ORIGINAL RESEARCH PAPER

Anesthesiology

EFFECT OF PREEMPTIVE GABAPENTINE ON POSTOPERATIVE ANALGESIA AND RESCUE ANALGESIC REQUIREMENTS IN TOTAL ABDOMINAL HYSTERECTOMY.

KEY WORDS: Gabapentine, preemptive analgesic, rescue analgesic

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ABSTRACT

Gabapentin was initially developed as a GABA-mimetic compound to treat spasticity, and has been shown to have potent anticonvulsive effects.Initially approved only for use in partial seizures, it soon showed promise in the treatment of chronic pain syndromes, especially neuropathic pain.Gabapentin has demonstrated analgesic effects in clinical trials as a preemptive analgesic and in acute postoperative pain management. Hence, the present study was designed to investigate whether pre-emptive use of gabapentin 300mg orally could reduce postoperative pain and rescue analgesic requirements in the initial 24 h in patients undergoing total abdominal hysterectomy. Gabapentin acts through a unique but poorly understood mechanism.Possible pharmacologic targets are selective activation of GABA-B receptors, enhancement of NMDA currents blocking AMPA receptor mediated transmission in the spinal cord.At clinically relevant concentrations, it decreases membrane voltage gated calcium currents (VGCC channels) in dorsal horn ganglion neurons. It has a high affinity for alpha -2-delta subunit of presynaptic VGCC channels and inhibits calcium influx and subsequent release of excitatory neurotransmitter by sensory neurons.It increases serotonin concentrations in brain.It has a selective effect on nociceptive process involving central sensitization. This effect on central sensitization plays an important role in reducing the postoperative pain when given pre emptively.

Materials and methods : This prospective observational study was conducted on 30 patients who underwent total abdominal hysterectomy under spinal anesthesia. Of these 15 patients were given gabapentin 300mg orally with sips of water 2h prior to the procedure and were denoted as Group G, while 15 patients were given placebo tablet 2h prior to the procedure and were denoted as Group P. Pain was assessed using the verbal rating scale(VRS) at 2h, 4h, 12h and 24h postoperatively. Morphine 4.5 mg intramuscularly was given as the rescue analgesic whenever VRS (Verbal rating scale) scores was more than or equal to 3. The time to first request for rescue analgesic was noted. The total morphine requirement in the 24 h postoperatively was studied.

Results: The gabapentine group and placebo group were comparable with respect to age(years), weight (kilograms),sex, duration of surgery(minutes) and ASA physical status and no statistically significant difference existed between the two groups. Patients in the gabapentine group G had significantly lesser pain scores at 2 hours, 4hours ,12 hours and 24 hours when compared to the placebo group. Also it was found that there is a significant effect of time on the level of pain and the levels of pain at 2hours and24 hours differed significantly from the level of pain at 4 hours and 12 hours.In the gabapentine group G decrease in pain levels is more rapid than the increase in pain levels which is more gradual while in the placebo group P there is a rapid increase in the level of pain and gradual decrease in the level of pain and pain scores reach the preoperative values only at approx .36 hours or longer postoperatively. The patients in the gabapentine group experienced greater prolongation of central neuraxial blockade as evidenced by the delay in request for rescue analgesia in the group.Also the rescue analgesic (morphine) consumption in the gabapentine group in the postoperative 24 hours was only half of that of the placebo group.

Conclusion: Thus the patients who had received gabapentine 300mg oral 2 hours prior to surgery had reduction in the intensity and duration of postsurgical pain,greater prolongation of central neuraxial blockade and lesser requirement of rescue analgesic when compared to the patients who had received placebo.

Introduction

The IASP (International Association for Study of Pain) defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. This definition recognizes the interplay between objective, physiological, sensory aspects of pain and its subjective, emotional and psychological components.The response to different pain is highly variable among persons and in the same person at different times. Uncontrolled postoperative pain may result in sympathetic nervous system activation causing a variety of potentially harmful physiologic responses that may adversely influence the extent of morbidity and mortality for the patients.

A revolution in the management of postoperative pain has occurred during the past two decades.

