Original Article

COMPARISON OF POSTOPERATIVE MEAN OPIOIDS CONSUMPTION IN PATIENT GIVEN PREOPERATIVE GABAPENTIN AND PLACEBO UNDERGOING MAJOR LAPAROTOMIES FOR LOWER ABDOMEN AND PELVIS

Muhammad Javed[*], Khaleel Ahmad[**], Anser Ali Butter[***]

[*]Assistant Professor Anesthesia, Nawaz Sharif Medical College, University of Gujrat, Gujrat.

[**]Assistant Professor Anesthesia, Nawaz Sharif Medical College, University of Gujrat, Gujrat.

[***]Assistant Professor, Rashid Latif Medical College, Lahore.

ABSTRACT:

OBJECTIVE: The objective of the study was to compare postoperative mean opioids consumption in patient given preoperative gabapentin and placebo undergoing major explorative laparotomies for lower abdomen and pelvis.

STUDY DESIGN: Randomized controlled trial

PLACE AND DURATION WITH DATES: Department of Anesthesiology, Hameed Latif hospital, Lahore, affiliated with College of Physicians & Surgeons of Pakistan, from 29-09-2009 to 29-03-2010.

METHODOLOGY: This was a randomized controlled trial included 150 patients undergoing major laparotomies who were divided in two equal groups. In group I, 75 patients received multivitamin tab. as placebo and in group II, 75 patients had Gabapentin. The two groups were compared for the consumption dose of opioids analgesia, postoperatively. T-test was applied for statistical difference. (p- Value < 0.05 was taken as significant. Data was collected on special designed proforma.

RESULTS: The mean dose of tramadol consumed by the patients in group I was 553.47 + 118.93 and in group II was 446.67+ 128.65 milligrams.

CONCLUSION: The preoperative administration of Gabapentin before major laparotomies is recommended to reduce the postoperative dose of opioids analgesia.

KEY WORDS: Gabapentin; postoperative analgesia; opioids consumption.

INTRODUCTION:

Management and Prevention of post operative pain and its complications are the main tasks in postoperative care and plays a key role in early mobilization and well-being of the patient.[1]

In the management of postoperative pain, opioids are the top level medications and morphine being the gold standard for comparison with other parental analgesics.[2] On the contrary, opioids carry a lot of side effects like respiratory depression, nausea and vomiting.[3] Postoperative pain management with minimal side effects, Multimodal analgesic regimes are being used; these involve the addition of drugs like NSAIDs, ketamine, paracetamol or combining local or regional analgesia with systemic opioids. The results of these studies have been reviewed by Spencer and Christopher.[4]

Preemptive analgesia is an analgesic treatment initiated before the start of surgical procedure. It was introduced to protect the central nervous system from deleterious effects of noxious stimuli, and the patient from the resulting allodynia, and increased pain.[5]

Corresponding Author:
Dr. Muhammad Javed, Assiatant Professor Anesthesia, Nawaz Sharif Medical College, University of Gujrat, Gujrat.
E-Mail: doctorhfd95@gmail.com
Contact No. 0323-4306256

Gabapentin, has been used as an anticonvulsant and antinociceptive drug, which is a structural analogue of gamma-amino butyric acid.[6]It binds mainly to the alpha-2-delta subunit of voltage-gated calcium channels. [7] The role of Gabapentin is established in neuropathic pain, diabetic neuropathy, post herpetic neuralgia and reflex sympathetic dystrophy.[8] It also has antihyperalgesic activity that selectively affect central sensitization.[9] The effictivity of GBP for the treatment of early post operative pain has been studied in many trials, over the last eight years. The surgical populations included in these studies were abdominal or pelvic surgery,[10,11] musculoskeletal surgery,[12] head and neck surgery,[13] breast surgery,[14] varicocele surgery[15] and thoracic surgery.[16]

Gabapentin is a second generation anticonvulsant used in the treatment of neuropathic pain. The top most priorities for its use in the perioperative setting, including preoperative anxiolysis, management of postoperative analgesia, prevention of chronic post-surgical pain, attenuation of haemodynamic response to direct laryngoscopy and intubation, prevention of postoperative nausea and vomiting (PONV), and postoperative delirium has been studied. In multiple studies oral gabapentin either in single or multiple doses ranging from 300 mg to 1200 mg; the results have shown a reduction in first request for postoperative analgesia, VAS score and opioid consumption during first 12-24 hours.[17] However reduction in opioids consumption is not associated with a reduction in the side effects. Gabapentin may lead to increased dizziness and sedation without decreasing the frequency of vomiting.[18]

Pandey et al determined the optimal dose of gabapentin for pain relief after lumbar diskectomy and suggested that 600mg gabapentin provides optimal analgesia with minimal side effects.[19] VAS score observed at 2,4,6,8,12 and 24 hours and fentanyl consumption was compared as the primary outcome measure in this study. This study design has been criticized since the patients fail to achieve similar pain scores. Morphine consumption was reduced (26.94±2.28 to 15.78±1.15mg) with 300mg gabapentin in another study.[20] Since the availability of morphine is often erratic in our setting, we will study the effect of 300mg gabapentin on 24 hours tramadol consumption.

