EVALUATION OF GABAPENTIN ON POSTOPERATIVE PAIN AND OPIOID CONSUMPTION FOLLOWING LAPAROSCOPIC CHOLECYSTECTOMY

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Summary

Gabapentin is reported to possess antihyperalgesic and antiallodynia properties. Recently, reports have indicated that gabapentin may have a place in the treatment of postoperative pain. In this study, we sought to role of preoperative use of gabapentin on postoperative pain and pethidine consumption following laparoscopic cholecystectomy.

Sixty patients of both sexes, ASA grade I and II underwent laparoscopic cholecystectomy were randomly allocated into two groups. Group A (n = 30) patients were premedicated with single dose of gabapentin(600 mg) 2 hours before operation and Group B (n = 30) with tab vitamin B complex as placebo. Operation was done under general anaesthesia. Postoperative analgesia was assessed in both groups subjectively by Visual Analogue Scale (VAS). Any patient of both groups with VAS score of more than three were administered intramuscular pethidine 1.5 mgkg-1 bodyweight for 24 hours. VAS Observations were made in postoperative ward at arrival and at 6, 12 and 24 hours for 24 hours. Total postoperative pethidine consumption and post operative side effects were also recorded.

Baseline data were comparable between the two groups. The mean VAS almost similar and less than 3 at different reading in both groups and the differences were statistically not significant. The mean total cumulative amount of pethidine administered over 24 hrs period was less in group A it was 117.31±14.13mg (Mean ± SD) and in group B was 221.23±16.25 mg (Mean ± SD) and the difference was statistically significant (p<0.01). Incidences of side effects like PONV and urinary retention were more in group B than group A and differences were statistically significant (p<0.01). Dizziness and Somnolence were more in group A than group B and difference was statistically significant (p<0.01).

Preoperative gabapentin significantly decreased postoperative opioid consumption and should be considered a potentially useful adjunctive in postoperative pain in patients undergoing laparoscopic cholecystectomy.

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Key words

Gabpentine; postoperative pain; laparoscopic cholecystectomy; pethidine

Introduction

Prevention and treatment of postoperative pain continues to be a major challenge in postoperative care and plays an important role in the early mobilization and well being of the surgical patient. A number of analgesic regimens can be used for pain relief during surgery. These regimens include the use of opioids, local anaesthetics, nonsteroidal anti-inflammatory drugs (NSAIDs), 2-agonists, and cyclooxygenase-2 inhibitors. The multiplicity of mechanisms involved in pain requires a multimodal analgesia regimen, suggesting that a combination of opioid and non-opioid analgesic drugs may improve analgesic efficacy and reduce opioid requirements and side-effects after surgery [1]. Gabapentin is a GABA analogue. It was originally developed for the treatment of epilepsy, and currently, gabapentin is widely used to relieve pain, especially neuropathic pain. It was shown to be effective in treating a variety of chronic pain conditions including post-hepatic neuralgia [2], diabetic neuropathy[3], complex regional pain syndrome[4], inflammatory pain [5], central pain [6], malignant pain [7], trigeminal neuralgia [8], HIV-related neuropathy [9], and headache [10]. Perioperative administration of gabapentine has been evaluated in recent studies [11,12]. Evidence suggests gabapentine is efficacious for postoperative analgesia, preoperatrive anxiolysis, and attenuation of the haemodynamic response to laryngoscopy and intubation and preventing chronic postoperative surgical pain postoperative nausea and vomiting and delirium [13,14].

The aim of present study was to assess postoperative analgesic benefit in patients administered gabapentin premedication for laparoscopic cholecystectomy under general anaesthesia and reduction in total post-operative requirements of opioid analgesics and side effects.

Materials and methods

It was as Randomised trial including sixty patients (thirty patients in each group) of both sexes age between 18-50 years, ASA physical status I and II scheduled to undergo elective laparoscopic cholecystectomy under general anaesthesia in CMH Chittagong and Dhaka from July 2008 to June 2010. Patients were selected by LOtary method. Patients with psychiatric illness, kidney disease, breast feeding and emergency operation were excluded from the study.

Pre-anaesthetic check up was done 24 hours prior to surgery and the procedure was explained to the patient and written consent was obtained from each patient. Permission was taken from departmental review board before starting the study. During the preoperative interview, patients were instructed how to assess postoperative pain by using the Visual Analogue Scale (VAS) 0-10, 0 = no pain, 10 = the worst imaginable pain.