Widespread recognition of the undertreatment ofacute pain by clinicians, economists,and health policy experts has led to the development of a national clinical practice guideline for acute pain management by the Agency for Healthcare Quality and Researchof the U.S. Department of Health and Human Services[1]. This landmark document includes acknowledgement of the historic inadequacies in perioperative pain management, importance of good pain control, need for accountability for adequate provisions of perioperative analgesia by healthcare institutions,and a statement on the need for the involvement of specialists in appropriate cases . Several professional societies have also developed clinical practice guidelines for acute pain management[2]. In 2000, the Joint Commission on Accreditation of Healthcare Organisations(JCAHO) unveiled new pain management standards. With their knowledge and familiarity with pharmacology, various regional techniques ,and the neurobiology of nociception, anesthesiologists are continually in the forefront of clinical and research advances in acute postoperative pain management. Anesthesiologists are leaders in the development of acute postoperative pain services,application of evidence –based practice to acute postopera tive pain, and creation of innovative approaches to acute pain management, all of which are a natural part of the anesthesiologist in becoming the "perioperative physician", a consultant and therapist throughout an institution, and a highly skilled expert in the operating room.

Definition of preemptive analgesia includes, what is administered before surgical incision,what prevents establishment of central sensitization resulting from incisional injury only i.e.intraoperative period or what prevents central sensitization resulting from incisional and inflammatory injuries i.e. intraoperative and postoperative period.

Gabapentine, introduced initially as an adjuvant antiepileptic drug is now being extensively studied for the purpose of preemptive analgesia. In this scenario,the purpose of my study is to find out the effect of preemptive oral gabapentin administration on postoperative pain and rescue analgesic requirements in total abdominal hysterectomy.

Objectives of the study

To study the effect of preemptive oral gabapentine on postoperative analgesia and rescue analgesic requirements in patients undergoing total abdominal hysterectomy under regional anesthesia namely spinal anesthesia.

Materials and methods

Ethical committee clearance as well as institutional approval was sought before the study was started .Informed written consent was obtained from each patient and family.

Study Area- Department of Anesthesiology and Critical Care , Academy of Medical Sciences,Pariyaram, Kannur district ,Kerala

Study Period- A period of one year from March 2014 to March 2015

Study Population—Consists of 30 female patients admitted in the hospital for total abdominal hysterectomy Study Sample

Inclusion Criteria:

(I) Age 40-60 years
(ii) ASA-PS --I or II
(iii) Duration of surgery—1to 3 hours

Exclusion criteria:

(I) Known allergy to gabapentine
(ii) Epilepsy
(iii) Previous treatment with gabapentine within a period of one month
(iv) Chronic pain syndromes
(v) Psychiatric disorders
(vi) Substance abuse
(vii) Impaired kidney or liver function
(viii) Patients who had received analgesics within 48 hours prior to surgery.
(ix) patients belonging to ASA grade I and II were considered for the study.

(I) Patient evaluation- A thorough evaluation of medical history and physical examination including preoperative heart rate, blood pressure, respiratory rate, oxygen saturation in room air are noted. The respiratory, cardiovascular, gastrointestinal and renal systems are evaluated for any impairment in function and patients classified according to American Society of Anesthesiologists grading. Only patients belonging to ASA grade I and II were considered for the study.

Investigations- A complete blood count, blood urea , serum creatinine estimation, liver function tests, urine analysis, electrocardiogram, chest radiography was done to rule out the presence of any coexisting diseases.

The study design was randomized and double blinded. Patients were randomly allocated into two equal groups of 15 each by a table of random numbers. Preoperatively , each patient was instructed on how to rate the pain on verbal rating scale (VRS). All study medications were given orally with sips of water 2h preoperatively by a staff nurse who was not involved in the study.Patients in study group G received tablet gabapentin 300mg, whereas in study group P patients received matching placebo.All patients were premedicated with midazolam 1.5 mg half an hour prior to surgery.Standard monitoring with electrocardiogram, pulse oximetry , noninvasive blood pressure and urine output with an indwelling catheter was initiated in the operation theatre .

