamethasone 8 mg (RD)	Incidence of vomiting (p-0.027) and the requirement of rescue antiemetic (p-value-0.003) was significantly less in RD compared to OD
Gowtham Raj K et al., [9] India, 2021	Middle Ear Surgery (MES) (60)	1) i.v. ondansetron 4 mg with dexamethasone 8 mg (OD) 2) Iv ramosetron 0.3 mg (R)	OD group showed 83% complete response which was higher than 57% of R group. Requirement of rescue antiemetic was less in OD group compared to R group (17% vs. 43%) Adverse effects- comparable
Mehta M et al., [13] India, 2021	Middle Ear Surgery (MES) (64)	1) i.v. granisetron 3 mg 2) Oral gabapentin 300 mg	No statistically significant difference in prevention of PONV No side-effects
Heidari M et al., [12] Iran, 2015	Middle Ear Surgery (MES) (90)	1) Granisetron 3 mg i.v. 2) Gabepentin PO 300 mg 3) Placebo	Incidence and severity of nausea and vomiting at different time intervals in Group I and Group II was significantly lower compared with Group III (p-value <0.05). Side-effects- no significant difference

[Table/Fig-9]: Studies which utilised dexamethasone-ondansetron and gabpentin for PONV [7-9,12,13].

The current study proves that the incidence of PONV was significantly less in group DO compared to Group G Prashanth Gowtham Raj SK et al., also proved that combination of DO was superior to ramosetron [9]. This was in contrast to studies done by Srivastava VK et al., and Shivakumar KP et al., as they proved that dexamethasone ondansetron combination is inferior to dexamathesone – palonoseteron and dexamethasone-ramosetron [7,8]. Dexamethasone improves the efficacy of other antiemetics by sensitising the pharmacologic receptors [9] and has an additive effect when combined with 5-HT3-RA [3,8]. Other mechanisms include prostaglandin antagonism, release of endorphins and bradykinin reduction [7]. Liu HM et al., performed a meta-analysis and proved that dexamethasone plus 5-HT3-RA with 5-HT3-RA alone in ear surgery showed pooled Risk Ratio (RR) of early and overall PONV of 0.79 and 0.46, respectively thus favouring the combination group in overall period (0-48 hrs) [2]. Hamza MA et al., showed that prophylactic administration of Dexamethasone 8 mg i.v. was more effective in preventing PONV than gabapentin (300 mg) in women undergoing abdominal surgeries [14]. Grant MC et al., and Heidari M et al., showed that incidence of PONV was significantly less in gabapentin group when compared to placebo [6,12]. In MES, Heidari M et al., and Mehta M et al., gabapentin (oral 300 mg one hour before anaesthesia) was compared with granisetron (3 mg i.v. given two minutes before induction of anaesthesia), a long acting and selective 5-HT3-RA showed no significant difference on the incidence of nausea and vomiting [12,13]. Dubey P et al., proved that single 300 mg dose of gabapentin reduced the incidence of PONV in maxillofacial surgeries over the first 24 hours when compared to ondansetron one hour prior to surgery [15]. Semira et al., showed that incidence of PONV was reduced with gabapentin (600 mg) and as effective as ondansetron (4 mg) or dexamethasone (8 mg) in laparoscopic cholecystectomy [16]. The present study utilised 300 mg gabapentin, however DO combination therapy was proved to be superior.

The need for rescue antiemetics in the present study was earlier in group G than group DO which was statistically significant. Prashanth Gowtham Raj SK et al., also found similar results with DO group [9]. Contrary to the current study, the requirement of rescue antiemetics was significantly more in group DO in studies done by Srivastava VK et al., and Shivakumar KP et al., [7,8]. Heidari M et al., showed that the time for first antiemetic was comparable between gabapentin and granisetron groups but longer when compared to placebo group (p-value <0.05) [12]. Though there was significant difference in the antiemetic effects extended by the two groups in present study (p-value=0.021), the total rescue antiemetic doses were comparable (p-value=0.501) similar to Semira et al., [16].

