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Original Article

Anaesthesia Section

Comparison between IV Paracetamol and Tramadol for Postoperative Analgesia in Patients Undergoing Laparoscopic Cholecystectomy

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ABSTRACT

Introduction: Efforts to use safer drug with minimal side effects for postoperative analgesia are growing day by day for surgeries of shorter duration or which may require day care only, search for ideal agent has been a never ending process.

Aim: The aim of the present study was to compare the efficacy of intravenous Paracetamol and Tramadol for post-operative analgesia in patients undergoing laparoscopic cholecystectomy.

Materials and Methods: This study was done at Department of Anaesthesiology, Era's Medical College, Lucknow, India. Sixty ASA-I or II patients between 18-55 years of age, scheduled for laparoscopic cholecystectomy were randomly allocated to two groups of 30 each. Group A received IV infusion of paracetamol 1g in 100 ml solution, while Group B received IV infusion of Tramadol 100 mg in 100 ml NS at 0 (first complain of pain postoperatively), 6, 12 and 18 hours respectively. Pain intensity was measured by a 10 point Visual Analogue Scale (0→no pain and 10→worst imaginable pain) VAS at T(0)→just before analgesic administration, at 0.5, 1.5, 3, 6, 12, 18 and 24 hours thereafter, in addition to HR, SBP, DBP.

Statistical Analysis: Chi-square test, Student t-test and p-values <0.05 was considered significant.

Results: During postoperative follow-up intervals, paracetamol showed significantly lower VAS scores as compared to tramadol at 1.5 hour, 3 hour, 6 hour, 12 hour and 24 hour follow up intervals. One patient in tramadol group had nausea postoperatively (p>0.05). No adverse effect attributable to paracetamol was noticed.

Conclusion: Intravenous Paracetamol can be advocated as an effective and safe analgesic agent for postoperative pain relief.

Keywords: Non-steroidal anti-inflammatory drugs, Postoperative pain, Visceral pain, VAS score

INTRODUCTION

Laparoscopic cholecystectomy is regarded as a daycare procedure that requires a shorter duration of hospital stay. Pain significantly reduces after laparoscopic cholecystectomy approach and it shorten the recovery period, therefore, reducing discharge time from 1 to 3 days to same day discharge with an earlier return to a normal life [1,2]. Studies have shown that laparoscopic surgery too causes postoperative pain in at least one-third of the patients and these patients have been seen taking more analgesics to alleviate pain [3]. The type of pain after laparoscopy differs from laparotomy which results mainly in parietal pain (abdominal wall), patients complain more of visceral pain after operative laparoscopy [4].

Different treatments have been proposed to relieve pain after laparoscopy. The choice of different drugs, the timing and route of their administration as well as the dosages are variable. Opioids and Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are generally used for management of postoperative pain after laparoscopic cholesystectomy. However, the clinical importance of infiltration of wounds with local anaesthetic agents, their intraperitoneal application, as well as the choice and dosages of these agents still remain controversial [5].

Paracetamol is the most commonly prescribed analgesic for the treatment of acute pain [6]. Its major advantages over NSAIDs are its lack of interference with platelet function and safe administration in patients with a history of peptic ulcers or asthma [7]. The main mechanism of action of Paracetamol is considered to be the inhibition of cyclooxygenase (COX) and recent findings suggest that it is highly selective for COX-2. Paracetamol is metabolised primarily in the liver into non-toxic products.

Researches have shown that besides its effective analgesic properties, paracetamol administered during perioperative period supports effective and speedy recovery in patients undergoing laparoscopic cholecystectomy [8,9].

Tramadol is a synthetic opioid which belongs to aminocylohexanol group, is an analgesic with central effect and weak opioid agonistic properties. Tramadol possesses weak agonist actions at the μ-opioid receptor with additional monoaminergic activity. This drug is also effective on noradrenergic and serotonergic neurotransmission. However, tramadol has shown to be failing in ensuring optimal analgesia in moderate to severe pain [10].

The aim of this study was to compare efficacy between intravenous Paracetamol and Tramadol for postoperative analgesia in patients undergoing laparoscopic cholecystectomy.

MATERIALS AND METHODS

The study was a prospective, randomized (simple randomization, computer generated) controlled trial and carried out in the Department of Anaesthesiology between January 2011 to December 2011 at Era's Lucknow Medical College and Hospital, Lucknow, India.