METHODOLOGY:

The randomized controlled trial was conducted at the Department of Anesthesiology, Hameed Latif hospital, Lahore, affiliated with College of Physicians & Surgeons of Pakistan.

After approval from ethical committee of the hospital and a written informed consent, 150 patients admitted through outdoor fulfilling the inclusion criteria were enrolled. After taking demographic history, the patients were divided randomly in two groups I and II by using random number table. Each patient in groups I received multivitamin tablet as a placebo and 300 mg Gabapentin in group II respectively with a sip of water 1hour before shifting to operation theatre. All patients received 0.05 mg/kg Intravenous (I/V) midazolam 15 minutes before shifting to operation theatre. Propofol 2mg/kg I/V was used for induction and rocuronium 0.6mg/kg Intra-venous for relaxation. Endotracheal tube or an LMA was employed according to direction of the attending anaesthetist. Anaesthesia was maintained with O2 and sevoflurane with intermittent positive pressure ventilation. All patients received 0.25mg/kg ketamine before skin incision and 1mg/kg tramadol 10 minutes after incision. The patients were shifted to the post anaesthesia care unit (PACU) after surgery; intensity of the pain was measured on the visual analogue scale (VAS) by anaesthesia resident blinded to group allocation.

They received 0.5mg/kg intravenous tramadol every time the VAS score is >3, which was repeated every 10 minutes till the score is <3. Total amount of tramadol consumed in 24 hours was noted. All this information was recorded in a pre-designed proforma.

Data analysis was computer based. Statistical package for social sciences (SPSS) version 10 was used for analysis.

Age and Opioid consumption for analgesia was presented as mean and SD in each group. Genders were presented as frequency and percentage. The mean opioid doses between

two study groups were compared by application of t- test as test of significance at p value ≤0.5.

RESULTS:

There was a significant statistical difference between the two groups in Tramadol consumption but no significant difference observed in Age, Sex and ASA status. In Group I, the mean age of the patients was 39.08 ± 9.79 years [range 20 – 60]. In Group II, the mean age of the patients was 40.80± 10.27 years [range 20 – 61] (Table 5) In group I, there were 47 (62.7%) male patients and 28 (37.3%) were female. The female to male ratio in this group was 1:1.68. In group II, there were 42 (56%) male patients and 33 (44%) were female. The female to male ratio in this group was 1:1.30. (Figure 5) In group I, there were 42 (56%) patients who were included in ASA Class 1 and 33 (44%) patients who were included in ASA Class 2. In group II, 34 (45.3%) patients and 41 (54.7%) patients were included in ASA Class 1 and ASA Class 2, respectively. (Figure 6) The mean dose of tramadol consumed by the patients in group I was 553.47 + 118.93 and in group II was 446.67+ 128.65 milligrams and in group II was 446.67+ 128.65 milligram. The two groups were also comparing for any statistical difference. Student t-test was applied and $p < 0.05$ which showed that there was a significant difference between the two groups. (Table 6)

Table 5: Distribution of patients by age (n=150)

Age in years	Group I		Group II	
	No. of patients	Percentage	No. of patients	Percentage
20 – 30	18	24	13	17.3
31 – 40	21	28	21	28
41 – 50	28	37.3	30	40
51 – 60	8	10.7	11	14.7
Mean + SD	39.08 + 9.79		40.80+10.27	
Range	20 – 60		21 – 60	

Table 6: Comparison of patients by the dose of tramadol consumption (n=150)

	Group I	Group II	p-value
Mean (SD) dose of tramadol consumed (in milligrams)	553.47 ± 118.93	446.67± 128.65	0.000 (< 0.05)

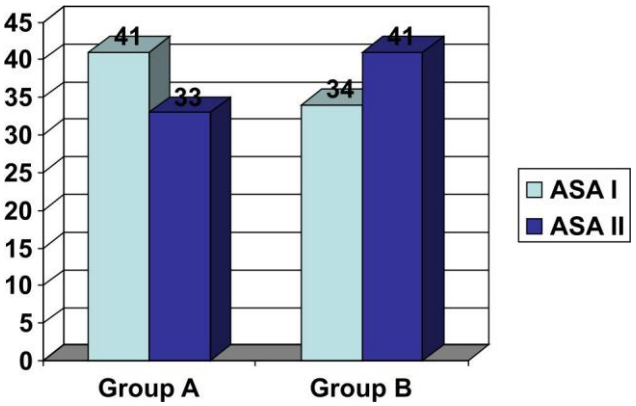

Figure 5: Distribution of patients by sex (n=150)

