International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Index Copernicus Value (2016): 79.57 | Impact Factor (2017): 7.296

A Comparative Study of Acetaminophen and Combination of Acetaminophen with Gabapentin for Post-Operative Analgesia for Open Cholecystectomy

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Abstract: ***Background: The relief of pain has always been a part of the anaesthesiologist's role in the most immediate postoperative period and the development of acute postoperative pain services has extended this interest beyond the post-anaesthesia care unit. To evaluate the effects of premedication with acetaminophen and combination of acetaminophen with gabapentin for post-operative pain relief, postoperative analgesic requirement and side effects in patients undergoing open cholecystectomy under general anesthesia. Methods and materials: This prospective randomized double blinded control study was conducted amongst sixty patients of ASA physical status I and II, age between 25-50 years, two groups 30 in each group to receive either Group A patients received tablet acetaminophen 15 mg/Kg, Group AG patients received tablet acetaminophen15 mg/kg and Capsule gabapentin 20 mg/kg two hours prior to the surgery. Patients were observed 12 hours postoperatively for pain via visual analogue scale (VAS), analgesic requirement and side effects. Results: It was observed that patients in gabapentin group had statistically significant lower pain score during the entire observation period in comparison to acetaminophen group. The total postoperative analgesic duration i.e. time from spinal analgesia to first dose of analgesic was 2.36 ± 0.71 hours in Group A whereas 10.69 ± 1.55 hours in Group AG, which was highly significant (P < 0.0001). The mean number of rescue analgesic dose requirement in the gabapentin group (1 ±0) was substantially lower than that of the acetaminophen group (2.72 ±0.46). The mean sedation scores were always higher in gabapentin group (4.36±0.49) as compared to acetaminophen group. Conclusions: Gabapentin significantly reduces post-operative pain and post-operative tramadol consumption with very minimal adverse effects.***

Keywords: open cholecystectomy, Postoperative pain, Gabapentin, acetaminophen, generalanaesthesia

1. Introduction

Postoperative pain relief is basic human right. Pain occurring after surgery is due to tissue damage. Post-operative pain is a major concern for both patients and physicians, [1, 2, 3]. which, when reduced, not only promotes comfort and recovery of the patient but also leads to a faster return to normal life, reduced length of stay and cost of treatment.[4, 5]Furthermore, patients with reduced post-operative pain have better pulmonary function tests.[7].The classic method of using opioids to control pain during and after surgery[5] is associated with a number of dose-related side effects (respiratory depression as the most important), which can be reduced with the co-administration of non-opioid analgesics to lower the opioid dosage.[8]

Various other drugs such as nonsteroidal anti-inflammatory drugs, local anaesthetic drugs, gabapentin, clonidine, and dexmedetomidine have been used to decrease the post-operative pain via different mechanism.

According to recent findings, aspirin and acetaminophen (paracetamol) are among the non-steroidal anti-inflammatory drugs (NSAIDs) that are probably more effective (either alone or in combination with opioids) than were previously considered.[10, 11]Gabapentin is another compound recently used in pain management studies.[12]It is a structural analogue of γ-aminobutyric acid which acts through central and peripheral mechanisms.[3] Gabapentin has been used orally in many studies to reduce post-operative pain.[13-16]

The aim of present study was to evaluate post- operative analgesic benefit in patients administered gabapentin and acetaminophen as premedication for surgery under general anaesthesia for open cholecystectomy and to compare their postoperative efficacy with respect to duration of analgesia, total post- operative requirements of analgesics and to study the side effects.

2. Method and Materials

After institutional Ethics committee approval was obtained and Patients were subjected to pre-anaesthetic assessment and informed consent was obtained from all the patients.In aprospective randomized double blinded control study was conducted amongst sixty patients scheduled for undergoing open cholecystectomy. Inclusion criteria withASA physical status I and II, age between 25-50 years, weight 40 to 65 kg, andexclusion criteria with chronic analgesic therapy, MAO inhibitor, corticosteroids drugs acting on central nervous system, pregnancy, lactationSuffering from nausea & vomiting.Eight hours for nil per mouth. Divided two groups 30 in each group to receive either Group A patients received tablet acetaminophen 15 mg/Kg, Group AG patients received tablet acetaminophen15 mg/kg and Capsule gabapentin 20 mg/kg two hours prior to the surgery with sips of water. Beforeadministration ofpremedication monitoring the blood pressure, pulserate, oxygen saturation, visual analogue scale, level of sedation.No other premedication was instituted.The patient was shifted to operation room and was connected for continuous monitoring of blood pressure,