A total number of 60 adult patients between 18-55 years of age ASA I or ASA II who were scheduled for elective laparoscopic cholecystectomy under general anaesthesia and who were ready to stay in hospital for 24 hours after surgery were enrolled. Pregnant and lactating patients, patients with known allergy to Tramadol or Paracetamol, patients on chronic analgesic medications, patients with significant coronary artery disease or ischemic myocardial disease, drug or alcohol abuse, chronic pulmonary disease, renal

failure, hepatic dysfunction, haemorrhagic disorder were excluded from the study.

Necessary approval and clearance for study was obtained from Institutional ethics committee. Informed consent was obtained from all the participants. The patients were randomly divided into two groups, group A (n=30): Comprised of patients who received intravenous Paracetamol (1g in 100 ml solution) and group B (n=30): Comprised of patients who received intravenous Tramadol (100 mg in 100 ml NS).

All the patients were visited the night before surgery. They were kept nil orally overnight. The patients were given Tab. Alprazolam (Alprax) 0.25 mg a night before surgery and two hours prior to surgery with a sip of water.

On arrival of patients to the operation theatre, intravenous line was initiated with 18G cannula. Preoperative recording of Heart Rate (HR), non invasive blood pressure (SBP, DBP, MAP) and arterial oxygen saturation (SpO_2) was carried out. All patients were premedicated with inj. Metoclopromide 10 mg and inj. Fentanyl (2 µg/kg) intravenously. All the patients were preoxygenated with 100% oxygen for 3 minutes. Induction of anaesthesia was carried out with inj. Propofol 2 mg/kg intravenously. Endotracheal intubation was facilitated with a paralyzing dose of inj Atracurium 0.5 mg/kg intravenously. Anaesthesia was maintained with oxygen-40%, nitrous oxide- 60% delivered through Bain's circuit using IPPV and a continuous infusion of inj Propofol (150 mcg/kg/min).

Muscle relaxation was maintained with intermittent doses of atracurium in aliquots of 0.1 mg/kg intravenously. At the conclusion of surgery residual muscle paralysis was reversed with inj. Neostigmine 50 µg/kg and inj. Glycopyrrolate 10 µg/kg intravenously. The patients were extubated following return of regular, rhythmic respiration when reasonably awake, after a gentle oral suction.

The parameter recordings included $Etco_2$, Heart Rate (HR), oxygen saturation (SpO_2), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP) perioperatively.

Initial dose of analgesic (either Tramadol 100 mg intravenous or Paracetamol 1g intravenous) was given to the patients in the postoperative period when the pain intensity, as observed on the VAS, showed a score >5. Thereafter, Tramadol 100 mg or Paracetamol 1g intravenous infusion was given at 6, 12 and 18 hours.

Pain intensity was measured based on a 10 point Visual Analogue Scale (VAS; 0-10 cm; 0= no pain and 10= worst imaginable pain).

VAS pain scores were obtained postoperatively at: just before analgesic administration (T0), 0.5 hours (T1), 1.5 hours (T2), 3 hours (T3), 6 hours (T4), 12 hours (T5), 18 hours (T6) and 24 hours (T7).

Any pain score above 5 on VAS was considered a breakthrough pain. It was managed by rescue analgesia with intravenous Diclofenac sodium 1.5 mg/kg, repeated as required. The patient having breakthrough pain were not included in the study but records were kept for comparison.

RESULTS

The observations made during above study were recorded on a proforma and the results obtained were analysed by appropriate statistical tests such as Chi-square test, Student's t-test and p <0.05 was considered significant.

Baseline data of both the groups were matched for age, weight, height, BMI and gender [Table/Fig-1].

At baseline (T0), mean SBP in Group A was 131.60±8.46 mm of Hg as compared to 131.73±9.20 mm of Hg in Group B, showing the 'between group' difference not to be significant statistically

SN	Variable	Group A	Group B	Significance of difference
1.	Mean Age±SD (yrs)	43.17±9.13	42.90±10.45	t=0.105; p=0.917
2.	Mean Weight±SD (kg)	56.20±8.51	59.63±7.15	t=1.692; p=0.096
3.	Mean Height±SD (cm)	154.97±10.52	157.03±9.38	t=0.803; p=0.425
4.	Mean BMI±SD (kg/m^2)	23.37±2.58	24.17±1.97	t=1.346; p=0.184
5.	Male: Female	16:14	16:14	χ^2=0; p=1

[Table/Fig-1]: Demographic Comparison.