All patients were preloaded with 10ml/kg of lactated Ringer's solution and spinal anesthesia was performed at L3- L4 interspace in right lateral position.Hyperbaric solution of 0.5% bupivacaine 3.4ml was given in the subarachnoid space.After confirmation of successful blockade and proper height of anesthesia, surgery was begun. Intraoperatively, patients were monitored using pulse oximetry,electrocardiogram ,noninvasive blood pressure evaluation.After surgery, patients were shifted to the Post Anesthesia Care Unit. Verbal rating scales were taken down by an independent physician who was not aware of the group allocation, on a scaleof 0- 4.When verbal rating scale was more than or equal to 3 or at any point of time when the patient demanded Morphine 4.5 mg boluses intramuscularly were given. Total number of morphine boluses and total morphine consumption (mg) was noted .The data was entered into the statistical software package SPSS 9. The mean+/- standard deviation from maximum pain scores in all patients in both groups at 2, 4, 12 , 24 h were calculated.Similarly, intravenous morphine consumption was calculated.A value of $P<0.05$ was considered significant. VRS scores were analyzed with 2-factor ANOVA for repeated measure. The total morphine consumption in each group in 24 h (Mean+/-standard deviation) was compared using unpaired 't' test.

Results and Observations

The study population of this prospective observational study comprised of 30 female patients who fulfilled the inclusion criteria and were undergoing total abdominal hysterectomy under spinal anesthesia.

Demographic and patient characteristics

Thirty female patients were included in the study.The demographic characteristics are presented in table 1.The age of the patients belonging to the gabapentin group designated as G, ranged from 34 to 46 years with a mean age of 42.93+/- 3.674 years .The age of the patients belonging to placebo group designated as P ,ranged from 35 to 50 years with a mean age of 46.33+/-1.474 years. There was no statistically significant difference in the two groups with respect to age (P= 0.284).

Group		N	Mean±SD	Std. Error mean	P Value
AGE	G	15	42.93±3.674	0.949	0.284
	P	15	46.33±11.475	2.963	NS

NS:Not Significant
SD:Standard Deviation
G :Gabapentine
P :Placebo

The weight of the patients belonging to the gabapentin group G ranged from 40 to 60 kg with a mean weight of 50.4+/-6.08 kg. The weight of the patients belonging to the placebo group ranged from 45 to 60 kg with a mean weight of 53.67+/-4.237 kg. There was no statistically significant difference in the two groups with respect to weight. (P = 0.099).

Group		N	Mean±SD	Std. Error mean	P Value
WT(KG)	G	15	50.40±6.080	1.57	0.099
	P	15	53.67±4.237	1.094	NS

NS:Not Significant
SD:Standard Deviation
G :Gabapentine
P :Placebo

ASA Physical status

13 out of 15 patients in the gabapentin group were ASA I, while 2 of the patients were ASA II were hypertensive. 11 out of 15 patients in the placebo group were ASA I while 4 of the patients were ASA II of which one patient had valvular heart disease- mild mitral stenosis, one patient had hypothyroidism and two patients had hypertension.

ASA GRADE * CASES1_Controls2 Crosstabulation

			CASES1_Controls2		
			case	control	Total
ASA GRADE	I	Count	13	11	24
		% within CASES1_Controls2	86.7%	73.3%	80.0%
		% of Total	43.3%	36.7%	80.0%
	II	Count	2	4	6
		% within CASES1_Controls2	13.3%	26.7%	20.0%
		% of Total	6.7%	13.3%	20.0%
Total		Count	15	15	30
		% within CASES1_Controls2	100.0%	100.0%	100.0%
		% of Total	50.0%	50.0%	100.0%

Chi-square test and Fischer's exact test was done to determine whether the ASA physical status was statistically significant between the gabapentin group G and placebo group P and P>0.05. There was no statistically significant difference in the ASA physical status between the two groups.

The duration of surgery in the gabapentin group ranged from 110 to 130 minutes, with a mean value of 123.8667+/- 5.91447 minutes. The duration of surgery in the placebo group ranged from 110 to 170 minutes with a mean value of 125.6667+/- 20.60398 minutes. Using Student's t test for independent samples, the difference in mean duration of surgery between the two groups were not found to be statistically significant.

