Indian Journal of Basic and Applied Medical Research; March 2021: Vol.-10, Issue- 2, P. 81 – 86
DOI: 10.36848/IJBAMR/2020/26215.55598

Original article:

Study of post-operative analgesics required to attenuate peri-operative pain

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Abstract:

Introduction: Many types of analgesics have been used alone or in combination for postoperative pain treatment. Postoperative pain is typically regarded as a type of nociceptive pain involving peripheral mechanoreceptor stimulation, inflammatory and neurogenic and visceral mechanisms, with a transient, reversible type of neuropathic pain.

Material and methods : 120 patients3 aged between 18 years and 65 years of either gender belonging to ASA Class I or Class II posted for elective abdominal surgeries under general anaesthesia were selected for the study. After obtaining the approval of the Institutional Ethics Committee and written informed consent from the patients, 120 patients were included.

Results: In present study intra operative mean fentanyl consumption in micro gram in gabapentin group was 126±28.899 and in control group was 124.667±29.034 with p value 0.8729 ($p>0.05$) shows no significant statistical difference in both the groups.

Conclusion : The postoperative pain scores were significantly less in 24 hrs post-operatively in the gabapentin group as compared to the placebo group without causing any adverse effect.

We will also like to conclude that oral gabapentin is a safe, effective, noninvasive preemptive analgesia for pain after abdominal surgeries under general anaesthesia.

Introduction:

Many types of analgesics have been used alone or in combination for postoperative pain treatment. Postoperative pain is typically regarded as a type of nociceptive pain involving peripheral mechanoreceptor stimulation, inflammatory and neurogenic and visceral mechanisms, with a transient, reversible type of neuropathic pain.[1] Though pharmacotherapy forms an integral part of management of acute pain, one has to look at various other methodologies to relieve post-operative pain.[2]

Surgical injury can lead to chronic pain is well established. The estimated incidence of chronic pain after various procedures are; leg amputation about 60%, thoracotomy 50%, breast surgery about 30%, cholecystectomy 10-20%, and inguinal hernioplasty about 10%. Predictive risk factors for chronic postoperative pain are: preoperative pain, repeat surgery, psychological vulnerability, a surgical approach with risk of nerve damage, moderate or severe intensity of acute postoperative pain, radiation therapy and anxiety.[3,4] So it is important to tackle postoperative pain at the earliest. The rationale behind preoperative use of gabapentin is, the gabapentin has a substantial inhibitory effect on the development and establishment of allodynia and

hyperalgesia. Hence this clinical study was undertaken to know whether preoperative use of gabapentin alters, first analgesic requirement time, and has any effect on postoperative pain scores in the first 24hrs after surgery.

Material and methods

120 patients3 aged between 18 years and 65 years of either gender belonging to ASA Class I or Class II posted for elective abdominal surgeries under general anaesthesia were selected for the study. After obtaining the approval of the Institutional Ethics Committee and written informed consent from the patients, 120 patients were included. The study population were randomly divided by computer generated numbers into 2 groups with 60 patients in each group (n=60). Preanaesthetic evaluation was done a day before the surgery. Patients were taught to read the visual analogue scale a day before the surgery.

Inclusion criteria:

Adult patients of either gender, aged between 18 – 65 years, belonging to ASA Class I or II without any co-morbid diseases scheduled for elective abdominal surgeries under general anaesthesia were included in the study.

1. Patients belonging to American Society of Anesthesiologists physical status I and II
2. Patients undergoing elective surgery under general anesthesia
3. Anticipated duration of surgery less than 4 h
4. Age group between 18 and 65 years
5. Weight range up to 20% of the ideal body weight for either sex
6. Hemodynamic ally stable

Exclusion criteria

1. Patients with a history of hypertension, diabetes, and liver disease
2. Patients with known neurological disease
3. Neurosurgical and cardiovascular surgical cases
4. Pregnant patients
5. Patients with known psychiatric disorders
6. Patients with anticipated difficult airway
7. Patients on antihypertensive drugs, sedatives, hypnotics, antidepressants, and drugs with effects on the nervous system
8. Patients already taking oral gabapentin
9. Patients allergic to opioids and Tramadol

Patients in the control group received oral placebo capsules and those in the gabapentin group received 600 mg gabapentin 1 h before surgery.

In the operating room, a crystalloid infusion was started through an IV cannula. Blood pressure (MAP), pulse rate (PR), and peripheral oxygen saturation (SPO2) were monitored. Pre-operative PR and systolic Blood pressure were noted and studied in both groups.

