

## **Effect of pre-emptive analgesia with Gabapentin on post-operative pain relief after total abdominal hysterectomy**

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### **Abstract**

The study was done to assess the pre-emptive analgesic effect of Gabapentin 300 mg on pain score and analgesic consumption within the first 24 hours after Total Abdominal Hysterectomy under Sub Arachnoid Block. It was a randomized double-blinded clinical trial. A total of 60 consenting female patients aged 30 to 60, belonging to ASA Grade I and II, undergoing TAH were allocated to one of the two groups (Gabapentin & Placebo) of 30 each. Gabapentin group were given Gabapentin 300 mg 2 hours prior to surgery. Surgery was performed under SAB. Post-operative pain was assessed using VAS score and rescue analgesic consumption in the form of Tramadol IV was noted. All patients completed the entire study. The Gabapentin group showed significantly lower VAS scores as compared to the placebo during the post-operative period. The total IV Tramadol consumption was also significantly lower compared to the placebo group during the initial 24 hours following surgery. Pre-emptive use of oral Gabapentin 300 mg significantly reduces the post-operative pain and reduces the rescue analgesic requirement during the initial 24 hours.

**Keywords:** Gabapentin, Pre-emptive analgesia

### **1. Introduction**

Pain, which is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, is a prominent and consistent complaint following surgical procedures. It is a major obstacle that prevents the early mobilization of the patient, amongst other hardships such as inability to breathe and cough adequately while compelling the patient to experience feelings of helplessness, fear, anxiety, low mood and loss of control. Therefore, prevention and treatment of pain takes top-most priority. While adequate pain relief could be considered a basic human right, failure to relieve pain is considered morally and ethically unacceptable. [1,2]

Postoperative pain and neuropathic pain have been traditionally considered distinct based on pathophysiology and treatment. Opioids, NSAIDs and Local Anaesthetics were used for acute pain and anticonvulsants and Tricyclic antidepressants were used for chronic pain. But considerable overlap has been observed in their pathophysiology. Allodynia and hyperalgesia are cardinal signs and symptoms of neuropathic pain, which are also often present after trauma and surgery.[3-4] Postoperative pain[1] is regarded as a

type of nociceptive pain involving peripheral mechanoreceptor stimulation. Surgical stimulation also leads to sensitization of dorsal horn neurons of spinal cord and contributes to increased pain sensitivity, also dubbed as central sensitization.

Opioids, which are the mainstay in post-operative pain control, alongside NSAIDs and COX-2 Inhibitors have various side-effects such as respiratory depression, gastric irritation and renal dysfunction because of which their usages have been restricted. The new ventures in acute pain research are the testing of new analgesics as well as combinations of analgesics and to assess whether need for opioids can be reduced. On the basis of various studies, Gabapentin (1-Aminomethyl Cyclohexanyl Acetic Acid) is a drug that significantly improves the quality of opioid analgesia, reduces opioid requirement, prevents or reduces opioid tolerance, without the side-effect profile of opioids, NSAIDs and COX-2 Inhibitors.[5-23]

Gabapentin has been used for the treatment of epilepsy since 1994. But in the subsequent years, it has demonstrated analgesic effect in diabetic neuropathy, post-herpetic neuralgia and neuropathic pain.[24-28] It affects

the nociceptive process by binding to the  $\alpha 2\delta$  subunit of voltage dependent calcium channels.[29,30] In pain models it has shown anti-hyperalgesic properties, possibly by reducing central sensitization, a prerequisite for postoperative hyperalgesia.

Pre-emptive analgesia is defined as an anti-nociceptive treatment that prevents the establishment of altered central processing of afferent input, which amplifies postoperative pain. It is a treatment that is initiated before and is operational during the surgical procedures, which results in reduced pain intensity and lower analgesic requirement, even after the analgesic effects of preemptive analgesic agents have worn off. [26,27]

This study was undertaken since most of the cases of Total Abdominal Hysterectomy are nowadays done under Sub Arachnoid Block, and studies on the pre-emptive analgesic effect of Gabapentin in Total Abdominal Hysterectomy under Sub Arachnoid Block is limited.

## 2. Materials and methods

### 2.1 Aims and Objectives

To evaluate the pre-emptive analgesic effect of Gabapentin 300 mg in reducing the pain and the requirement of rescue analgesic in the initial 24 hours in patients undergoing Total Abdominal Hysterectomy under Sub Arachnoid Block.