Group Statistics

GROUPS		Mean±SD (min)		
Surgery duration	G	123.8667	±	5.91447
	P	125.6667	±	20.60398

VRS SCORES

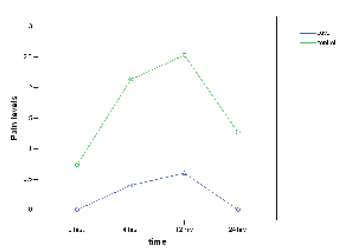
GROUPS		Mean ± Std. Deviation	N
2hrs	G	.00 ±.000	15
	P	.73 ±1.280	15
	Total	.37 ±.964	30
4hrs	G	.40 ±1.056	15
	P	2.13 ±1.598	15
	Total	1.27 ±1.596	30
12hrs	G	.60 ±1.121	15
	P	2.53 ±1.506	15
	Total	1.57 ±1.633	30
24hrs	G	.00 ±.000	15
	P	1.27 ±1.751	15
	Total	.63 ±1.377	30

Source	SS	df	MS	F	P Value
Between subjects					
Treatment	60.21	1	60.21	27.26	<0.001
Error	61.83	28	2.21		
Within subjects					
Time	27.63	3	9.21	7.39	<0.001
Treatment x time	6.43	3	2.14	1.72	0.169
Error	104.7	84	1.25		

The patients in the gabapentin group G had VRS scores of 0 .00+/- 0.000 at 2 h, 0.40 +/-1.056 at 4 h , 0.60 +/- 1.121 at 12 h and 0.00 +/_0.000 at 24 h. The minimum pain levels were at 2h and 24h postoperativel y 0.00 +/- 0.000, while the maximum pain level was at 12 h postoperatively 0.6 +/-1.121. The patients in the placebo group P had VRS scores of 0.73 +/-1.280 at 2 h, 2.13 +/- 1.598 at 4 h , 2.53 +/- 1.506 at 12 h and 1.27 +/- 1.751 at 24 h. The minimum pain level was at 2 h postoperatively and the maximum pain level was at 12 h postoperatively, unlike the group G where the pain levels at 24 h were also minimum. To determine whether the level of pain differed with respect to the treatment , mixed ANOVA was done and P<0.001, thus there was a statistically significant difference in the levels of pain between the gabapentin group Gand placebo group P.

Result of mixed anova

Also, averaging the effects of treatment, there is a significant effect of time on the level of pain and using the LSD Post hoc test, it was seen that the levels of pain at 2 h and 24 h differed significantly from the level of pain at 4h and 12 h, There was no interaction between the type of treatment and time.

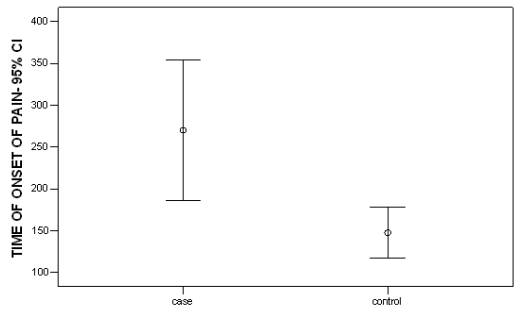


Time of first request for rescue analgesic namely morphine

The time of first request for rescue analgesic(morphine 4.5 mg intramuscularly) in the gabapentin group G was 270+/-150.89 min (Mean +/-SD) after the surgery ,while in the placebo group P the first request for rescue analgesic was 147.53+/- 54.575 min (Mean+/- SD) after the surgery. This was analyzed by 't ' test and found to to be statistically significant.

