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Effect of Oral Gabapentin used as Preemptive Analgesia to Attenuate Post Operative Pain in Patients undergoing Maxillofacial Surgeries

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ABSTRACT

Background: Gabapentin was used as an anticonvulsant drug but has now shown to have analgesic effects. Some patients develop chronic postsurgical pain, which lasts for months and there are no other causes to which the pain can be attributed. Therefore, pain control in post-op patients is of critical importance and multimodal analgesic practices are gaining trend. **Objective:** To determine the effect of oral gabapentin given pre-operatively on post-operative pain in patients undergoing maxillofacial surgeries. **Study Design:** Randomized controlled trial. **Settings:** Department of Anesthesia, Ayub Teaching Hospital, Abbottabad Pakistan. **Duration:** Six months from January 2019 to June 2019. **Methods:** All the patients aged 20 to 70 years who were categorized as physical status I or II according to the American Society of Anesthesiologists (ASA), and were scheduled to have maxillofacial procedures that were expected to last between 120 and 180 minutes were included. Participants were divided into 2 different groups randomly: Group A received gabapentin 600 mg and Group B received placebo two hours preoperatively. The pain score was noted at 0, 2, 6, and 12 hours and patient satisfaction was observed at 24 hours post-operatively. Data collection was done by using a study proforma and analysis was done by using SPSS version 26. **Results:** Patients in Group A (Gabapentin group) had statistically significant results (p-value <0.05) at 0, 2, 6 and 24 hours for post-operative analgesia. Patient satisfaction was found in 90.0% of patients of gabapentin group as compared to placebo group. **Conclusion:** Single oral dose of gabapentin given preoperatively was observed to be the effective for post operative analgesia and decreased rescue analgesia consumption.

Keywords: Gabapentin, Maxillofacial surgery, Pain scores, Patient satisfaction.

INTRODUCTION

Gabapentin was initially introduced as an anticonvulsant drug but is now shown to have anti hyperalgesic effects. It is a Gamma-aminobutyric acid (GABA) analogue but does not operate by acting on GABA receptors in any excitatory or inhibitory manner.[1] For pain modulation, it works on the L-type calcium channel in the spinal cord and the dorsal root ganglions. The targets are "alpha; delta subunits" of the dorsal horn neurons leading to decreased neurotransmitter release because of unavailability of calcium. In addition to its central effects, it also works on peripheral neurons. It inhibits the excitation of C-fibres to stimuli, which decreases pain sensation, via voltage gated calcium channels and blocking N-methyl D-aspartate receptors and a-amino methyl propionic acid. Surgical trauma causes release of chemical signals in the form of cytokines and bradykinin which increase the sensation of pain. Post-operative pain has high prevalence and the mainstay of analgesia are opioids, though some non-steroidal anti-inflammatory drugs are also used. But due to the wide array of side effects as; respiratory depression, somnolence, hypotension, nausea and vomiting, bradycardia, constipation and pruritus, multimodal drugs are used to attain synergy and decrease the dose of

opioids required. Gabapentin is one of the drugs used for such purposes.[1,2]

The effects of gabapentin are diverse including the side effects. Most common side effect is dizziness. Others include fatigue, somnolence and ataxia, which are potentially troublesome in elderly and those with gait abnormalities. It has yielded curative results in treating post-poliomyelitis.[3] Gabapentin 600 mg an hour before anesthesia for thyroid surgery has been evaluated by Lee *et al*. with significant decrease in visual analogue scale (VAS) for pain and incidence of post-op sore throat at 6 and 24 hours after surgery.[4]

From a meta-analysis of 133 randomized controlled trials done by Doleman B *et al*. showed that there was statistically significant reduction in post-op pain and analgesics requirement in the first 24 hours after the use of gabapentin before anesthesia.[3] They also concluded that the dose requirement was less in general anesthesia when compared to spinal anesthesia. It was also reported that the analgesia was directly related to the dose of opioid use in the control group. Decreased pruritis, less patient anxiety and increased patient satisfaction have also been recorded. The maximum and median effective dose for analgesia have been shown to be 600 or 900mg and 1500mg respectively and the same effects have been recorded in those to whom the drug was given post-operatively. The sedative side effect of gabapentin may benefit some patients if it is administered pre-operatively.[3,4]

