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Original Article

Effects of Preemptive Gabapentin on Postoperative Pain Control and Opioid Consumption after Abdominal Hysterectomy

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ABSTRACT

Background: *Preemptive analgesia is an analgesic state that is initiated before surgery in order to prevent the establishment of central sensitization evoked by the incisional and inflammatory injuries occurring during surgery and in the early postoperative period. Preemptive analgesia can both decrease the severity and duration of pain and also can delay the pain. There are different methods and techniques present now a days to obtain preemptive analgesia. Gabapentin is a drug which was introduced recently and it is used in various field of anaesthesia practice. Gabapentin have been shown to be beneficial in postoperative pain following various surgery. The present study was carried out to evaluate the effect of preemptive oral gabapentin on postoperative pain control and opioid consumption in patients undergoing abdominal hysterectomy.* ***Method:*** *In this prospective randomized double-blind study, Total 60 patients of ASA grade I, II planned for Total Abdominal Hysterectomy were selected randomly according to selection criteria. Sixty patients divided into two groups, 30 patients underwent total abdominal Hysterectomy received gabapentin 600 mg (Group-G) and 30 patients received placebo (Group-P) orally two hours prior induction of anesthesia. All patients instructed preoperatively for the pain visual analogue scale (VAS) and verbal rating scale for measurement and assessment of the quality of pain. All patients were given 100 mg suppository diclofenac every 8 h. If VAS score more than 4 a top up dose of pethidine 0.5mg/kg was administered intravenously. Total pethidine consumption during initial 12 hours postoperative period was recorded for each patient.* ***Result:*** *Patients in the placebo group had higher VAS*

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score, just after operation during zero hour mean VAS score was 6.3±0.95 and 8.2±0.25 in group G & group P respectively. During the second hours compared with the gabapen¬tin groups, mean VAS score was 5.2±0.47 and 7.4±0.68 in group G & group P respectively. Six hours after the surgery, both groups showed downward trends of the pain VAS, but significantly in group G. Mean score was 4.1±0.32 and 6.2±0.51 in group G & group P respectively. ***Conclusion:*** *Present study shows that pre-emptive use of oral Gabapentin significantly reduces the post-operative pain and reduces the opioid (pethidine) consumption in patient undergoing Total Abdominal Hysterectomy.*

Keywords: *Preemptive analgesia, gabapentine, postoperative pain, abdominal hysterectomy*

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INTRODUCTION

Preemptive analgesia, a treatment that is initiated before surgery in order to prevent the establishment of central sensitization evoked by the incisional and inflammatory injuries occurring during surgery and in the early postoperative period. Postoperative pain, a type of acute pain, that affects recovery from surgery and anaesthesia. The goal of postoperative pain relief is to achieve optimal analgesia, facilitating a quick return to normal physiological function[1]. The idea behind preemptive analgesia is not simply that it reduces nociception and stress during surgery, although these are obviously worthwhile goals. Primarily, three different classes of drugs are utilized for the treatment of postoperative pain (anti-inflammatories, local anesthetics, and opioids). Unfortunately, long-term clinical use of these agents is limited by their side effects[2]. Gabapentin, a structural analogue of gamma-amino butyric acid, has been discovered very recently and used as an antinociceptive drug and is claimed to be effective in preventing neuropathic component of acute nociceptive pain of surgery[1]. Preemptive gabapentin significantly decreases opioid consumption and post operative pain in patient undergoing lower extremity orthopaedic surgeries under spinal anaesthesia[3]. Gabapentin has more recently extended into the management of more acute conditions[4]. Therefore, when used as a preemptive analgesic, gabapentin may reduce acute postoperative pain[2]. The use of gabapentin in acute postoperative pain management has been evaluated in different studies. Thus, purpose of the study to observe the effect of oral preemptive gabapentin on postoperative pain and opioid requirements in patients undergoing total abdominal hysterectomy.