GROUPS (Time of first request for rescue analgesia)	N	Mean +-Standard deviation	P value
G	15	270.00+-150.890	
P	15	147.53+-54.575	.006

Error bar diagram showing the difference between the time of first request for rescue analgesia between gabapentine and placebo group

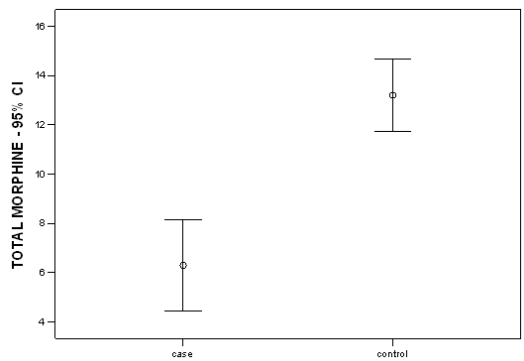


Total dose of rescue analgesic consumption (Morphine 4.5mg boluses intramuscular on demand)

Total morphine Groups	N	Mean+- Standard Deviation	
G	15	6.30+-3.316	.000
P	15	13.20+-2.671	

The total dose of rescue morphine given was found to be 6.3+/- 3.316 mg (Mean +/-SD) in the gabapentin group G , while in the placebo group P, it was found to be 13.2+/-2.671 mg.This difference was found to be statistically significant as P< 0.05.

Error bar diagram showing the difference between total morphine used between cases and controls.



DISCUSSION

Pain is a physiological consequence of impending or actual tissue injury that serves a vital protective function. However, pain can become a disease itself when it occurs or persists in the absence of tissue damage or following appropriate healing of injured tissue. Chronic pain becomes tremendously disabling and has considerable negative impact on quality of life. Gabapentin was initially developed as a GABA-mimetic compound to treat spasticity, and has been shown to have potent anticonvulsive effects.Initially approved only for use in partial seizures, it soon showed promise in the treatment of chronic pain syndromes, especially neuropathic pain. Gabapentin has demonstrated analgesic effects in clinical trials as a preemptive analgesic and in acute postoperative pain management. However ,there have not been much studies about the pre-emptive use of gabapentin in cases conducted under regional anesthesia and its effect on

postoperative requirement of rescue analgesic. Hence, the present study was designed to investigate whether pre-emptive use of gabapentin 300mg orally could reduce postoperative pain and rescue analgesic requirements in the initial 24 h in patients undergoing total abdominal hysterectomy.Gabapentin acts through a unique but poorly understood mechanism.Possible pharmacologic targets are selective activation of GABA-B receptors, enhancement of NMDA currents blocking AMPA receptor mediated transmission in the spinal cord.At clinically relevant concentrations, it decreases membrane voltage gated calcium currents (VGCC channels) in dorsal horn ganglion neurons. It has a high affinity for alpha -2-delta subunit of presynaptic VGCC channels and inhibits calcium influx and subsequent release of excitatory neurotransmitter by sensory neurons. It increases serotonin concentrations in brain.It has a selective effect on nociceptive process involving central sensitization. This effect on central sensitization plays an important role in reducing the postoperative pain when given pre emptively.

This prospective observational study was conducted on 30 patients who underwent total abdominal hysterectomy under spinal anesthesia. Of these 15 patients were given gabapentin 300mg orally with sips of water 2h prior to the procedure and were denoted as Group G, while 15 patients were given placebo tablet 2h prior to the procedure and were denoted as Group P. Pain was assessed using the verbal rating scale(VRS) at 2h, 4h, 12h and 24h postoperatively .Morphine 4.5 mg intramuscularly was given as the rescue analgesic whenever VRS scores was more than or equal to 3. The time to first request for rescue analgesic was noted. The total morphine requirement in the 24 h postoperatively was studied.

Demographic and patient characteristics were studied statistically .There was no significant difference between the Group G and the Group P with respect to age (years) .When the weight of the patients (kilograms) in the gabapentin group G was compared with the weight of the patients in the placebo group P there was no statistically significant difference between the two groups. The ASA physical status of both groups were compared and there was no statistically significant difference between the two groups .The duration of surgery (minutes) was compared in both groups and there was no significant difference between the two groups. Thus both the gabapentin group G and the placebo group P were comparable with respect to age , weight , ASA physical status and duration of surgery.

