#### DEXAMETHASONE PROPHYLAXIS ON INCIDENCES OF POST-OPERATIVE NAUSEA AND VOMITING (PONV) IN PATIENTS UNDERGOING GYNECOLOGICAL SURGERIES UNDER SPINAL ANESTHESIA

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**ABSTRACT: BACK GROUND:** Nausea and vomiting are the most common distressing symptom in the post-operative period. It can result in delayed hospital discharge and increased hospital cost. The present study was done to assess the effect of dexamethasone prophylaxis on the incidences of nausea and vomiting in post-operative period in patients undergoing gynecological surgeries. **MATERIAL AND METHODS:** A total number of 66 patients, aged between 20 to 65 years, posted for elective gynecological surgeries under spinal anesthesia were included in the study. Patients were randomized into two groups of 33 patients each, and the study group (group-D) received Inj. Dexamethasone 8 mg intravenously as prophylactic antiemetic 1 hour before surgery whereas control group (group-N) received normal saline. Post-operatively, the frequency of nausea and vomiting were observed and its influences on postoperative analgesia were also noted. RESULTS: In our study, 4(12.1%) patients in group-D and 8(24.2%) patients in group-N had nausea and vomiting in the intraoperative period (p value=0.202). 24.2% patients in group-D had vomiting in the postoperative period as compared to 72.7% in group-N and group D patients had significant reduction in incidences of nausea and vomiting in immediate post-operative period compared to group N (p-value 0.016). Accordingly, the mean requirement of rescue antiemetic was less in group-D compared to Group-N. Further, patients in group-D had better VAS scores compared to patients in group-N in post-operative period. **CONCLUSION:** Use of Dexamethasone prior to subarachnoid block in patients undergoing gynecological surgeries reduces the incidence of nausea and vomiting and the requirement of antiemetic in the postoperative period, and better post-operative analgesia.

**KEYWORDS:** Dexamethasone, Subarachnoid Block, Post-operative Nausea and Vomiting, Gynecological surgeries.

**INTRODUCTION:** Post-operative nausea and vomiting (PONV) is a common, troublesome and potentially hazardous complication of anaesthesia and surgery, with an estimated incidence as high as 70-80% in high risk patients.<sup>1,2</sup> Pain is not always the patients prime concern in the post-operative period, many patients will place or have nausea and vomiting as the most unpleasant consequence. There are a number of factors influencing the occurrence of PONV which may be briefly summarized as: patient factors, pre-operative factors, intra-operative factors (anesthetic and surgical factors) and post-operative factors. The advantages of prophylactic drug therapy are early ambulation and decreased morbidity.<sup>1</sup>

Nausea and vomiting during regional anesthesia for abdominal and gynecological surgeries still remains a significant problem not only for the patient, but also for the anesthesiologist and the surgeon as well. The etiology of intraoperative nausea and vomiting is complex; it may be attributed

to surgical stimulation, hypotension, vagal stimulation and certain drugs used during intraoperative period. Though reported incidence of PONV with regional anesthesia is lower compared to general anesthesia, its deleterious effects to the individual patient is not different.<sup>2</sup>

Gynecological surgeries are identified as one of the major risk factor for PONV.<sup>3</sup> When severe, nausea or vomiting may be associated with wound dehiscence, bleeding, electrolyte imbalance, dehydration and pulmonary aspiration of gastric contents in post-operative period, resulting in prolonged hospital stay and increased health care cost.<sup>4</sup> Therefore, the prevention and treatment of PONV always remained an important responsibility of anesthesia care provider.

Various prophylactic antiemetic drugs have been used for the prevention and control of PONV. Dexamethasone is effective in reducing the incidence of post-operative nausea and vomiting (PONV) in patients undergoing adeno-tonsillectomy, thyroidectomy, cholecystectomy, and abdominal hysterectomy, <sup>4</sup> with limited side effects during postoperative period. Further, it has been reported to have an additional advantage of reducing fatigue, pain and total analgesic requirement in post-operative period.<sup>5, 6</sup>

Though, many literatures are available on the use of dexamethasone as prophylactic antiemetic in major gynecological surgeries under general anesthesia, its use under spinal anesthesia is limited. Therefore, the present study was done primarily to find out the effects of dexamethasone prophylaxis on incidences of nausea and vomiting in patients undergoing gynecological surgeries under subarachnoid block.

