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Original Research

Comparative Study Of Intravenous Paracetamol Versus Intravenous Diclofenac For Postoperative Pain Relief In Elective Laparoscopic Cholecystectomy

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ABSTRACT

Background: Laparoscopic cholecystectomy is the preferred surgical technique for uncomplicated cholecystectomy. Recommended approach for post operative pain management is to initiate the treatment with analgesics such as paracetamol, NSAIDS followed by adjunctive use of opioids to treat more acute pain symptoms. Present study was aimed to compare intravenous paracetamol versus intravenous diclofenac for postoperative pain relief in elective laparoscopic cholecystectomy.

Material and Methods: Present study was prospective double blinded Randomised controlled study, conducted patients between 18 - 65 years, ASA physical status I/II, posted for laparoscopic cholecystectomy. 80 cases were randomly divided as Group A (75 mg Diclofenac: 40 cases) & Group B (1 gm Paracetamol: 40 cases).

Results: In present study difference in VAS score in group A & group B at all points was statistically not significant except at 6 Hours where difference in VAS score in both group was statistically significant (P value 0.02). After comparing the Visual Rating Scale (VRS) scores of both groups to assess postoperative pain, it was found that VRS score in group A was higher than group B at 15 minutes, 30 minutes & 6 hours and was statistically significant. It was found that 26 (65%) of patients in group A required rescue analgesic whereas 18(45%) in group B required rescue analgesic. However, the difference observed was statistically not significant (P= 0.072). It was found that 3 (7.5%) of patients in group B experienced an adverse effect whereas 6 (15%) in group A had an adverse effect. The difference was statistically not significant. (P=0.061).

Conclusion: Paracetamol is considered superior to diclofenac in laparoscopic cholecystectomy as paracetamol gives better & prolonged analgesia than Diclofenac as evidenced low VAS & VRS score and also lesser requirement of rescue analgesia.

Keywords: Paracetamol, diclofenac, laparoscopic cholecystectomy, postoperative analgesia.

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INTRODUCTION

Laparoscopic cholecystectomy is the preferred surgical technique for uncomplicated cholecystectomy. Pain after laparoscopic cholecystectomy is usually acute in character that starts with the surgical trauma and ends with tissue healing.[3] Although the pain following a

laparoscopic cholecystectomy is less intense than open surgery, patients often suffer visceral pain with coughing, respiratory movements and mobilization and shoulder pain secondary to peritoneal insufflations, A direct and significant correlation between shoulder pain and delay in returning to normal daily activities has been reported.[2]

The origin of the pain after the laparoscopic Cholecystectomy surgery is multifactorial,[2,3,4] as pain arising from incision site being somatic pain, Pain from the gall bladder bed being mainly visceral in nature and shoulder pain is mainly due to the residual CO2 irritating the diaphragm. Prolonged pain can reduce physical activity and increased risk of deep vein thrombosis. In addition there can be widespread effects on gut and urinary tract motility which may lead to postoperative ileus, nausea, vomiting and urinary retention. [1,4,7,8] Therefore, Adequate analgesia is of utmost importance for early ambulation and discharge reducing hospital stay adequate analgesia is of utmost importance. [3,4]

Recommended approach for post operative pain management is to initiate the treatment with analgesics such as paracetamol, NSAIDS followed by adjunctive use of opioids to treat more acute pain symtoms.[5] Postoperative pain relief is of utmost importance and growing evidence suggests that treatment of postoperative pain should be multimodal and opioid sparing to accelerate recovery and avoid potential side effects.[6,7] Present study was aimed to compare intravenous paracetamol versus intravenous diclofenac for postoperative pain relief in elective laparoscopic cholecystectomy.

MATERIAL AND METHODS

Present study was prospective double blinded Randomised controlled study, conducted in department of anaesthesiology, at XXX medical college & hospital, XXX, India. Study duration was of 18 months (February 2018 to July 2019). Study approval was obtained from institutional ethical committee.

