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Original Research Article

Evaluation of analgesic efficacy of two different doses of Pregabalin for attenuation of post-operative pain in laparoscopic cholecystectomy

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Abstract

Introduction: Literature established the role of pregabalin in the pain management. However, there are limited studies in attenuating postoperative pain after laparoscopic cholecystectomy (LAC). So, we evaluate the analgesic effect of two different doses of Pregabalin for attenuation of post-operative pain in laparoscopic cholecystectomy
Methodology: In this randomized prospective study, 120 patients were allocated into three groups of 40 each. Group A, B and C received Tab Vitamin, Tab Pregabalin 75 mg and 150 mg respectively 1 hour before the expected time of anesthesia. Postoperative efficacy among these three groups was compared with respect to increase in duration of analgesia, reduction in postoperative pain scores, total postoperative requirements of analgesics and side effects.
Results: Pregabalin does not reduce pain intensity during 24-hr following LAC as compared to placebo. No difference in need for rescue analgesic, time for need of first rescue analgesic dose and amount of fentanyl and Diclofenac requirement in three groups was observed. No other side effect was reported in any of the groups at any post-operative interval**.**
Conclusion: The findings in present study suggested that Pregabalin does not provide a better preemptive pain control than placebo in cases undergoing LAC.
Keywords: Pregabalin, Postoperative Pain, Cholecystectomy.

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1. Introduction

Early Postoperative pain after laparoscopic Cholecystectomy (LAC) remains a clinical challenge for anaesthesiologist [1]. Various studies have explained unwanted impacts of unmitigated pain with utmost physiological effects on the body systems. Numerous drugs and techniques have been used to produce analgesia but each is associated with some side effects. Most commonly used drug opioids leads to respiratory side effects, nausea, vomiting and urinary retention [2].

Since time of onset for noxious stimulus is known during LAC surgery, preemptive analgesia provides attractive option for reducing postoperative morbidity. Pregabalin, a structural analogue of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) has shown a good analgesic efficacy against post-operative pain in surgical procedures with fewer side effects as compared to other conventionally used preemptive drugs [3, 4].

In the present study an attempt was made to evaluate the efficacy of two different doses of Pregabalin for attenuation of post-operative pain after LAC in a placebo-controlled randomized trial.

2. Materials and Methods

After obtaining institutional review board approval and informed parental consent, this prospective double

blinded randomised control trial was carried out in a tertiary care hospital. Out of a total of 163 patients listed for surgery during the study period, 28 patients did not meet inclusion criteria and 13 patients were not included due to refusal and 2 cases were ***cancelled.*** A total of 120 patients in ASA physical status grade I or II, between 20 - 60 years of age, with BMI ≤ 30 for males and ≤ 35 for females, undergoing elective LAC surgery under general anaesthesia (GA) were enrolled. Patients with known allergy / Hypersensitivity to the study drug, history of motion sickness or prior severe postoperative nausea and vomiting (PONV) and on chronic steroid therapy were excluded from the study. Patients with having renal or hepatic dysfunction, any chronic medical illness (diabetes mellitus, hypertension) or those with history of drug abuse/alcohol abuse/chronic pain or daily ingestion of analgesics or any NSAIDS <24 hours before surgery were excluded.

According to a computer-generated randomization chart, the patients were assigned to one of the three treatment groups. Patients in group A (n=40) received placebo (Vitamin tablet) and patients in group B (n=40) received 75 mg pregabalin tablet and patient in group C(n=40) received 150 mg pregabalin tablet orally as premedication 1 hr before induction of GA. The test drug was administered by a nurse who was blinded to drug assignment. Standardized anaesthetic management for induction of GA using Propofol 2 mg Kg^{-1} i.v., Inj. Fentanyl 1.5 $mcgKg^{-1}$ i.v. and Inj. Atracurium 0.5$mgKg^{-1}$ i.v. followed by tracheal intubation was done for the groups. Maintenance was done with 2% Sevoflurane in 70% nitrous oxide and 30% oxygen. At the end of surgery, residual neuromuscular blockade was antagonized with glycopyrrolate 0.02$mgKg^{-1}$ and Neostigmine 0.05 $mgKg^{-1}$, and the trachea was extubated while the child was awake.

Monitoring of vitals was done throughout the operative procedure and postoperatively patients at 2 hrs, 6 hrs, 12 hrs and then at 24 hrs post-procedure intervals. Pain scores were recorded on visual analogue scale (VAS) of 100 units at 2, 6, 12 and 24 hrs. Incidence of PONV was noted along with side effects such as headache, dizziness, diplopia and shivering. Time required for first dose of analgesic after the procedure was recorded. Total number of analgesic doses required during 24-hr period was also noted.