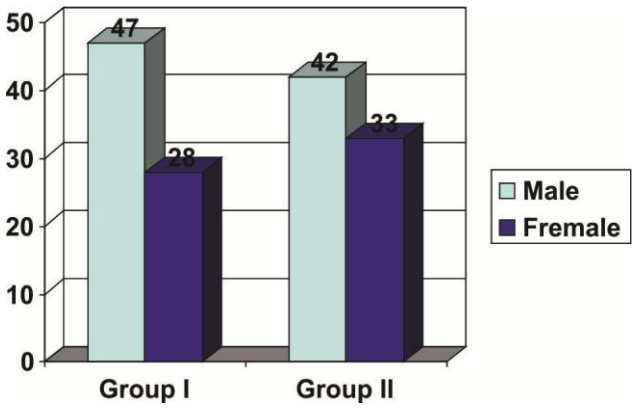

Figure 6: Distribution of patients by ASA Classification (n=150)

DISCUSSION:

We found favorable results of preoperative Gabapentin administration which showed a

significant reduction in the consumption of opioids after major laparotomies (553.47 ± 118.93 milligrams without Gabapentin and 446.67± 128.65 milligrams with Gabapentin).
Gabapentin has been used as a preemptive analgesia in multiple studies for the postoperative pain in different surgeries. There is variation of results among different authors.
A study was conducted by Parikh HG, et al. [21] on 60 patients who were divided into two groups. Group A received 600mg gabapentin and group B oral received placebo 1 h prior to surgery. Anesthesia was given and surgery was performed. Visual analog score (VAS) was used to assess post-operative pain at extubation (0 h) 2,4,6,12 and 24 h post-operatively. Intravenous Tramadol was used as post-operative analgesia. 2mg/kg was given in the Post Anesthesia Care Unit as the first dose, and repeated at 8 and 16 h. Rescue analgesia was given with Diclofenac 1.5mg/kg, slow intravenous. The total doses of rescue analgesia in both the groups were noted. Results: The VAS scores at 0, 2, 4, 6, 12, and 24 h were 1.9 vs. 2.4 (P=0.002), 2.3 vs. 3.0 (P=0.000), 3.2 vs. 3.7 (P=0.006), 2.9 vs. 4.4 (P=0.000), 3.6 vs. 4.6 (P=0.000), and 3.7 vs.4.6 (P=0.000), respectively. Numbers of patients requiring rescue analgesia with Diclofenac were 3 vs. 14 (P=0.004). Conclusion of this study was that a single dose of oral gabapentin given pre-operatively enhanced the analgesic effect of tramadol and also decreases the need of rescue analgesia.
Al-Mujadi H, et al [13] used gabapentin 1200 mg or placebo two hours prior to induction of anesthesia to patients going for elective thyroidectomy. Postoperatively pain was assessed on a visual analogue scale at rest and during swallowing in the first 24 hr. Morphine 3 mg iv was given to all patients every five minutes until visual analogue scale scores were 4 or less at rest, and 6 or less with swallowing. Total morphine consumption for each patient was recorded from zero to 24 hr postoperatively. Overall, there was significant reduction in pain score at rest and swallowing in the gabapentin group when compared with the placebo sgroup.Total postoperative morphine consumption in the Gabapentin group was 15.2 ± 7.6 mg (mean ± SD) vs 29.5 ± 9.9 mg in the placebo group ($P < 0.001$). Like our study, the results of this study were in favor of Gabapentin before surgery.
In a systemic review carried out by Metheisen Ole, et al. [22] the postoperative outcome of Gabapentin were studied in terms of postoperative pain. 1529 patients were included Twenty-three trials. In 12 of 16 studies with data on postoperative opioid requirement, the reported 24-hour opioid consumption was significantly reduced with gabapentin. Quantitative analysis of five trials in abdominal hysterectomy showed a significant reduction in morphine consumption [weighted mean difference (WMD – 13 mg, 95% confidence interval (CI) -19 to -8 mg)], and in early pain scores at rest (WMD – 11 mm on the VAS, 95% CI -12 to -2 mm) and during activity (WMD -8 mm on the VAS; 95% CI -13 to -3 mm), favoring gabapentin. Like our study, this study also favored the use of preoperative Gabapentin for reduction of morphine consumption
The above discussion suggests that Gabapentin effectively reduced the postoperative opioids consumption. Different clinical trials have used different outcome parameters. However, most of the studies have used visual analogue score for pain measurement and the demand or quantity of analgesia consumed by the patient.

CONCLUSION:

Gabapentin when used preoperatively in major laparotomies can significantly reduce the postoperative consumption of analgesia. So, it is recommended that Gabapentin should be given before the major abdominal surgeries. However, multi-center studies for a longer period are required to better estimate of outcomes.

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SR #	AUTHOR NAME	CONTRIBUTION
1	Dr. Muhammad Javed	Main Author
2	Dr. Khaleel Ahmad	Data Collection
3	Dr. Anser Ali Buttar	References collection