### 2.2 Outcome variables for this Clinical Trial

Pain score by visual analogue scale (VAS) over 24 hours postoperatively. Rescue analgesic requirement over 24 hours postoperatively. This study was conducted at Dr. SMCSI Medical College, after getting approval from the Institutional Ethical Committee. Informed written consent was obtained from all patients who participated in the study.

### 2.3 Study method:

- Randomized Double-blinded Clinical Trial
- The patients were randomly assigned to one of the two groups, Gabapentin group and Placebo group using "slips of paper in a box" technique.

### 2.4 Inclusion criteria:

- Female patients
- Age group 30-60 years
- ASA Grade I and II
- Undergoing TAH

### 2.5 Instrument used for the study:

- The Visual Analogue Scale, which shows markings from 0 - 10, in which 0 = "No pain" and 10 = "Worst pain imaginable"

### 2.6 Outcome variables

- VAS Pain scores
- The amount of rescue analgesic consumption in the form of Tramadol IV

### 2.7 Exclusion criteria:

- Denial of consent
- Allergy to Gabapentin
- Consumption of NSAID in last 48 hours
- Patients Suffering from epilepsy, liver disease, renal disease or chronic pain syndrome
- Patients who have psychiatric illness

### 2.8 Sample size

A total number of 60 patients divided into 2 groups with 30 patients in each group.

### 2.9 Methodology

On the day prior to surgery, clinical examination of the patients was done; Visual Analog Scale was explained. 2 hours prior to surgery, patients were premedicated with Tab. Ranitidine 150 mg, Tab. Metoclopramide 10 mg and a staff nurse not involved in the study gave the study medicine. Group A - Tab. Gabapentin 300 mg; Group B - matching placebo. After shifting the patients to the operating theatre, Inj. Midazolam 1mg IV was administered and Sub Arachnoid Block was performed with 3.5ml 0.5% Hyperbaric Bupivacaine +25mcg Fentanyl and level was assessed.

After surgery, the patients were shifted to the recovery room and were given Tramadol 50mg IV as initial loading dose. Subsequently Tramadol 25mg IV was given on patient demand. Lockout interval was 15 min and 4-hour limit was 300 mg. VAS scores were assessed by an independent physician at 2, 4, 8, 12 and 24 hrs after surgery. Total amount of Tramadol IV consumption at same time intervals was also recorded.

60 patients who fulfilled the inclusion criteria were included in the study; divided into two groups, 30 patients in the study group (Gabapentin) [Group A] and 30 patients in the placebo group [Group B]. All the patients were able to complete the entire study. Data from the 60 patients were then analyzed.

### 2.10 Statistical Analysis

Statistical analysis was performed using the SPSS software. Demographic data was analyzed; unpaired 't' test for age and weight and chi-square test for ASA status. Rescue analgesic requirement during the postoperative period and VAS score over 24-hour period were analyzed with unpaired 't' test. Data were described by Mean and standard deviation. A 'p' value of <0.05 was considered statistically significant.

### 3. Results and Observation

The groups were comparable with respect to age, weight (Table 1) and ASA status (Table 2)

**Table 1: Comparison of sample based on age and weight**

	Placebo (N=30)		Gabapentin (N=30)		t	p
	mean	sd	mean	sd		
Age	43.6	5.5	46.0	6.8	-1.548	0.127
Weight	59.8	9.8	59.3	9.0	0.205	0.838

**Table 2: Comparison of sample based on ASA status**

ASA	Placebo		Gabapentin		Total		$\chi^2$	df	p
	N	%	N	%	N	%			
I	19	63.3	17	56.7	36	60	0.278	1	0.598
II	11	36.7	13	43.3	24	40			
Total	30	100	30	100	60	100			

The intra – operative hemodynamic values were also comparable in both the groups. (Table 3)

**Table 3: Comparison of Intra-operative hemodynamic values**

	Placebo (N=30)		Gabapentin (N=30)		t	p
	mean	sd	mean	sd		
Pulse Rate	86.1	11.5	88.1	12.9	-0.635	0.528
Systolic Bp	125.1	13.0	124.3	11.1	0.236	0.814
Diastolic Bp	78.7	10.4	76.9	9.6	0.672	0.504
Oxygen Sat	99.9	0.4	99.9	0.4	-0.308	0.759

Post-operative pain was assessed using the Visual Analogue Scale in both groups and it was observed that the Gabapentin group consistently showed lower scores at 2, 4, 8, 12 and 24 hours following surgery.