The data so obtained was analyzed using Statistical Package for Social Sciences Version 15.0. Chi-square test was used to compare the incidence of PONV and other side effects between study groups. Fisher exact test was used wherever the expected frequency of a cell shall be less than 5. Change in vitals was compared using paired "t"- test. ANOVA and independent samples "t"-test was used to compare among/ between groups for the outcome variables. Confidence level of the study was kept at 95%, hence a "p" value less than 0.05 indicated statistically significant difference.

3. Observation and Results

Demographic parameters and clinical characteristics were comparable between the groups [Table 1]. All patients were done under LAC and received premedication and GA. Gall bladder disease was the most common diagnosis in study group A and B whereas symptomatic Cholelithiasis was the most common finding in study group C. Gall stone disease with common bile duct stone was the least common diagnosis. Pain right hypochondrium and upper abdominal pain were the most common presenting complaints in all the groups followed by nausea and pain abdomen, dyspepsia and pain abdomen and dyspepsia alone respectively.

At all the time intervals except at 24 hrs VAS were lowest in Gp C. At 24 hrs interval, VAS was lowest in Gp A. VAS was maximum in group A at 2 hrs. At 6 and 12 hrs intervals VAS in Gp A and Gp B was same and higher as compared to Gp B. At 24 hours, VAS in both the study groups was same and higher than control group. At none of the time intervals, a significant difference in VAS was observed among the groups ($p>0.05$) [Table 2]. At 24 hrs, no episode of nausea was reported in any of the groups [Table 2]. At 12 and 24 hrs, no episode of vomiting was reported in any of the groups [Table 2]. No complaint of headache, shivering, dizziness or diplopia was reported in any of the groups at any post-operative interval. No difference among groups was observed with respect to mean time for need of first rescue analgesic and mean dosage of fentanyl and Diclofenac used as rescue analgesics ($p>0.05$) [Table 3].

Table 1: Demographic profile and clinical characteristics of patients in groups [MEAN ± SD]

Patient data	Group A (n=40) mean±SD	Group B (n=40) mean±SD	Group C (n=40) mean±SD	P value
Mean Age	37.85±6.88	36.17±5.28	36.70±7.41	0.80
Gender M/F	13/27	15/25	10/30	0.48
Mean BMI	23.44±1.81	23.29±1.47	23.16±1.41	0.75
ASA grade (I/II)	36/4	35/5	36/4	0.91
Duration of surgery (min)	54.4±7.9	54.8±7.7	55.5±7.7	0.80
IO fluid requirement (ml)	1022.5±155.2	1018.8±153.0	1035.0±154.9	0.88

All values expressed as mean ± SD or as expressed otherwise. M= Male, F= Female, BMI=Body mass Index, IO= Intraoperative, SD= Standard deviation.

Table 2: Intergroup Comparison of postoperative pain, Nausea and Vomiting at different time intervals [MEAN ± SD]

	Time Interval	Group A (n=40) Mean±SD/%	Group B (n=40) Mean±SD/%	Group C (n=40) Mean±SD/%	Significance of difference (Kruskall Wallis test)	
					"χ^2"	"p"
VAS	2 hrs	3.0±1.2	2.9±1.2	2.7±1.2	1.15	0.56
	6 hrs	1.6±0.9	1.6±0.9	1.3±1.0	2.02	0.36
	12 hrs	1.0±0.8	1.0±0.8	0.9±0.7	0.58	0.74
	24 hrs	0.9±0.8	1.0±0.8	1.0±0.8	0.10	0.94
Postoperative nausea	2 hrs	6(15)	5(12.5)	6(15)	0.145	0.930
	6 hrs	4(10)	3(7.5)	4(10)	0.207	0.902
	12 hrs	1(2.5)	1(2.5)	0(0.0)	1.023	0.600
	24 hrs	0(0.0)	0(0.0)	(0.0)	-	-
Postoperative vomiting	2 hrs	3(7.5)	4(10)	4(10)	0.207	0.902
	6 hrs	4(10)	4(10)	2(5)	0.900	0.638
	12 hrs	0(0.0)	0(0.0)	0(0.0)	-	-
	24 hrs	0(0.0)	0(0.0)	0(0.0)	-	-

VAS= Visual Analogue Score

Table 3: Need for rescue analgesic, time duration for need of first rescue analgesic and dose and type of analgesic drug requirement [Mean ± SD]

Variable	Group A (n=40)	Group B (n=40)	Group C (n=40)	Significance of difference	
				χ^2	P
Need for rescue analgesic	26(65)	25(62.5)	24(60)	0.48	0.78
Time for need of first rescue analgesic	236.5	230.9	170.0	0.59	0.55
Fentanyl(µgm)	58.1± 6.6	58.0±6.2	55.4±5.9	1.46	0.23
Diclofenac(mg)	114.4± 36.2	113± 36.2	107.3± 28.1	0.30	0.73

4. Discussion

Our results showing that the trial drug Pregabalin did not perform better than a placebo. These findings are similar to those reported in literature. Paech *et al* reported that 100 mg pregabalin does not reduce acute pain or improve recovery after minor surgery [5]. In present study no significant difference in time for first rescue analgesic, number of patients requiring rescue analgesic and analgesic need of fentanyl and Diclofenac was observed among the three groups thus rendering the fact that either of two dosages of pregabalin are no better than a placebo. Jokela *et al* also made similar observations for 75 mg and 150 mg oral Pregabalin dosage [6].

