

A Comparative Study of Intravenous Paracetamol and Ketorolac for Postoperative Analgesia Following Laproscopic Cholecystectomy

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Abstract: ***Background and Aims:** The present study compared the analgesic efficacy of paracetamol and ketorolac for postoperative pain in patients undergoing laparoscopic cholecystectomy. **Study Design:** Prospective randomized double blinded study. **Material and Methods:** Total of 60 patients aged 18-58 years with ASA physical status I or II of either sex, scheduled for elective laparoscopic cholecystectomy under general anaesthesia were included in this study. Patients were allocated to two equal groups of 30 each by sealed envelope method. Patients were premedicated with intravenous glycopyrrolate (0.01mg/kg) and fentanyl (2mcg/kg). After preoxygenation with 100% oxygen for 3 min, patients were induced with IV propofol (2mg/kg) followed by succinyl choline (1.5mg/kg) to facilitate laryngoscopy and tracheal intubation. Anaesthesia was maintained with sevoflurane, nitrous oxide 60% in oxygen, and vecuronium in incremental dosages of 0.02 mg/kg. Group P received an IV infusion of Paracetamol 1gm 30 minutes prior to end of surgery and Group K received 30mg ketorolac iv. The mean arterial blood pressure and SpO2 were recorded prior to induction, after induction and monitored every 15 minutes till the end of surgery and extubation. Once residual neuromuscular blockade was reversed with 0.05mg/kg neostigmine and 0.01mg/kg glycopyrrolate and extubation criteria met, patients were extubated and shifted to the postoperative room. **Results:** Statistical analysis was done using SPSS software. p values <0.05 were considered significant. There was no statistical difference between the two groups in terms of age and demographic data as well as hemodynamic parameters. The VAS score at 3 and 6 hours was found to be lower in the ketorolac group. **Conclusion:** Single dose intravenous ketorolac can be recommended as an effective and safe alternative to intravenous paracetamol for postoperative pain following laparoscopic cholecystectomy.*

Keywords: Intravenous paracetamol, ketorolac, postoperative analgesia

1. Introduction

The International Association for the study of pain defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.”¹

All surgical procedures are associated with pain which increases the metabolic responses, autonomic reflexes, nausea, muscle spasm, ileus, all of which contribute to increased postoperative morbidity and mortality.² It is hence important to ensure adequate postoperative pain relief to improve the surgical outcome as well as to rehabilitate the patient at the earliest.

Phillipe Mouret in 1987 introduced the technique of laparoscopic cholecystectomy and ever since this procedure has gained immense popularity due to fewer complications and lower postoperative complications.³ Acute pain following laparoscopic cholecystectomy is multifactorial and starts with surgical trauma and ends with healing of tissues.^{4,5,6} Pain following laparoscopic cholecystectomy can be either somatic or visceral in origin. Pain arising from the surgical site is somatic in origin while that arising from the gall bladder bed is visceral. Some patients may also complain of shoulder pain post the procedure due to irritation of the diaphragm by the residual CO2.

Paracetamol is one of the most commonly used drugs for the treatment of acute pain. Because of its good safety profile intravenous paracetamol is an important component of a multimodal regimen for analgesia.⁷

NSAIDs act by inhibiting prostaglandin synthesis by inhibiting the key enzyme, cyclooxygenase. Ketorolac acts by causing inhibition of both cyclooxygenase and lipooxygenase enzymes, thereby inhibiting prostaglandin and leukotriene synthesis. As a result, ketorolac is a more potent NSAID in comparison to other drugs of the same class.

2. Study Design, Materials and Methods

After obtaining approval from the Institution ethical committee and written informed consent from the patients, 60 patients of either sex belonging to ASA category 1 and 2, aged between 18-58 years posted for elective laparoscopic cholecystectomy were selected and the study was carried out. Patients having contraindications to paracetamol or to NSAIDs and those having cardiovascular, renal, respiratory comorbidities or history of allergy to the study drugs were excluded after preoperative assessment. Randomization was carried out by sealed envelope method. All patients were explained details of Visual analogue scale (VAS) prior to surgery. All patients were premedicated with tablet ranitidine 150mg and tablet diazepam 5mg on the night prior to surgery.