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Table 1: INDEPENDENT T-TEST FOR COMPARISON OF MEAN VAS IN TWO GROUPS

VAS	GROUP	N	MEAN	SD	P value	SIGNIFICANCE
VAS 0h	GABAPENTIN	60	1.9	0.71	0.037	Significant
	CONTROL	60	2.3	0.70		
VAS 2h	GABAPENTIN	60	2.3	0.92	0.004	Significant
	CONTROL	60	3.0	0.72		
VAS 4h	GABAPENTIN	60	3.2	0.73	0.017	Significant
	CONTROL	60	3.7	0.75		
VAS 6h	GABAPENTIN	60	3.3	0.80	<0.001	Significant
	CONTROL	60	4.2	0.76		
VAS 12h	GABAPENTIN	60	3.7	0.71	<0.001	Significant
	CONTROL	60	4.6	0.67		
VAS 24h	GABAPENTIN	60	3.9	0.79	0.003	Significant
	CONTROL	60	4.8	0.73		

POST OPERATIVE RESCUE ANALGESIA:

In present study post operative rescue analgesia was provided with inj. tramadol 2 mg/kg IV given if patients demand and only if VAS >4.

Rescue analgesia was required in 6 cases in gabapentin group and 28 cases in control group with *p*-value 0.004. This shows significant difference between requirements of post-operative rescue analgesia in both groups.

FIRST ANALGESIC REQUIREMENT TIME:

The first analgesic requirement time in the postoperative period in the gabapentin group (7.667±3.786 hrs) was significantly more than ($p<0.05$) in the placebo group (4.462±1.45 hrs).

Table No. 2: First analgesic requirement time

GROUP	MEAN (hr)	SD	*p*-value	SIGNIFICANCE
GABAPENTIN	7.67	3.79	0.023	SIGNIFICANT
CONTROL	4.46	1.45		

PULSE RATE:

Mean basal pulse rate in gabapentin Group was 86.47 ± 14.15 per min and in control Group was 84.33 ± 14.23 per min. (*p =0.559*) Mean maximum intra-operative pulse rate in gabapentin group was 105.73 ± 12.466 per min and in control group was 106.90 ± 12.466 per min. Thus there was no statistically significant difference in mean Basal and Maximum pulse rate in both the groups. ($P > 0.05$)

Table 3: INDEPENDENT T-TEST FOR EQUALITY OF MEAN
PRE-OP PULSE RATE (per min) IN TWO STUDY GROUPS

GROUP	N	MEAN	SD	*P*-value	SIGNIFICANCE
GABAPENTIN	60	86.47	14.15	0.5599	
CONTROL	60	84.33	14.23		Not Significant

Table 4: INDEPENDENT T-TEST FOR COMPARISON OF MEAN
MAXIMUM INTRA-OP PULSE RATE (per min) IN TWO STUDY GROUPS
SYSTOLIC BP:

GROUP	N	MEAN	SD	*P*-value	SIGNIFICANCE
GABAPENTIN	60	105.73	12.46	0.7126	Not Significant

Mean basal systolic arterial pressure was 129.80 ± 9.342 mm Hg in gabapentin group and 130.13 ± 10.673 mm Hg in control group (P > 0.05). Mean maximum systolic arterial pressure was 140.53 ± 9.81 mm Hg in gabapentin group and 142.87 ± 10.11 mm Hg in control group. This difference was found to be statistically not significant (P > 0.05).

Table 5: INDEPENDENT T-TEST FOR EQUALITY OF MEAN
PRE-OP SYSTOLIC BP (mmHg) IN TWO STUDY GROUPS

GROUP	N	MEAN	SD	*P*-value	SIGNIFICANCE
GABAPENTIN	60	129.80	9.342	0.9018	
CONTROL	60	130.13	10.673		Not Significant

Table 6: INDEPENDENT T-TEST FOR COMPARISON OF MEAN
MAXIMUM INTRA-OP SYSTOLIC BP (mmHg) IN TWO STUDY GROUPS

GROUP	N	MEAN	SD	*P*-value	SIGNIFICANCE
GABAPENTIN	60	140.53	9.81	0.4472	Not Significant
CONTROL	60	142.47	10.11		

Adverse effects

Gabapentin is well tolerated with few serious adverse effects. Reviewing data from controlled clinical trials conducted prior to 1995, Ramsay[39] reported that somnolence (20%), and dizziness (18%), ataxia (13%) and fatigue (11%) were the most common side-effects. The relative safety of gabapentin is supported by case reports of massive overdoses of the drug in which serious toxicity was absent.

