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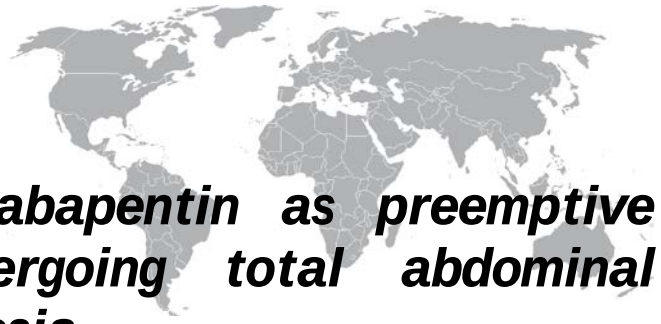
Original Article



To evaluate the role of Gabapentin as preemptive analgesic in patients undergoing total abdominal hysterectomy in spinal anesthesia

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ABSTRACT

Background. Preemptive analgesia is an antinociceptive treatment that prevents establishment of altered processing of afferent input. Gabapentin, a structural analogue of gamma-amino butyric acid, has been used as an anticonvulsant and antinociceptive drug and is claimed to be more effective in preventing neuropathic component of acute nociceptive pain of surgery.

Methods Fifty patients of ASA grade I and II were assigned to receive oral 600mg Gabapentin or Placebo 2 hours before surgery. Surgeries were conducted under spinal anesthesia. Post operatively pain was assessed by visual analogue score (VAS) at 2, 4, 8, 12 and 24 hrs. Patients were given rescue analgesic on demand. Sedation score and total numbers of analgesics during first 24 hours postoperatively were noted.

Results. Gabapentin group resulted in faster onset of motor and sensory block, significantly longer duration of analgesia, substantial reduction in post-operative pain and the rescue analgesics. Patients remained in sleeping but co- operative state and Gabapentin group were not associated with side effects when compared with placebo group.

Conclusions. Preemptive use of Gabapentin 600mg orally significantly prolongs the analgesia with reducing postoperative pain and rescue analgesics in patients undergoing total abdominal hysterectomy under spinal anesthesia.

Keywords: abdominal surgery, gabapentin, pre-emptive analgesia, post-operative analgesia

INTRODUCTION

Preemptive analgesia is defined as an antinociceptive treatment that prevents the establishment of altered central processing of afferent input, which amplifies postoperative pain (1). By decreasing the altered central sensory processing, preemptive analgesia is thought to consequently decrease the incidence of hyperalgesia and allodynia after surgery (2). Gabapentin has demonstrated analgesic effects in clinical trials as a pre-emptive analgesic and in acute postoperative pain management; however, experience with gabapentin is limited (3, 4).

Postoperative pain affects recovery from surgery and anesthesia. The use of opioids by patient-controlled analgesia (PCA) is popular but limited by side effects and by the fact that certain types of pain respond poorly to opioids (5). Because of the multiplicity of mechanisms involved in postoperative pain, a multimodal analgesia regimen, with a combination of opioid and non-opioid analgesic drugs is often used to enhance analgesic efficacy and reduce opioid requirements and side effects (6).

Gabapentin is an anticonvulsant, structurally related to gamma aminobutyric acid. Experimental models of neuropathic pain and inflammatory hyperalgesia demonstrate that gabapentin has an effective antinociceptive or antihyperalgesic action, in addition to be an anticonvulsant (1). Gabapentin has been demonstrated to act within the spinal cord or brain to reduce sensitization of dorsal horn neurons (7).

Gabapentin and pregabalin both have been used in the treatment of neuropathic pain as well as post-operative pain with good results (8). Gabapentin and morphine have synergistic analgesic effects in animals and in humans (9-11). In a recent study, a single dose of oral gabapentin reduced postoperative morphine consumption and movement-related pain after radical mastectomy (12). Numerous studies showed that opioids when used as an adjunct in spinal anesthesia has a contributing action in the onset of sensory and motor block. Therefore, we designed the present study to evaluate the role of single dose of 600 mg of Gabapentin as pre-emptive analgesia in patients undergoing total abdominal Hysterectomy in Spinal anesthesia and to study the effect of Gabapentin on onset of sensory and motor block.

METHODOLOGY

After obtaining the approval of the Institutional Ethics Committee, written informed consent was obtained from the patients. 50 patients of ASA physical status I-II in age group 18-65 years undergoing elective total abdominal hysterectomy under Spinal Anesthesia whose anticipated duration of surgery was less than 4 hours, were included for the study. Patients with contraindications to spinal anesthesia or major neurological, cardiovascular, metabolic, respiratory, renal disease or coagulation abnormalities were excluded.