On shifting to the operating rooms, an 18G cannula was secured and all patients were started on Ringer lactate solution at the rate of 8-10ml/kg/hr. Standard ASA monitors NIBP, ECG and Pulse oximeter were attached to the patients. Patients were premedicated with intravenous glycopyrrolate (0.01mg/kg) and fentanyl (2mcg/kg). After preoxygenation with 100% oxygen for 3 min, patients were induced with IV propofol (2mg/kg) followed by succinyl choline (1.5mg/kg)

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to facilitate laryngoscopy and tracheal intubation. Anesthesia was maintained with sevoflurane, nitrous oxide 60% in oxygen, and vecuronium in incremental dosages of 0.02 mg/kg. Group P received intravenous paracetamol 1g (in 100ml infusion) and group K received intravenous ketorolac 30mg 30 minutes prior to the end of surgery. Once the residual neuromuscular blockade was reversed with 0.05mg/kg neostigmine and 0.01mg/kg glycopyrrolate and extubation criteria met, patients were extubated. The mean arterial blood pressure and SpO₂ were recorded prior to induction, after induction and monitored every 15 minutes till the end of surgery.

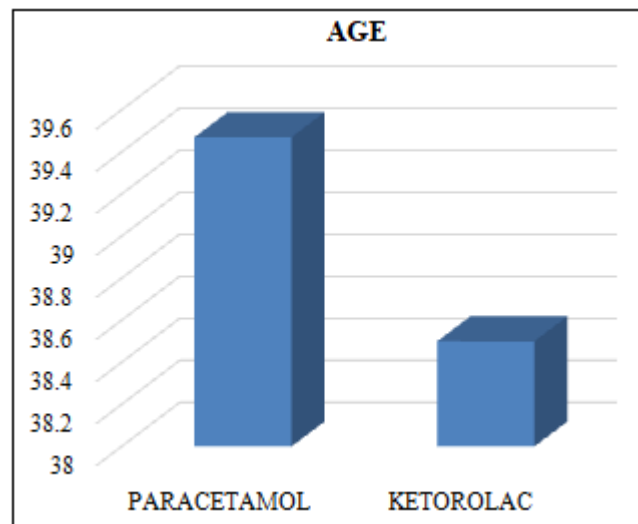
Patients were shifted to the postoperative room to monitor the hemodynamic data, postoperative pain and other adverse events every 15 minutes for the first 1 hour and then 3 and 6 hrs later. Postoperative pain was assessed using the VAS scale. Rescue analgesia in the form of tramadol 50mg IV was administered when the VAS score recorded was more than 3. The requirement of rescue analgesic was recorded at the end of 6 hours.

3. Statistical Analysis

All statistical methods were carried using SPSS 23 for Windows. $P < 0.05$ was considered significant and $p < 0.01$ was considered highly significant.

4. Results

All cases were selected from general surgery/gastroscopy departments. All the 60 patients completed the study. Demographic profile of the patients in terms of age and gender were comparable and there was no significant inter-group difference (Graph 1 and 2).