Inclusion criteria

- Patients between 18 - 65 years, ASA physical status I/II, posted for laparoscopic cholecystectomy, willing to participate in present study

Exclusion criteria

- Hypersensitivity/ History of allergic reactions to paracetomol, diclofenac and other NSAIDS
- Those whose pain evaluation was judged unreliable because of neurological disease or treatment with steroids, NSAIDS and opioids before surgery
- If there was any complication during surgery or operation has to be converted to open cholecystectomy
- Difficulty in breathing, bronchial asthma or exertion related chest pain, Liver disease like jaundice, ascites or altered liver function tests, renal disease or altered real function test, Patients with bleeding diathesis, Cardiovascular system illness
- History of alcoholism and drug abuse, History of psychiatric disease
- Patients with chronic backache, chronic abdominal pain or patients treated with analgesia

Study was explained to patients in local language & written consent was taken for participation & study. Total sample size of study was – 80 cases, patients were randomly assigned to either group by Sampling method or sampling technique was Simlple random sampling as Group A (75 mg Diclofenac: 40 cases) & Group B (1 gm Paracetamol: 40 cases). All patients were explained the use of VAS (Visual analogue scale) and VRS (Visual rating Prince Henry Scale). The observer was blinded to the solution instilled.

The patient was premedicated with Injection Glycopyrollate 0.2mg IM before entering the operation theatre. After an intravenous line (18 or 20G) is secured, monitors including ECG, pulse oximeter, Sphygmomanometer, capnogram were attached. Injection Midazolam (0.03mg/Kg) and Injection Fenatnyl (2Ug / kg) were given for sedation, amnesia, analgesia.

All patients received IV Pantoprazole 40 mg and IV Ondansetron 4 mg.
Pre-oxygenation was done for 5 min following which induction had been done with Injection Thiopentone 5mg/kg or Propofol 2mg/kg and Injection Succinylcholine 1.5mg/kg injection. After securing the airway with endotracheal intubation, further anaesthesia was maintained on sevoflurane with 60:40 of N_2O and O_2 with intermittent doses of Injection Vecuronium using a closed circuit. Intraoperative monitoring of pulse, BP, Saturation, $ETCO_2$ was done. Ventilation was adjusted to maintain end tidal carbon dioxide between 25-40 mm Hg. CO_2 Insufflation rate was kept as 5l/ min. During surgery all patients received intravenous ringer lactate. After removal of Gallbladder the study drug was administered by randomization. Neuromuscular blockade was reversed adequately at the end of the surgery with Injection Glycopyrrolate 8 ug/kg and Inj. Neostigmine 0.05 mg/kg and after thorough oral suction, patients were extubated. Post operatively patients were monitored for 12 hrs. Baseline variable like pulse rate, respiratory rate, blood pressure, oxygen saturation were recorded for each patient. The patients were given rescue analgesia in the form of injection Tramadol 1mg/kg slow intravenously when VAS was more than or equal to 4 and VRS was more than or equal to 3.
Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

RESULTS

Mean age in group A was 39.28 $\pm$ 13.11 and the mean age in group B was 40.53$\pm$12.65 with a p value of 0.665 indicating statistically not significant, In group A there were 18 (45%) female and 22(55%) male patients and in group B there were 23(57.5%) females and 17(42.5%) male patients, difference was statistically not significant (p value= 0.263). On statistical analysis, association found was not significant (P value of 0.812) which means that both the groups had equal distribution of ASA grade I and II patients. Thus the patients were demographically similar in both groups means group A and group B with respect to age, sex and ASA grading.

Table 1: General characteristics

	Group A	**Group B**	**p value**
Mean age (mean ± SD)	39.28 ± 13.11	40.53 ± 12.65	0.665
Sex			
Female	18 (45%)	23 (57.5%)	0.263
Male	22 (55%)	17 (42.5%)	
ASA grade			
1	27 (67.50%)	26 (65%)	0.812
2	13 (32.50%)	14 (35%)	

Visual Analogue Scale was used to assess postoperative pain. In present study difference in VAS score in group A & group B at all points was analysed by unpaired T-test and P value was more than 0.05 throughout indicating statistically not significant except at 6 Hours where difference in VAS score in both group was statistically significant (P value 0.02)

Table 2: Comparison of VAS scores between two groups

Timing	**Group A**		**Group B**		**P value**	**Significance**
	Mean	**SD**	**Mean**	**SD**		
0 MIN	0.98	0.77	1.08	0.83	0.577	Not Significant
15 MIN	2.08	1.44	2.43	1.30	0.257	Not Significant

30MIN	2.98	1.17	3.13	1.47	0.615	Not Significant
1 HR	3.43	1.15	3.45	1.34	0.929	Not Significant
2 HR	3.68	1.00	3.73	1.15	0.836	Not Significant
4 HR	3.43	1.26	3.28	1.22	0.590	Not Significant
6 HR	3.58	1.17	2.95	1.08	0.02	Significant
12 HR	2.48	0.91	2.63	1.00	0.485	Not Significant

After comparing the Visual Rating Scale (VRS) scores of both groups to assess postoperative pain, it was found that VRS score in group A was higher than group B at 15 minutes, 30 minutes & 6 hours and was statistically significant.