Patients in the gabapentin group G had significantly lower VRS scores when compared with the placebo group P at 2h (0.00+/- 0.000 vs 0.73+/- 1.280) , at 4h (1.056 vs 2.13 +/- 1.598) , at 12h (0.60+/- 1.121 vs 2.53+/- 1.506) and 24h (0.00+/- 0.000 vs 1.27+/- 1.751). Statistical analysis has revealed that there is a significant difference in the level of pain between the gabapentin group and the placebo group. Thus , patients in the gabapentin group had lower levels of pain at all time-points measured postoperatively when compared with the placebo group. Gabapentin as preemptive analgesic has a significant effect in reducing the pain postoperatively , when compared to the placebo, at all time points observed . After a single oral dose of 300mg gabapentin, mean maximum plasma concentrations are attained in 2-3 h.The preemptive administration of gabapentin approximately 2h before surgery appears optimal in order to attain maximal plasma concentration at time of surgical stimuli.

Also, averaging the effect of treatment, it was found that there is a significant effect of time on the level of pain and the levels of pain at 2h and 24h differed significantly from the level of pain at 4h and 12h.In Group G pain level is at the minimum (VRS = 0.00+/- 0.000)at 2h postoperatively, then increases gradually to 4h postoperatively , further pain levels increase at a lesser rate upto 12h postoperatively, reaching the maximum pain level at 12h postoperatively and then starts decreasing steeply and at 24h postoperatively reaches the baseline value i.e. the pain level at 2h postoperatively. The decrease in pain levels is more rapid than the increase in pain levels which is more gradual.

In the placebo group P,pain level at 2h postoperatively is the minimum compared to all other time-points, increases at a rapid rate to 4h postoperatively and further increases more gradually upto 12 h where the pain level is at the maximum value and then starts decreasing at a more rapid rate upto 24h postoperatively. A t 24h ,the pain level is less than at 4h and 12h, but never reaches the the value at 2h postoperative, in contrast to group G.If the curve is extrapolated, the pain level reaches the VRS scores at 2h only at approx 36 hours or longer

Comparing group G and group P, patients in both groups had lowest pain scores at 2h postoperatively, in both groups pain started increasing from 2h ,through 4h and reached a maximum at 12h postoperatively after which the pain scores started decreasing and at 24h reached lower levels . Comparatively lower pain scores at 2h maybe due to the residual effect of spinal anesthesia given, after which the spinal anesthesia may have worn off and all inflammatory mediators due to the incisional and tissue injury have come into play at 4h and maximum pain levels at 12h due to large numbers of inflammatory mediators active at that point of time .Thereafter , healing process slowly has begun and hence inflammatory injuries have started reducing and hence pain levels are declining to much lower values at 24h. Even though the trend in the increasing and decreasing of pain scores are similar in both groups, the pain scores in the gabapentin group at all points of time measured are significantly less than in the placebo group and the pain at 24h postoperatively has reduced to the pain levels at 2h postoperative i.e, the pain has reached the baseline value within 24h ,while in the placebo group the pain does not reduce to the baseline value within 24 h ,it reaches the baseline pain levels only after 36h or longer period of time.In other words, the patients in the placebo group experienced higher levels of pain for a longer period of time when compared with the gabapentin group. Thus ,preemptive gabapentin not only reduces the intensity but also the duration of postoperative pain after abdominal hysterectomy under spinal anesthesia.

In animal models of nociception, gabapentin reduces hypersensitivity associated with nerve injury, inflammation, and pain after surgery. Mechanical hyperalgesia surrounding the wound in postoperative patients, and experimental, heat –induced secondary hyperalgesia share a common mechanism—central neuronal sensitization—that may contribute to some aspects of postoperative pain.Antihyperalgesic drugs such as gabapentin may have a role in postoperative pain.Gabapentin has potential in reducing the central neuronal sensitization and thus reducing the postoperative pain.