Graph 1: Demographic Data

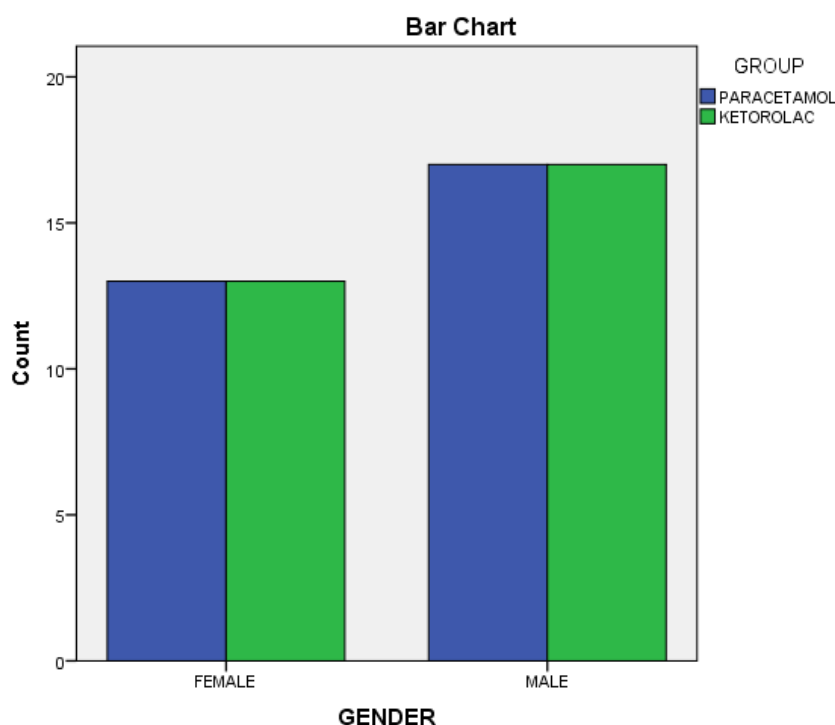
Table 1

	Group	N	Mean	Std. Deviation	t	Df	P Value
Age	Paracetamol	30	39.47	10.474	0.357	58	0.722
	Ketorolac	30	38.5	10.504			

Table 2

Table 2

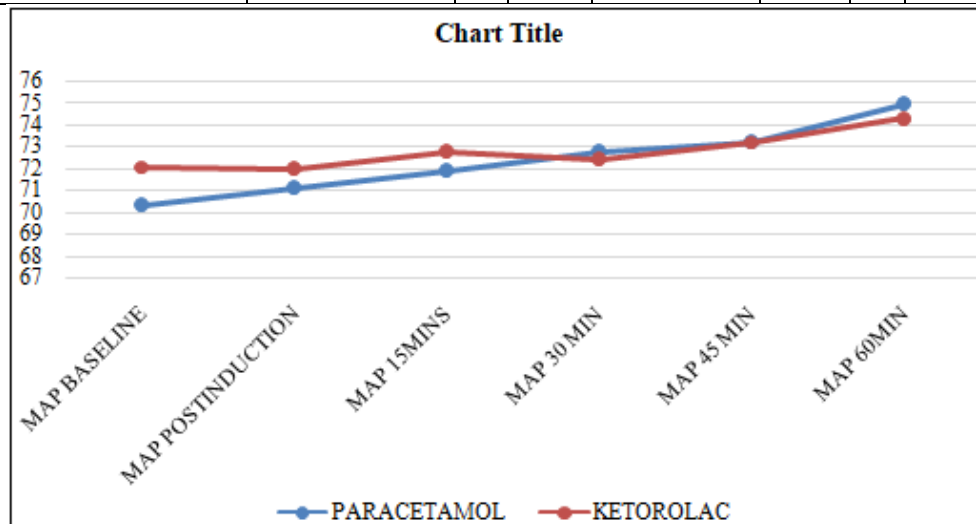
Crosstab					
			GROUP		Total
			Paracetamol	Ketorolac	
Gender	Female	Count	13	13	26
		% within GROUP	43.3%	43.3%	43.3%
	Male	Count	17	17	34
		% within GROUP	56.7%	56.7%	56.7%
Total		Count	30	30	60
		% within GROUP	100.0%	100.0%	100.0%



Graph 2: Showing Gender Comparison

Table 3

	GROUP	N	Mean	Std. Deviation	t	Df	P VALUE
MAP BASELINE	PARACETAMOL	30	70.3	7.831	-0.933	58	0.355
	KETOROLAC	30	72.07	6.807			
MAP POSTINDUCTION	PARACETAMOL	30	71.1	6.37	-0.52	58	0.605
	KETOROLAC	30	72	7.027			
MAP 15MINS	PARACETAMOL	30	71.87	4.995	-0.611	58	0.543
	KETOROLAC	30	72.8	6.708			
MAP 30 MIN	PARACETAMOL	30	72.77	4.819	0.228	58	0.821
	KETOROLAC	30	72.43	6.399			
MAP 45 MIN	PARACETAMOL	30	73.2	4.902	0	58	1
	KETOROLAC	30	73.2	6.52			
MAP 60MIN	PARACETAMOL	30	74.97	5.543	0.477	58	0.635
	KETOROLAC	30	74.3	5.286			



