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Anaesthesiology

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GABAPENTIN AS PRE-EMPTIVE ANALGESIC AGENT GIVEN TO ABDOMINAL HYSTERECTOMY PATIENTS FOR POST OPERATIVE ANALGESIA

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ABSTRACT

Background and Aims: The study was undertaken to assess the safety and efficacy of preoperative single oral dose of gabapentin for postoperative benefit in patients undergoing abdominal hysterectomy under spinal anaesthesia and to assess the other effects such as duration of analgesia with total analgesic requirement, measurement of postoperative sedation scores and side effects of oral gabapentin.

Methods: Patients were randomly assigned into two groups of 30 in each. Group G received gabapentin (300 mg); Group P received a placebo orally 2 h before surgery. Sevearity of postoperative pain was analyzed by Visual Analogue Score at rest and movement, Time of rescue analgesic and by Post-operative complications.

Results: On comparison, the T1 score is significantly greater in Group G (183.00 ± 19.81) compared to Group P (172.33 ± 11.50)) whereas, the total Tramadol consumption was significantly lower in Group G (221.33 ± 40.32) compared to Group P (289.00 ± 21.31). The mean Ramsay sedation scores for Group G were between 2.20±0.41 h to 2.93±0.25 h and for Group P were between 2.00±0.00 h to 2.27±0.45 h. The adverse effect such as nausea, vomiting and dizziness were noted in the ratio of 3:4, 2:2 and 1:0 in Group G and Group P patients respectively this showed there is no discrepancy in the side effects.

Conclusion: Single dose of gabapentin administered 2 h before surgery provides better pain control as compared to placebo. It prolongs the duration of analgesia, reduces the total analgesic requirement during the postoperative period.

INTRODUCTION

Post-operative pain is not purely nociceptive and evokes a neuroendocrine response to pain and can lead to increased incidence of deep vein thrombosis, vascular graft failure, and myocardial ischemia. Various techniques are employed to treat this pain, which includes the use of opioids by patient-controlled analgesia is popular, but limited by side-effects and by the fact that certain types of pain respond poorly to opioids. Methods used for post-operative pain relief after spine surgery include non-steroidal anti-inflammatory drugs, analgesic suppository, parenteral opioids, intermittent intramuscular injections, infiltration of local anaesthetics at incision site, antihyperlgesic drugs like gabapentin and pregabalin etc.. However, the surgical incision leads to sensitization, leading to hyperalgesia and allodynia seen as movement evoked pain in the postoperative patient. Anticonvulsants have shown promising results while treating chronic neuropathic pain[1]. Several reviews have shown the utility of anticonvulsants as adjuvant drugs as a result of their opioid sparing effects[2,3]. Pre treatment with gabapentin, a drug used for neuropathic pain acts on peripheral sodium channels, voltage dependent calcium channels, and decreases glutaminergic transmission in the spinal cord. It inhibits central neuronal sensitization and hyperalgesia by acting on calcium channels located at postsynaptic and presynaptic junctions resulting in the inhibition of the calcium influx thereby decreasing excitatory amino acid neurotransmission. By decreasing the central sensory input processing, gabapentin is considered to provide preemptive analgesia hence, decreasing the incidence of hyperalgesia and allodynia after surgery.

The present study was undertaken to evaluate the efficacy of a single oral dose of gabapentin (300 mg) on the duration of postoperative analgesia in patients undergoing surgeries in spinal anesthesia (SA).

MATERIALS AND METHODS

A Prospective double blinded randomized control study was conducted after receiving the institutional ethical committee approval. Before including the patients for the study, all the patients were explained about the procedures and a written informed consent was obtained. The 60 patients who were planned to undergo surgery under spinal anaesthesia were randomly divided in to two groups and assigned as Group G (Gabapentin) and Group P (Placebo).

