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Original article:

Study of intra operative haemodynamic stability of oral gabapentin to attenuate peri-operative pain

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Abstract:

Introduction: Pain has been a major concern of mankind since time immemorial and it has been the subject of ubiquitous efforts to understand and treat it.The postoperative period is an integral part of the surgical experience of a patient.

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: Mean VAS taken post-operatively at 12 hr for gabapentin group was 3.667± 0.711 while that for control group was 4.633±0.669. t value was 5.124. Degree of freedom was 58 and *p*-value <0.001. ($p<0.05$) Thus there was significant difference between mean VAS at 12 hr in both study groups.

Conclusion: Based on the results obtained from our study we conclude that, the preoperative administration of 600 mg of oral gabapentin an hour before the surgery significantly ($p<0.0001$) decreases patients requirement for rescue analgesic compared with placebo.

Introduction:

Pain has been a major concern of mankind since time immemorial and it has been the subject of ubiquitous efforts to understand and treat it.The postoperative period is an integral part of the surgical experience of a patient. If the surgery is an injury, then allowing the patient to suffer postoperative pain is like adding insult to injury. Postoperative pain affects recovery from anaesthesia and surgery.[1] Peripheral tissue injury provokes peripheral sensitization (a reduction in the threshold of nociceptor afferent peripheral terminals) and central sensitization (an activity dependent increase in excitability of spinal neurons.[2,3]) These changes contribute to the post injury pain hypersensitivity state which manifests as an increase in the responsiveness to noxious stimuli and a decrease in the pain threshold, both at the site of injury and in the surrounding uninjured tissue.[2,3] The preemptive treatment could be directed at the periphery, at inputs along sensory axons, and at central neurons. Different treatment regimens could be used at different times relative to surgery to maximize the prevention of pain in response to different levels of sensory inputs.[2,3]

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.

Results:

120 patients 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. Following peri-operative parameters were studied.

Age of the patients was between 18 to 65 years. The mean age of the patients in Gabapentin Group was 44.20 ± 14.35 years and in Control Group was 44.07 ± 14.59 years which was statistically not significant. ($P > 0.05$)

Patients in both groups were comparable on the basis of type of surgery. 14 patients in Gabapentin group were posted for cholecystectomy while 12 patients in control group were posted for cholecystectomy (laparoscopic / open). 20 patients in Gabapentin group were posted for appendicectomy while 22 patients in

control group were posted for appendicectomy (laparoscopic / open). 14 patients in Gabapentin group were posted for renal surgeries while 16 patients in control group were posted for renal surgeries (nephrectomy / nephrolithotomy / pyelolithotomy). 12 patients in Gabapentin group and 10 patients of control group were posted for other gastrointestinal (GI) surgeries (feeding gastrostomy / jejunostomy).

Table1: COMPARISON OF TYPE OF SURGERIES IN BOTH GROUPS

TYPE OF SURGERY	GABAPENTIN GROUP	CONTROL GROUP
CHOLECYSTECTOMY	14(23.33%)	12(20%)
APPENDICECTOMY	20(33.33%)	22(36.66%)
RENAL SURGERIES	14(23.33%)	16(26.66%)
OTHER G.I. SURGERIES	12(20%)	10(16.66%)
TOTAL	60	60

MEAN DOSE OF INTRA-OP INJ. FENTANYL:

Fentanyl 2µg/kg was administered intravenously for pre-medication. Surgeries lasting for more than 1 h were given a repeat dose of fentanyl 1µg/kg at the end of the first hour of induction. Any increase in the pulse rate and MAP when not settling down by deepening the plain of anesthesia was given fentanyl 0.05 µg/kg subsequently. Intra-operative fentanyl requirement in both the groups were studied. The mean Intra-operative fentanyl requirement in gabapentin group was 165.50 ± 26.04 µg and in control Group was 176.67± 27.96 µg. Hence Groups were comparable. Difference was statistically insignificant. (P > 0.05)

Table 2: INDEPENDENT t-TEST FOR COMPARISON OF MEAN DOSE OF INTRA-OP INJ. FENTANYL (µg) IN TWO GROUPS

GROUP	N	MEAN	SD	*P*-value	SIGNIFICANCE
GABAPENTIN	60	165.50	26.04	0.1122	Not Significant
CONTROL	60	176.67	27.96		

MEAN VAS TAKEN AT 0 Hr

Mean VAS taken immediate post-operatively in PACU at 0 hr for gabapentin group was 1.9± 0.712 while that for control group was 2.3±0.702. t value was 2.183. Degree of freedom was 58 and *p* value was 0.0372. ($p<0.05$) Thus there was significant difference between mean VAS at 0 hr in both study groups.

Table 3: INDEPENDENT T-TEST FOR COMPARISON OF MEAN VAS AT 0h IN TWO GROUPS

MEAN VAS TAKEN AT 2 Hr

GROUP	N	MEAN	SD	*P*-value	SIGNIFICANCE
GABAPENTIN	60	1.9	0.712	0.0372	Significant

Mean VAS taken post-operatively at 2 hr for gabapentin group was 2.333 ± 0.922 while that for control group was 2.967±0.718. t value was 3.159. Degree of freedom was 58 and *p* value was 0.0037. ($p<0.05$) Thus there was significant difference between mean VAS at 2 hr in both study groups.