**Table 4: Comparison of VAS at different time periods in both groups**

	Placebo (N=30)		Gabapentin (N=30)		t	p
	mean	sd	mean	sd		
VAS Score 2	6.0	1.0	5.2	0.9	3.262	.002
VAS Score 4	5.9	1.2	4.9	1.0	3.541	.001
VAS Score 8	4.5	0.9	3.9	0.9	2.572	.013
VAS Score 12	4.0	0.9	3.2	0.9	3.618	.001
VAS Score 24	3.3	1.0	2.7	1.0	2.155	.035

At the 2<sup>nd</sup> hour, the VAS scores were lower in the Gabapentin group compared to the Placebo group (5.2±0.9 vs. 6.0±1 respectively;  $P < 0.05$ )

At the 4<sup>th</sup> hour, the VAS scores were lower in the Gabapentin group compared to the Placebo group (4.9±1 vs. 5.9±1.2 respectively;  $P < 0.05$ )

At the 8<sup>th</sup> hour, the VAS scores were lower in the Gabapentin group compared to the Placebo group (3.9±0.9 vs. 4.5±0.9 respectively;  $P < 0.05$ )

At the 12<sup>th</sup> hour, the VAS scores were lower in the Gabapentin group compared to the Placebo group (3.2±0.9 vs. 4.0±0.9 respectively;  $P < 0.05$ )

At the 24<sup>th</sup> hour, the VAS scores were lower in the Gabapentin group compared to the Placebo group (2.7±1 vs. 3.3±1 respectively;  $P < 0.05$ )

Therefore Gabapentin group showed significantly lower VAS scores as compared to the placebo group (5.2±0.9, 4.9±1, 3.9±0.9, 3.2±0.9 and 2.7±1 vs. 6.0±1, 5.9±1.2, 4.5±0.9, 4.0±0.9, 3.3±1 at 2, 4, 8, 12 and 24 hours respectively;  $P < 0.05$ ), during the post-operative period.

The rescue analgesic requirement in the form of Tramadol IV was also assessed at 0 - 2, 2 - 4, 4 - 8, 8 - 12 and 12 - 24 hours following surgery. Gabapentin group showed a lower Tramadol consumption at all these time intervals.

**Table 5: Comparison of rescue analgesic requirement in both groups**

	Placebo (N=30)		Gabapentin (N=30)		t	p
	mean	sd	mean	sd		
Rescue AR 0-2	80.8	15.7	72.5	16.5	2.004	0.050
Rescue AR 2-4	98.3	27.8	70.0	19.0	4.606	0
Rescue AR 4-8	64.2	15.7	45.0	17.9	4.421	0
Rescue AR 8-12	61.7	17.0	32.5	11.7	7.740	0
Rescue AR 12 -24	59.2	13.9	50.0	20.8	2.009	0.049
Rescue AR Total	363.3	51.2	270.0	49.3	7.195	0.000

Between 0 – 2 hours, the tramadol consumption was  $72.5 \pm 16.5$  mg in the Gabapentin group compared to  $80.8 \pm 15.7$  mg in the Placebo group. ( $P < 0.05$ )

Between 2 – 4 hours, the tramadol consumption was  $70 \pm 19$  mg in the Gabapentin group compared to  $98.3 \pm 27.8$  mg in the Placebo group. ( $P < 0.05$ )

Between 4 – 8 hours, the tramadol consumption was  $45 \pm 17.9$  mg in the Gabapentin group compared to  $64.2 \pm 15.7$  mg in the Placebo group. ( $P < 0.05$ )

Between 8 – 12 hours, the tramadol consumption was  $32.5 \pm 11.7$  mg in the Gabapentin group compared to  $61.7 \pm 17$  mg in the Placebo group. ( $P < 0.05$ )

Between 12 – 24 hours, the tramadol consumption was  $50 \pm 20.8$  mg in the Gabapentin group compared to  $59.2 \pm 13.9$  mg in the Placebo group. ( $P < 0.05$ )

