# Efficacy of Methylprednisolone and Etoricoxib Combination to attenuate Post-operative Pain and Nausea/Vomiting in Laparoscopic Surgeries

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# ABSTRACT

Background and Aims:Pain and PONV (postoperative nausea and vomiting) are common complaints in the period following surgery. A multimodal approach targeting the reduction of postoperative pain with an opioid-sparing analgesic along with an antiemetic medication would minimize opioid consumption and its associated side effects. We evaluated the efficacy of methylprednisolone 125 mg IV taken along with oral 120 mg etoricoxib on postoperative pain and PONV in patients undergoing laparoscopic surgeries

Material and methods:A prospective, randomized, double-blind study was conducted on 70 patients aged between 18 and 60 years with ASA grade 1 and 2 posted for elective laparoscopic surgeries. The test group was given a combination of methylprednisolone 125mgIV (given just before induction)& etoricoxib120mg oral (given 1 hr before surgery). (Group A, n=35) while control group received normal saline IV and a placebo per oral(Group B, n=35). Duration and quality of analgesia was assessed by visual analogue scale (VAS) score at 2,4,6,8,10,12,16,20 and 24hr as primary objective. Total dose of rescue analgesic(injection Fentanyl 50 mcg) in first 24 hours, peri-operative hemodynamic change and post op nausea vomiting (PONV) were observed as secondary objective.

Result:Demographic profiles were comparable. Duration of postoperative analgesia was significantly prolonged(p<0.05) in Group A(7.57 $\pm$ 1.04hrs) as compared to Group B(3.05 $\pm$ 0.5hrs). Group A showed a significant reduction in postoperative fentanyl consumption in the form of rescue analgesic(p<0.05). Group A also showed significant reduction in the incidence of PONV(p<0.05).

Conclusion: We conclude that single-dose administration of methylprednisolone IV along with oral etoricoxib has better analgesic efficacy in comparison to placebo for patients undergoing laparoscopic surgeries.

KEYWORDS: Etoricoxib, Methylprednisolone, PONV, post-

operative pain, laparoscopic surgery.

# **INTRODUCTION:**

Laparoscopic surgeries are minimally invasive surgeries that are safe and advantageous because they reduce the hospital stay and lead to better convalescence after surgery. They are increasingly being termed as outpatient procedures.The most crucial step in the postoperative recovery period is the optimal control of early postoperative pain and postoperative nausea and vomiting. Effective perioperative pain management poses a significant challenge for healthcare practitioners.<sup>[1]</sup>

Since time immemorial, opioids have been the mainstay drugs for management of postoperative pain, despite their manifold adverse effects such as respiratory depression, PONV and physical dependence. So a multimodal approach using combination of opioid and non- opioid analgesics or a mixture of non-opioid analgesics given as pre-emptive analgesic improve pain relief, minimize opioid consumption and opioid associated side effect. <sup>[2]</sup>Pre-emptive analgesia is an anti-nociceptive treatment, which prevents central hyper-excitability, central sensitization evoked by the incisional and inflammatory injuries occurring during surgery and early postoperative period via altering the afferent input involved in pain. <sup>[3]</sup>

Etoricoxib is a selective inhibitor of cyclooxygenase-2 (COX-2),an enzyme involved in pain and inflammation. Its extensively used because of its wide safety profile (GI, CVS, renal), good oral bioavailability, rapid onset of action and long plasma half life. <sup>[4]</sup>Along with its opioid sparing analgesic effect it has its proven benefits in acute (postoperative) and chronic(arthritis) pain management. Laparoscopic surgeries have remarkably high incidence of PONV .Glucocorticoids likemethylprednisolone have shown to decrease pain, PONV and postoperative fatigue. They have also shown to have opioid sparing analgesic effect similar to NSAIDs. <sup>[4–6]</sup>Hence etoricoxib was combined with methylprednisolone in our study to attenuate pain and PONV.