METHOD:

In this prospective randomized double-blind study, Total 60 patients with ASA grade I, II planned for Total Abdominal Hysterectomy were selected randomly according to selection criteria. Then equal number of envelopes containing either gabapentin tablet or placebo was made. Then a non-researcher physician gave a code number in every envelop. This code number was also noted in data collection sheet and was decoded during data analysis. Sixty patients divided into two groups. 30 patients of experimental group (Group G) received gabapentin 600 mg (Group-G) and 30 patients received placebo (Group-P) orally two hours before induction of anaesthesia in total Abdominal Hysterectomy. All patients instructed preoperatively for the pain visual analogue scale (VAS) and verbal rating scale for measurement and assessment of the quality of pain. After entering the operating room, patients received 10 mL/kg of Ringer's solution. Heart rate, Blood pressure and arterial oxygen saturation (SpO2) was monitored. Preoxygenation with 100% oxygen done and then Anaesthesia is

induced by fentanyl (2µg/kg), thiopental (6 mg/kg), and vecuronium (0.1 mg/kg) had used to facilitate intubation. Patients then ventilated with 100% oxygen and intubated with an adequately sized cuffed tube. Anesthesia was maintained using a mixture of oxygen (33%), nitrous oxide (66%) and halothane. Vecuronium and fentanyl used for intraoperative relaxation and analgesia. Surgery was initiated while patients become supine. After surgery, the muscle relaxants were reversed using neostigmine (40 µg/kg) and atropine (20 µg/kg). After extubation and ensuring adequate ventilation, patients is transferred to the recovery care unit and then to the ward. All patients received 100 mg suppository diclofenac every 8 h. Postoperative pain was measured using a visual analogue scale. Patients with a pain score >4 was treated with 0.5mg/kg intravenous Pethidine. The amount of Pethidine consumption and pain level at 0h, 2h, 6h, 12h after surgery, Heart rate, SBP, DBP, MBP, SpO_2, Respiratory rate were recorded. Postoperative complications including vomiting and dizziness also recorded. In case of nausea and vomiting, Ondansetron 8mg IV was given. This information, together with the demographic characteristics of the patients and the duration of surgery were analyzed. All collected data sheet checked very carefully to identify the error in the data. Data processing work consist of registration schedules, editing computerization, preparation of dummy table, analyzing and matching of data.

RESULTS

Demographic data and baseline parameters of both groups were comparable. There were no significant differences in age, sex, ASA grading between groups.

Table I: Age distribution of the patients (n=60)

Age (years)	**Number of patients**		**P value**
	N=30 Group-G	N=30 Group-P	
Mean ± S.D.	45.8±11.5	46.7±9.8	**0.7494^{ns}**

ns= not significant

P value reached from unpaired t test.

While studying the distribution of cases by age it was found that majority of the patients i.e. 66.6% (n=40) were between 35-50 years, 18.3% (n=11) were age <35 years. Mean age was found to 45.8±11.5 years in group-G while 46.7±9.8 years in group-P (Table I). The difference was not statistically significant (p>0.05) between two groups. In this study we found that body mass index (kg/m^2) was almost similar in both groups, the difference was not statistically significant (p>0.05) between two groups. Maximum 37(61.66%) of women (63.33% in group-G & 60.0% in group-P) had observed normal weight (Table II)

Table II: Distribution of study subjects according to BMI (n=60)

Body mass index (kg/m^2)	**Number of patients**		**P value**
	N=30 Group G	N=30 Group P	
Mean ± S.D.	25.34±4.85	25.96±3.97	**0.5900^{ns}**

ns= not significant P value reached from unpaired t test.

Table III shows ASA status of the study patients, it was observed that almost two third (63.3% & 60.0%) patients had ASA grade I in group G and group P respectively. The difference was not statistically significant (p>0.05) between two groups.

Table III: Distribution of the study patients according to types of American Society of Anaesthesiologist (ASA) status (n=60)

ASA status	***Group G*** ***n (%)***		***Group P*** ***n (%)***		**P value**
	n	*%*	*n*	*%*	
I	19	63.3	18	60.0	
II	11	36.6	12	40.0	**0.7882^{ns}**

ns= not significant
P value reached from chi square test.

Patients in the placebo group had higher VAS score, just after operation during zero hour mean VAS score was 6.3±0.95 and 8.2±0.25 in group G & group P respectively. The difference was statistically significant. During the second hours compared with the gabapentin groups, mean VAS score was 5.2±0.47 and 7.4±0.68 in group G & group P respectively. The difference was statistically significant. Six hours after the surgery, both groups showed downward trends of the pain VAS, but significantly in group G. Mean score was 4.1±0.32 and 6.2±0.51 in group G & group P respectively. The difference was statistically significant. At the 12th hour, almost all patients had lower VAS score. Mean score was 2.91±0.23 and 3.0±0.27 in group G & group P respectively (Table IV). The difference was statistically not significant. So overall finding suggested that, premptive use of gabapentin reduced the postoperative pain significantly.