In United States of America about 51.4 million surgeries are performed annually. Of these patients, around 75% experience post-op pain which decreases their quality of life and increases morbidity. Some patients develop chronic postsurgical pain, which lasts for as long as two months and there are no other causes to which the pain can be attributed. Therefore, pain control in post-op patients is of critical importance and multimodal analgesic practices are gaining trend. Another meta-analysis presented the fact that there was no heterogeneity and no publication bias in the data that gabapentin effectively reduced post-op pain and the dose of opioid required for different surgeries. Most of the surgeries in which gabapentin had been studied were elective.[5-7]

In addition to this, it has been shown to be useful in the treatment of the post-herpatic neuralgia, neuropathic pain, diabetic neuropathy and reflex sympathetic dystrophy. The goal behind conducting this study was to find out the impact that oral gabapentin administered prior to maxillofacial surgery has on the level of post-operative pain among patients undergoing maxillofacial surgical procedures.[8-11]

METHODS

This randomized double blinded study was conducted at Department of Anesthesia, Ayub Teaching Hospital, Abbottabad Pakistan over a period of six months from January 2019 to June 2019.

After taking the ethical committee approval, a total of 60 cases aged between 20 to 70 years of either gender, who were categorized as physical status I or II according to the American Society of Anesthesiologists (ASA), and were scheduled to have maxillofacial procedures that were expected to last between 120 and 180 minutes were included.

Patients who had already taken antidepressants, calcium channel blockers, or sedatives other than those prescribed by protocol within 24 hours of the scheduled surgery, having renal insufficiency, hypersensitivity to opioids, known asthmatic, history of acute peptic ulcer disease and those having coagulopathy and contraindications to drug used were excluded.

After randomization by lottery method, ASA I-II, participants were divided into 2 different groups and given gabapentin in doses of 600 milligrams two hours before the operation in the subjects of Group A and cases of the group B were control (not given gabapentin). The post-operative analgesia requirement in patients undergoing head and neck surgeries in the setup of Ayub Teaching Hospital, Abbottabad. Patients' satisfaction was also inquired 24 hours postoperatively. After shifting the patient to operating room, a large bore IV line was secured and crystalloid infusion was started, mean arterial blood pressure, heart rate, and oxygen saturation were noted. Fentanyl (2 µg/kg) was used with the anesthesia. Propofol (2 mg/kg) and atracurium (0.5 mg/kg) were given, and the patient were maintained with isoflurane with the fresh flow of the gas of 21/min. The participants' lungs were ventilated mechanically. After the surgeries, the patient's level of pain was measured by visual analogue scale (VAS), (1-10 cm) where 0 cm = "no pain" and 10 cm = "worst pain imaginable at time points 0, 2, 6, and 24 hours. The measurements were all taken by the same anesthetic resident that was blind to the study.

Data was collected through interview-based questions after consent from the patients and was analyzed using SPSS version 21. Independent sample t-test was used for analyzing numerical data and Chi-square test was applied for analyzing categorical data. $P \leq 0.05$ was considered statistically significant.

RESULTS

A total of 60 patients were comparatively studied; divided by two groups. The mean age of the patients of

group A was 44.3 ± 10.6 years and 37.5 ± 12.5 years of placebo group B. Mean weight of group A paticepnats was 62.9 ± 7.5 kg and 59.7 ± 6.8 kg of placebo group B. In group A 15 cases were males and 15 were females, while in plcebo group B the 18 were males and 12 were females. Average duration of surgery was 2.75 ± 0.6 and 2.50 ± 0.8 was in group B. Table 1

Table 1: Discriptive statistics of demographic cherecteristics (n=60)

Variables	Group A (n=30)	Group B (n=30)
Age (years)	44.3 ± 10.6	37.5 ± 12.5
Weight	62.9 ± 7.5	59.7 ± 6.8
Gender (Male/female)	15/15	18/12
Duration of surgery	2.75 ± 0.6	2.50 ± 0.8

Group A= Gabapentin. Group B = Placebo

Postoperative pain score was significantly decreased in Gabapentin consumed group A as compared to placebo group B, p-values were quite significant as shown in table 2.

