TO EVALUATE THE ROLE OF GABAPENTIN AS A PREEMPTIVE ANALGESIC IN PATIENTS UNDERGOING TOTAL ABDOMINAL HYSTERECTOMY UNDER SPINAL ANAESTHESIA

Gunavathi Kandappan[1], Thiruvarul Santhoshini Raju[2]

[1]Assistant Professor, Department of Anaesthesia & Critical Care Medicine, Meenakshi Medical College, Kanchipuram.
[2]Assistant Professor, Department of Anaesthesia & Critical Care Medicine, SRM Medical College, Chennai.

ABSTRACT

AIM OF THE STUDY

To evaluate whether Gabapentin when given orally preoperatively at a dose of 300 mg has an effect on postoperative pain and analgesic requirement in patients undergoing total abdominal hysterectomy under spinal anaesthesia. The study also evaluates the side effects associated with administration of Gabapentin.

METHODOLOGY

This is a prospective, randomised, single blinded case controlled study. This study was conducted in total of 60 patients who underwent elective abdominal hysterectomy in our institute over a period of four months. Patients were randomly allocated into two groups: Group G (Gabapentin Group) and Group P (Placebo Group).

Patients in Group G received Gabapentin 300 mg orally and Group P patients received placebo capsules with sips of water two hours before surgery. Time since spinal anaesthesia to first requirement of analgesic (T), total analgesic requirement in first 24 hours, visual analogue scale (VAS) scores at rest and movement, Ramsay sedation score, side effects of the drug like somnolence, dizziness, confusion, nausea, vomiting were recorded in first 24 hours postoperatively.

RESULT

Single oral dose of Gabapentin 300 mg when given preoperatively reduces the postoperative pain scores and total tramadol consumption in patients undergoing abdominal hysterectomy under spinal anaesthesia. Sedation was the only significant side effect observed with the Gabapentin usage. Thus, Gabapentin can be considered as an adjunct in treating postoperative pain.

CONCLUSION

Oral Gabapentin 300 mg given preoperatively as preemptive analgesic is effective in total abdominal hysterectomy patients under spinal anaesthesia without any significant complications.

KEYWORDS

Gabapentin, Preemptive Analgesia, Hysterectomy, Pain.

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INTRODUCTION: Postoperative pain is one of the most feared problem among patients coming for surgery. Pain following hysterectomy is often multifactorial, produced from different sources. Pain arising from either the incisional site, deeper visceral structures and movement such as during straining, coughing or mobilisation may be severe. Abdominal procedure is more invasive than vaginal procedure and produces more pain. Proper management of postoperative pain leads to early mobilisation, short hospital stay, less hospital costs and increased patient satisfaction.[1] Pain control regimens must be tailored according to the needs of individual patient taking into account their age, medical condition, physical condition, level of anxiety, surgical procedure and response to agents administered.

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Corresponding Author:
Dr. Gunavathi Kandappan,
Department of Anaesthesia and Critical Care Medicine,
Meenakshi Medical College, Enathur, Kanchipuram.
E-mail: drguna83mmc@gmail.com
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Major goal of postoperative pain management is to minimise the dose of medication, to lessen the side effects and provide adequate analgesia. This can be achieved by multimodal approach to pain management.[2] Kehlet and Dahl were the first ones to describe the concept of combining multiple analgesic techniques in 1993, to improve outcome following surgery. This concept was introduced to maximise analgesic benefits and to reduce the incidence of opioid-related adverse effects. Multimodal analgesia is achieved by combing different analgesics that act by different mechanisms at different sites in the nervous system. To attain maximum benefit, pain management must be initiated in the preoperative period, continued intraoperatively and in the postoperative period.