Graph 3: graph showing mean arterial pressure

Comparison of the MAP BASELINE between the two groups shows that MAP BASELINE is higher in KETOROLAC group with a t value of -0.933 and is statistically non significant with a p value of 0.355

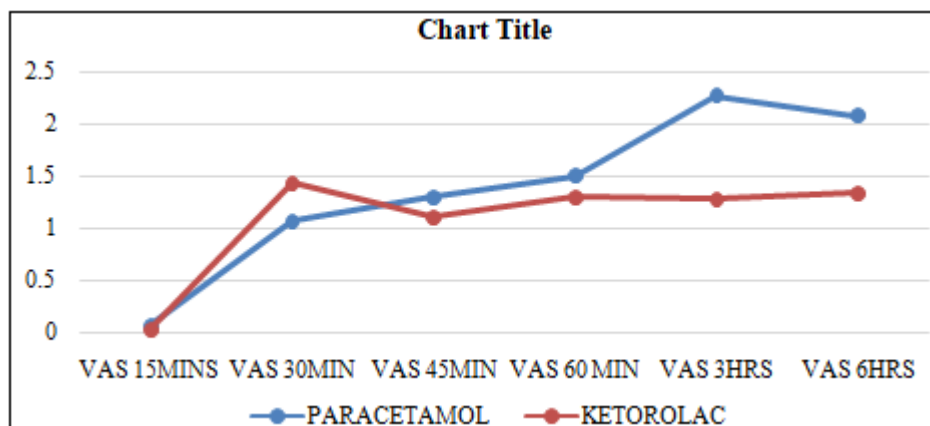
Comparison of the MAP 30 MIN between the two groups shows that MAP 30 MIN is higher in PARACETAMOL group with a t value of 0.228 and is statistically non significant with a p value of 0.821

Comparison of the MAP POSTINDUCTION between the two groups shows that MAP POSTINDUCTION is higher in KETOROLAC group with a t value of -0.52 and is statistically non significant with a p value of 0.605

Comparison of the MAP 45 MIN between the two groups shows that MAP 45 MIN is higher in PARACETAMOL group with a t value of 0 and is statistically non significant with a p value of 1

Comparison of the MAP 15MINS between the two groups shows that MAP 15MINS is higher in KETOROLAC group with a t value of -0.611 and is statistically non significant with a p value of 0.543

Comparison of the MAP 60MIN between the two groups shows that MAP 60MIN is higher in PARACETAMOL group with a t value of 0.477 and is statistically non significant with a p value of 0.635



Graph 4: Graph showing changes in VAS Score

Table 4

	GROUP	N	Mean	Std. Deviation	t	Df	P Value
VAS 15MINS	PARACETAMOL	30	0.07	0.254	0.584	58	0.561
	KETOROLAC	30	0.03	0.183			
VAS 30MIN	PARACETAMOL	30	1.07	0.691	-1.876	58	0.066
	KETOROLAC	30	1.43	0.817			
VAS 45MIN	PARACETAMOL	30	1.3	0.651	1.18	58	0.243
	KETOROLAC	30	1.1	0.662			
VAS 60 MIN	PARACETAMOL	30	1.5	1.042	0.935	43.29	0.355
	KETOROLAC	30	1.3	0.535			
VAS 3HRS	PARACETAMOL	30	2.27	0.785	5.814	58	<0.001
	KETOROLAC	30	1.27	0.521			
VAS 6HRS	PARACETAMOL	30	2.07	0.907	3.317	58	0.002
	KETOROLAC	30	1.33	0.802			

