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Evaluating Gabapentin as a Pre-Emptive Analgesic During Combined Spinal Epidural Anesthesia in Patients Undergoing Total Abdominal Hysterectomy

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ABSTRACT
Pain management during and after major surgeries such as total abdominal hysterectomy remains a significant clinical challenge as the post-operative period is a vulnerable period that triggers various hemodynamic instability, pain, etc. These can be handled better by adopting certain pre-operative measures like the use of preemptive analgesics like Gabapentin and reducing the need for opioids. We aimed to evaluate the efficacy, safety, quality of analgesia and side effects of Gabapentin as a pre-emptive analgesic by comparing it with that of a placebo. It was a Comparative study of Sixty female in patients undergoing total abdominal hysterectomy of American Society of Anaesthesiologists (ASA) grade I and grade II, between the age group 35-60 years selected by simple random sampling technique. They were divided into two groups of thirty each. Group-G (Gabapentin)-received Tab. Gabapentin 300mg orally, 2 hours before the surgery with sips of water. Group P-P (placebo)- received none. All patients received a combined spinal epidural anaesthesia followed by epidural top ups for pain relief. The outcome was compared between the groups for the mean time of onset of sensory block, total number of epidural bolus in 24 hrs, hemodynamic changes and the VAS at 2, 4, 8, 12 and 24 hours. SPSS for Windows (version 22.0) was used for analysis. Group- G showed significantly lower VAS scores postoperatively compared to Group- P with a p value<0.0001 at every interval. Significantly reduced requirements of the number of epidural top-ups were demonstrated in Group- G compared to Group- P postoperatively, p<0.5. Intra operatively Hemodynamic were well maintained in Group-G when compared to Group-P as seen with significant differences in mean arterial blood pressures between the two groups p<0.001. Pre-emptive use of Tab. Gabapentin 300mg orally significantly reduces the number of post-operative epidural bolus requirements and post-operative pain in patients undergoing total abdominal hysterectomy under combined spinal epidural anaesthesia Maintaining stable intra operative Hemodynamic.

INTRODUCTION

Pain is perfect miserie, the worst of evils and, excessive, overturns all patience"- John Miller (Paradise Lost). Anaesthesia as a subject by itself originated in an endeavor to offer pain relief to the patient during surgical procedures and in the postoperative period. However acute pain following surgery has been managed inadequately because of a wide variety of myths and fears. The incidence of post-operative pain is between 25-76%[1,2]. This uncontrolled pain in the postoperative period triggers adverse hemodynamic responses and effects like delayed recovery and chronic pain. There has been a revolution in the last three decades in the management of acute pain. An increased knowledge regarding the pathophysiology of pain, advances in pharmacological options and extensive use of regional techniques like continuous epidural analgesia have brought about changes in pain management in the perioperative period[3]. Preoperative predictors of pain include anxiety, age, sex, patient psychology, socioeconomic factors and surgery. In the earlier periods analgesia was restricted to surgical and postoperative period. However, this was associated with lot of morbidity to the patient in terms of surgical stress and increased requirements for analgesics in the postoperative period which were associated with various adverse effects[4,5]. The concept of pre-emptive analgesia which has been recently introduced involves administering an analgesic drug prior to a noxious stimulus such as surgical skin incision. This analgesic administration is supposed to decrease surgical stress response as well as postoperative analgesic requirements. Various drugs like opioids, NSAIDs, antiepileptic drugs are being used for purpose of pre-emptive analgesia. Opioids act at peripheral, posterior horn of spinal cord as well as CNS level to offer pre-emptive analgesia. NSAIDs preferentially act at peripheral site to offer pre-emptive analgesia. Antiepileptic drugs act at CNS level to offer pre-emptive analgesia[6]. Gabapentin is a GABA analogue which was introduced as an anti-epileptic and later proved to be effective in neuropathic pain. More recently, it has been studied to treat acute post-operative pain.

MATERIALS AND METHODS

It was a Comparative study on Sixty female in patients undergoing total abdominal hysterectomy of American Society of Anaesthesiologists (ASA) grade I and grade II, between the age group 35-60 years selected by simple random sampling technique divided into two groups of thirty each. Group-G (Gabapentin)-received Tab. Gabapentin 300mg orally, 2 hours prior to the surgery with sips of water. Group P-P (placebo)-received none.

Inclusion Criteria:

- Female patients aged 30-60 years.
- ASA physical status I or II.
- Scheduled for elective total abdominal hysterectomy under combined spinal-epidural anesthesia.
- Consent to participate in the study.