Discussion:

In the present study with oral gabapentin 600 mg given 1 hr prior to surgery, no adverse effects were noted in gabapentin group. In present study intra operative mean fentanyl consumption in micro gram in gabapentin group was 126±28.899 and in control group was 124.667±29.034 with p value 0.8729 (p>0.05) shows no significant statistical difference in both the groups. Similar results were found in study conducted by Parikh et al.[5] (2010) mean fentanyl consumption intra operatively in gabapentin group was 146.3±32.3 and in control group was 148.3±28.7(p>0.054) showing statistically insignificant difference in both groups.

In randomized double blind placebo controlled study conducted by Grover et al.[6] (2009) on women undergoing total mastectomy with axillary dissection under GA, similar results were observed. Patients received 600 mg gabapentin pre operatively. Intra operative analgesia was given in the form of morphine 0.1 mg /kg IV. Any hypertension or tachycardia (>25%of baseline) was treated with morphine 0.05 mg /kg IV. Intra operative morphine consumption was similar in both the groups. Pandey et al.[7] (2005) conducted a similar study where total fentanyl consumption both intra and post operatively up to 24 hrs were studied. Mean fentanyl consumption in gabapentin group was 563±252 micro gm and in that for control group was 924.7±417.5 with p value<0.05. Significant difference was observed in total analgesic consumption.

In present study post operative rescue analgesia was provided with inj. tramadol 2 mg/kg IV given if patients demand and only if VAS >4. Rescue analgesia was required in 6 cases in gabapentin group and 28 cases in control group with *p*-value 0.004. This shows significant difference between requirements of post-operative rescue analgesia in both groups. In study conducted by Parikh et al.[5] (2010) similar results were found. Rescue analgesia was provided with inj. diclofenac 1.5 mg/kg IV slowly. Numbers of patients requiring rescue analgesia were 3 in gabapentin group as compared to 14 in control group with p value 0.004 which shows significant difference between requirements of post operative rescue analgesia in both groups.

In study conducted by Behdad et al[8] (2012), post operative rescue analgesia was provided with morphine. Study showed significant difference between numbers of patients requiring rescue analgesia with inj. morphine in both groups at 1 hr post operatively. However there was no significant difference in number of patients requiring post operative rescue analgesia with inj. morphine in both groups at 6, 12 and 24 hrs.

Khan et al.[8] (2013) studied post operative analgesia with oral pre medication gabapentin 1200 mg 2 hr prior to surgery in patients undergoing abdominal hysterectomy. Post-operative rescue analgesia was provided with inj. Nalbuphine. Mean post operative nalbuphine consumption (mg) was 13.21±4.708 and that in control group was 24.31±9.276 with *p*-value <0.001 showing significant difference in post operative rescue analgesia requirement in both groups. The mean time for first analgesic requirement in the postoperative period in the gabapentin group was 7.667±3.786 hrs. And that for control group was 4.462±1.45 hrs. This shows that the mean time for first dose of rescue analgesic in post operative period for gabapentin group was significantly more than (p<0.05) in the placebo group. Grover et al.[6] (2009) conducted double blind placebo controlled study on 50 women undergoing total mastectomy with axillary dissection under GA. Gabapentin group received 600mg oral gabapentin while control group received oral placebo capsules 1 hr before surgery

Time of First dose of rescue analgesia required was significantly longer in gabapentin group than in control group. (p<0.001) Similar results were observed by Behdad et al.[40] (2012)

Gabapentin is well tolerated with few serious adverse effects. Reviewing data from controlled clinical trials conducted prior to 1995, Ramsay[39] reported that somnolence (20%), and dizziness (18%), ataxia (13%) and fatigue (11%) were the most common side-effects. The relative safety of gabapentin is supported by case reports of massive overdoses of the drug in which serious toxicity was absent. In present study with oral gabapentin 600 mg given 1 hr prior to surgery, no adverse effects were noted in gabapentin group.

Conclusion:

The postoperative pain scores were significantly less in 24 hrs post-operatively in the gabapentin group as compared to the placebo group without causing any adverse effect.

We will also like to conclude that oral gabapentin is a safe, effective, noninvasive preemptive analgesia for pain after abdominal surgeries under general anaesthesia.

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Date of Publishing: 05 March 2021
Author Declaration: Source of support: Nil, Conflict of interest: Nil
Ethics Committee Approval obtained for this study? YES
Was informed consent obtained from the subjects involved in the study? YES
For any images presented appropriate consent has been obtained from the subjects: YES
Plagiarism Checked: Urkund Software

DOI: 10.36848/IJBAMR/2020/26215.55598