Preemptive Analgesia: The concept of pain prevention was first introduced by Crile in 1913 and later developed by Wall and Woolf. Preemptive analgesia is defined as analgesic intervention given before noxious stimulus to attenuate or block sensitisation of central and peripheral pain pathway, which amplifies postoperative pain. In preemptive analgesia, anti-nociceptive treatment is started before and is operational

during the surgical procedure so that the physiological consequences of nociceptive transmission are reduced. Because of this protective effect on nociceptive pathways, preemptive analgesia is more effective than analgesic treatment initiated after surgery. Thereby preemptive analgesia reduces immediate postoperative pain and prevents the development of chronic pain. Preemptive analgesia helps to prevent the neurological and biochemical consequences of noxious input to central nervous system.[3]

Gabapentin is a second generation anticonvulsant drug introduced in 1993 for treatment of refractory partial seizures.[4] Later it was found to be effective in treating chronic pain conditions like postherpetic neuralgia, diabetic neuropathy, trigeminal neuralgia, HIV-related neuropathy, complex regional pain syndromes, inflammatory pain and malignant pain.[5] Recently its use has been extended for management of postoperative pain.[6] Sedation and dizziness are most common side effects of gabapentin.[7] Our study has been conducted to find out the effect of oral gabapentin 300 mg in patients undergoing abdominal hysterectomy patients.

MATERIALS AND METHODS: This is a prospective, randomised, single blinded case controlled study. This study was conducted in 60 patients who underwent elective abdominal hysterectomy in our institute over a period of four months. Institutional Ethical Committee clearance was obtained.

Inclusion Criteria:

- American Society of Anaesthesiologists physical status I and II patients.
- Age group of 20-60 years.
- Patients posted for elective abdominal hysterectomy.

Exclusion Criteria:

- Known Sensitivity to Gabapentin.
- History of Seizure Disorder.
- History of Gabapentin Consumption.
- Known Psychiatric Disorder.
- Chronic Pain Syndromes.
- Liver or Renal Disease.
- History of Drug Abuse.
- Recent Intake of Analgesics in Past 24 hours.

Patients satisfying inclusion criteria were randomly allocated by closed envelope method into two groups: Group G (Gabapentin Group) and Group P (Placebo Group). They were informed preoperatively about the nature of the study and informed written consent was obtained from all the patients. They were informed about the visual analogue scale. Patients in Group G received Gabapentin 300 mg orally and Group P patients received placebo capsules with sips of water two hours before surgery. All patients were premedicated with Inj. ranitidine 50 mg and metoclopramide 10 mg intravenously one hour before surgery. Inside the operating room, monitors (ECG, NIBP, Pulse Oximetry) were connected. Bladder was catheterised to monitor urine output. Intravenous access established with 18G cannula. All patients were preloaded with 10 mL/kg of Ringer's lactate solution.

Under strict aseptic precautions, 4 mL of hyperbaric solution of 0.5% bupivacaine given in lumbar subarachnoid space. After confirming adequate height of blockade, patients were sedated with 1 to 2 mg of midazolam intravenously. At the end of surgery, patients were shifted to ward. VAS scores were assessed at rest and during movement in the immediate postoperative period (0 hour) and at 1, 2, 4, 6, 12 and 24 hours postoperatively. Patients were given Inj. Tramadol 2 mg/kg intravenously (IV) when the VAS score was 4 or greater.

Subsequently, Inj. Tramadol of 1 mg/kg IV was given every 15 minutes until VAS score was less than 4. Dosage not to exceed 250 mg at one time and 600 mg per day. Time since spinal anaesthesia to first requirement of analgesic (T), Total analgesic requirement in first 24 hours, VAS scores at rest and movement, Ramsay sedation score (1–Anxious, Agitated, or restless; 2– Co-operative, oriented and tranquil; 3–Responds to command; 4 –Asleep but has a brisk response to light glabellar tap or loud auditory stimulus; 5 – Asleep but has a sluggish response to light glabellar tap or loud auditory stimulus; 6-Asleep, no response), side effects of the drug like somnolence, dizziness, confusion, nausea, vomiting were recorded in first 24 hours postoperatively.

STATISTICAL ANALYSIS: The data collected was analysed using statistical software package SPSS 16.0. Quantitative data was analysed using students t-test and qualitative data was analysed using chi-square test. P value of less than 0.05 is considered statistically significant.