Exclusion Criteria:

- Known allergy or contraindication to gabapentin or other study medications.
- History of chronic pain or use of opioid analgesics in the past 6 months.
- Patients with significant psychiatric or neurological disorders.
- Renal or hepatic impairment.
- Body mass index (BMI) >s35 kg/m².
- Pregnant or lactating women.

Combined Spinal-Epidural Anesthesia: All patients received a standardized combined spinal-epidural anesthetic technique. The spinal component involves administering 0.5% hyperbaric bupivacaine with or without an opioid (e.g., fentanyl), while the epidural catheter was being placed for postoperative analgesia. General proforma was be used for collection of data from individual patients and for recording different parameters. In our clinical study, 60 female patients undergoing elective TAH belonging to ASA grade 1 and grade 2 between the age groups 35-60 years were selected by simple random sampling technique and divided into two groups of 30 each.

Group-G (Gabapentin): received Tab.Gabapentin 300mg orally,2 to 3 hours prior to the elective surgery with sips of water.

Group-P (Placebo): received none.

In all patients epidural catheter was inserted at L1-L2 inter space at a depth of 10cms for intra operative and post operative top ups. Subarachnoid block was achieved in all patients using Inj. Bupivacaine 0.5%(H) 3.2-3.4ml in the lower L3-L4 inter space. Post-operatively, Visual Analogue Score (VAS) was noted at 2, 4, 8, 12 and 24 hours. Epidural top with 10cc 0.125% Inj. Bupivacaine was administered and the total number of boluses demanded along with the use of any other analgesic in the first 24 hours were noted.

Statistical Analysis: Data was analyzed using SPSS software version [24.0]. Continuous variables (e.g., VAS scores, opioid consumption) was presented as mean ± standard deviation and analyzed using the independent t-test or Mann-Whitney U test as appropriate. Categorical variables (e.g., incidence of PONV, adverse events) was analyzed using the

chi-square test or Fisher's exact test. A p-value of <0.05 was considered statistically significant.

RESULTS AND DISCUSSIONS

In the current study it was found that there were no statistically significant differences in terms of demographic properties or ASA grading and thus the data were comparable between both the groups. The majority of the participants belonged to age group between 41-50 years in the Gabapentin group whereas belonged to between 31-50 years in the placebo group. Difference between the two groups is statistically insignificant. p=0.9 (Table 1). (Table 2) suggests 36.7% of the patients in the Gabapentin group and 46.7% in the Placebo group belonged to ASA grade 1 while 63.3 % of the patients in the Gabapentin group and 53.3% in the Placebo group belonged to ASA grade 2. The difference between the groups with regard to distribution of ASA physical status is not significant. No complications were seen in the participants of the Placebo group and 73.3% of the patients in the Gabapentin group. Dizzines was seen in 3.3%, sedation in 13.3% and nausea in 10% of the patients in the Gabapentin group. The differences between the groups is statistically significant (Table 3).

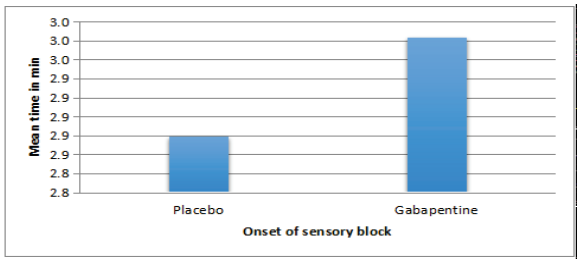

Fig. 1: Comparison of Onset of Sensory Block

The mean time of onset of sensory block in Gabapentin group was observed to be 2.98mins compared to 2.80mins in the Placebo group. The difference between the groups is statistically in significant p<0.3 (Fig. 1).