All eligible patients were randomized in to two groups. Group A (n = 30) patients, were premedicated with single dose of gabapentin(600 mg) 2 hours before operation and Group B (n = 30) with tab vitamin B complex as placebo. Operation was done under general anaesthesia with controlled ventilation. All patients received oral diazepam (5 mg) at night before surgery. Pethidine 1 mgkg-1 and diazepam 0.1 mgkg-1 were slowly given intravenously before induction of general anesthesia. Induction was done with thiopentone 5 mgkg-1. After intubation with vecuronium 0.1 mgkg-1, anaesthesia was maintained with 70% nitrous oxide in oxygen, halothane 0.5-1% and muscle relaxation was maintained with incremental doses of vecuronium. Patient's heart rate, blood pressure, respiratory rate, SpO_2 and $ETCO_2$ were monitored and recorded in every 5 minutes interval. After completion of operation the patients were extubated by reversal of muscle relaxant and then admitted to the postoperative ward for 24 hours. Postoperative analgesia was assessed in both groups subjectively by Visual Analogue Scale (VAS). Any patient of both groups with VAS score of more than three were administered intramuscular pethidine 1.5 mgkg-1 bodyweight for 24 hours. VAS Observations were made in postoperative ward at arrival and at 6, 12 and 24 hours for 24 hours. Patient's heart rate, blood pressure, respiratory rate and SpO_2 were observed accordingly. Total postoperative pethidine consumption and side effects like post operative nausea and vomiting (PONV), dizziness; urinary retention and somnolence were also recorded.

All statistical analysis was carried out using SPSS (Statistical Package for social sciences) 17.0 for windows. All results are expressed as mean ± standard deviation (SD) or in frequencies as applicable. Results are considered statistically significant if $p< 0.05$.

Results

Patient's demographics and preoperative data were similar and fairly comparable in both groups and differences were statistically not significant (Table-I). Duration of surgical procedure and duration of anaesthetic procedure were similar in both groups and differences were statistically not significant (Table-I). No patient was withdrawn from the study. Operating conditions were pronounced satisfactory by the surgeon concerned in all the cases.

The pain intensity was measured by visual analogue scale in both groups. Statistical analysis revealed no significant difference in pain severity at arrival in postoperative ward and at 6, 12 and 24 hours (Table-II). The mean VAS almost similar and less than 3 at different reading in both groups which indicate adequate postoperative analgesia was maintained in both groups.

The mean total cumulative amount of pethidine administered over 24 hrs period following the end of surgery was less in group A compared to group B. Mean dose of pethidine in group A was 117.31+14.13mg (Mean + SD) where as in group B was 221.23+16.25 mg (Mean + SD) and the difference is statistically significant $P<0.01$ (Table-III). Incidence of postoperative side effects like PONV, dizziness, urinary retention and somnolence were recorded and shown in (Table-IV). Incidence of PONV and urinary retention and were more in group B than group A and differences were statistically significant ($p<0.01$). Dizziness and Somnolence were more in group A than group B and difference was statistically significant ($p<0.01$).

Table I : Demographic and Perioperative data

Characteristics	Group A (n=30)	Group B (n=30)	P Value	Result
Age(Years)	40.7+5.11	39.1+5.03	0.094	NS(student 't' test , unpaired)
Body weight (Kg)	56.4+6.2	57.2+5.9	0. 279	NS(student 't' test, unpaired)
Height (Cm)	153.25+3.49	152.65+4.04	0.087	NS(student 't' test , unpaired)
Sex				
Male	10(33.34)	11(36.66%)	0.768	NS(chi square test)
Female	20(66.66%)	19(63.34%)	0.789	NS(chi square test)
ASA physical status				
I	22(73.33%)	23(76.66%)	0.776	NS(chi square test)
II	08(26.67%)	07(23.34%)	0.784	NS(chi square test)
Duration of Surgery (min)		67.9+10.3	69.2+9.8	0.836 NS(student 't' test , unpaired)
Duration of Anaesthesia (min)		77.6+12.8	79.3+13.1	0.821 NS(student 't' test , unpaired)

Values are expressed in Mean + SD and Percentage
NS– Not significant

Table II : Mean pain score (VAS) after surgery

Measurement time	Group A (n=30)	Group B (n=30)	P Value	Result Student 't' test, (unpaired)
After surgery	2.87+1.8	2.98+1.7	0.251	NS
After 6 hours	2.79+1.5	2.91+1.6	0.089	NS
After 12 hours	2.59+1.7	2.86+1.6	0.098	NS
After 24 hours	1.97+1.4	2.01+1.5	0.213	NS

Values are expressed in Mean + SD
NS– Not significant

Table III : Mean total dose of pethidine administered over 24 hours period following surgery