Overall, the rescue analgesic consumption in the form of IV Tramadol was lower in the Gabapentin group compared to the placebo group ( $72.5 \pm 16.5$ ,  $70 \pm 19$ ,  $45 \pm 17.9$ ,  $32.5 \pm 11.7$ ,  $50 \pm 20.8$  vs.  $80.8 \pm 15.7$ ,  $98.3 \pm 27.8$ ,  $64.2 \pm 15.7$ ,  $61.7 \pm 17$ ,  $59.2 \pm 13.9$  at 0 - 2, 2 - 4, 4 - 8, 8 - 12 and 12 - 24 hours respectively;  $P < 0.05$ ) following surgery. Total IV tramadol consumption was also significantly low in the Gabapentin group ( $270 \pm 49.3$  mg) compared to the placebo group ( $363.3 \pm 51.2$  mg).

As regarding the side effects, in the Gabapentin group, 3 patients had nausea and 4 patients had sedation while in the placebo group, 3 patients had nausea, 2 patients had vomiting, 3 patients had sedation and 1 patient had both nausea and vomiting.

#### 4. Discussion

Pain is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” by The International Association for the Study of Pain (IASP).[31,32] It is a subjective experience based on an individual's early life experiences related to injury. Moreover, variations in individual's complaint of pain, pain behaviours and response to pain management strategies, even in identical clinical circumstances have been observed. This reflects the multidimensional nature of the pain experience, with psychological, physiological, social/environmental and pharmacological factors playing a part.[1] Therefore, treatment also must take into consideration, all these factors.

In about 50% of all surgical procedures, treatment for pain relief is thought to be inadequate.[33] While painful experiences are immediately displeasing, they can inerasably leave a mark on the nervous system, which leads to amplification of the response to subsequent noxious stimuli (hyperalgesia) and causing typically painless sensation to be experienced as pain (allodynia). It

is sometimes followed by the development of a chronic condition that produces continuous pain long after surgery. Prior painful experiences are a known predictor of increased pain and analgesic use in subsequent surgeries.[34, 35]

##### 4.1 Preemptive analgesia [39-41]

The practice of treating pain only after its perception is slowly being supplanted by a preventive approach. Development of central sensitization and hyper excitability occurs after surgical incision and results in the amplification of post-operative pain.

One of the most critical observations concerning central sensitization is the role played by the first phase of the pain response. Opiates administered before the first phase and reversed with opiate antagonist naloxone before the expected onset of the second phase, were capable of preventing this late stage of the pain response. Thus, preventing the initial neural cascade could lead to long-term benefits by eliminating the hypersensitivity produced by noxious stimuli.

Animal experiences demonstrated the benefits of preventing central sensitization by infiltrating with local anaesthetics, an approach that was particularly effective with pain associated with differentiation, as might occur with amputation. Collectively, results like these led to the concept of preemptive analgesia, initiating an analgesic regimen before the onset of the noxious stimulus to prevent central sensitization and limit the subsequent pain experience.

Preemptive analgesia is a treatment that is initiated before and is operational during the surgical procedure in order to reduce the physiologic consequences of nociceptive transmission provoked by the procedure.[27] Owing to this protective effect on the nociceptive pathways, preemptive analgesia has the potential to be more effective than a similar analgesic treatment initiated after surgery. It results in reduced pain intensity and lower analgesic requirements, even after the analgesic efforts of the preemptive agents have worn off. Consequently there is,

- Reduction of immediate post-operative pain
- Prevention of development of chronic pain

The precise definition of preemptive analgesia is one of the controversies in the field of medicine and contributes to the question of whether preemptive analgesia is clinically relevant.

Definition of preemptive analgesia include[40] what is administered before surgical incision, what prevents establishment of central sensitization resulting from incisional injury only or what prevents central sensitization from incisional and inflammatory injuries.

## 4.2 Efficacy

Despite solid demonstrations of its effects in some animal models, considerable controversy surrounds the use of preemptive analgesia in clinical settings. This controversy exists because not all clinical trials of preemptive analgesia have resulted in clear demonstration of its efficacy.[42,43] In evaluating clinical trials of preemptive analgesia, the timing of the intervention is only one factor. It is also essential to consider the ability of the intervention to prevent central sensitization and whether other aspects of the perioperative pain experience may be of sufficient duration and intensity to mask any intraoperative benefits from the preemptive analgesia.[44]

Many clinical protocols have mirrored the laboratory studies using animals that gave birth to the concept of preemptive analgesia. However, these animal experiments employed painful stimuli of intensity and duration. Therefore, it should not be surprising that interventions with a limited capacity for preventing central sensitization, when applied for only a small portion of the perioperative period, fail to demonstrate a preemptive analgesic effect.