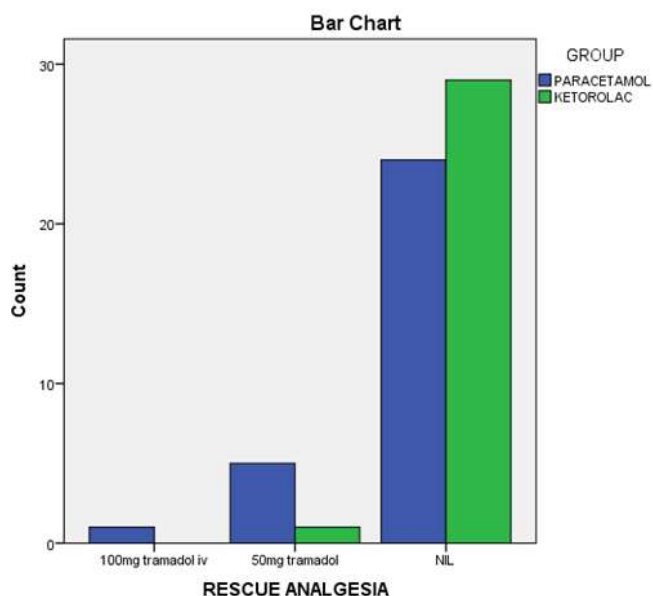
Comparison of the VAS 3HRS between the two groups shows that VAS 3HRS is higher in PARACETAMOL group with a t value of 5.814 and is statistically significant with a p value of <0.001

Comparison of the VAS 6HRS between the two groups shows that VAS 6HRS is higher in PARACETAMOL group with a t value of 3.317 and is statistically significant with a p value of 0.002

On analyzing the effect of the two drugs on the VAS score, it was found that both the drugs had a comparable effect upto 60 minutes postoperatively. At the end of 3 and 6 hours respectively, patients who received ketorolac were found to have a more favourable VAS score in comparison to the paracetamol groups