**METHODS:** After institutional approval and written informed consent from all 66 female patients, aged between 20 to 65 years, belonging to American Society of Anesthesiologists Physical Status 1 and 2, undergoing gynecological surgeries under subarachnoid block (SAB) were included in our study.

Patients with gastrointestinal disease, previous history of PONV, history of motion sickness, those who had received opioids, antiemetic drugs, steroids or NSAIDS or who had hypersensitivity to any of the drugs used in the study period, were excluded from this study. All patients' age, weight, height, and body mass index (BMI) were noted. Patients were kept nil per orally for overnight before anesthesia and were premedicated with tablet Alprazolam 0.5 mg orally, the night before and 2 hours prior to surgery. Patients were randomly allocated to receive 2 ml of either 8 mg dexamethasone (Group- D) or normal saline (Group- N) intravenously, 1 hour before SAB.

On arrival in the operation theatre, continuous ECG, non-invasive blood pressure, and pulseoximeter were attached, and baseline values of heart rate, blood pressure, and SpO<sub>2</sub> were recorded.

All patients were preloaded with Ringers lactate (10 ml/kg). Heart rate with continuous electrocardiogram, non-invasive blood pressure, pulse oximetry (SpO<sub>2</sub>) were monitored throughout the surgery. All patients received oxygen at the rate of 3-5 L/min using nasal prongs/face mask. Under all aseptic precautions, SAB was performed in lateral position (left/right) using 25 G Quincke's spinal needle, at  $L_2$ - $L_3$  or  $L_3$ - $L_4$  interspace with 3.0 ml of 0.5 % hyperbaric bupivacaine injected intrathecally. The level of sensory blockade after 10 minutes of performing SAB was noted using sterile pin prick method and the surgery was allowed to start only when a sensory level of T-8 was achieved.

In the intra operative period, hypotension (Systolic BP <30% of the baseline value or Systolic BP <90mm of Hg) was treated with intravenous fluids and boluses of inj. Mephentermine 3 mg,

bradycardia (Heart Rate <60/minute with hypotension or <50/minute without hypotension) was treated with inj. Atropine 0.6 mg intravenously and any occurrences of nausea and vomiting (as defined and graded below) was treated with inj. Ondansetron 4 mg, intravenously as a rescue antiemetic and was recorded.

Nausea was defined as a subjectively unpleasant sensation associated with an urge to vomit. Retching was defined as spasmodic, rhythmic contraction of respiratory muscle without expulsion of gastric contents. Vomiting was defined as forceful expulsion of gastric contents in our study. PONV was graded<sup>7</sup> as follows:

- 0- no nausea and no vomiting,
- 1- nausea/retching without vomiting,
- 2- nausea with vomiting < 3 episodes,
- 3- Nausea with vomiting > 3 episodes.

Post-operatively, incidence of PONV was documented at various intervals. Immediately after shifting the patient to recovery room we considered it as 'zero hour', and at 1, 2, 4, 8 and 24 hours from the 'zero hour' post operatively, and any episode of nausea and vomiting of grade 2 and 3 were treated with inj. Ondansetron 4mg intravenously and recorded.

After the surgical procedure, when the level of sensory block receded to T-10 level or patient complained of pain, intramuscular inj. Diclofenac sodium 75 mg was given and was repeated 8 hourly after first injection up to 24 hours. Postoperative pain was assessed using 10 cm visual analogue scale<sup>8</sup> (VAS, 0=no pain, 10=worst pain imaginable) in accordance with intervals of PONV documentation up to 24 hrs.

Statistical analysis was performed using SPSS (version11.5) software. Pearson Chi-square test and Fisher's exact test were performed to compare qualitative variables. Independent sample t-test (unpaired t-test) and Mann-Whitney U test were performed for comparing quantitative variables. A p-value of less than 0.05 was considered to be statistically significant.

**RESULTS:** This study on 66 female patients undergoing gynecological surgeries showed no statistical significance between the two groups on patient characteristics like age, height and weight including mean baseline values of hemodynamic parameters. Duration of surgery was not statically significant between the two study groups.