The study design was randomized and double blind. Patients were randomly allocated into 2 equal groups of 25 each with the help of a computer-generated table of random numbers and later then both the groups were compared with the parameters obtained i.e. age, weight, height, body mass index. In the preoperative room all study medications were given orally with sips of water 2 hours preoperatively by Anesthesia technician who was not involved in the study and the concept of a visual

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Table 1: *Visual Analogue Score*

Score	Criteria
0	No pain
1,2,3	Mild pain
4,5,6	Moderate pain
7,8,9	Severe pain
10	Worst imagining pain

Table 2: *Ramsay sedation Score*

Score	Description
0	Awake and anxious
1	Awake and calm
2	Awake and co- operative
3	Sleeping but co- operative
4	Deep sedation, but quick reaction to pain stimuli
5	Deep sedation, but slow reaction to pain stimuli
6	Deep sedation, but no reaction to painful stimuli

Table 3: *Bromage Scale*

Score	Description
1	Complete block (unable to move feet / knees)
2	Almost Complete block (able to move feet only)
3	Partial block (just able to move knees)
4	Detectable weakness of hip flexion while supine (full flexion of knees)
5	No detectable weakness of hip flexion while supine
6	Able to perform partial knee bend

analog scale (VAS) (Table 1) was introduced. Patients in study Group received tablet Gabapentin 600mg, whereas in placebo group patients received matching placebo tablet.

In the operating room, a crystalloid infusion was started through an IV cannula. Mean arterial blood pressure, heart rate (HR), and peripheral oxygen saturation (SpO_2) were monitored and Ramsay sedation score (Table 2) was noted no other premedication was given.

All patients were preloaded with 15 ml.kg-1 of lactated Ringers' solution and spinal anesthesia was given at interspace L2-L3 or L3-L4 in left lateral position with 3.5 ml of hyper baric solution of 0.5 % bupivacaine. After confirmation of the successful blockade, sedation score was noted.

When the patient was placed in the supine position, the level of sensory block was assessed and recorded as loss of sensation to pin prick, checking in a caudal to cephalic direction. Mean time for sensory blockade onset, to achieve T_{10} and T_6 level was noted. Motor block was recorded according to the Bromage scale (Table 3).

In post-operative period pain assessment was carried out by VAS (Table 1) and duration of motor block was assessed by Bromage scale. Intramuscular diclofenac (75 mg) was given in the gluteal region as a rescue analgesic on demand and at that time, VAS score was recorded. Duration of effective analgesia was measured as time from the time to shift after completion of surgery as 1st request for analgesic either in the recovery room or in ward. Patient was kept under observation or a total period of 24 hours to observe for the total number of doses of analgesic required and any side-effects.

Statistical Analysis

Sample size was decided in consultation with statistician. Twenty-five was the smallest number in each group, where any results could be statistically significant hence this number was selected. Two sample paired T-Test was used to find out significance between two samples. Data was reported as mean±SD. A *P*-value of < 0.05 was considered statistically significant.

RESULTS

Both the groups were comparable with respect to age, gender, weight, height, body mass index (Table 4), ASA status, type of surgery and duration of surgery (Table 5).

The mean time of onset of Motor block was 126.6 ± 11.5 seconds, 31.28 ± 3.64 seconds in placebo and Gabapentin group and to attain sensory level T_{10} 195.8 ± 19.65 sec and 86.76 ± 4.33 sec and for T_6 level 206.96 ± 19.65 and 101.76 ± 3.67 seconds in placebo group and Gabapentin group respectively which was highly significant as shown in Table 5.

Table 4: *Demographic Data*

	Gabapentin group	Placebo Group	P value
Mean age	42.88 ± 7.98	45.76 ± 9.37	>0.05
Mean wt (Kgs)	52.90 ± 6.65	53.96 ± 6.18	>0.05
Mean Ht (mts)	1.58 ±0.0728	1.58 ± 0.070	>0.05
Mean BMI (kg/m2)	21.21 ± 2.78	21.67 ± 3.5	>0.05

Table 5: *Characteristics of sensory and motor block*

		Gabapentin group	Placebo group	P value
Motor block (seconds)		31.28 ± 3.64	126.6 ± 11.5	<0.001
Sensory Block (seconds)	T_{10} level	86.76 ± 4.33	195.8 ±19.65	<0.001
	T_6 level	101. 76 ±3.67	206.96 ± 19.65	<0.001
Duration of surgery (min)		148.84 ± 15.26	148.84 ± 15.26	>0.05
Total duration of analgesia after surgery was over (1st rescue analgesic) (hours)		6.16 ± 0.71	2.16 ± 0.23	<0.001

Table 6: *Total no. of rescue analgesics given within 24 hours*

No. of doses	Gabapentin group n= 25		Placebo group n=25		P value
	No. of patients	%	No. of patients	%	
3	19	76	2	8	<0.001
4	5	20	6	24	
5	1	4	16	64	
Vas score at 1st rescue analgesic	2.3 ± 0.42		3.1 ± 0.71		<0.05
Mean no. of doses in 1st 24 hours	3.28 ± 0.54		4.6 ± 0.65		<0.001