Selection of cases

Patients posted for below umbilical surgeries of American Society of Anesthesiologists (ASA) Class I/II Belongs to the age group of 20–60 years of both sex. Height of the patient between 150 and 180 cm. Duration of surgery < 3 hours

Exclusion criteria

Patients having known sensitivity to gabapentin. History of seizure disorder. Known psychiatric disorder. Chronic pain syndromes. Liver or renal disease. History of drug abuse. Recent intake of analgesics in past 24 hours was excluded from the study.

Demographic data

The demographic data for all the patients were compared with regards to age, height, weight, sex and ASA physical status.

Study design

A single-blind, randomized, placebo-controlled study was done on 60 ASA Grades I and II patients who were randomly selected and assigned as two groups and each group contains 30 patients scheduled to undergo elective abdominal hysterectomy. Patients in the study group received gabapentine oral dose 300mg/kg and patients in the control group received placebo capsule with sip of water 2 hours before the surgery. All the patients were premeditated with Inj. Ranitidine 50 mg and metoclopramide 10 mg intravenously one hour before surgery. All patients were preloaded with 10ml/kg of Ringer's locate solution and 4 ml of hyperbaric solution of 0.5% bupivacaine given in lumbar subarachnoid space.

At the end of surgery, patients were shifted to ward. Visual analogue scale (VAS) scores were assessed at rest and during movement in the immediate postoperative period (0hr) and at 2, 4, 6, and 12 h post operatively. Patients were given Inj. Tramadol 2 mg/kg intravenously when the VAS score was 4 or greater. Subsequently Inj. Tramadol of 1mg/kg IV was given every 15 min 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 h, VAS scores at rest and movement, Ramsay sedation score[4], side effects like somnolene, dizziness, confusion, nausea, vomiting were recorded in first 12 h postoperatively.

Statistical analysis

The statistical analysis was done using the statistical programming software Statistical Package for the Social Sciences - SPSS Statistics (version 11- SPSS Inc., Chicago, Illinois, USA). Baseline variables

between the two groups were compared using Chi-square test. The mean of two groups were compared using student t-test.

RESULTS

Demographic data

Demographic data of all patients were compared with regards to age, height, weight, sex and ASA physical status. The p values between the two groups were not statistically significant **(Table 1).**

Table 1: Demographic data Comparison

S.No	Demographic Data	Group G (n=30)		Group P (n=30)	pValue
1	Age (years)	Mean	43.97	43.10	0.786
		S.D	12.93	11.65	
2	Height (cm)	Mean	155.87	156.30	0.748
		S.D	3.88	6.23	
3	Weight (kg)	Mean	58.27	56.57	0.202
		S.D	5.25	4.96	
4	Sex (M / F)	Number	27/3	22/8	0.095
		Percentage	90/10	73.3/26.7	
5	ASA (I / II)	Number	24/6	24/6	0.078
		Percentage	80/20	80/20	

The mean duration of surgery were found to be for Group G was 102.50 ± 14.67 and for Group P was 109 ± 17.68 min, which is not significant with the P value of 0.127. Hence there is no difference between groups with regard to duration of surgery.

All patients were monitored for VAS scores at rest and with movement by making the patients to sit in the immediate postoperative period at 0, 2, 4, 6, and 12 hours and presented in **Table 2**. This shows that the mean VAS scores at rest (0 hr) and with movement were significantly lower in Group G when compared to Group P patients.

Table 2: VAS Score at Rest and with Movement

Time Intervals (in Hrs.)	GROUP	N	Rest			Movement		
			Mean	Std. Deviation	P value	Mean	Std. Deviation	P value
0	Group G	30	1.00	0.00	n/a	1.10	0.31	0.001
	Group P	30	1.00	0.00		1.47	0.51	
2	Group G	30	3.67	0.88	<0.0001	4.93	0.98	0.006
	Group P	30	4.63	1.10		5.67	1.03	
4	Group G	30	3.13	0.43	<0.0001	4.20	0.48	<0.0001
	Group P	30	3.73	0.69		4.83	0.70	
6	Group G	30	2.90	0.55	<0.0001	3.96	0.61	<0.0001
	Group P	30	3.60	0.77		4.71	0.74	
12	Group G	30	2.27	0.52	<0.0001	3.27	0.52	<0.0001
	Group P	30	3.27	0.52		4.30	0.53	