OBSERVATION: Demographic profile (Age, Height, Weight, ASA Status, Number of Patients) in both the groups are identical. [Table 1]. In the immediate postoperative period (0 hr.), VAS score at rest was found to be 1 in both Group G and Group P. This may be due to the effect of spinal anaesthesia. The mean VAS scores at rest during postoperative period of 1, 2, 4, 6, 12 and 24 hours in group G patients were 3.50, 3.67, 3.13, 2.90, 2.27 and 1.67 respectively; and in Group P patients, the mean VAS scores were 5.73, 4.33, 3.73, 3.60, 3.23 and 2.03 respectively. The P value at all-time intervals were less than 0.05. This shows that the mean VAS scores at rest were significantly lower in group G compared to group P patients. [Table 2].

The mean VAS scores with movement at 0, 1, 2, 4, 6, 12 and 24 hours of postoperative period in group G patients were 1.10, 4.17, 4.93, 4.20, 4.20, 3.27, 2.13 respectively and in group P patients the mean scores were 1.47, 6.73, 5.50, 4.77, 4.76, 4.30, 2.57 respectively. The P value at all-time intervals were less than 0.05. This shows that the mean VAS scores with movement were significantly less in group G patients compared to group P at all-time intervals [Table 3]. T1 is the time interval between providing spinal anaesthesia and administration of first dose of tramadol. It was found that this Time interval was 183.0 minutes in group G and 172.33minutes in group P. The P value was found to be 0.01, which is considered significant. This indicates that T1 score is significantly greater in group G

compared to group P [Table 4]. Postoperative analgesia was provided with intravenous tramadol for all patients. In group G patients, average dose of tramadol required was 232.33 mg and in group P, the dosage required was 285.83 mg.

The P value was found to be 0.0001. Hence, it was found that total tramadol consumption was significantly lower in group G patients compared to group P [Table 5].

Postoperatively, all patients were assessed for the level of sedation using Ramsay sedation score periodically at 0, 1, 2, 4, 6, 12, and 24 hours. The mean sedation scores at 0, 1, 2, 4, 6, 12 and 24 hours of postoperative period were 2.93, 2.37, 2.30, 2.23, 2.33, 2.57 and 2.37 respectively in group G; and in group P, the scores were 2.27, 2.00, 2.07, 2.00, 2.10, 2.20 and 2.13 respectively. The P value at all-time intervals was less than 0.05. This shows that the level of sedation was significantly higher in group G patients compared to group P [Table 6].

During the postoperative period, all patients were monitored for complications periodically. In both the groups out of 30 patients, 24 patients did not develop any complications. Nausea was noted in 3 patients in group G and in 4 patients in group P. Vomiting occurred in 2 patients in each group. Dizziness was found in 1 patient of group G and none developed dizziness in group P. The P value was found to be 0.77 which is insignificant [Table 7].

RESULTS

- Reduction in postoperative pain scores both at rest and during movement at all-time intervals of 0, 1, 2, 4, 6, 12 and 24 hours postoperatively in group G patients.
- Reduction in total tramadol consumption during initial 24 hours of postoperative period in group G patients.
- Prolongation of the time to first analgesic requirement in group G patients.
- Sedation scores were higher in group G patients, but is well tolerated.
- The incidence of other side effects like nausea, vomiting , dizziness were found to be less in both the groups and were found to be statistically not significant.

No. of Patients	Group G	Group P	P value
Age	46.40±5.26	46.80±5.50	0.77 (Not Significant)
Height	156.23±3.93	155.70±4.44	0.62 (Not Significant)
Weight	58.40±5.16	56.83±4.74	0.23 (Not Significant)
ASA Status			

Table 1: Demographic Values of Both the Study Groups

Duration	Group-G Mean±SD	Group-P Mean±SD	t-value	Df=58 p-value
0 hour	1.00±0.00	1.00±0.00	-	-
1 hour	3.50±1.55	5.73±1.74	5.25	0.000
2 hours	3.67±0.88	4.33±0.66	3.31	0.002
4 hours	3.13±0.43	3.73±0.69	4.03	0.000
6 hours	2.90±0.55	3.60±0.78	4.06	0.000
12 hours	2.27±0.52	3.23±0.50	7.31	0.000
24 hours	1.67±0.48	2.03±0.49	2.93	0.01

Table 2: VAS at Rest

* Not Significant.