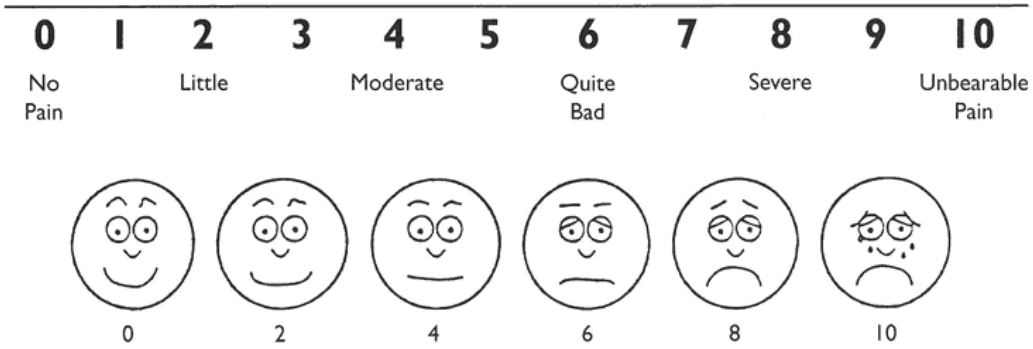
heart rate, ECG, end tidal carbon dioxide and oxygen saturation.

Surgery was conducted in similar way in allpatients using injection Thiopentone sodium 5mg/kg, atracurium 0.5mg/kg and fentanyl 2µg/kg and maintained with Isoflurane 0.5%to1% and nitrous oxide 60% and oxygen 40% and atracurium in titrated dose.Patients were reversed with 0.05mg/kg, Neostigmine and 0.01mg /kg glycopyrolate.

Heart rate, blood pressure, pulse rate, oxygen saturation, respiratory rate, VAS score, any episode of nausea/ vomiting and level of sedation were noted on arrival to the PACU and this was recorded as the baseline score (0 hours). These were also noted hourly for 4 hours and subsequently at 6, 8, 12, 16, 20 and 24 hours. Tramadol was used as rescue analgesic based on patient's demand and the time and frequency and total consumption of rescue analgesic was noted. Nausea, vomiting and other side effects are noted 19. Two or more emetic episodes were treated with Intravenous metoclopramide 0.2mg/ kg . Sedation was scored using Ramsay sedation score.

Levels 1-3: Patient awake
Level 1-Anxious, agitatedor restless or both
Level 2-Cooperative, oriented and tranquil
Level 3-Responds to commands only.
Levels 4-6 Patient asleep
(Responds to light glabellar tap or loud auditory stimuli)
Level 4- Brisk response
Level 5.Sluggish responsLevel
Level 6. No response.

Pain was assessed postoperatively by visual analogue scale immediate postoperatively and every two hourly thereafter, which was explained to the patient during preoperative visit. The 10cm VAS was used and shown to all the patients on pre-operative visit, its two end points: 0 or 10 corresponding to "No Pain" or "Worst Imaginable Pain" respectively



In PACU blinding done, the anaesthetist or staff nurse monitoring VAS scale, time of first rescue analgesia (VAS score of more than three were administered tramadol1mg/kg intramuscularly). Injection Tramadol 1mg /kg was given over 2-3 minutes intravenously and after a further 30 minutes VAS was observed. Further increment of 20 mg was given if VAS = 40mm and the total dose (maximum 400 mg/24 hours) were recorded, number of rescue analgesia, and duration of post-operative analgesia, sedation and complication. Total dose of analgesic in first 24 hours was recorded.

Statistical analysis

Thirty was the smallest number in each group, where any results could be statistically significant hence this number was selected. Kruskul Wallis chi-square testwas used to find out significance between two samples. Data was reported as mean value ± S.D. A P value less than 0.05 was considered statistically significant. Yate's chi square test was selected for discrete samples.