Postoperatively all patients were monitored for VAS scores periodically. When the VAS score at rest is 4 or greater, patients were given Tramadol 2 mg/kg intravenously as initial dose and subsequently given at a dose of 1 mg/kg or on patients demand. Care was taken not to exceed the limit of Tramadol 250 mg/day and 600 mg/day. So the time interval between providing spinal anaesthesia and administration of first dose of Tramadol (T1) and the total dosage of Tramadol required for each patient during postoperative period upto 24 h was calculated and presented in **Table 3**. The result showed that T1 score is significantly greater in Group G compared to Group P whereas, the total Tramadol consumption was significantly lower in Group G patients comparable to Group P.

Table 3: T1 Score and Tramadol Dose

GROUPS	N	T1 Score (min)			Tramadol Dose mg/kg		
		Mean	Std. Deviation	P value	Mean	Std. Deviation	P value
Group G	30	183.00	19.81	0.013	221.33	40.32	<0.0001
Group P	30	172.33	11.50		289.00	21.31	

Level of Sedation

Patients in the study groups who received intravenous gabapentin were noted to be more sedated as compared to the placebo group. The Ramsay sedation score was recorded at different time intervals from 0 h to 12 h and observed the mean sedation scores of postoperative period were between 2.20±0.41 h to 2.93±0.25 h for Group G and between 2.00±0.00 h to 2.27±0.45 h for Group P patients.

Adverse Effects

During the postoperative period, all the patients were monitored for complications periodically. Nausea, vomiting and dizziness were noted in the ratio of 3:4, 2:2 and 1:0 in Group G and Group P patients respectively. This shows that there is no significant difference in the incidence of side effects between both groups.

DISCUSSION

The study was undertaken to assess the safety and efficacy of preoperative single oral dose of gabapentin for postoperative benefit in patients undergoing abdominal hysterectomy under spinal anaesthesia. Gabapentin dosage of 300 mg[5,6] was selected for this study because of its oral bioavailability is 60% and decreases with increasing dosage. The results of the study shows that gabapentin 300 mg given 2 h before surgery significantly reduces postoperative pain scores, analgesic requirement, prolongs the time for requirement of first analgesic dose without increasing the incidence of side effects except for sedation.

In a study by Elina et al.,[7] it was found that one dose of gabapentin ranging from 300 – 1200 mg when given preoperatively reduces opioid consumption by 20 – 60 %. They also found that the dose of gabapentin used did not have any effect on opioid consumption. In this study, during the postoperative period it was found that the VAS scores at rest and movement were significantly less (P Value <0.05) in gabapentin group compared to placebo group at 0, 2, 4, 6, and 12 hours.

Dirks et al.,[8]concluded that the patients undergoing mastectomy, gabapentin was found to reduce the pain scores with movement but not at rest and at the same study. Turan et al.,[9] in patients undergoing abdominal hysterectomy, gabapentin produced a significantly lower VAS scores both during rest and movement at 1, 4, 8, 12, 16, 20 and 24 hours. Gee et al.,[10] was found gabapentin mediated by its binding to $\alpha 2\delta$ subunit of voltage gated calcium channels in dorsal horn of spinal cord, which are upregulated during noxious stimuli. Later the study conducted by Hurley et al.,[11] binding of gabapentin to calcium channel results in reduced calcium influx thereby reducing release of excitatory aminoacids involved in nociception. As similar to Al-mujadi et al.,[12], Turan et al.,[9] and Pandey et al.,[5] in our study also the requirement of Tramadol in 24 h period was found to be lower 221.33 mg in Group G (gabapentin) when compared to Group P (289.00 mg).