Table 7: *Ramsay sedation score*

Scores	Gabapentin group	Placebo group	P value
Pre-induction hours	3.1 ± 0.49	1	<0.001
0	3	1	
1	3.4 ± 0.5	1.8 ± 0.22	
3	3.4 ± 0.25	1.4 ±0.41	
6	3.2 ± 0.43	1	
9	3.2 ± 0.33	1	

Table 8: *Side effects*

	Placebo group n=25		Gabapentin group n=25		P value
Hypotension	0		2	8%	>0.05
Bradycardia	-		-		
Vomiting	2	8 %	1	4%	>0.05
Nausea	-		-		

The mean numbers of doses of rescue analgesia in first 24 hours in Gabapentin group and placebo group was 3.28 ± 0.54 and 4.6 ± 0.65 hours respectively. p value is <0.001 which is highly significant (Table 6).

Patients were sleeping but co-operative i.e. ramsay sedation score 3 in gabapentin group while almost all the patients were calm and cooperative in placebo group ramsay sedation score was 1 and 2 as shown in Table 7.

Both the groups were hemodynamically stable in pre, intra and postoperatively though two patients had hypotension in intraoperative period in Gabapentin group which could be managed with single dose of 6mg mephentermine intravenously and one patient in gabapentin group and 2 patients in placebo group had vomiting which was treated with single dose of tablet domperidone since it was after when the nill –by-mouth hours were cleared.

DISCUSSION

Pre-incisional analgesia has been shown to be more effective in control of postoperative pain by protecting the central nervous system from deleterious effects of noxious stimuli and resulting allodynia, and increased pain. Gabapentin have antiallodynic and antihyperalgesic properties useful for treating neuropathic pain and may also be beneficial in acute postoperative pain. Several studies have reported the usefulness of Gabapentin in perioperative settings resulting in reduced postoperative pain, postoperative analgesic

requirement, side effects, prolongation of analgesia, and higher patient satisfaction (8, 13-15).

In our study we have demonstrated that 600 mg of Gabapentin taken 2 hours before total abdominal hysterectomy surgery resulted in faster onset of motor and sensory block, longer duration of analgesia, substantial reduction in post-operative pain and the rescue analgesics and patients remained in Sleeping but co-operative state (Ramsay sedation score3) and that Gabapentin group was not associated with side effects when compared with placebo.

The pre-emptive administration of gabapentin approximately two hours before surgery appears optimal in order to attain maximal plasma concentrations at the time of surgical stimuli. In animal models of nociception, gabapentin reduces hypersensitivity associated with nerve injury, inflammation, and pain after surgery (16-18).

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 (19). It has also been demonstrated that a 600mg single dose of gabapentin enhanced the effect of morphine, but side effects appeared in approximately 40% of volunteers when these drugs were used concomitantly (10).

In another study, gabapentin was shown to reduce the requirement of fentanyl (20), tramadol (21) for postoperative pain relief in patients. It also reduced the number of postoperative epidural bolus requirement and postoperative pain in patients undergoing total abdominal hysterectomy under combined spinal epidural anesthesia (22) and it also prolonged post spinal analgesia 8.98 ± 5.38 hours in Gabapentin group whereas 14.17 ± 6.67 hours in pregabalin group (highly significant) as in study by Saraswat and Arora (23) and in other study by Bafna and Krishnamoorthy (24) post spinal analgesia was 535 ± 32.86 min in pregabalin group and 302 ± 24.26 min in gabapentin group in comparison to control group 151.83 ± 16.21 min which was again highly significant.

Gabapentin is usually well tolerated. and has few side effects and minor interactions with other drugs when used for the treatment of chronic pain (20) but we did not observe any significant side effects associated with a single oral dose of Gabapentin which are comparable with other studies (20-24).

CONCLUSIONS

Based upon the findings of this study, we suggest that single oral dose of gabapentin 600 mg is effective for early onset of sensory and motor block. It prolongs the analgesia and reduces postoperative pain and rescue analgesic requirement without altering the intraoperative hemodynamics. It also calms and sedates the patient makes them cooperative and non-anxious which can be taken as contributory factor for the post-operative recovery.