Table- IV: Assessment of pain sensation using Visual Analogue Scale (VAS) (n=60)

VAS score	***Group G*** ***N=30***		***Group P*** ***N=30***		**P value**
	Mean±SD		**Mean±SD**		
0 hr after surgery	6.3	±0.95	8.2	±0.25	**0.0001^{s}**
2 hr After surgery	5.2	±0.47	7.4	±0.68	**0.0001^{s}**
6 hr after surgery	4.1	±0.32	6.2	±0.51	**0.0001^{s}**
12 hr after surgery	2.91	±0.23	3.0	±0.27	**0.1699^{ns}**

s= significant, ns= not significant
P value reached from unpaired student t-test

Intensity of pain was higher in placebo group as compared with gabapentine group. Downhill trend of changes of Visual Analogue Pain Score was observed in both groups with progression of time, but significantly in gabapentine group (Fig.1).

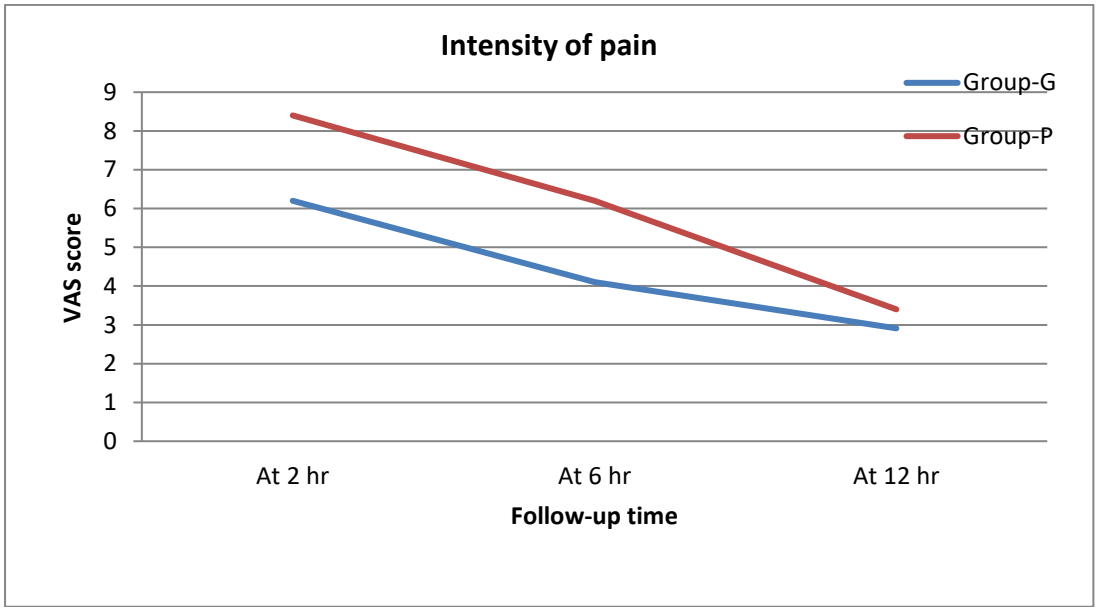

Figure- 1: Comparison of pain intensity between groups (n=60)

Just after surgery at zero-hour maximam patient of both groups experienced moderate to severe pain but patients of placebo group complaints more pain than gabapentin group and the difference was statistically significant. More number of patients in placebo group experiencing pain than gabapentin group 2 hours after surgery and the difference was statistically significant ($p<0.001$). 6 hour after surgery patient in placebo group also experienced more pain than gabapentine group and the difference was statistically significant ($p<0.001$). After 12 hours of surgery maximum patient in both group experienced less pain and the difference was not statistically significant (Table V).