Duration	Group-G Mean±sd	Group-P Mean±sd	t-value	Df=58 p-value
0 hour	1.10±0.31	1.47±0.51	3.39	0.001
1 hour	4.17±1.98	6.73±1.91	5.10	0.000
2 hours	4.93±0.98	5.50±0.78	2.48	0.02
4 hours	4.20±0.48	4.77±0.68	3.72	0.000
6 hours	4.20±0.49	4.76±0.67	3.73	0.000
12 hours	3.27±0.52	4.30±0.54	4.19	0.000
24 hours	2.13±0.43	2.57±0.68	2.95	0.005

Table 3: VAS Score with Movement

Duration in Minutes	Group-G	Group-P
Mean	183.00	172.33
Sd	19.81	11.50
Range	150 - 225	155 - 200
t-Value	2.55	
Df	58	
p-value	0.01 (Significant)	

Table 4: T1 Score is the Time from Spinal Anaesthesia to Requirement of First Analgesic Dose

	Group-G	Group-P
Mean	232.33	285.83
Sd	22.54	23.46
Range	200 – 300	250 – 335
t-Value	9.01	
Df	58	
p-value	0.000 (Significant)	

Table 5: Tramadol Consumption

Duration	Group-G Mean±sd	Group-P Mean±sd	t-value	Df=58 p-value
0 hour	2.93±0.25	2.27±0.45	7.07	0.000
1 hour	2.37±0.49	2.00±0.00	4.10	0.000
2 hours	2.30±0.47	2.07±0.25	2.41	0.02
4 hours	2.23±0.43	2.00±0.00	2.97	0.004
6 hours	2.33±0.48	2.10±0.31	2.45	0.03
12 hours	2.57±0.50	2.20±0.41	3.10	0.003
24 hours	2.37±0.49	2.13±0.35	2.13	0.04

Table 6: Ramsay Sedation Score

Complications	Group-G		Group-P	
	Number	%	Number	%
No Complication	24	80.00	24	80.00
Nausea	3	10.00	4	13.30
Vomiting	2	6.70	2	6.70
Dizziness	1	3.30	0	-
Chi-square value	1.14			
Df	3			
p-value	0.77 (Not Significant)			

Table 7: Complications

DISCUSSION: Multimodal approach to control postoperative pain is considered as best therapeutic option.[8] Role of anticonvulsants in the treatment of acute postoperative pain has been demonstrated by many clinical studies.[9] This study was done to assess whether gabapentin when given preoperatively has a role in reducing acute postoperative pain in patients undergoing abdominal hysterectomy.

Analgesic action of gabapentin is found to be mediated by its binding to α 2δ subunit of voltage gated calcium channels in dorsal horn of spinal cord which are up regulating noxious stimuli.[10] Gabapentin when given 2 to 3 hours orally prior to surgery, reaches the peak plasma concentration and brain concentration.[11] Many studies have proved that gabapentin is effective when given at a dose of 300 mg Panah Khahi.[12,13] Many studies have proved that gabapentin when given at a dose of 300 to 1000 mg reduces the opioid consumption by 20- 60%.[14,15,16] The time of requirement for the first dose of analgesia is long when gabapentin in given as a presumptive analgesic.[17] Similar results have been obtained in this study as well. Gabapentin also prolongs the time for rescue analgesia when used in intravenous regional anaesthesia.[18] In a study conducted in a patient undergoing mastectomy under GA, gabapentin was found to reduce pain scores with movement but not at rest.[19,20] Few studies proved that gabapentin reduced VAS scores both at movement and at rest significantly.[21] Similar results have been proved in our study as well.

Gabapentin is associated with side effects like nausea, vomiting, dizziness, confusion, headache, ataxia and weight gain.[22] In this study, side effects like nausea and vomiting were less in both the groups. Only one patient belonging to group G developed dizziness which was not statistically significant. Few studies found that the incidence of sedation was high in group G.[23] which is similar to our study.

CONCLUSION: This study demonstrates that a single oral dose of gabapentin 300 mg when given preoperatively reduces the postoperative pain scores and total tramadol consumption in patients undergoing abdominal hysterectomy under spinal anaesthesia. Sedation was the only significant side effect observed with the gabapentin usage. Thus, gabapentin can be considered as an adjunct in treating postoperative pain.

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