REFERENCES

1. Kissin I. Preemptive analgesia. Anesthesiology. 2000;93:1138-43.
2. Wilder-Smith OH. Pre-emptive analgesia and surgical pain. Prog Brain Res. 2000;129:505-24.
3. Chiaretti A, Viola L, Pietrini D, et al. Preemptive analgesia with tramadol and fentanyl in pediatric neurosurgery. Childs Nerv Syst. 2000;16:93-9.
4. Fassoulaki A, Patris K, Sarantopoulos C, Hogan Q. The analgesic effect of gabapentin and mexilentine after breast surgery for cancer. Anesth Analg. 2002;95:985-91.
5. Dickenson A. Neurophysiology of opioid poorly responsive pain. Cancer Surv. 1994;21:5-16.
6. Fishman S, Borsook D. Opioids in pain management. In: Benzon H, Raja S, Molloy RE, Strichartz G, eds. Essentials of pain medicine and regional anesthesia. New York: Churchill Living-stone. 1999.p.51-4.
7. Feng Y, Cui M, Willis WD. Gabapentin markedly reduces acetic acid-induced visceral nociception. Anesthesiology. 2003;98:729-33.
8. Tiippana EM, Hamunen K, Kontinen VK, Kalso E. Do surgical patients benefit from perioperative gabapentin/pregabalin? A Systematic Review of Efficacy and Safety. Anesth Analg. 2007;104:1545-56.
9. Shimoyama M, Shimoyama N, Inturrisi CE, Elliott KJ. Gabapentin enhances the antinociceptive effects of spinal morphine in the rat tail-flick test. Pain. 1997;72:375-82.
10. Eckhardt K, Ammon S, Hofman U, et al. Gabapentin enhances the analgesic effect of morphine in healthy volunteers. Anesth Analg. 2000;91:185-91.
11. Caraceni A, Zecca E, Martini C, De Conno F. Gabapentin as an adjuvant to opioid analgesia for neuropathic cancer pain. J Pain Symptom Manage. 1999;17:441-5.
12. Dirks J, Fredensborg BB, Christensen D, et al. A randomized study of the effects of single dose gabapentin versus placebo on postoperative pain and morphine consumption after mastectomy. Anesthesiology. 2002;97:560-4.
13. Rorarius MGF, Mennander S, Suominen P, Rintala S, Puura A, Pirhonen R, Salmelin R, Haanpää M, Kujansuu E and Yli-Hankala A. Gabapentin for the prevention of postoperative pain after vaginal hysterectomy. Pain. 2004;110:175-181.
14. Al-Mujadi H, A-Refai AR, Katzarov MG, Dehrab NA, Batra YK, Al-Qattan AR. Preemptive Gabapentin reduces postoperative pain and opioid demand following thyroid surgery. Canadian Journal of Anesthesia. 2006:53:268-273.
15. Turan A, Kaya G, Karamanlioglu B, Pamukcu Z, Apfel CC. Effect of oral gabapentin on postoperative epidural analgesia. British Journal of Anaesthesia. 2006;96:242-6.
16. Cheong JK, Pan HL, Eisenach JC. Antiallodynic effect of intrathecal gabapentin and its interaction with clonidine in a rat model of postoperative pain. Anesthesiology. 2000;92:1126-31.
17. Field MJ, Holloman EF, McCleary S, et al. Evaluation of gabapentin and S-(_)-3-isobutylgaba in a rat model of postoperative pain. J Pharmacol Exp Ther. 1997;282:1242-6.
18. Dirks J, Petersen KL, Rowbotham MC, Dahl JB. Gabapentin suppresses cutaneous hyperalgesia following heat/capsaicin sensitization. Anesthesiology. 2002;97:102-6.
19. Dirks J, Moiniche S, Hilsted KL, Dahl JB. Mechanisms of postoperative pain: clinical indications for a contribution of central neuronal sensitization. Anesthesiology. 2002;97:1591-6.

20. Pandey CK, Sahay S, Gupta D, Ambesh SP, Singh RB, Raza M, Singh U, Singh PK. Preemptive gabapentin decreases postoperative pain after lumbar discoidectomy. Can J Anaesth. 2004;51:986-9.
21. Turan A, Karamanlioglu B, Memis, Dilek, Usar, Pinar. The analgesic effect of Gabapentin after total abdominal hysterectomy. Anesthesia & Analgesia. May 2004;98(5):1370-1373
22. Verma A, Arya S, Sahu S, Lata I, Pandey HD, Singh H. To Evaluate the Role of Gabapentin as Preemptiv Analgesic in Patients Undergoing Total Abdominal Hysterectomy in Epidural Anaesthesia. Indian Journal of Anaesthesia. 2008;52(4):428-431.
23. Saraswat V, Arora V. To Evaluate the Role of Gabapentin as Preemptive Analgesic in Patients Undergoing Total Abdominal Hysterectomy in Epidural Anaesthesia. Indian Journal of Anaesthesia. 2008;52(6):829-834.
24. Bafna U, Rajarajeshwaran K, Khandelwal M, Verma AP. A comparison of effect of preemptive use of oral Gabapentin and pregabalin for acute post-operative pain after surgery under spinal anesthesia. Journal of Anaesthesiology Clinical Pharmacology. 2014;30(3):373-7.

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