Characteristics	Study Group	<b>Control Group</b>	t-value	p-value		
Age (in years)	44.61±9.19	42.21±9.296	1.052	0.297		
Weight (in kg)	56.15±5.386	56±4.841	0.12	0.905		
Height (in cms)	151.24±2.646	152.12±2.52	1.38	0.172		
BMI	24.59±2.649	24.20±2.378	0.636	0.527		
Duration of surgery (in minutes)	96.88±18.735	95.85±11.851	0.267	0.792		
Baseline HR	79.12±4.973	78±5.579	0.862	0.392		
Baseline MAP	91.76±2.670	91.33±3.397	0.564	0.575		
Table 1: Demography and hemodynamic parameters						

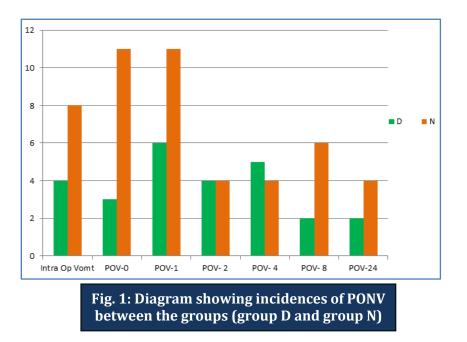
Intra-operatively, the dexamethasone group had only nausea in 4(12.1%) patients compared to saline group who had nausea in 5(15.2%) and vomiting in 3(9.1%) patients and was not significant. Immediately after surgery in the recovery room 11(33.3%) patients in the saline group had experienced nausea and vomiting which was statistically significant (p-value 0.016) compared to 3(9.1%) patients in dexamethasone group in our study. At other intervals observed, the incidence of nausea or vomiting between groups were not statistically significant but incidences of grade 2 and grade 3 PONV were clinically significant between the groups at 1<sup>st</sup> hour (6.1% in group D versus 27.3% in group N), and at 4<sup>th</sup> hour (0% in group D versus 9.1% in group N). Incidences of PONV between the groups were not significant both clinically and statistically at 8<sup>th</sup> hour and 24<sup>th</sup> hour intervals.

The VAS scores at intervals 'zero' hour and  $1^{st}$  hour post-operatively between the two groups were statistically highly significant with p-value <0.001 and was significant at  $8^{th}$  hour and  $24^{th}$  hour intervals (p-value= 0.001 in both intervals). Statistically there is no difference in VAS scores between the two groups at  $2^{nd}$  and  $4^{th}$  hour intervals.

Nausea & Vomiting	Group D		Group N		p-value	
Nausea & vointing	Present	Absent	Present	Absent		
Intra-Op	4(12.1%)	29(87.9%)	8(24.2%)	25(75.8%)	0.202	
POV-0	3(9.1%)	30(90.9%)	11(33.3%)	22(66.7%)	0.016	
POV-1	6(18.2%)	27(81.8%)	11(33.3%)	22(66.7%)	0.159	
POV- 2	4(12.1%)	29(87.9%)	4(12.1%)	29(87.9%)	1.000	
POV- 4	5(15.2%)	28(84.8%)	4(12.1%)	29(87.9%)	0.500	
POV-8	2(6.1%)	31(93.9%)	6(18.2%)	27(81.8%)	0.258	
POV-24	2(6.1%)	31(93.9%)	4(12.1%)	29(87.9%)	0.672	
Table 2: Comparison of incidences of nausea and vomiting between the two groups						