Table 2: Mean postoperative pain score (VAS) comparision in both groups (n=60)

Pain assessemnt	Pain score (VAS)		p-value
	Group A	Group B	
Immidiatly after surgery	3.6 ± 1.1	3.1 ± 1.8	0.02
At two hours	2.9 ± 1.3	5.0 ± 1.0	0.001
At 6 hours	2.8 ±1.3	4.4 ± 0.7	0.02
At 24 hours	2.5 ± 1.5	3.9 ± 1.0	0.003

Group A= Gabapentin. Group B = Placebo

In group A, 90.0% subjects who received Gabapentin 2 hours pre operatively were found satisfied as compared to 60% of the patients who received placebo. Table 3

Table 3: Frequency of aptients satisfaction comparision in both groups (n=60)

Variable	Pain score (VAS)		p-value
	Group A	Group B	
Patients satisfaction at 24 hours	27(90.0%)	18(60.0%)	0.02

Group A= Gabapentin. Group B = Placebo

DISCUSSION

The analgesic efficacy of 600 milligrams of gabapentin was demonstrated by this study in patients who were undergoing maxillofacial surgery. Patients who received gabapentin 2 hours prior to surgery, in comparison to the placebo group, they had considerably lower VAS scores at all times and used less rescue analgesia for pain treatment. A study conducted by Fabritius ML. *et al* as a meta-analysis of one hundred and twenty-two randomized clinical trials showed that the studies with low risk of bias had no consistent morphine sparing effect due to gabapentin. Through analysis of all the studies, all groups showed reduction in morphine requirement in 24 hours. There was statistically significant difference between different dose groups for analgesia. The highest positive response of gabapentin analgesia was seen in the smallest and highest dose groups which was 0-350mg (p=0.04) and >1050 mg (p=0.2) respectively. Other groups were 351-700mg and 701-1050mg which showed reduction of 3.4 mg (p=0.12) and 1.1 mg (p=0.01) of morphine respectively. They concluded that due to high risk of bias in studies, data was not showing a steady systemic dose dependent increase of analgesia.

Our results show that there is statistically significant decrease in the need of rescue analgesics in patients who were administered gabapentin pre-operatively. Another randomized clinical trial of 202 patients demonstrated that there was no delay of time to pain cessation in the cases. Though there was increased rate of cessation of opioids after surgery. Thasleem A. *et al* showed that by administering 1200 mg of gabapentin 2 hours preoperatively showed that there was excellent relief of postoperative pain in cases as compared to controls (p=0.0001). Thus, they concluded that per oral gabapentin has a promising role in post-operative analgesia. In a double-blinded randomized study done by Zeng M. *et al*. The cases received 600mg per oral gabapentin a night before surgery and then another dose two hours before induction of anesthesia Acute post-operative pain at rest (p=0.001) and with movement (p=0.000) within 24 hours were found to be reduced in gabapentin group. "Rai A. *et al* and Dhaliwal P, *et al* showed significant reduction in post-operative opioid need in patients undergoing breast cancer surgeries and otorhinolaryngological surgeries respectively.[14,15] It has been observed in several studies done earlier that gabapentin when given before surgical stimulus, alleviates acute nociceptive and inflammatory pain responses as consistent with the results of our study.[15, 16] Considering the outcomes of this study, it is believed that patients undergoing maxillofacial procedures benefit from gabapentin 600 mg's ability to decrease postoperative pain and decrease the analgesia requirements also. Assuming that Gabapentin is widely tolerated drug, it seems to have less adverse effects and also have fewer interaction when combined with other medications when it applied to the management of persistent pain conditions. In this study did not find any major side effect linked with its (gabapentin) single oral dose, therefore enhancing its safety profile.[17.18]

CONCLUSION

In conclusion, a single oral dose of gabapentin when given preoperatively has commendable effects on post-operative pain relief and thus decreasing the amount of

rescue analgesia consumption. However, more research needs to be done in a broad range of surgical procedures and patient categories in order to examine the efficacy of this medicine either on its own or in conjunction with other analgesics, whether as additive effects or synergistic benefits.

LIMITATIONS

There were no significant limitations.