#### **MATERIAL AND METHODS:**

A prospective, double-blind clinical study was initiated after clearance from institutional ethical committee. Sample size was calculated to be 35 patients to be randomly allocated in each group keeping a power of 0.8,  $\alpha$  error of 0.05 and allowing for study error and attrition. A total of 70 patients were assigned to either test group(A) receiving combination of tab etoricoxib 120 mg and iv methylprednisolone 125 mg or control group(B) receiving placebo tablet with sterile water iv using computer generated table of random numbers. Patients were given either a combination of tab etoricoxib 120 mg (1 hour prior to induction) and iv methylprednisolone 125 mg (just before induction)in Group A while control Group B received a placebo tablet and sterile water iv. All patients included in the study were kept nil per oral for 8 hrs. <sup>[7]</sup>Routine vital parameters including pulse oximeter, NIBP, ECG were attached and monitored intraoperatively. The anesthesia technique was standardized for both groups. Patients were induced with 3  $\mu$ g/kg of fentanyl IV and 2 mg/kg of propofol IV; orotracheal intubation was facilitated by 0.08 mg/kg of vecuronium IV. Anaesthesia was maintained by inhalational sevoflurane with oxygen and nitrous oxide. At the end of the surgery, residual neuromuscular paralysis was antagonized with neostigmine at 0.04 mg/kg and glycopyrrolate at 0.01 mg/kg IV. Following reversal, the patients were extubated and shifted to the post-anesthesia care unit (PACU). Pain was assessed perioperatively using standard 10 cm visual analog scale with 0 corresponding to no pain and 10 worst possible pain.<sup>[8]</sup>

VAS score was noted subsequently after every 2 hrs at wards. The time in minutes from the end of surgery to the first analgesia request was noted together with total analgesia consumed in the first 24 hrs. In addition, the incidence of PONV(using four-point ordinal scale),sedation (assessed using Ramsey Sedation Scale),total number of rescue analgesic (inj fentanyl 50 $\mu$ g) doses.Haemodynamic parameterswere recorded both intra and post-operatively for first 24 hours.<sup>[9, 10]</sup>

Statistical analysis was done using the SPSS version 20 software. Standard qualitative and quantitative tests were used to compare the data. (e.g. unpaired student — t test, Chi-square test etc). A p value < 0.05 with a power of 80% was considered statistically significant.

#### **RESULTS:**

Both groups were comparable in terms of demographic profile such age, sex, height, weight, ASA physical status, site of surgery with no statistical significant difference between two groups.

The duration of analgesia was longer (7.57  $\pm$  1.04 hrs) in Group A than Group B (3.05  $\pm$  0.9 hrs) and the difference

was statistically significant (p=0.02). Table 1

Parameters	Group A (n=35)	Group B (n=35)	p value
Age(years)	40.40 ±12.9	38.89 ±13.41	
Sex (Male/Female)	23/12	20/15	p>0.05
Weight (kgs)	59.34±8.73	62.57±5.63	
ASA (I/II)	31/4	32/3	

#### Table 1: Comparison of demographic data in two groups

Mean VAS scores were significantly low in group A than group B at postoperative time, 2 hrs (0 vs 1.4); 4 hrs (1.28 vs 2.8) and 6 hrs (2.2 vs 3.42); after which the difference became insignificant. Figure 1 Mean number of analgesic doses required in Group A was  $1.31 \pm 0.50$ , were as in Group B was  $1.771\pm0.6897$  for first 24 hours. There was statistically significant difference between two groups (p value = 0.0203).Table 2Table 3

Duration	Group A (n=35)		Group B (n=35)		
gesia	No. of patients	Per- cent	No. of patients	Per- cent	
2hr	00	0	08	22.85	
3hr	00	00	18	51.4	
4hr	00	00	07	20.0	
5hr	00	00	01	2.85	p value
6hr	07	20.0	01	2.85	0.0006
7hr	08	22.85	00	0.0	
8hr	13	37.14	00	0.0	
9hr	07	20.0	00	0.0	
Mini- mum	6 hr		2 hr		
Maxi- mum	9 hr		6 hr		
$Mean \pm SD$	7.57±1.04 hr		3.05±0.5hr		

# Table 2: 2: Comparison of duration of analgesia in twogroups

22.85% of patients in Group A complained PONV compared to 51.42% in Group B which was statistically significant. (p<0.001).All the patients remained haemodynamically stable throughout the period of study. There was no statistically significant difference between the groups.Hypotension and sedation was noted in some

	Group A(n=35)			Group B(n=35)			
Total Analgesic doses in first 24hr	No. of doses	No. of patients	Percent	No. of doses	No. of patients	Percent	
	0	0	0	0	0	0	
	1	23	65.71	1	2	5.71	p value
	2	12	34.29	2	12	34.29	0.0203
	3	0	0	3	14	40	
	4	0	0	4	7	20.0	
Mean No. of dose $\pm$ SD	$\textbf{1.31}\pm\textbf{0.50}$			2.79±085			

Table 3: 3: Comparison of dose of rescue analgesic in first 24 hrs in two groups

patients of both the groups and was statistically insignificant.