3. Results

Demographic data (age, sex, weight and duration of surgery) was comparable in two groups

Table 1: Demographic Data in both group

		Group A (n = 30)	Group AG (n = 30)	*P Value*
Age (years)		38.4 ± 7	38.5 ±7	0.9535 (> 0.05)
Weight (kg)		53.6 ±5.96	52.6 ± 5.92	0.8432 (>0.05)
Sex	male	24	30	0.7405 (>0.05)
	female	76	70	
Duration of surgery [hrs]		2.76 ±0.34	2.68 ±0.33	0.33 (>0.05)

Table 2: Statistical comparison of rescue analgesics in both groups

Variable		Group A	Group AG	P Value
No of Rescue Analgesia		2.72 ±0.46	1 ±0	0.0001 Significant
Amount of Rescue Analgesia		282.4 ±41.3	104.8 ±11.9	0.0001 Significant
Post-operative Sedation Score		1.28 ±0.46	4.36± 0.49	0.0001 Significant
Complication	Yes	3(10%)	5 (16.66%)	0.2317 Not significant
	No	27(90%)	25 (83.4%)	
Duration of Post-operative Analgesia(hrs)		2.36 ± 0.71	10.69 ± 1.55	0.0001 Significant

The average time of first rescue analgesic consumption for group A, and AG was 2.36 ± 0.71 and10.69 ± 1.55 hours respectively. When all the groups were compared together, the difference was highly significant (p-value<0.01).The average number of rescue analgesics given to the patients in group A, 2, 3 and AG was 2.72 ±0.46 and 1 ±0 (significant

difference when compared together). The average total rescue analgesic consumption for group A and AG was 282.4 ±41.3and 104.8 ±11.9 mg respectively (significant, when compared together). Ramsay sedation score level both group A and AG was 1.28 ±0.46 and 4.36± 0.49 respectively (significant, when compared together). Intergroup comparisons are given in Table2.Visual analogue scale when compared (table3) in both groups together had significant difference. On comparing group A with group AG the difference in pain after surgery was highly significant at 2, 3, 4, 6 hours (P Value<0.05).No other significant complications.

Table 3: VAS SCALE in both groups

	Group A	Group AG	P value
Preoperative	1 ±0	1 ±0	_
Post operative0 hr	1 ±0	1 ±0	_
1 hr	1 ±0	1 ±0	_
2hrs	2.6 ±2.2	1 ±0	0.0001 Significant
3hrs	3.96 ±2.34	1.2 ±0.5	0.0001 Significant
4hrs	1.96 ±0.35	2.08 ±0.28	0.0185 Significant
6hrs	2 ±0.29	2.62± 0.33	0.0393 Significant
8 hrs	2.96±o.61	2.96±0.54	0.9258
12hrs	5.36±0.91	5.48±0.59	0.8777
18hrs	2.8±0.82	2.64±0.49	0.6342
24hrs	4±0.29	3.96±0.2	0.5716

Table 4: PONV

level	Group A no of patient-3(10%)	Group AG no of patient-5(16.66%)	P value
1	1	1	0.5742 not Significant
2	1	0	
3	0	1	
4	1	3	

4. Discussion

Post-operative pain is one of the most feared and is probably the most prevalent of all pain conditions, yet in many cases it continues to be inadequately controlled. Various drugs through different routes have been tried to produce adequate analgesia in patients after surgery. Gabapentin is a newer antiepileptic drug with minimal side-effects which has been used for post-operative analgesia.

Preincisional analgesia has been shown to be more effective in control of postoperative pain by protecting the central nervous system from deleterious effects of noxious stimuli and resulting allodynia, and increased pain. Gabapentin have anti allodynic and anti hyperalgesic properties useful for treating neuropathic pain and may also be beneficial in acute postoperative pain. Several studies have reported the usefulness of Gabapentin and pregabalin in perioperative settings resulting in reduced postoperative pain, postoperative analgesic requirement, side effects, prolongation of analgesia, and higher patient satisfaction.18-21

Demographic variables were comparable the two Groups. The duration of surgery and anaesthesia were also comparable among thetwo Groups (P>0.05)(table1).

Fassoulaki and others 6 did not observe any difference in time of first rescue analgesic consumption after preoperative administration of 1200mg of oral Gabapentin but on the contrary Turan and associates21 found a highly significant difference between the Gabapentin and Placebo Groups.