Table 3: Comparison of VRS scores between two groups

Timing	**Group A**		**Group B**		**P value**	**Significance**
	Mean	**SD**	**Mean**	**SD**		
0 MIN	1.30	0.46	1.15	0.36	0.111	Not Significant
15 MIN	1.70	0.69	1.38	0.63	0.030	Significant
30MIN	2.10	0.74	1.63	0.77	0.006	Significant
1 HR	2.23	0.77	2.23	0.62	1.000	Not Significant
2 HR	2.25	0.67	2.45	0.55	0.149	Not Significant
4 HR	2.90	0.81	2.65	0.62	0.126	Not Significant
6 HR	3.18	0.75	2.53	0.88	0.001	Significant
12 HR	2.58	0.59	2.35	0.66	0.114	Not Significant

(Unpaired t test) ($P < 0.05$ – Significant)

The rescue analgesic requirements of both the groups were analysed by applying Chi square test. It was found that 26 (65%) of patients in group A required rescue analgesic whereas 18(45%) in group B required rescue analgesic. However, the difference observed was statistically not significant (P= 0.072)

Table 4: Rescue analgesia in both groups

Rescue drug required	**Group A**	**Group B**	**Total**
No	14 (35%)	22 (55%)	36(45%)
Yes	26 (65%)	18 (45%)	44(55%)
Grand Total	40 (100%)	40 (100%)	80(100%)

$\chi^2 = 3.232$, DF=1 P = 0.072 (Not significant) *(Chi square test)*

It was found that 3 (7.5%) of patients in group B experienced an adverse effect whereas 6 (15%) in group A had an adverse effect. The difference was statistically not significant. (P=0.061)

Table 5: Adverse reaction in both groups

Adverse reaction	**Group A**	**Group B**	**Total**
Gastritis	2(5.0%)	0(0.0%)	2(2.5%)
Nausea	3(7.5%)	0(0.0%)	3(3.75%)
Vomiting	1(2.5%)	3(7.5%)	4(5.0%)

$\chi^2 = 5.625$, DF=1, P = 0.061 (Not significant)

DISCUSSION

Laparoscopic cholecystectomy becomes the most popular trend in recent days because of lower post-operative morbidity including faster recovery time, reducing hospital stay, minimal pain and fewer complications.[2,3] Laparoscopic cholecystectomy continues to be the gold standard in management of cholelithiasis.[9] Laparoscopic cholecystectomy is the preferred surgical