# DISCUSSION

Pain is a subjective sensation, however its undertreatment can lead to various physical, emotional and psychological sequelae. Inadequate treatment of postoperative pain leads to prolonged hospital stay, delayed recovery and more economic burden to patient.<sup>[11]</sup>

As part of pre-emptive multimodal analgesia, use of opioid and non-opioid analgesics that act at different sites within the central and peripheral nervous systems has found to prevent postoperative pain. [11-13] Opioids are associated with emesis, risk of respiratory depression and addiction. NSAID's are the most commonly used analgesics for acute pain control. COX-2 inhibitors like etoricoxib are associated with fewer adverse effects than conventional NSAIDs and hence more preferred. <sup>[14, 15]</sup>Celik EC et al used NSAIDs as along with general anesthesia and found total reduction in post op analgesic consumption but their study was limited by unsatisfactory VAS score and various side effect.Bisgaard used dexamethasone with selective COX-2 inhibitors where as Gautam S et al and Romundstad et al used methylprednisolone with etoricoxib all noticed good analgesia with opioid sparing effect. [16–19]

Use of methylprednisolone along with etoricoxib significantly prolonged duration of action with reduce number of rescue analgesic doses in present study as seen by Boonriong et al and others. <sup>[18–20]</sup>Lierz et al and Ko-iam et al used etoricoxib as preemptive analgesia in therapeutic knee arthroscopy surgeries and abdominal surgeries respectively and showed reduced VAS score at different time intervals as seen in our study.As very less number of studies have noted VAS score at different time interval, there is scope for future studies to note the same. <sup>[21, 22]</sup>

Glucocorticoids like methylprednisolone are well known for their analgesic(membrane stabilization), antiinflammatory, immune modulating and antiemetic effects. <sup>[18]</sup>Potential side effects of glucocorticoids include gastrointestinal bleeding, impaired wound healing, susceptibility of wound site infection, but with 125mg single dose many studies have ruled out the same. <sup>[18–20]</sup> Present study showed combining methylprednisolone with etoricoxib not only prolongs analgesia but also reduces PONV. Hence this combination can be used as multimodal approach to attenuate pain and PONV.

World is behind laparoscopic surgeries because of its wide variety of advantages over open surgeries but at the same time pain from port site, peritoneal stretch is associated with PONV. <sup>[18]</sup>To combat this, the concept of multimodal analgesia and preemptive analgesia is vast developing rather than single analgesic technique for better pain relief.

Nausea often accompanies pain so drug which reduces pain and PONV together would be a boon to pain physicians in post op patients. Gautam et al, Lunn et al concluded from their studies that a single dose of methylprednisolone decreases the incidence of PONV and reduces the consumption of ondansetron.<sup>[18, 23]</sup> Whereas Konuganti et al conducted their study using dexamethasone and concluded that the glucocorticoid played an important role in alleviating patient discomfort related to nausea and vomiting. <sup>[23, 24]</sup>All the patients of both groups remained haemodynamically stable throughout the study period. It was in accordance with other studies like Lierz et al, Shuying et al and Ko-iam et al. <sup>[21, 22, 25]</sup> This is evident by the fact that there was good analgesia throughout the period of study. The concept of multi modal analgesia is well-established for management of pain and has to be used regularly in order to provide speedy recovery of patients at hospital

### CONCLUSION

Single dose of intravenous methylprednisolone and oral etoricoxib combination used as preemptive analgesic significantly reduces postoperative pain and PONV in patients undergoing laparoscopic surgeries.

#### LIMITATION:

Single dose etoricoxib does not infer the long term benefits to the patients. Although both the drugs are safely used there is lack of evidence for drugs interaction between them and assessment of visual analog scale score is subjective.

#### REFERENCES

- 1. Jakobsson JG. Pain management in ambulatory surgery-A review. Pharmaceuticals. 2014;7:850–65.
- Mariano ER, Fishman S, Crowley M. Management of acute perioperative pain. Accessed date ; 2019,. Available from: https://www.uptodate.com/contents/ management-of-acute-perioperative-pain.
- Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. Lancet. 2006;367:1618–1625.
- Gautam S, Agarwal A, Das PK, Agarwal A, Kumar S, Khuba S. Evaluation of the efficacy of methylprednisolone, etoricoxib and a combination of the two substances to attenuate postoperative pain and PONV in patients undergoing laparoscopic cholecystectomy: a prospective, randomized, placebo-controlled trial. Korean J Pain. 2014;27:278–84.
- Steffens JP, Santos FA, Sartori R, Pilatti GL. Preemptive dexamethasone and etoricoxib for pain and discomfort prevention after periodontal surgery: A double-masked, crossover, controlled clinical trial. J Periodontol. 2010;81:1153–60.
- Sandhu T, Paiboonworachat S, Ko-Iam W. Effects of preemptive analgesia in laparoscopic cholecystectomy: a double-blind randomized controlled trial. Surg Endosc. 2011;25:23–30.
- Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. Anesthesiology. 2011;114:495–511.
- Chooi CS, White AM, Tan SG, Dowling K, Cyna AM. Pain vs comfort scales after Caesarean section: a randomized trial. Br J Anaesth. 2013;110:780–787.