Variable	Group A (n=30)	Group B (n=30)	P Value	Result Student 't' test, (unpaired)
Mean dose of pethidine (mg)	117.31+14.13	221.23+16.25	P<0.01	Significant

Values are expressed in Mean + SD
P < 0.01 – Statistically significant

Table IV : Incidence of side effects during postoperative period

Side effects	Group A (n=30)	Group B (n=30)	P Value	Result (Chi Square test)
PONV	1(3.33%)	5(16.66%)	P<0.01	Significant
Dizziness	4(13.33%)	1(3.33%)	P<0.01	Significant
Urinary retention	1(3.33%)	5(16.66%)	P<0.01	Significant
Somnolence	4(13.33%)	1(3.33%)	P<0.01	Significant

Values are expressed in Percentage
P < 0.01 – Statistically significant

Discussion

Opioids remain the mainstay for postoperative analgesia, especially following major surgery. Pain, however, is a multi-factorial phenomenon that cannot be controlled adequately with simple monotherapy with opioids alone [15]. Furthermore, opioid use is associated with dose-related adverse effects such as respiratory depression, nausea, vomiting, urinary retention, itching, and sedation. Opioids also reduce gastrointestinal (GI) motility, which may contribute to postoperative ileus 16,17]. Their ability to control pain on movement also is limited, which may delay early mobilization and aggressive postoperative rehabilitation [18]. To improve pain relief, and reduce the incidence and severity of adverse effects, a multi-modal approach to postoperative analgesia should be used.

Bangladeshi patients are usually of small or medium built and relatively lesser body weight than their western counter parts. Considering the pharmacokinetic studies, and mean body weight of patients being 60 kg it is hypothesized that a single dose of 600mg of gabapentin would be safe and effective given two hours before surgery [19].

The results of this study showed that a single dose of 600 mg gabapentin given two hours before surgery significantly reduced the need for postoperative pethidine consumption during the first 24 hr postoperatively. The mean VAS was less than 3 in both groups during different time periods during postoperative period, which indicate adequate postoperative analgesia was maintained in both group.

Pretreatment with a single dose of gabapentin blocked the development of hyperalgesia (which is N-methyl-D-aspartate mediated NMDA) and tactile allodynia [which is -amino-3 hydroxy-5-methyl-4-isoxazolaproprionate (AMPA) and metabotropic receptor-mediated] for up to two days in a rat model of postoperative pain, while gabapentin one hour after intervention reduced symptoms for only three hours [20]. Previous clinical studies with gabapentin for postoperative analgesia have shown promising results. A single dose of oral gabapentin 1200 mg administered preoperatively resulted in 50% reduction in movement related pain two and four hours after radical mastectomy [21]. Oral gabapentin 1200 mg administered one hour before surgery decreased pain scores in the early postoperative period and postoperative morphine consumption in spinal surgery patients, while decreasing morphine-associated side effects [22]. In an another study, gabapentin 3000 mg administered before and during

the first 24 hr after abdominal hysterectomy reduced morphine consumption by 32%, without significant effects on pain scores at rest or during mobilization [23]. Rorarius et al. demonstrated that a single dose of 1200 mg gabapentin given two to 2.5 hrs before induction of anesthesia reduced the need for additional postoperative pain treatment by 40% during the first 20 postoperative hours in patients undergoing vaginal hysterectomy [24]. Our results are consistent with these studies. Pain scores at rest and during swallowing were significantly reduced in gabapentin-treated patients. Despite differences in surgical procedures, a significant effect of gabapentin on postoperative analgesic requirements was observed in most of the above studies.

Incidence of postoperative complications like PONV, dizziness, urinary retention and somnolence were observed in both groups. Incidences were less with gabapentine then with placebo and differences were statistically significant ($P<0.01$) regarding PONV and urinary retention. These side effects such as nausea, vomiting, urinary retention, it were associated with dose-related opioid use. Dizziness and Somnolence were more with gabapentine and difference were statistically significant ($p<0.01$). Somnolence and dizziness are the two most common side effects associated with gabapentin. The incidence reported in present study is similar to earlier studies [25]. This is usually not disabling and antianxiety effect has been found to be beneficial in some studies [19].

Conclusion

In conclusion, our findings suggest that gabapentin should be considered a potentially useful adjunctive, antihyperalgesic agent for the treatment of postoperative pain in patients undergoing laparoscopic cholecystectomy. The total postoperative opioid consumption is significantly less with gabapentine. It can be used as part of multimodal postoperative pain therapy if not as sole analgesic.

Disclosure

All the authors declared no competing interest.

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