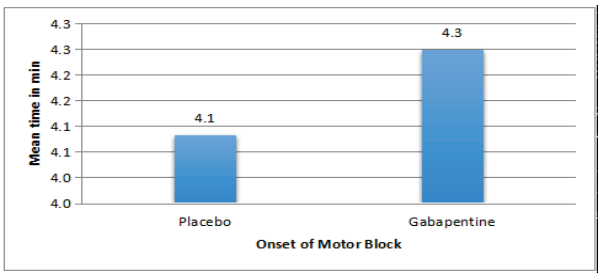

Fig. 2: Comparison of Onset of Motor Block

The mean time for the onset of motor block was observed to be 4.3mins in gabapentin group whereas 4.1 in the placebo group. The differences between the groups is statistically insignificant. p<0.3 (Fig. 2). The maximum level of sensory blockade achieved in gabapentin group is T8 in 76.7% and 66.7% in the placebo group. The difference between the groups is statistically insignificant. p<0.6. The majority of the patients in the gabapentin group 73.3% had a level of sensory blockade of T10 whereas 53.3% in the placebo group had a level of sensory blockade of T 10. The differences between the groups is statistically insignificant p<0.3 (Table 4). Intra operative complications were seen in 43.3% of the patients in gabapentin group and 46.7% in the placebo group.56.7% of the patients in the gabapentin group and 53.3% of the patients in the placebo group had no complications and is statistically insignificant. p<0.8 (Table 5). Total number of epidural boluses demanded in the gabapentin group is lower compared to the placebo group and is statistically significant. p<0.0001. (Table 6). As per (Table 7) around 53.4% of the patients in both the groups had no intra operative complications. Bardycardia was seen in 13.3 % of the patients in placebo group whereas 43.3 % of the patients in the Gabapentin group developed intra operative hypotension. The differences between the groups was statistically insignificant. p=0.3.

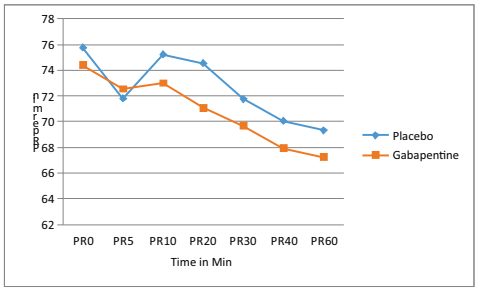

Fig. 3: Comparison of Pulse rate

Mean pulse rate changes were comparable in both groups and is found to be statistically insignificant. p=0.3 (Fig. 3). Post-operative VAS scores at every interval was significantly lower in Gabapentin group in comparison with the placebo group. p<0.001 (Table 8).

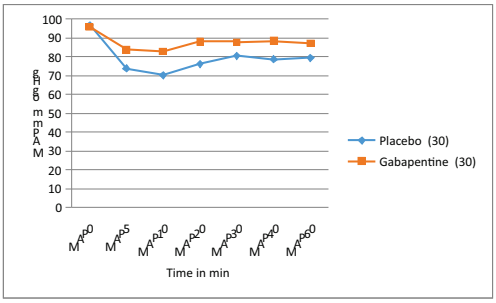

Fig. 4: Comparison of MAP

Table 1: Comparison of Groups with Age

	Placebo		Gabapentin		
Age in Yrs	No	%	No	%	Total
31-40	13	43.3	11	36.7	24
41-50	13	43.3	15	50.0	28
51-60	4	13.3	4	13.3	8
Total	30	100	30	100	60

Table 2: Comparison of ASA Grade Between Groups

	Placebo		Gabapentine		
ASA_GRD	No	%	No	%	Total
1	14	46.7	11	36.7	25
2	16	53.3	19	63.3	35
Total	30	100	30	100	60

Table 3: Comparison of Pre-Operative Complications

	Placebo		Gabapentin		
POCIA	No	%	No	%	Total
Dizziness	0	0	1	3.3	1
Nausea	0	0	3	10.0	3
None	30	100	22	73.3	52
Sedation	0	0	4	13.3	4
Total	30	100	30	100	60

Table 4: Comparison of Maximum level of Sensory Block

	Placebo		Gabapentine		
MSOSB	No	%	No	%	Total
T6	10	33.33	7	23.3	17
T8	20	66.7	23	76.7	43
Total	30	100	30	100	60

Table 5: Comparison of Intra-Operative Complications

	Placebo		Gabapentin		
IOC	No	%	No	%	Total
NO	16	53.3	17	56.7	33
YES	14	46.7	13	43.3	27
Total	30	100.0	30	100.0	60

Table 6: Total Number of Epidural Bolus in 24 hrs

	Placebo		Gabapentin		
Tnoeb_24	No	%	No	%	Total
3.00	0	0	8	26.6	8
4.00	0	0	11	36.7	11
5.00	30	100	11	36.7	41
Total	30	100	30	100	60

Table 7: Intra-Operative Complications

	Placebo		Gabapentin		
IO complications	No	%	No	%	Total
Nil	16	53.4	16	53.4	32
Bradycardia	4	13.3	1	3.3	5
Hypotension	10	33.3	13	43.3	23
Total	30	100	30	100	60