However, in another study Jokela *et al* reported preemptive Pregabalin to be a better analgesic for post-operative pain control reducing the need of postoperative analgesia but at a higher dosage of 300 mg and 600 mg respectively which was also associated with side effects [7]. The results observed by Chang *et al* who proposed two 300 mg perioperative doses of pregabalin at 12 h apart intervals to prevent and attenuate post-operative shoulder pain also undermine the utility of pregabalin as an effective analgesic drug [8].

In present study, the utility of drug was tested at a much lower (75 mg and 150 mg) single dose regimen and did not show any better result as compared to placebo.

The controversy around use of pregabalin as a preemptive analgesia remains a topic of debate owing to availability of limited literature on the issue.

However, Zhang *et al* who carried out a systematic review of 11 valid randomized controlled trials using pregabalin for acute postoperative pain made conclusions similar to observation made in present study with respect to its ability of controlling the pain [9]. Although they reported that preemptive use of pregabalin reduces opioid consumption and opioid related adverse effects after surgery. However, in present study, we did not notice a reduction in opioid reduction or post-operative analgesic need in either of two groups using 75 mg and 150 mg oral pregabalin as a preemptive drug. Keeping in view these findings at a higher dosage, it might be considered that the dosage in present study was much lower and the response being dose-dependent does not conform to the observations of systematic review of Zhang *et al*.

The findings in present study are a trend that paves the way for further experimentations at a higher dosage as no side effects were noticed at the targeted dosages in present study and given the reported efficacy of pregabalin at 300 and 600 mg dosages but with a higher side effect profile. A dosage schedule in between 150 mg and 300 mg should be subjected to evaluation.

5. Conclusion

The findings in present study thus suggested that pregabalin at a dosage of 75 mg and 150 mg does not provide a better preemptive pain control than placebo in cases undergoing laparoscopic cholecystectomy and requires further investigation for optimum dosages.

Financial Disclosure

The authors declared that this study has received no financial support.

Ethics Committee Approval

Ethics committee approval was received for this study from the ethics committee of Command hospital, Lucknow, India

Informed Consent

This study performed in humans was approved by the Institutional Review Board and written informed consent was obtained from all patients or parents of minors.

Conflict of Interest

No conflict of interest was declared by the authors.

References

[1]. Lau H, Brooks DC. Predictive factors for unanticipated admissions after ambulatory laparoscopic Cholecystectomy. *Arch Surg.* 2001 Oct; 136(10):1150-3.

[2]. Shoar S, Esmaeili S, Safari S. Pain Management after Surgery: A Brief Review. *Anesth Pain.* 2012; 1(3):184-6.

[3]. Chizh BA, Gohring M, Troster A, Quartey GK, Schmelz M, Koppert W. Effects of oral pregabalin and aprepitant on pain and central sensitization in the electrical hyperalgesia model in human volunteers. *Br J Anaesth.* 2007; 98(2): 246-54.

[4]. Shneker BF, McAuley JW. Pregabalin: a new neuromodulator with broad therapeutic indications. *Ann Pharmacother.* 2005; 39(12):2029-37.

[5]. Paech MJ, Goy R, Chua S, Scott K, Christmas T, Doherty DA. A randomized, placebo-controlled trial of preoperative oral pregabalin for postoperative pain relief after minor gynecological surgery. *Anesth Analg.* 2007; 105(5):1449-53.

[6]. Jokela R, Ahonen J, Tallgren M, Haanpää M, Korttila K. Premedication with pregabalin 75 or 150 mg with ibuprofen to control pain after day-case gynaecological laparoscopic surgery. *Br J Anaesth*. 2008; 10(6): 834-40.

[7]. Jokela R, Ahonen J, Tallgren M, Haanpaa M, Korttila K. A randomized controlled trial of perioperative administration of pregabalin for pain after laparoscopic hysterectomy. *Pain.* 2008; 134(1-2):106-12.

[8]. Chang SH, Lee HW, Kim HK, Kim SH, Kim DK. An evaluation of perioperative pregabalin for prevention and attenuation of postoperative shoulder pain after laparoscopic cholecystectomy. *Anesth Analg.* 2009; 109(4):1284-6.

[9]. Zhang J, Ho K-Y, Wang Y. Efficacy of pregabalin in acute postoperative pain: a meta-analysis. *Br J Anaesth* 2011; 106(4): 454-62.