SUGGESTIONS / RECOMMENDATIONS

Further comprehensive research should be conducted on this comparison.

CONFLICT OF INTEREST / DISCLOSURE

None.

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REFERENCES

1. Salama E. Amer A. The effect of pre-emptive gabapentin on anaesthetic and analgesic requirements in patients undergoing rhinoplasty: A prospective randomised study. Indian Journal of Anaesthesia. 2018;62(3):197.
2. Chang C, Challa C. Shah J, Eloy J. Gabapentin in Acute Postoperative Pain Management. BioMed Research International. 2014:2014:1-7.
3. Doleman B, Heinink T, Read D, Faleiro R, Lund J. Williams J. A systematic review and meta-regression analysis of prophylactic gabapentin for postoperative pain. Anaesthesia. 2015:70(10):1186-1204.
4. Chamberlain R. Arumugam S. Lau C. Use of preoperative gabapentin significantly reduces postoperative opioid consumption: a meta-analysis. Journal of Pain Research. 2016;9:631-640.
5. Fabritius ML, Wetterslev J. Mathiesen O, Dahl JB. Dose-related beneficial and harmful effects of gabapentin in postoperative pain management post hoc analyses from a systematic review with meta-analyses and trial sequential analyses. J Pain Res. 2017:10:2547-2563.
6. Hah J. Mackey SC., Schmidt P, et al. Effect of Perioperative Gabapentin on Postoperative Pain Resolution and Opioid Cessation in a Mixed Surgical Cohort, A Randomized Clinical Trial. JAMA Surg. 2018;153(4):303-311
7. Thasleem, A., Isaac, M. and Vigish, V. Oral gabapentin for postoperative pain relief after lower limb surgery a randomized controlled trial. Indian Journal of Clinical Anaesthesia, 2017;4(1);37-40.
8. Rosner H. Rubin L, Kestenbaum A. Gabapentin adjunctive therapy in neuropathic pain states. Clin J Pain. 1996;12:56-8.
9. Backonja M, Beydoun A, Edwards KR, et al. Gabapentin for the symptomatic treatment of painful neuropathy in patients with diabetes mellitus: a randomized controlled trial. JAMA. 1998;280:1831-6.
10. Rowbotham M, Harden N, Stacey B, Bernstein P, Magnus-Miller L. Gabapentin for the treatment of postherpetic trial. JAMA. 1998;280:1837-42
11. Mellick GA, Mellick LB. Reflex sympathetic dystrophy treated with gabapentin. Arch Phys Med Rehabil. 1997;78:98-105.
12. Zeng M, Dong J, Lin N, Zhang W, Zhang K, Peng K, Wang D, Zhao Y, Peng Y, Han R. Preoperative gabapentin administration improves acute postoperative analgesia in patients undergoing craniotomy: a randomized controlled trial. Journal of Neurosurgical Anesthesiology. 2019 Oct 1;31(4):392-8.
13. Rai, A., Khan, J., Dhaliwal, J., Busse, J., Choi, S., Devereaux, P. Preoperative pregabalin or gabapentin for acute and chronic postoperative pain among patients undergoing breast cancer surgery: A systematic review and meta-analysis of randomized controlled trials. Journal of Plastic, Reconstructive & Aesthetic Surgery, 2017;70(10), pp.1317 1328.
14. Dhaliwal P, Shah C, Kumar S, Chauhan D. Pre-emptive oral gabapentin for post-operative pain relief in patients undergoing middle ear surgeries-a prospective study. International journal of scientific research 2018:7(1):239-240.
15. Rorarius MG, Mennander S, Suominen P, Rintala S. Puura A. Gabapentin for the prevention of postoperative pain after vaginal hysterectomy. Pain 2004; 110: 175-81.
16. Dirks J, Moiniche S, Hilsted KL., Dahl JB. Mechanism of postoperative pain: clinical indications for contribution of central neuronal sensitization. Anesthesiology 2002; 97: 1591-6.
17. Mao J. Chen LL, Gabapentin in pain management. Anesth Analg 2000;91:680-7
18. McLean MJ, Morrell MJ, Willmore LJ, et al. Safety and tolerability of gabapentin as adjunctive therapy in a large, multicenter study. Epilepsia 1999:40:965-72.