Table 8: Comparison for VAS

	Placebo (30)			Gabapentine (30)			
	Mean	SD	Median	Mean	SD	Median	P
VAS2HRS	5.97	1.13	6.00	2.50	.68	2.00	<0.0001
VAS4HRS	6.20	.85	6.00	2.80	.66	3.00	<0.0001
vas8HRS	6.17	.80	6.00	3.07	.74	3.00	<0.0001
VAS12HRS	5.90	.85	6.00	2.70	.54	3.00	<0.0001
VAS24_HRS	7.00	.	.	3.03	.68	3.00	0.065

Mean arterial pressures in Gabapentin group were well maintained when compared to placebo group. the differences between the groups is statistically significant. p<0.001.(Fig. 4). The age distribution between the two groups shows a minor difference, with the majority in the Gabapentin group falling within the 41-50 age range, while the placebo group had a broader range between 31-50 years. However, this difference was statistically insignificant (p=0.9), indicating that age was not a confounding factor in the

study. Similarly, the distribution of ASA physical status between the two groups was not significantly different, with both groups having a nearly equal proportion of patients in ASA grade 1 and 2. This suggests that the patients were comparable in terms of their baseline physical health[7,8]. A notable finding was the incidence of complications and side effects. While no complications were observed in the placebo group, 26.7% of patients in the Gabapentin group experienced some form of complication, such as dizziness (3.3%), sedation (13.3%) and nausea (10%). The statistically significant difference here suggests that Gabapentin may have a higher side effect profile in the context of pre-emptive analgesia during combined spinal-epidural anesthesia[8]. The study observed the maximum level of sensory blockade achieved during the procedure. In the Gabapentin group, 76.7% of patients achieved a T8 level, compared to 66.7% in the placebo group. A majority in both groups had a sensory blockade level at T10. However, the differences in sensory blockade levels between the two groups were statistically insignificant ($p<0.6$ and $p<0.3$), indicating that Gabapentin did not significantly influence the level of sensory blockade which is similar to few studies[9,10]. The study found that mean pulse rate changes were comparable between the groups and statistically insignificant ($p=0.3$). However, post-operative VAS (Visual Analog Scale) scores were significantly lower in the Gabapentin group compared to the placebo group ($p<0.001$), indicating better pain management in the Gabapentin group. Additionally, mean arterial pressures were better maintained in the Gabapentin group, with statistically significant differences ($p<0.001$). These findings highlight Gabapentin's effectiveness in managing post-operative pain and maintaining hemodynamic stability. In a similar study conducted by Ho *K et al.* on effects of pre operative Gabapentin or Clonidine in decreasing post operative pain patients who have undergone abdominal hysterectomy in which 300mg of Gabapentin or 100 microgram of Clonidine was administered to the patients an hour before the surgery. It was concluded that the VAS pain scores were significantly lower in Gabapentin group compared to the placebo group[8]. Epidural boluses were administered on demand to both the groups using 0.125% of 10cc Inj. Bupivacaine. In a study by HO k *et al.* demonstrated significantly lower consumption of analgesics like morphine in the Gabapentin group compared to the Placebo group[8]. Similar results were observed in a study by Moore AS *et al.* demonstrating significantly lower usage of analgesics in Gabapentin group compared to the placebo group[9]. A study by Pinto R[10], demonstrated decreased consumption of morphine in the group which received Tab. Gabapentin prior to the surgery in patients undergoing spinal surgery. In a study conducted by Moore *et al.* comparing the effect of Gabapentin and Pregabalin on post operative pain in patients undergoing infra umbilical surgeries under subarachnoid block a single dose of 1200mg showed significantly decreased VAS scores postoperatively[9]. In a study by Habib AS *et al.* demonstrated significant lower VAS scores post operatively with a single higher dose of Gabapentin with no significant differences in the side effects between the two groups[11]. A study conducted byFassolauki[12], using 300mg Gabapentin or 100 microgram Tramadol or placebo 2 hours prior to laparoscopic cholecystectomy demonstrated significantly lower pain scores at all time intervals post operatively in comparison to the rest of the groups.

CONCLUSION

The study demonstrates that while Gabapentin may introduce some side effects like dizziness, sedation, and nausea, it significantly improves post-operative pain management and maintains better hemodynamic stability compared to a placebo. The lack of significant differences in sensory blockade levels and intra operative complications between the groups suggests that Gabapentin's primary benefit in this context lies in its post-operative effects rather than its intra operative impact. These findings could guide clinical decision-making in the use of Gabapentin for pre-emptive analgesia in similar surgical settings.

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