In a study by Verma A et al[34], the effect of gabapentin 300mg or placebo 2h prior to abdominal hysterectomy under combined spinal epidural anesthesia was observed. Postoperatively, patients in gabapentin group had significantly lower VAS scores at 2, 4 ,8, 12 and 24 h postoperatively as compared to the placebo ($P < 0.05$) .This study had similar results compared to our study even though rescue analgesia was through epidural boluses of 0.125% bupivacaine , whereas in our study morphine 4.5mg boluses intramuscularly was given when VRS scores where more than or equal to 3.Thus they concluded that oral preemptive gabapentin 300mg significantly reduces the postoperative pain and the number of postoperative epidural bolus requirement in patients undergoing abdominal hysterectomy under combined spinal epidural anesthesia.These findings are similar to our result.In the study by Pandey CK et al[35], where the effect of preemptive use of gabapentin 300mg on postoperative pain and fentanyl consumption in patients after single-level lumbar discoidectomy was studied, patients in the gabapentin group had significantly lower VAS scores at all timeintervals than those in the placebo group $P<0.05$. The total fentanyl consumed after surgery in the first 24h in the gabapentin group was significantly less than in the placebo group, $P< 0.05$. These findings are also similar to our results except that the pain scale used was VAS , while we used VRS scores and the rescue analgesic was fentanyl, while we used morphine.

In our study,in the gabapentin group G, the time to first demand for rescue analgesic was 270+/- 150.890 minutes ,when compared with placebo group P which was 147.53+/- 54.575 minutes. The perception of severe pain in the gabapentin group was delayed by almost double the time when compared to the

placebo group .The patients who had received gabapentin preemptively had more prolongation of the central neuraxial blockade which was statistically significant when compared with the placebo group which perceived pain much earlier . Thus these patients had lesser requirement for rescue analgesic in the subsequent period, prolonged analgesia,better patient satisfaction and lesser chance for development of chronic pain.From this we infer that, gabapentin by its effect on central neuronal sensitization leads to prolongation of central neuraxial blockade and this helps in immediate postoperative analgesia and further reduction of other parenteral analgesics.

In a study by Kohli m et al, the effect of preoperative pregabalin (gabapentinoid like gabapentin) on postoperative analgesic requirements in patients undergoing hysterectomy under spinal anesthesia was studied. Pregabalin like gabapentin is a gabapentinoid,being an oral drug would be easy for the patients to take and also its prolongation of the neuraxial block helps in immediate postoperative analgesia and further reduction of other parenteral analgesics. Thus, gabapentin may also cause prolongation of neuraxial block similar to pregabalin.Ghai A et al compared pregabalin with gabapentin for postoperative pain in abdominal hysterectomy. They concluded that a single dose of 300mg pregabalin given 1-2h prior to surgery is superior to 900mg gabapentin and placebo after abdominal hysterectomy. Both pregabalin and gabapentin were found to be better than placebo. Thus in this study also, it was found that time to first request for analgesia was longer in the gabapentin group placebo group.when compared to placebo. In our study, though the dose of gabapentin was 300mg compared to 900 mg in the above mentioned study, the time to first request for analgesia in the gabapentin group was longer than in the placebo group.T herefore gabapentine in the dose of 300mg is enough to produce prolongation of spinal anesthesia further into the postoperative period as opposed to 600mg in the above study.

In our study, in the gabapentin group, the total consumption of rescue analgesic namely morphine in the 24h immediate postoperative period was almost half of that consumed by the placebo group and P<0.000, i.e., there is a significant difference in the morphine consumption postoperatively between the two groups. The patients in the gabapentin group had lesser requirement for postoperative rescue analgesic requirement in the immediate 24 h postoperatively, when compared with the the placebo group.The lesser requirement for morphine leads to lesser incidence of opioid side effects like vomiting, pruritus ,respiratory depression etc. Thus gabapentin pre emptively,reduces the total analgesic consumption in the immediate postoperative period.