In our study, we also observed a very highly significant difference in the time of first rescue analgesic consumption in patients who consumed acetaminophen and combination of Gabapentin with Acetaminophen. which indicates that Gabapentin might have potentiated the analgesic effect of Acetaminophen.

The difference in the number of rescue analgesic consumption was very significantly reduced in patients who consumed combination of Gabapentin with Acetaminophen (Group AG) in comparison to patients who did consume Acetaminophen.

Similar results were observed in patients of ear-nose-throat surgery in a study conducted by Turan and associates. In the present study Gabapentin and Acetaminophen combination (Group 4) reduced the total analgesic requirement (Tramadol) by 51% in comparison to the control Group (P<0.001).

The difference in total rescue analgesic consumption noticed by addition of Acetaminophen and Gabapentin on comparison to acetaminophen alone was statistically found to be significant during first 24 hours post-operatively which could be because of short half-life of acetaminophen of just 2-3 hours and a weak anti-inflammatory action.

Similarly patients who consumed Gabapentin along with Acetaminophen had lower VAS scores at all time intervals in comparison to the patients who consumed Acetaminophen alone but the difference was statistically significant only at 1, 2, 3, 4 and 6 hours post-operatively.

In this study incidence of Postoperative nausea and vomiting not significant in the both groups (table4).Uses of tramadol as rescue analgesic in the present study don't increase the incidence of PONV. Some of the few studies statistically increase in the incidence of PONV was also noticed. 1, 2, 3, 22, 23, 24

Sedation was discovered to be another major drawback due to consumption of Gabapentin. A significantly high number of patients group AG (patients who consumed Gabapentin) had sedation of level 4, 5 or 6 in comparison to in Group A (patients who did not consume Gabapentin). Similar increase in level of sedation as a result of administration of Gabapentin was noticed in some research works of post-operative analgesia 1, 2, 3, 4, 5, 23, 24. The above mentioned results of our study demonstrated that it may be possible to protect the patient and the patient's nociceptive system, from the negative effects of noxious stimuli by protective premedication with combination of various antihyperalgesic and analgesic drugs and Gabapentin is a useful agent.

5. Conclusion

The total postoperative analgesic duration increased in AG group was10.69 ± 1.55 hours. The mean number of rescue analgesic dose requirement in the gabapentin group was substantially lower than that of the acetaminophen group. The mean sedation scores were always higher in gabapentin group (4.36± 0.49) as compared to acetaminophen group.

Premedication with antihyperalgesic and analgesic agents helps to reduce the postoperative pain scores and effective for providing better postoperative pain relief. Lower and delayed requirements of rescue analgesics and higher levels of sedation with other minimal side effects.