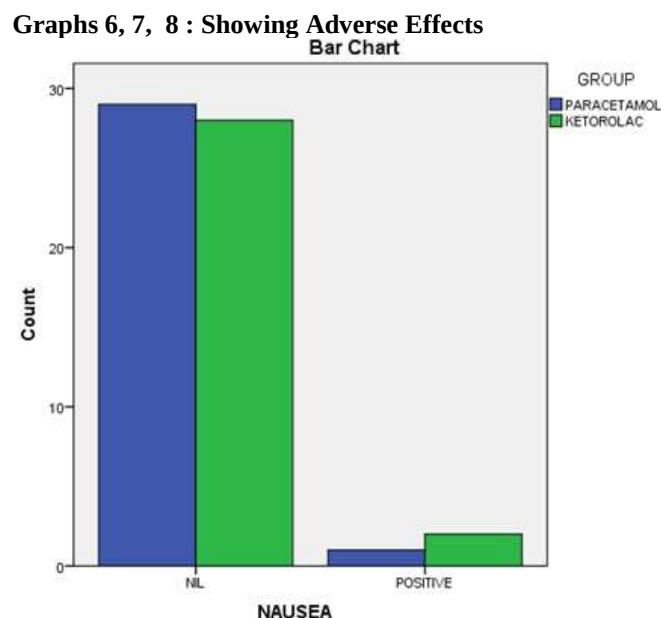
Table 5

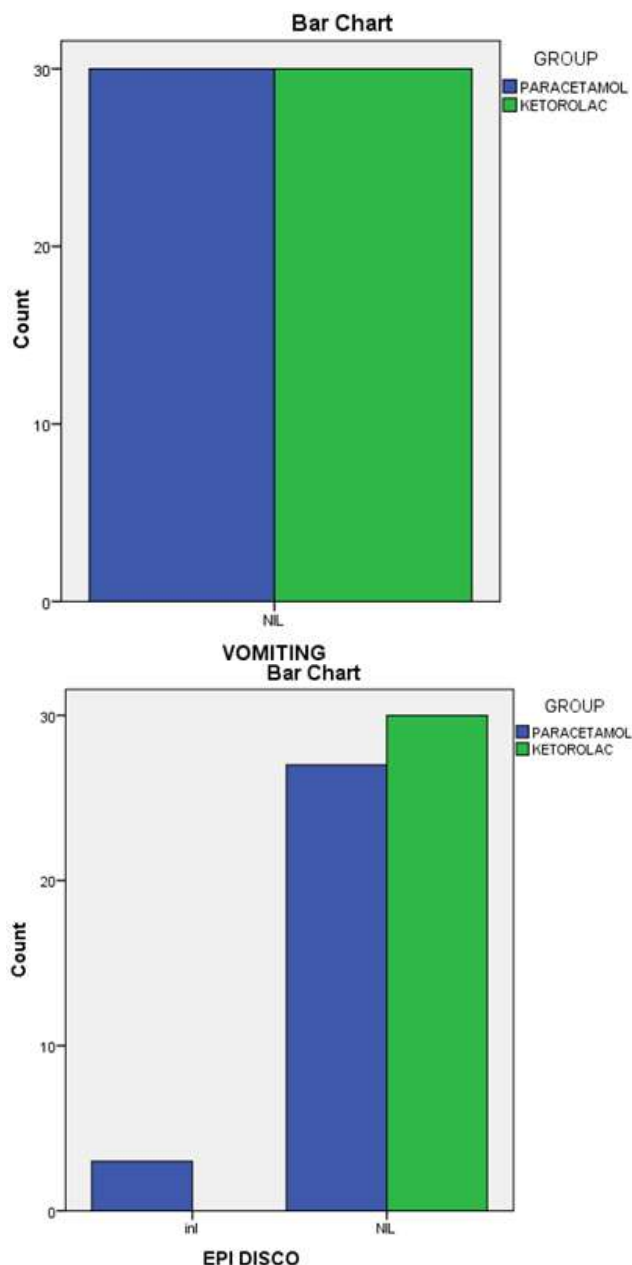
			GROUP		Total
			PARACETAMOL	KETOROLAC	
Rescue Analgesia	100mg tramadol iv	Count	1	0	1
		% within GROUP	3.3%	0.0%	1.7%
	50mg tramadol	Count	5	1	6
		% within GROUP	16.7%	3.3%	10.0%
	NIL	Count	24	29	53
		% within GROUP	80.0%	96.7%	88.3%
Total		Count	30	30	60
		% within GROUP	100.0%	100.0%	100.0%



Graph 5: Showing rescue analgesia requirement

In the paracetamol group a total of 6 patients received rescue analgesic in comparison to 1 patient in the ketorolac group. However it was not found to be statistically significant.





When adverse effects such as nausea, vomiting and epigastric discomfort were assessed, the two groups did not show any statistical significance.

5. Discussion

Pain following laproscopic cholecystectomy can be multifactorial. It can arise either from the surgical site, intra abdominal or referred pain due to irritation of the diaphragm⁸. In general NSAIDs and opioids are the drugs most commonly used in the postoperative unit for management of acute pain following laparoscopic cholecystectomy. Paracetamol, which is non opioid has emerged to be a good analgesic and has been associated with faster recovery rates.⁹

In this study, the analgesic efficacy of the two drugs, paracetamol and ketorolac were evaluated with respect to the post operative VAS scores at various intervals. It was observed that both the drugs had a good hemodynamic profile with no significant adverse effects. There was no significant change in MAP in patients of either group both

intra and postoperatively. However, in terms of analgesic efficacy, patients who received ketorolac were found to be pain free and was associated with a more favourable VAS score at 3 and 6 hours post procedure compared to the group that received paracetamol.

Clinically the analgesic efficacy of paracetamol is comparable to that of aspirin but less effective in comparison to the other NSAIDs.¹⁰

In a study conducted by Boccara *et al.* the preemptive use of paracetamol and ketoprofen for postoperative analgesia following laparoscopic cholecystectomy was evaluated and it was found ketoprofen was superior to paracetamol in terms of analgesic efficacy¹¹

Watcha *et al.* in their study concluded that oral ketorolac when administered preoperatively provides better postoperative analgesia in comparison to acetaminophen or placebo in children undergoing myringotomy.¹² Hyllested *et al.* suggested in their study that NSAIDs were superior to paracetamol with respect to pain scores in elective orthopedic and dental procedures. However they also opined that paracetamol can be a good alternative in high risk patients owing to its fewer adverse effects as compared to NSAIDs.¹³

6. Conclusion

In summary, single dose intravenous ketorolac can be recommended as an effective and safe alternative to intravenous paracetamol for postoperative pain relief following laparoscopic cholecystectomy.

7. Limitations

- 7.1. Small sample size
- 7.2 Lack of placebo arm

Source(s) of support

NIL

Presentation at a meeting

NIL

Conflicting Interest

NIL

Acknowledgement

NIL

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