Tiippana et al evaluated randomized controlled trials examining the analgesic efficacy, adverse effects, and clinical value of gabapentinoids in postoperative pain (gabapentin/ pregabalin). They found out that gabapentinoids effectively reduce postoperative pain, opioid consumption, and opioid-related adverse effects after surgery. Hurley RW et al did a meta-analysis on the analgesic effects of perioperative gabapentin on postoperative pain. Based on this review ,they concluded that perioperative oral gabapentin is a useful adjunct for the management of postoperative pain that provides analgesia through a different mechanism than opioids and other analgesic agents and would make a reasonable addition to a multimodal analgesic treatment plan. In the study by Pandey et al[35], they found that in addition to decreasing the severity of postoperative pain, pre emptive gabapentin also decreased the total fentanyl consumed after surgery in the first 24h when compared to the placebo group. This result was similar to our study except that the rescue analgesic used in our study was morphine in comparison to fentanyl in the study quoted above.Grover VK et al[38] did a randomized placebo-controlled double blind trial and concluded that a single dose of gabapentin 600mg administered 1h prior to surgery produced significant and effective postoperative analgesia after total mastectomy and axillary dissection without significant side effects. This study differed from our study in that the dosage of gabapentin was 600mg compared to our study where gabapentin 300mg was used and the surgery was done under general anesthesia whereas our study was done under spinal anesthesia, but the rescue analgesic in both studies was morphine. Thus according to our study, a smaller dose of gabapentin even 300mg could produce reliably good reduction in the intensity and duration of postoperative pain.

Sen H et al[46], compared the preventive effects of perioperative ketamine and gabapentin on early and chronic pain after elective hysterectomy.They concluded that gabapentin and ketamine are similar in improving early pain control and in decreasing opioid consumption ; however gabapentin also prevented chronic pain in the first 6 postoperative months.

Summary

- This was a prospective observational study done to find out the effect of oral gabapentin as pre emptive medication on postoperative analgesia and rescue analgesic requirements in total abdominal hysterectomy.
- Of the 30 patients included in the study 24 patients were ASA I and 6 patients were ASA II. In the gabapentin group, two patients were ASA II and in the placebo group, four patients were ASA II.
- 15 patients were given gabapentin 300mg tablets orally 2h prior to sugery while the other 15 patients were given placebo tablets prior to hysterectomy which was performed under spinal anesthesia.
- The gabapentin group and placebo group were comparable with respect to age (years), weight (kilograms), sex, duration of surgery(minutes) and ASA physical status and no statistically significant difference existed between the two groups.
- T he monitoring of the patients intraoperatively included : continuous electrocardiography (ECG), noninvasive blood pressure (NIBP) , pulseoximetry (Sp O2) and urine output.
- Postoperatively, the patients were evaluated for pain by the Verbal Rating Scores at 2h, 4h, 12h and 24h, the time of first request for rescue analgesia was noted and the total analgesic requirement in the immediate postoperative 24h was also studied.
- All the values are expressed as mean +/- standard deviation. S tudent's t test and mixed ANOVA was used for statistical analysis and P<0.05 was considered significant.
- All the 15 patients in the gabapentin group had significantly reduced intensity and duration of pain postoperatively, when compared to the placebo group at all points of time as evident from the VRS scores of the two groups.
- In the patients in the gabapentin group , the first request for analgesia occurred much later than that of the placebo group, almost twice the time had elapsed before the patients in the gabapentin group demanded analgesia.
- Thus, they experienced greater prolongation of central neuraxial blockade when compared to the placebo group.
- The rescue analgesic (morphine) consumption in the gabapentin group in the postoperative 24h was only about half of that of the placebo group.
- Thus, the patients who had received gabapentin300mg oral 2h prior to surgery had reduction in the intensity and duration of postsurgical pain, greater prolongation of central neuraxial blockade and lesser requirement of rescue analgesic when compared to the patients who had received placebo.

Conclusion

Oral preemptive gabapentin 300mg reduces the intensity and duration of postoperative pain after total abdominal hysterectomy under spinal anesthesia.

Pre emptive gabapentin prolongs the central neuraxial blockade and delays the onset of postoperative Pre emptive gabapentin prolongs the central neuraxial blockade and delays the onset of postoperative pain in patients undergoing abdominal hysterectomy under spinal anesthesia.

Gabapentin reduces the total opioid analgesic consumption in the immediate 24h postoperative period and thus may be used as a component of multimodal analgesia.

However, further trials are required with larger sample size.