## 4.3 Strategies [45]

Preemptive analgesia strategies have involved interventions at one or more sites along the pain pathway. These strategies have included infiltration with local anesthetics, nerve blocks, epidural block, subarachnoid block, intravenous analgesics and anti-inflammatory drugs. For example, infiltrating the incision site with long-acting local anesthetic bupivacaine, after administering general anaesthesia and before incision was found to be more effective for hernia repair pain than either spinal anaesthesia or general anaesthesia alone and these benefits appeared to last many days.

Although spinal anaesthesia clearly provides a better intraoperative block of the surgical stimulus, the more effective post-operative analgesia produced by infiltration with a long-acting local anaesthetic may have been an important factor in preventing central sensitization. During routine laparoscopy with general anaesthesia, infiltrating with local anaesthetic before incision was found to be more effective than infiltrating with saline before incision or infiltrating with local anaesthetic at the conclusion of the procedure. There were no differences among patients who received either saline or local anaesthetic at the conclusion of the procedure. Blockade of peripheral nerves with local anaesthetics can have a beneficial effect on pain after hernia repair, outlasting the duration of the nerve block even when the repair is performed with spinal anaesthesia. Intravenous opiates or ketamine administered before incision can lead to a decrease in wound hyperalgesia days after the surgery.[46] Anti-inflammatory drugs may play an

important role in peri-operative pain management by reducing the inflammatory response in the periphery and thereby decreasing sensitization of the peripheral nociceptors. This should help attenuate central sensitization.

## 4.4 Targets of pre-emptive analgesia

From a conceptual point of view, the peri-operative period can be divided into three fairly distinct phases: Pre-operative, intra-operative and post-operative.[41]

Certain factors contribute to the development of acute post-operative pain, within these three phases. These factors include:

- Pre operative noxious inputs and pain.
- Noxious intra-operative inputs arising from the cutting of skin, muscles, nerves and bones, wound retraction etc.
- Post operative noxious inputs including those arising from the inflammatory responses and ectopic neural activity in the case of post surgical nerve injury.

Each of these factors can contribute both to peripheral and central sensitization and each is a legitimate target for a pre-emptive analgesic approach.

The relative contribution of these three factors to acute post-operative pain is dependent on, transmission of noxious afferent information from the periphery to the spinal cord and brain.[42,43] The clinical importance of these findings for those receiving general anaesthesia during surgery is that while they are unconscious, the processes leading to the sensitization of dorsal horn neurons are unaffected by general anaesthesia or routine doses of opioids. This sets the stage for increased post surgical pain and increased requirement for analgesic and therefore blocking the same leads to a decrease or absence of pain.

Since its introduction into the anaesthesia literature, the concept of preemptive analgesia has evolved, based on confirmatory and contradictory evidence from clinical studies, new developments in basic science and critical thoughts. This evolution has led to progress in our understanding of the mechanisms that contribute to pre-emptive analgesia.

Preemptive analgesia is defined as “analgesic intervention provided before surgery to prevent or reduce subsequent pain.”[3,4] By preventing central sensitization using nociceptive blockers by regional analgesia, we may be able to produce a painless post surgical state. The use of preemptive analgesia was reported in various surgical procedures, such as in limb surgeries, laparoscopic procedures, mastectomy and vaginal hysterectomy. Regarding abdominal hysterectomy, there are conflicting results regarding the value of preemptive analgesia. Since hysterectomy is the most frequent major surgical



procedure performed in gynecology and it is estimated that by the age 64 years 40% of women will have had a hysterectomy, it would be of great value to optimize pain treatment in these patients.