(p=0.954). At T1, mean SBP in Group A was 126.40±10.92 mm of Hg as compared to 126.00±10.69 mm of Hg in Group B. At T2, both the groups showed a slight decrease in mean SBP, 123.17±7.92 (Group A) and 124.20±8.76 (Group B). This was followed by an increase in both the groups at T3 and T4 intervals. At T5 interval, both the groups showed the mean SBP values close to baseline values, followed by a slight increase at T6 interval which remained almost stabilized at T7. At T7, mean SBP in Group A was 127.47±6.26 mm of Hg as compared to 128.87±9.16 mm of Hg in Group B. At none of the time intervals, the difference between two groups was significant statistically (p>0.05) [Table/Fig-2].

For DBP- At baseline (T0), mean DBP in Group A was 79.40±6.83 mm Hg as compared to 78.83±8.31 mm Hg in Group B. At T1 mean DBP in Group A was 78.13±5.74 mm of Hg as compared to 78.03±5.60 mm of Hg in Group B. At T2, both the groups showed a slight decrease in mean DBP to reach at 75.37±7.62 (Group A) and 75.40±7.75 (Group B). At T3, a further decrease in mean DBP was observed, taking the mean value in Group A to 71.38±10.72 mm of Hg as compared to 73.97±8.12 mm of Hg in Group B. This was followed by an increase in both the groups at T4 interval followed by a decrease at T5 and T6 intervals. At T6 interval, both the groups showed the mean DBP values close to baseline values followed by a slight increase at T6 interval which remained almost stabilized at T7. At none of the time intervals, the difference between two groups was significant statistically (p>0.05) [Table/Fig-3].

SN	Time interval	Group A (n=30)		Group B (n=30)		Significance of difference	
		Mean	±SD	Mean	±SD	T	"p"
1.	T0	131.60	8.46	131.73	9.20	-0.058	0.954
2.	T1	126.40	10.92	126.00	10.69	0.143	0.886
3.	T2	123.17	7.92	124.20	8.76	-0.479	0.634
4.	T3	129.73	7.18	130.27	8.05	-0.271	0.787
5.	T4	133.20	6.45	135.53	7.21	-1.321	0.192
6.	T5	124.77	6.99	125.87	7.67	-0.581	0.564
7.	T6	127.67	8.19	128.07	5.77	-0.219	0.828
8.	T7	127.47	6.26	128.87	9.16	-0.691	0.492

[Table/Fig-2]: Comparison of mean SBP between two groups at different time intervals.

SN	Time interval	Group A (n=30)		Group B (n=30)		Significance of difference	
		Mean	±SD	Mean	±SD	T	"p"
1.	T0	79.40	6.83	78.83	8.31	0.288	0.774
2.	T1	78.13	5.74	78.03	5.60	0.068	0.946
3.	T2	75.37	7.62	75.40	7.75	-0.017	0.987
4.	T3	71.38	10.72	73.97	8.12	-1.052	0.297
5.	T4	88.77	6.94	91.80	6.17	-1.789	0.079
6.	T5	83.13	7.95	84.03	8.45	-0.425	0.672
7.	T6	75.87	6.87	75.77	8.37	0.051	0.960
8.	T7	76.80	6.47	77.20	5.40	-0.260	0.796

[Table/Fig-3]: Comparison of mean DBP between two groups at different time intervals.

As compared to baseline, mean change in heart rate was maximum at T4 interval in Group A and T5 interval in Group B. In Group A, at all time intervals, except at T4 and T5, mean heart rate was lower as compared to baseline but it was significant statistically only at T1. At T4 and T5 intervals, in both the groups, mean heart rate was significantly higher as compared to baseline. In Group B, mean heart rate was lower than baseline only at T1 interval and the difference was significant (p=0.005). At all the other intervals, mean heart rate was higher than baseline, but the increase was significant statistically only at T4, T5 and T7 intervals [Table/Fig-4].

At baseline (T0), mean VAS score in Group A was 6.30±0.99 as compared to 6.20±1.30 in Group B, thus showing no significant difference between the two groups (p=0.738). However, at T1 and T2, mean VAS score in Group A (3.10±0.61 and 2.53±0.63 respectively) was significantly lower as compared to that in Group B (3.47±0.51 and 3.03±0.93 respectively). At T3, mean VAS score in Group A (3.03±0.67) was lower as compared to that in Group B (3.23±0.77) yet the difference was not significant statistically (p=0.289). At all the other time intervals, Group A had mean VAS scores lower than Group B, but the difference was not significant statistically at T6 and T7 intervals (p>0.05) [Table/Fig-5].

None of the patients in either group required rescue analgesic. Only one (3.3%) case in Group B complained of nausea and vomiting. The patient was managed with inj Ondansetron 4 mg i.v. No other side effect was noticed in either of the two groups.