- Akhavanakbari G, Entezariasl M, Isazadehfar K, Mirzarahimi T. The effects of oral pregabalin on post-operative pain of lower limb orthopedic surgery: a double-blind, placebo-controlled trial. Perspect Clin Res. 2013;4:165–173.
- Mackey DC, Butterworth JF, Mikhail MS, Morgan GE, Wasnick JD. Morgan and Mikhail's Clinical Anesthesiology. New York, NY: McGraw-Hill Education LLC; 2013,.
- Gan TJ, Joshi GP, Viscusi E, Cheung RY, Dodge W, Fort JG. Preoperative parenteral parecoxib and follow-up oral valdecoxib reduce length of stay and improve quality of patient recovery after laparoscopic cholecystectomy surgery. Anesth Analg. 2004;98:1665–73.
- Oliveira D, Almeida GS, Benzon MD, Mccarthy HT, J R. Perioperative single dose systemic dexamethasone for postoperative Pain: A meta-analysis of randomized controlled trials. Anesthesiology: The Journal of the American Society of Anesthesiologists. 2011;115:575– 88.
- 13. Waldron NH, Jones CA, Gan TJ, Allen TK, Habib AS. Impact of perioperative dexamethasone on postoperative analgesia and side-effects: systematic review and meta-analysis. Br J Anaesth. 2013;110:191–200.
- 14. Chung F, Ritchie E, Su J. Postoperative pain in ambulatory surgery. Anesth Analg. 1997;85:808–824.
- 15. Kehlet H. Surgical stress: the role of pain and analgesia. Br J Anaesth. 1989;63:189–95.
- 16. Çelik DEC, Kara E, Koc. Ahmet Murat Yayik. The comparison of single dose preemptive intravenous ibuprofen and paracetamol on postoperative pain scores and opioid consumption after open septorhinoplasty: a randomised controlled study. European Archives of Oto-Rhino-Laryngology. 2018;275:2259–63.
- 17. Bisgaard T. Analgesic treatment after laparoscopic cholecystectomy: a critical assessment of the evidence. Anesthesiology. 2006;104:835–881.
- Puura A, Puolakka P, Rorarius M, Salmelin R, Lindgren L. Etoricoxib pre-medication for postoperative pain after laparoscopic cholecystectomy. Acta Anaesthesiol Scand. 2006;50:688–93.
- Romundstadl, Breivikh, Niemig, Helle A, Stubhauga. Methylprednisolone intravenously 1 day after surgery has sustained analgesic and opioid-sparing effects. Acta Anaesthesiol Scand. 2004;489:1223–1254.
- Boonriong T, Tangtrakulwanich B, Glabglay P, Nimmaanrat S. Comparing etoricoxib and celecoxib for preemptive analgesia for acute postoperative pain in patients undergoing arthroscopic anterior cruciate ligament reconstruction: a randomized controlled trial. BMC Musculoskeletal Disorders. 2010;11:1–5.

- 21. Lierz P, Losch H, Felleiter P. Evaluation of a single preoperative dose of etoricoxib for postoperative pain relief in therapeutic knee arthroscopy. Acta Orthop. 2012;83:642–649.
- 22. Ko-Iam W, Paiboonworachat S, Pongchairerks P, Junrungsee S, Sandhu T. Combination of etoricoxib and lowpressure pneumoperitoneum versus standard treatment for the management of pain after laparoscopic cholecystectomy: a randomized controlled trial. Surgical endoscopy. 2016;30:4800–4808.
- Lunn TH, Kristensen BB, Andersen LØ, Husted H, Otte KS, Gaarn-Larsen L. Effect of high-dose preoperative methylprednisolone on pain and recovery after total knee arthroplasty: a randomized, placebo-controlled trial. Br J Anaesth. 2011;106:230–238.
- Konuganti K, Rangaraj M, Elizabeth A. Pre-emptive 8 mg dexamethasone and 120 mg etoricoxib for pain prevention after periodontal surgery: A randomised controlled clinical trial. J Indian Soc Periodontol. 2015;19:474–480.
- Shuying L, Xiao W, Peng L, Tao Z, Ziying L, Liang Z. Preoperative etoricoxib reduces length of stay on ambulatory laparoscopic cholecystectomy. Int J Surg. 2014;12:464–472.

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