#### 4.5 Clinical trials

Hussain Al-Mujadi *et al*[18] in a randomized double-blinded clinical trial using Gabapentin 1200 mg vs placebo, given two hours prior to induction of anesthesia to patients undergoing elective thyroidectomy with a study group of 35 patients each, showed that a single dose of 1200 mg Gabapentin given 2 hours before surgery reduces the need for post operative morphine consumption during the first 24 hours post operatively. Pain scores at rest and during swallowing were significantly lower in the Gabapentin treated patients. They suggested that Gabapentin should be considered as a potential useful adjunctive, anti hyperalgesic agent for the treatment of acute post-operative pain in patients undergoing thyroidectomy.

Pandey *et al*[17] in a randomized double-blinded clinical trial to evaluate the comparative pre-emptive effect of Gabapentin and tramadol on acute post operative pain and fentanyl requirement, in laparoscopic cholecystectomy with 459 patients assigned to receive 300 mg Gabapentin and 100 mg tramadol or placebo, found that patients in the Gabapentin group had significantly lower pain scores at all time intervals during the first 24 hours post operative period. Sedation, nausea, retching and vomiting were the commonest side effects on the Gabapentin group. They concluded that the pre-emptive use of Gabapentin significantly decreases post operative pain and rescue analgesic requirement in laparoscopic cholecystectomy.

Dirks *et al*[15] in their study using oral Gabapentin 1200 mg vs placebo given 1 hour pre operatively in patients undergoing radical mastectomy found that the pain intensity and PCA morphine consumption were significantly less in Gabapentin group of patients, during the first 24 hours post operative period with no significant side effects.

Turan *et al*[12] also conducted a randomized double-blinded clinical study in patients undergoing spinal surgery by giving oral Gabapentin 1200 mg/day or placebo 1 hour preoperatively. There was reduction in VAS pain scores and also considerable reduction in PCA morphine consumption in Gabapentin group of patients. Also vomiting and urinary retention were less in the Gabapentin group.

Rorarius *et al*[50] also found that Gabapentin 1200 mg reduced the need for additional post operative pain treatment by 40% during the first 20 postoperative hours.

Farsoulaki *et al*[51] conducted a randomized double blinded clinical study in patients undergoing

radical mastectomy by giving oral Gabapentin 1200 mg/day or placebo for 10 days post operatively, initiated on the evening before surgery. They assessed the pain scores and the codeine and paracetamol requirement for zero to ten days post operatively. They observed that there was considerable reduction in VAS pain scores and analgesic consumption with no significant side effects.

Secondary hyperalgesia is a pain state, which may develop during and after surgery and is manifested clinically as mechanical allodynia, that is the perception of pain in response to normally innocuous mechanical stimuli in normal tissue surrounding an area of tissue trauma. The development of this pain state has been shown previously to be dependent on activation of NMDA receptors located at the dorsal horn of spinal cord.

Pain after abdominal hysterectomy can be multifactorial. Incision pain, pain from deeper (visceral) structures and particularly dynamic pain such as during straining, coughing, or mobilizing can be quite severe. In one study, the authors found that visceral pain dominated during the first 48 hours after hysterectomy. Although local anesthetics have been injected into the surgical wound in numerous studies, the effect is equivocal; some studies show a good effect, whereas others show no effect. In a systematic review of the use of incisional local anesthetics, Moiniche *et al*[14] found inconclusive results after all operations except inguinal herniorrhaphy, for which local anesthetics provided up to seven hours of analgesia. In most studies on TAH, the authors have not assessed pain at different sites and therefore it is difficult to conclude the true benefit of subcutaneously placed catheters for incisional pain during major abdominal surgery.

In this study, we tried to find out whether Gabapentin 300 mg given 2 hours prior to surgery reduced the post-operative pain and the requirement of rescue analgesic during the first 24 hours post operatively. Oral administration of Gabapentin approximately 2 hours prior to surgery appears rational in attaining maximal plasma concentration at the time of surgical stimuli. The dose was in accordance with the recommended single dose of Gabapentin for the treatment of neuropathic pain (300 mg to 1200 mg three times daily). We opted for the lowest dose of 300 mg, as it was found that increasing the dose of Gabapentin to 600 mg or above had no additional benefit. Gabapentin was administered prior to surgery on the basis of finding in laboratory animals that pre treatment with Gabapentin is more effective and longer lasting than post treatment. Pre treatment with a single dose of Gabapentin blocked the development of hyperalgesia, which is NMDA mediated and tactile allodynia, which is AMPA and metabotropic receptor mediated for up to 2 days in a rat

model of post operative pain, while Gabapentin 1 hour after intervention reduced symptoms for only 3 hours.