Table- V: Assessment of quality of pain/severity of pain by Verbal Rating Scale (n=60)

	Group G N=30		***Group P N=30***		***P value***
	n	**%**	**n**	**%**	
0 hr after surgery					
Mild =(1-3)	2	6.66	0	0	
Moderate=(4-6)	20	66.67	12	40	
Severe=(7-10)	8	26.7	18	60	
					<0.001[s]
2 hr after surgery					
Mild =(1-3)	5	16.67	1	3.33	
Moderate=(4-6)	19	63.33	17	56.7	
Severe=(7-10)	6	20	12	40	
					<0.001[s]
6 hr after surgery					
Mild =(1-3)	18	60	5	16.7	
Moderate=(4-6)	12	40	21	70	
Severe=(7-10)	0	0	4	13.3	
					<0.001[s]

12 hr after surgery					
Mild =(1-3)	22	73.3	20	66.67	
Moderate=(4-6)	08	26.7	10	33.33	
Severe=(7-10)	0	0	0	0	
					>0.05^{ns}

s= significant, ns= not significant
P value reached from chi-square test.

Rescue medication was needed more in placebo group than group-G and the difference was statistically significance ($p<0.05$). in this study post operative pain was treated according to operational definition. All patients was given 100 mg suppository diclofenac every 8 h. If pain not alleviated and pain score >4, rescue medication was given as Inj. Pethidine 0.5mg/kg intravenous. The mean (± SD) amount of Pethidine used in the placebo group (55.6±12.8 mg) was significantly more than in the gabapentin group (25.8±5.2 mg; P=0.0001). There was a significant increase in Pethidine use in the placebo group (Table VI).

Table- VI: Trends of use of rescue medication (Pethidine) amongst the study population (n=60)

Rescue medication	**Number of patients**		**P-value**
	N=30 Group G n(%)	***N=30 Group P n (%)***	
Inj. Pethidine	12(40%)	24(80%)	
Mean±SD	25.8±5.2 mg	55.6±12.8 mg	**0.0001^{s}**

s = significant

P value reached from unpaired t test.

Nausea and vomiting was lower for the gabapentin group, compared with the placebo group (Table VII); this difference was statistically significant (P <0.05).

Table- VII: Evaluation of any adverse events (n=60)

Complication	**Number of Patient**		**P-value**
	Group G (N=30) n (%)	***Group P (N=30) n (%)***	
Hypersensitivity or rash	0	0	
Hypotension	0	0	
Nausea, vomiting	7(23.33%)	18(60.00%)	**0.0043^{s}**
Cardiovascular collapse	0	0	
Myoclonus	0	0	

s= significant, ns= not significant
P value reached from chi square test

DISCUSSION

Total of 60 patients were included to determine the effectiveness of preemptive gabapentin on postoperative pain control and opioid consumption after abdominal hysterectomy. Age distribution of the patients were between 35-50 years. Mean age difference was not statistically significant between two groups. Similar findings were observed in total abdominal hysterectomy where selected patient allocated to one of the three groups of gabapentin, tramadol and placebo. Unpaired t test showed that the three groups were not significantly different, in terms of age[5].

In this study. It was observed that mean body mass index was almost similar in both groups and the difference was not statistically significant. Bhatia et al[1] in their study also showed similar mean body mass index in patient undergoing abdominal hysterectomy. Kinney et al[6] in their study with elective thoracotomy shows mean body mass index was higher in Gabapentin and placebo group. This was due to selection of both male and female patient.

It was observed that almost two third patients had ASA grade I in group G and group P respectively. The difference was also not statistically significant between two groups. Similar data also shown in other studies where maximum patient had ASA grade I[2,7]. In another study, where patient selected for preemptive gabapentin went for elective thoracotomy shows maximum patient had ASA II or III[6]. This result probably due to presence of various coexisting lung disease.

In this study, day before surgery patients were instructed about the Visual Analogue Scale (VAS), Patients in the placebo group had higher VAS, during the 0 and 2 hours, compared with the gabapentin groups. Mean verbal pain score was higher in group P then in group G. The difference was statistically significant.