Table 4: INDEPENDENT T-TEST FOR COMPARISON OF MEAN VAS AT 2h IN TWO GROUPS

MEAN VAS TAKEN AT 4 Hr

GROUP	N	MEAN	SD	*P*-value	SIGNIFICANCE
GABAPENTIN	60	2.3	0.922	0.0037	Significant
CONTROL	60	3.0	0.718		

Mean VAS taken post-operatively at 4 hr for gabapentin group was 3.233 ± 0.728 while that for control group was 3.70±0.750. t value was 2.54. Degree of freedom was 58 and *p*-value was 0.0169. ($p<0.05$) Thus there was significant difference between mean VAS at 4 hr in both study groups.

Table 5: INDEPENDENT T-TEST FOR COMPARISON OF MEAN VAS AT 4h IN TWO GROUPS

GROUP	N	MEAN	SD	*P*-value	SIGNIFICANCE
GABAPENTIN	60	3.2	0.728	0.0169	
CONTROL	60	3.7	0.750		Significant

MEAN VAS TAKEN AT 6 Hr

Mean VAS taken post-operatively at 6 hr for gabapentin group was 3.333± 0.802 while that for control group was 4.2±0.761. t value was 7.345. Degree of freedom was 58 and *p*-value <0.001. ($p<0.05$) Thus there was significant difference between mean VAS at 6 hr in both study groups.

Table 6: INDEPENDENT T-TEST FOR COMPARISON OF MEAN VAS AT 6h IN TWO GROUPS

GROUP	N	MEAN	SD	*P*-value	SIGNIFICANCE
GABAPENTIN	60	3.3	0.802	<0.001	Significant

MEAN VAS TAKEN AT 12 hr

Mean VAS taken post-operatively at 12 hr for gabapentin group was 3.667± 0.711 while that for control group was 4.633±0.669. t value was 5.124. Degree of freedom was 58 and *p*-value <0.001. ($p<0.05$) Thus there was significant difference between mean VAS at 12 hr in both study groups.

Table 7: INDEPENDENT T-TEST FOR COMPARISON OF MEAN VAS AT 12h IN TWO GROUPS

MEAN VAS TAKEN AT 24 Hr

GROUP	N	MEAN	SD	*P*-value	SIGNIFICANCE
GABAPENTIN	60	3.7	0.711	<0.001	Significant

Mean VAS taken post-operatively at 24 hr for gabapentin group was 3.933± 0.785 while that for control group was 4.767±0.728. t value was 4.087. Degree of freedom was 58 and *p*-value was 0.003. ($p<0.05$) Thus there was significant difference between mean VAS at 24 hr in both study groups.

Table 8: INDEPENDENT T-TEST FOR COMPARISON OF MEAN VAS AT 24h IN TWO GROUPS

GROUP	N	MEAN	SD	*P*-value	SIGNIFICANCE
GABAPENTIN	60	3.9	0.785	0.003	Significant
CONTROL	60	4.8	0.728		

Discussion:

Postoperative pain which is very unpleasant and physiologically stressful is very common problem in postoperative period.Today, the knowledge on mechanism of production of acute pain has advanced sufficiently over the past decade. So that rational rather than empirically derived therapy can be used by aiming specifically at interrupting the mechanism responsible for the generation of clinical pain. This concept is more relevant in the management of surgical pain than in any other scenario.[4]

Pain in the postoperative period does not bear a direct relationship with the surgical injury. Due to peripheral and central hypersensitivity or the wind up phenomenon post operative pain is always more severe for any surgical injury. Any therapeutic regimen that will prevent or modulate this sensitization should be helpful in the effective management of postoperative pain. Preemptive analgesia is one such intervention. The underlying principle would be that therapeutic intervention is made in advance of pain rather than in reaction to it. Numerous antihyperalgesic methods and drugs have been evaluated in order to reduce the central neuronal hyperexcitability which theoretically, may amplify postoperative pain.[5]Although gabapentin has been used in the treatment of neuropathic pain syndromes, it has also demonstrated potent antihyperalgesic properties in preclinical and clinical studies, without affecting acute nociception.[6,7,8]

Mean VAS taken immediate post-operatively in PACU at 0 hr in present study for gabapentin group was 1.9 ± 0.712 while that for control group was 2.3 ± 0.702. t value was 2.183. Degree of freedom was 29 and *p* value was 0.0372 which is less than 0.05. This shows significant difference between mean VAS at 0 hr in both study groups. In placebo controlled study conducted by in Parikh et al.[8] (2010) similar results were found when oral gabapentin 600 mg was administered 1hr prior to patients undergoing elective abdominal surgeries under GA. Mean VAS at 0 hr in gabapentin group was 1.9 ± 0.7 and control 2.3 ± 0.4 with *p* value 0.02 showing significant difference between mean VAS at 0 hr in both groups. Khan et al.[9] (2013) used gabapentin 1200mg

1 hr pre-operatively to study post operative analgesia in patients of abdominal hysterectomy under GA against placebo. Mean VAS at 0 hr for gabapentin group was 4.79 ± 1.388 and for control group was 8.03 ± 0.848 with *p*- value 0.000 showing significant difference between mean VAS at 0 hr in both groups. (Table 19)

Conclusion

Based on the results obtained from our study we conclude that, the preoperative administration of 600 mg of oral gabapentin an hour before the surgery significantly ($p<0.0001$) decreases patients requirement for rescue analgesic compared with placebo.

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