Previous clinical studies with Gabapentin for post-operative analgesia have shown promising results. In an earlier study by Hussain-Al-Mujadi *et al*, pre-emptive use of Gabapentin 2 hours prior to thyroidectomy significantly reduced the VAS scores at rest and during swallowing when compared to placebo group.

In our study, the post-operative pain was assessed using the VAS scores. A Visual Analogue Scale (VAS) is a measurement instrument that tries to measure a characteristic or attitude that is believed to range across a continuum of values and cannot easily be directly measured. For example, the amount of pain that a patient feels ranges across a continuum from none to an extreme amount of pain. From the patient's perspective, this spectrum appears continuous and their pain does not take discrete jumps, as a categorization of none, mild, moderate and severe would suggest. It was to capture this idea of an underlying continuum that the VAS was devised.

Operationally, a VAS is usually a horizontal line, 100 mm in length, anchored by word descriptors at each end. The patient marks on the line, the point that they feel represents their perception of their current state. The success of the tool depends on the patient's interpretation of the scale and not all patients may be able to translate a sensory experience into a linear format.

Additionally, patients with impaired vision or muscle co-ordination may find it difficult to utilize this tool. However, Briggs and Closs 1999[47] state that there is evidence to support validity and reliability of the VAS and that it correlates well with other pain intensity tools.

All patients of this study were familiarized on the use of the VAS scale pre-operatively and in post-operative period. VAS scores were assessed by a physician unrelated to the study at 2, 4, 8, 12 and 24 hours post-operatively.

VAS scores and analgesic requirement:

Gabapentin group showed significantly lower VAS scores as compared to the placebo group ( $5.2 \pm 0.9$ ,  $4.9 \pm 1$ ,  $3.9 \pm 0.9$ ,  $3.2 \pm 0.9$  and  $2.7 \pm 1$  vs.  $6.0 \pm 1$ ,  $5.9 \pm 1.2$ ,  $4.5 \pm 0.9$ ,  $4.0 \pm 0.9$ ,  $3.3 \pm 1$  at 2, 4, 8, 12 and 24 hours respectively;  $P < 0.05$ ), during the post-operative period. The rescue analgesic consumption in the form of IV Tramadol was lower in the Gabapentin group compared to the placebo group ( $72.5 \pm 16.5$ ,  $70 \pm 19$ ,  $45 \pm 17.9$ ,  $32.5 \pm 11.7$ ,  $50 \pm 20.8$  vs.  $80.8 \pm 15.7$ ,  $98.3 \pm 27.8$ ,  $64.2 \pm 15.7$ ,  $61.7 \pm 17$ ,  $59.2 \pm 13.9$  at 0 - 2, 2 - 4, 4 - 8, 8 - 12 and 12 - 24 hours respectively;  $P < 0.05$ ) following surgery. Total IV tramadol consumption was also significantly low in the Gabapentin group ( $270 \pm 49.3$  mg) compared to the placebo group ( $363.3 \pm 51.2$  mg).

Turan *et al*[12] in a study on 50 patients for abdominal hysterectomy had given 1200 mg Gabapentin 1

hour before surgery versus placebo. Tramadol was given as rescue analgesic by PCA, after assessing the pain by VAS. He found that the VAS scores were significantly lower in the Gabapentin group for up to 20 hours post-operatively.

Rorarius *et al*[50] also observed that Gabapentin 1200 mg reduced the need for additional post-operative pain treatment by 40% during the first 20 post-operative hours.

Similarly, in our study also, we noticed a significant reduction in the analgesic requirement and VAS scores in the first 24 hours following surgery. Majority of the patients in both groups did not experience any significant side effects except few cases of sedation and nausea in both groups.

The inference of this study is that Gabapentin when administered 2 hours prior to surgery, significantly reduced VAS pain scores and rescue analgesic requirement during the initial 24 hours post-operatively.

## 5. Conclusion

From this study, we conclude that

- Pre-emptive use of oral Gabapentin 300 mg significantly reduces the post-operative pain as assessed by the VAS scores during the initial 24 hours.
- There is a concomitant reduction in the post-operative rescue analgesic requirement during the initial 24 hours.

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