After a single oral dose of 300 mg of gabapentin, mean maximum plasma concentration was attained in 2-3 hours and has bio-availability of 60%. It does not bind with plasma proteins and the elimination half-life is 5-7 hours [15]. This explains the severity of PONV seen in group G in present study at four and six hours (p-value=0.033 and p-value=0.009). Varied doses (gabapentin 300-1200 mg) given 1-2 hours prior to surgical incision and in various surgeries (laparoscopic, spine, abdominal) showed reduction severity of PONV [6]. Though the severity is varied in above studies, the rescue antiemetic acting with different mechanisms facilitate in the treatment of PONV.

Established timing for DO combination showed dexamethasone (4-8 mg) at induction and ondansetron (4 mg) at end of surgery when given as i.v. bolus is an effective treatment for PONV in MES postoperatively [2,3,24]. However, there is paucity in literature on the appropriate dose, timing and the frequency interval required for gabapentin and hence further studies are required to provide adequate evidence.

In the present study, low doses of dexamethasone (0.1 mg/kg) and gabapentin 300 mg were used and the results were comparable for duration of analgesia and rescue analgesic requirement (p-value >0.5)

[Table/Fig-7]. Both dexamethasone and gabapentin are alternative non opioid analgesic in the multimodal approach of postoperative pain management. They also reduce intraoperative and postoperative opioid use. Gan TJ et al., similarly proved a reduction in need for analgesics with dexamethasone when added to 5-HT3-RA [3]. Waldron NH et al., conducted a meta-analysis and proved that a single dose of i.v. dexamethasone has beneficial effect on postoperative pain by modulating the systemic physiological responses and anti-inflammatory mediators [26]. Postoperative analgesic effects of gabapentin is mediated via alpha 2/delta subunit of voltage sensitive calcium channels, inhibiting the voltage activated sodium channels downstream and finally the nociceptive signal pathways [6]. Optimal pre-emptive dose of gabapentin for postoperative pain relief is 600 mg [27]. Unlike upward dosing trend in efficacy of chronic pain management of gabapentin, there is a ceiling effect beyond 600 mg in acute pain. This is attributed to the saturated transport system and dose dependent absorption [28]. Kim KM et al., found no significant difference in pain scores and requirement of rescue analgesics between gabapentin, ramoseteron and gabapentin-ramosetron groups [29]. Further studies should focus on dosing of gabapentin and postoperative analgesia as the primary end point.

Various adverse events reported in existing literature with DO combination were headache and dizziness and with gabapentin are excessive sedation, dizziness, somnolence, light-headedness, headache and dry mouth [2,6]. Preoperative gabapentin is also associated with significant increased rates of postoperative sedation (RR=1.22; 95% CI, 1.02-1.47; p-value=0.03) compared with control [6]. The current study did not show any significant increase in sedation in gabapentin group [Table/Fig-8] which was similar to the results of Grant MC et al., with gabapentin dosing of 300 mg (RR=2.91; 95% CI, 0.19-43.70; p=0.44; P for heterogeneity=0.005; I2=87%) [6]. Kim KM et al., similarly found no significant difference in sedation scores with or without gabapentin [29]. Sedation effect of gabapentin is related to its central nervous system effects and are dose dependent with more impact on dose >1200 mg which can prolong postanaesthesia care unit stay [6]. A combination of prophylactic antiemetics with multimodal action is the mainstay of treatment of PONV resulting in fewer side-effects of each drug [10].

Limitation(s)

The limitation in the present study was the use of single and low dose of the gabapentin compared to the already established DO combination in MES. Another limitation being the involvement of female genders and non smokers in both groups. Unavoidable factors were different surgeons and their experience on complexity of surgery. Further studies are warranted on multicentre basis with dose response (optimal dose and dose intervals) of gabapentin to establish the efficacy and safety for its antiemetic and analgesic effects.

CONCLUSION(S)

The present study showed that dexamethasone-ondansetron combination reduced the incidence and severity of PONV in MES and is a better prophylactic antiemetic therapy than gabapentin alone. The combination therapy proved to be definitely more efficacious in prevention of both early and late PONV and hence can be recommended for prophylaxis of PONV in MES.

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