References

[1] KartikSyal, et al, "Protective Premedication": A Comparative Study of Acetaminophen, Gabapentin and Combination of Acetaminophen with Gabapentin for Post-Operative AnalgesiaJ Anaesth Clin Pharmacol 2010; 26(4): 531-536.
[2] V Saraswat, Vishal Arora et al. Preemptive Gabapentin vs Pregabalin for Acute Postoperative Pain after Surgery under Spinal AnaesthesiaIndian Journal of Anaesthesia 2008; 52 (6):829-834
[3] Pandey CK, Singhal V, Kumar M, Lakra A, Ranjan R, Pal R, et al. Gabapentin provides effective postoperative analgesia whether administered pre-emptively or post-incision. Can J Anaesth 2005; 52:827-31
[4] Durmus M, Kadir But A, Saricicek V, IlksenToprak H, OzcanErsoy M. The post-operative analgesic effects of a combination of gabapentin and paracetamol in patients undergoing abdominal hysterectomy: A randomized clinical trial. ActaAnaesthesiolScand 2007;51:299-304.
[5] Rawal N, Berggren L. Organization of acute pain services: A low-cost model. Pain 1994;57:117-23..
[6] Fassoulaki A, Patris K, Sarantopoulos C, Hogan Q. The analgesic effect of Gabapentin and Mexiletine after breast surgery for cancer. AnesthAnalg 2002; 95: 985-91.
[7] Ballantyne JC, Carr DB, deFerranti S, Suarez T, Lau J, Chalmers TC, et al. The comparative effects of postoperative analgesic therapies on pulmonary outcome: Cumulative meta-analyses of randomized, controlled trials. AnesthAnalg 1998; 86:598-612.
[8] Cook RJ, Sackett DL. The number needed to treat: A clinically useful measure of treatment effect. BMJ 1995; 310:452-4.
[9] P.F.White. The changing role of non-opioid analgesic techniques in the management of postoperative pain.Anesthesia and Analgesia. 2005; 101:S5–S22.
[10] Mackaness CR, Hussain SK, Hobbs GJ, Spendlove JL, Majeed A. Effect of general anaesthesia and surgery on the kinetics of intravenous propacetamol. Br J Anaesth 1999;82:121-6.
[11] Chandrasekharan NV, Dai H, Roos KL, Evanson NK, Tomsik J, Elton TS, et al. COX-3, a cyclooxygenase-1 variant inhibited by acetaminophen and other analgesic/antipyretic drugs: Cloning, structure, and expression. Proc Natl AcadSci U S A 2002; 99:13926-31.
[12] Maneuf YP, Gonzalez MI, Sutton KS, Chung FZ, Pinnock RD, Lee K. Cellular and molecular action of the putative GABA-mimetic, gabapentin. Cell Mol Life Sci 2003;60:742-50.
[13] Katzung BG, Masters SB, Trevor AJ. Basic & Clinical Pharmacology. New York: McGraw-Hill Medical; 2011.
[14] Amin SM, Amr YM. Comparison between preemptive gabapentin and paracetamol for pain control after adenotonsillectomy in children.Anesth Essays Res 2011;5:167-70.
[15] Hassani V, Manoochehripour M, Nojoomi M. Study of the effects of intravenous paracetamol with different doses on opioid sparing during and after upper limb surgeries. Razi J Med Sci 2008;15:109-15.
[16] Imani F, HasaniV, BazarganiB, Entezari S, Mirdehghan M. Evaluation of oral gabapentin premedication on postoperative pain after thoracotomy. Razi J Med Sci 2009;16:73-9.
[17] Peerman MH. Single dose intravenous ondansetron in the prevention of post-operative nausea and vomiting.Anaesthesia 1994; 49: 16-23. 20. Ramsay MA, Savege TM, Simpson BR. Controlled sedation with alphaxaone–alphadolone. BMJ 1974; 2: 656-59.
[18] Tiippana E M, Hamunen K, Kontinen V K and Kalso E. Do surgical patients benefit from perioperative gabapentin/pregabalin? A Systematic Review of Efficacy and Safety.AnesthAnalg 2007;104:1545-1556.
[19] Rorarius M G F, Mennander S, Suominen P, Rintala S, Puura A, Pirhonen R, Salmelin R, Haanpää M, Kujansuu E and Yli-Hankala A. Gabapentin for the prevention of postoperative pain after vaginal hysterectomy. Pain 2004;110:175-181.
[20] Al-Mujadi H, A-RefaiA R, Katzarov M G, Dehrab N A, Batra Y K and Al-Qattan A R. Preemptive gabapentin reduces postoperative pain and opioid demand following thyroid surgery. Canadian Journal of Anesthesia 2006:53:268-273.
[21] Turan A, Kaya G, Karamanlioglu B, Pamukcu Z and Apfel C C. Effect of oral gabapentin on postoperative epidural analgesia. British Journal of Anaesthesia 2006;96:242– 6.
[22] Turan A, Karamanlioglu B, Memis D, Usar P, Pamukcu Z, Ture M. The analgesic effect of Gabapentin after total abdominal hysterectomy.AnesthAanalg 2004; 98: 1370-3
[23] Pandey CK, Priye S, Singh S, Singh U, Singh RB, Singh PK. Preemptive use of Gabapentin significantly decreases post-operative pain and rescue analgesic requirements in laparoscopic cholecystectomy. Can J Anaesth 2004; 51: 358-63.
[24] Pandey CK, Navkar DV, Giri PJ, Raza M, Behari S, Singh RB and others. Evaluation of the optimal preemptive dose of Gabapentin for post-operative pain relief after diskectomy. J NeurosurgAnesthesiol 2005; 17: 65-68.