According to the study conducted by McLean et al.,[13], Dirks et al.,[8] and Pandey et al.,[5] the use of gabapentin is associated with side effects like nausea, vomiting, sedation, dizziness, confusion, headache, ataxia and weight gain were found to be similar in both placebo and gabapentin groups. In this study the incidence of side effects like nausea and vomiting was less in both placebo and gabapentin group and also there was no statistically significant difference between them. As like the study by Pandey et al.,[5] the sedation scores in this study at 0 , 2 ,4 , 6 and 12 h were higher in Group G when compared to Group P .

CONCLUSION

This study demonstrates that a single oral dose of gabapentin 300 mg when given preoperatively reduces the postoperative pain scores and total Ttramadol consumption in patients undergoing abdominal hysterectomy under spinal anaesthesia. The incidence of other side effects like nausea, vomiting, dizziness was found to be less in both the groups. Thus the gabapentin can be considered as an adjunct in treating postoperative pain and the finest armamentarium of anesthesiologist which can be used as a part of multimodal therapy.

REFERENCES

1. Mao J, Chen LL. Gabapentin in pain management. Anesth Analg 2000;91:680-7.
2. Gilron I. Review article: The role of anticonvulsant drugs in postoperative pain management: A bench-to-bedside perspective. Can J Anaesth 2006;53:562-71.
3. Hurley RW, Cohen SP, Williams KA, Rowlingson AJ, Wu CL. The analgesic effects of perioperative Gabapentin on postoperative pain: A meta-analysis. Reg Anesth Pain Med 2006;31:237-47.
4. Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedation with alphaxalone-alphadolone. Br Med J. 1974 22; 2(5920): 656-9.
5. Pandey CK, Shio P, Surendra S, Uttam S, Ram BS, Prabhat KS, Pre-emptive use of gabapentin significantly decreases postoperative pain and rescue analgesic requirements in laparoscopic cholecystectomy, Can J Anesth 2004; 51(4): 358–63.
6. Panah KM, Yaghooti AA, Marashi SH, Nadjafi A. Effect of pre-emptive gabapentin on postoperative pain following lower extremity orthopaedic surgery under spinal anaesthesia. Singapore Med J 2011; 52(12):879-82.
7. Elina MT, Katri H, Vesa KK, Eija K. Do Surgical Patients Benefit from Perioperative Gabapentin/Pregabalin? A Systematic Review of Efficacy and Safety. Anesthesia & Analgesia 2007; 104 (6):1545-56.
8. Dirks J , Fredensborg BB , Christensen D , Fomsgaard JS , Flyger H , Dahl JB. A randomized study of the effects of single-dose gabapentin versus placebo on postoperative pain and morphine consumption after mastectomy. Anesthesiology 2002: 97(3):560-64
9. Turan A, Karamanlioğlu B, Memiş D, Usar P, Pamukçu Z, Türe M. The analgesic effects of gabapentin after total abdominal hysterectomy. Anesth Analg. 2004; 98(5):1370-3.
10. Gee NS, Brown JP, Dissanayake VU, Offord J, Thurlow R, Woodruff GN. The novel anticonvulsant drug, gabapentin (Neurontin), binds to the alpha2delta subunit of a calcium channel. J Biol Chem 1996; 271(10):5768-76.
11. Hurley RW, Chatterjea D, Rose Feng M, Taylor CP, Hammond DL. Gabapentin and pregabalin can interact synergistically with naproxen to produce antihyperalgesia. Anesthesiology 2002;97 (5):1263-73.
12. Al-Mujadi H, A-Refai AR, Katzarov MG, Dehrab NA, Batra YK, Al-Qattan AR. Pre-emptive gabapentin reduces postoperative pain and opioid demand following thyroid surgery. Can J Anesth 2006; 53:268-73.
13. McLean MJ, Morrell MJ, Willmore LJ, Privitera MD, Faught RE, Holmes GL, Magnus-Miller L, Bernstein P, Rose-Legatt A. Safety and tolerability of gabapentin as adjunctive therapy in a large, multicenter study. Epilepsia 1999;40(7):965-72.