Khan et al.[8] In another study used preemptive gabapentin 1200mg group showed significantly lower mean VAS score than the control group for the patient undergoing abdominal hysterectomy at zero and 2 hours after surgery. Ucak et al[9], they used a gabapentin dose of 1200 mg one hour before surgery. In this study, postoperative pain scores were significantly lower in the gabapentin group when compared to the placebo group, but they used large dose of gabapentin as preemptive analgesic. Panah khahi et al. explored the efficacy of preemptive use of 300 mg gabapentin on reduction of postoperative pain after internal fixation of the tibia this study showed that the pain score was significantly lower in gabapentin group compared to the placebo group 2 hours after the completion of surgery, but surgery was done under spinal anaesthesia[9]. Farzi et al[5] in the comperative study showed that patients in the placebo group had higher VAS score during the 2 hours after surgery compared with the gabapentin (600mg) and tramadol (100mg) group, but tramadol group developed adverse effect like nausea and vomiting, drowsiness. Bharti et al.[10] in their study showed 600 mg preemptive gabapentin significantly reduce pain scores 2 hours after total mastectomy compared with placebo group. Kinney et al[6] evaluate the role of preoperative gabapentin in patients receiving epidural analgesia undergoing thoracotomy showed no significant difference between gabapentin and placebo group. Eidy et al.[11] studied the comperative effect of pregabalin and gabapentin on postoperative pain after laparoscopic cholecystectomy showed significant decrease of pain score in gabapentine group in compare with placebo group but in this study, they used 800 mg gabapentin tablet.

Six hours after the surgery, both groups showed downward trends of the pain VAS,

but significantly in group G. Mean VAS score was statistically significant. Modak et al[2] in their study use preemptive gabapentin for the patient undergoing abdominal hysterectomy, after 6 hours, mean visual analogue score decrease significantly in gabapentin group compare to the placebo group.

At the 12th hour, almost all patients had lower mean VAS score in both group and the difference were not statistically significant. Frouzanfard et al[12] in their study, they also find that 12 hours after surgery there was significant decrease of mean VAS score in gabapentin group in compare with placebo group. Eidy et al.[11] studied the comperative effect of pregabalin and gabapentin on postoperative pain after laparoscopic cholecystectomy showed significant decrease of pain score in gabapentine group in compare with placebo group but in this study, they used 800 mg gabapentin tablet

In this study quality of pain also evaluated by verbal rating scale, where patients in the placebo group had more moderate to severe pain, during the zero and second hours compared with the gabapentin groups. Then severity of pain decreases gradually. At the 12th hour, almost all patients had mild pain. More number of patients in placebo group experiencing pain than gabapentin group 0 and 2 hours after surgery and the difference was statistically significant. 6 hours after surgery patient in placebo group experienced more pain than gabapentine group and the difference was statistically significant. After 12 hours of surgery maximum patient in both groups experienced less pain and the difference also not significant.

Need for use of rescue medication was more in placebo group than group-G and the difference was statistically significance, In this study The mean (± SD) amount of Pethidine used in the placebo group was significantly more than in the gabapentin group. In another prospective randomized placebo-controlled study observed the mean number of rescue analgesic dose requirement in the gabapentin group was substantially lower than that of the control group. Gabapentin significantly reduces post-operative pain and post-operative tramadol consumption with very few side effects[3].

In this study nausea and vomiting was higher for the placebo group, compared with the groups G; however, this difference was statistically significant. Findings consistent with result of other study. Nausea and vomiting score were lower for the gabapentin group, compared with the two other groups; however, this difference was not statistically significant. Nausea and vomiting scores, for the gabapentin and tramadol groups, showed different trends, until 12 hours after the operation, and similar trends afterwards. For the gabapentin group, nausea score was lower in the first hour and increased during the next 12 hours[5].

Another important property of gabapentin is absence of major drug interactions and serious adverse effects. Various authors in their respective studies evaluating gabapentin on postoperative pain showed no significant side effects in gabapentin group as compared to control patients. In a study, two patients of the gabapentin group complained of symptom of dizziness[4]. Nausea/vomiting and dizziness are among the most common adverse effects seen after the administration of tramadol and these adverse effects treated by using ondansetron[5]. However, dose titration schedule and slow initiation therapy have been proposed to reduce tramadol induced adverse effects.

The results of our study clearly showed that the preemptive use of gabapentin significantly reduces postoperative pain and hence narcotic/opioid requirements in patients underwent total abdominal hysterectomy, thereby minimizing the side effects of narcotics.

CONCLUSION

It was concluded that preemptive oral gabapentin (600 mg) had significant effect

on reducing postoperative pain and postoperative opioids requirement in patients undergoing abdominal hysterectomy and thereby minimizing the side effects of opioids.

Conflict of interest: There is no conflict of interest and financial interest to report.

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