Nausea and	Group D				Group N			
Vomiting grades	0	1	2	3	0	1	2	3
Intra-Op Vomiting	29(87.9%)	4(12.1%)	0(0.0%)	0(0.0%)	25(75.8%)	5(15.2%)	2(6.1%)	1(3%)
PONV-0	30(90.9%)	2(6.1%)	1(3%)	0(0.0%)	22(66.7%)	3(9.1%)	4(12.1%)	4(12.1%)
PONV-1	27(81.8%)	4(12.1%)	2(6.1%)	0(0.0%)	22(66.7%)	2(6.1%)	6(18.2%)	3(9.1%)
PONV- 2	29(87.9%)	1(3%)	3(9.1%)	0(0.0%)	29(87.9%)	0(0.0%)	3(9.1%)	1(3%)
PONV- 4	28(84.8%)	5(15.2%)	0(0.0%)	-	29(87.9%)	1(3%)	3(9.1%)	-
PONV- 8	31(93.9%)	0(0.0%)	2(6.1%)	-	27(81.8%)	4(12.1%)	2(6.1%)	-
PONV-24	31(93.9%)	2(6.1%)	0(0.0%)	-	29(87.9%)	3(9.1%)	1(3%)	-
Table 3: Comparison of Grades of Nausea and Vomiting between the two groups								

VAS at different intervals	Group	Median	p-value		
VAS-0	D	1	n<0.001		
VA3-0	Ν	3	p<0.001		
VAS-1	D	1	p<0.001		
VA3-1	Ν	2	p<0.001		
VAS-2	D	2	0.27		
	Ν	2	0.27		
VAS-4	D	2	0.36		
VA3-4	Ν	2	0.30		
VAS-8	D	2	0.001		
VA3-0	Ν	3			
VAS-24	D	2	0.001		
v A3-24	Ν	3	0.001		
Table 4: Comparison of VAS Score between the groups					



**DISCUSSION:** Dexamethasone is a synthetic steroid known for its anti-inflammatory properties has been shown to be an effective antiemetic in patients receiving cancer chemotherapy.<sup>9-11</sup> Though, few investigations have failed to demonstrate post-operative antiemetic and analgesic affects, several studies have shown that dexamethasone effectively decreases the incidence of PONV, and better postoperative analgesia. The exact mechanism of dexamethasone induced antiemetic and analgesic effects still remains to be fully understood. However, it has been postulated to be related to inhibition in the synthesis of prostaglandins, associated with triggering of emesis and inflammatory response.<sup>13</sup> Antagonism of 5HT-receptors in the central nervous system is another possible mechanism of antiemetic effects of dexamethasone.<sup>8, 9</sup>

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The onset of dexamethasone antiemetic action is thought to be 1–2 hour allowing time to diffuse across the cell membrane and alter gene transcription.<sup>14</sup> Administration of steroids 60 min or more before surgical trauma may be important in minimizing pain and inflammation. Similarly, dexamethasone is a more effective antiemetic when given before induction of anesthesia than at the end of surgery.<sup>15, 16</sup>

With the prophylactic use of dexamethasone, we observed a reduction of PONV incidences by 48.5% in dexamethasone group compared to control group which is similar to the findings of studies by Khatiwada S et al<sup>17</sup> and Tjeng et al<sup>18</sup> who showed 28% and 32% reduction in incidence of PONV respectively. As female patients and gynaecological surgeries itself are high risk factors for increased incidence of PONV, the higher reductions in incidences of PONV was expected in our study with the prophylactic use of dexamethasone compared to saline group.

This also reflected in the reduction in doses of rescue antiemetic in the postoperative period in the dexamethasone group similar to previous studies. The major reduction of incidence of PONV in our study occurred in early post-operative period than later half of the study period. In our study, incidences of PONV were not significant between the two groups in later half of the study, but the number of patients with severe vomiting was more in control group compared to dexamethasone group.

The meta-analysis by De Oliveira et al<sup>19</sup> and studies by Thomas et al<sup>20</sup> and BisGaard T et al<sup>6</sup> showed reduction in post-operative pain and requirement of analgesics after the prophylactic use of dexamethasone<sup>21</sup>; similarly, we observed significantly low pain scores in dexamethasone group of our study, even though we had administered analgesia to patients of both the groups at similar intervals of the study. Dexamethasone use shown to reduce pain, analgesic requirement and duration of convalescence in post-operative patients. A study by Ming-Shan Chen, et al showed no difference in pain scores between their dexamethasone group and control group.<sup>8</sup>

We conclude that prophylactic use of dexamethasone prior to SAB in patients undergoing gynecological surgeries reduces the incidence of nausea and vomiting and requirement of antiemetic and improved analgesia in the postoperative period, with better patient satisfaction. We recommend randomized, controlled trials in larger samples to further strengthen our results.

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