technique for uncomplicated cholecystectomy. Pain after laparoscopic cholecystectomy is usually acute in character that starts with the surgical trauma and ends with tissue healing.[1]
Although the pain following a laparoscopic cholecystectomy is less intense than open surgery, patients often suffer visceral pain with coughing, respiratory movements and mobilization and shoulder pain secondary to peritoneal insufflations, The creation of pneumoperitoneum increases the intra-abdominal pressure which shifts the diaphragm cephalad and reduces diaphragmatic excursions. This can led to basal atelectasis, intrapulmonary shunting and ventilation perfusion mismatch which can delay postoperative recovery, lengthen the hospital stay and increase morbidity.
An optimal peri-operative experience encompasses effective pain control with minimal side effects from anesthetic and analgesic drugs. The goals are to facilitate recovery of the surgical patient, enhance patient satisfaction and improve cost effectiveness. Therefore, Adequate analgesia is of utmost importance for early ambulation and early recovery[3,4] and growing evidence suggests that treatment of postoperative pain should be multimodal and opioid sparing to accelerate recovery and avoid potential side effects.[6,7]
T. S. Göröcs et al.,[10] noted that, mean self-reported pain intensity on the VAS was 33.2 at 15 min after end of surgery and was reduced to 19.2 at patient discharge (−13.9 points). Relative pain reduction was similar in the three surgery subtypes. The majority of patients achieved a VAS score < 30 mm and were classified as responders; i.v. paracetamol was well tolerated and no serious adverse events and only one possibly drug-related adverse event was reported. The majority of physicians (80.5%) and patients (81.6%) rated the efficacy, and satisfaction with therapy respectively, as very good or good.
Debashish Paul et al.,[11] observed that at 4 hr interval, difference in VAS Score is insignificant. Following that there is gradual increase in VAS Score in the diclofenac group. The mean VAS Score at 24 hr interval is 1.97(±.1.40) in Group-A and it is 2.33(±1.92) in Group -B. There is higher VAS Score in Group-B compared to Group-A but difference is statistically insignificant (P-Value =0.401). Insignificant difference in VAS Score at this time interval can be explained by the fact that patients with higher VAS Score in group-B were administered rescue analgesia by this time. They noted significant outcome (p-values are 0.0005 at 0 hrs, 0.003 at 2 hrs, 0.001 at 6 hrs, 0.0005 at 12 hrs) in VAS pain score in between the two groups at different intervals.
To minimize opioid related side effects (somnolence and sedation, nausea and vomiting, sleep disturbances, urinary retention and respiratory depression), prophylactic use of opioids in the postoperative period is avoided.[12] A multimodal approach to pain control including a combination of analgesic options such as regional techniques and non-opioid analgesics have shown improved analgesia with early mobilization and reduced opioid side effects in postoperative patients. lower incidence of adverse effects and improved analgesia has been demonstrated with multimodal analgesia techniques, which may provide for shorter hospitalization times, improved recovery and function[13,14] and possibly decreased healthcare costs.
In present study, Tramadol 1mg/kg was used as rescue analgesic. The rescue analgesic requirements of both the groups were analysed by applying Chi square test. It was found that 26 (65%) of patients in group A required rescue analgesic whereas 18(45%) in group B required rescue analgesic. However, the difference observed was statistically not significant (P= 0.072). The adverse effects of both the groups which were analyzed by applying chi square test. It was found that 3 (7.5%) of patients in group B experienced an adverse effect whereas 6 (15%) in group A had an adverse effect. The difference was statistically not significant.(P=0.061)
Karki AJ et al.,[15] found that mean duration of first rescue pethidine in paracetamol group was 46.15±21.25 min whereas in diclofenac group was 35.88±10.13 min was statistically significant (P value 0.031). The mean dose of requirement of rescue pethidine in 24 hours was 109.38±35.22 mg in paracetamol group and 124.19±35.04 mg in diclofenac group (p value

0.135). So study concluded that, Pre-emptive iv paracetamol 15 mg/kg is effective than iv diclofenac 1 mg/kg for prolonging the duration of immediate post operative analgesia and reduces (13%) the total pethidine consumption in 24hours. None of the patients had experienced any untoward side effects of paracetamol or diclofenac in this study.

Raymond S. S. et al.,[16] found that time to first rescue medication was significantly ($P < 0.001$) longer for both active groups than for placebo but was not significantly different between the two active groups. The median (95% confidence interval) times to first rescue medication were 3 (1.4–4.0) h for intravenous acetaminophen, 2.6 (1.6–4.0) h for propacetamol, and 0.8 (0.6 – 1.1) h for placebo. The analyses of median time to rescue medication performed among responders (defined as subjects who had a reduction inpain intensity of at least one unit) showed that the median times for first rescue medication were 4.0 (3.3–4.3) h for intravenous acetaminophen, 3.8 (2.5–5.2) h for propacetamol, and 1.6 (1.0 –2.6) h for placebo. In adverse effects.

Recent advances in pathophysiology of pain has led to the concept of pre-emptive analgesia which states that it may be possible to prevent or reduce the central neural hyper-excitability that contributes to enhanced postoperative pain.[5] Pain associated with tissue damage results in prolonged modulation of the somatosensory system, with increased responsiveness of both peripheral and central pain pathways.[17] Experimental evidence suggests that it may be possible, and indeed preferable, to prevent or 'pre-empt' the neuro-physiologic and biochemical consequences of anoxious input to the CNS rather than to begin treatment when these consequences are already established.

CONCLUSION

Paracetamol is considered superior to diclofenac in laparoscopic cholecystectomy as paracetamol gives better & prolonged analgesia than Diclofenac as evidenced low VAS & VRS score and also lesser requirement of rescue analgesia. Paracetamol should be given in laparoscopic cholecystectomy as it provides good analgesia, diclofenac had more adverse effect like gastritis, vomiting & nausea than paracetamol.

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