SN	Time interval	Group A				Group B			
		MD	SE	"t"	"p"	MD	SE	"t"	"p"
1.	T1	-5.60	1.33	4.20	<0.001	-3.87	1.28	3.02	0.005
2.	T2	-1.73	1.58	1.10	0.281	0.67	1.64	-0.41	0.687
3.	T3	-0.17	2.00	0.08	0.934	3.00	2.09	-1.43	0.163
4.	T4	9.53	1.50	-6.37	<0.001	11.63	1.45	-8.04	<0.001
5.	T5	9.17	2.14	-4.29	<0.001	12.00	2.26	-5.30	<0.001
6.	T6	-2.73	2.14	1.28	0.212	2.17	2.02	-1.07	0.292
7.	T7	-0.93	2.06	0.45	0.654	2.07	0.55	-3.72	0.001

[Table/Fig-4]: Comparison of Change in heart rate in two groups as compared to baseline.

SN	Time interval	Group A (n=30)		Group B (n=30)		Significance of difference	
		Mean	±SD	Mean	±SD	T	"p"
1.	T0	6.30	0.99	6.20	1.30	0.336	0.738
2.	T1	3.10	0.61	3.47	0.51	-2.537	0.014
3.	T2	2.53	0.63	3.03	0.93	-2.443	0.018
4.	T3	3.03	0.67	3.23	0.77	-1.071	0.289
5.	T4	3.53	0.68	4.20	0.66	-3.837	<0.001
6.	T5	3.43	0.63	3.97	0.93	-2.610	0.012
7.	T6	2.93	0.83	3.03	1.03	-0.414	0.681
8.	T7	2.20	0.61	2.53	0.68	-1.996	0.051

[Table/Fig-5]: Comparison of mean VAS scores between two groups at different time intervals.

DISCUSSION

Postoperative pain management is one of the most important and an ever challenging task for an anaesthesiologist. Postoperative pain is variable in duration, intensity and character and is the main factor delaying discharge of patients undergoing day-care procedures including laparoscopy and hence adding to the hospital cost. Pain after laparoscopic surgery may vary in quality and localization and is reported in several trials to be incisional, intra-abdominal, or referred (shoulder tip). The aetiology is complex, it could be due to damage to abdominal wall structures, visceral trauma, inflammation [4,11] or peritoneal irritation because of carbon dioxide entrapment beneath the haemidiaphragms [12].

Generally, NSAIDs and opioids are administered for postoperative pain management, however, owing to their controversial results [5,13] they are losing their value as a drugs of choice. Paracetamol, a non-opioid has emerged to be effective, which leads to faster recovery in patients undergoing laparoscopic cholecystectomy [6,8,9] while tramadol which has agonist actions at μ- opioid receptors also gained momentum owing to its central analgesic effect and weak opioid agonistic properties [14].

In the present study, a comparison of analgesic effect and side effects of intravenous infusion of paracetamol and intravenous infusion of tramadol was carried out for postoperative pain relief in patients undergoing laparoscopic cholecystectomy under general anaesthesia.

Blood pressure levels as well as heart rate in both the groups were comparable throughout the study period, though a decrease in blood pressure levels and heart rate was observed in early follow up intervals at 30 min, 1.5 hour and 3 hour time intervals. The initial high scores of haemodynamic parameters could be a result of post-surgical stress response. Although operative stress response is much reduced in laparoscopic cholecystectomy, yet postoperative pain itself is accompanied with a stress response [15].

Although tramadol has been reported to reduce blood pressure and increase heart rate in some cases [16] yet in present study though the blood pressure lowering effect of tramadol was observed in the early intervals itself, the increase in heart rate was observed from 1.5 hour interval only. However, the increase in haemodynamic parameters at 6 and 12 hours intervals could be attributed to return of pain as the blood levels of the drugs decline with time.

Studied done earlier on postoperative pain management using Tramadol and Paracetamol have not reported any significant clinical impact of these two drugs on haemodynamics [17-20].

In a study conducted by Shabir et al., one group received Bupivacaine (0.5%) 20ml, instilled in gallbladder bed and the undersurface of diaphragm and infiltration of port wounds [21]. In other group, Tramadol (100mg) was given Intramuscularly (IM) at the completion of elective laparoscopic cholecystectomy. The assessment of postoperative analgesia was done using Visual Analogue Scale (VAS) at hourly intervals for first four hours and then 24 hours also. Vital signs like Spo_2, HR, NIBP, RR were recorded six hourly for 24 hours postoperatively. Tramadol group had better analgesic effect as compared to Bupivacaine group.

In the present study, both the drugs showed effective control on pain scores in short time only. It was observed that mean scores indicative of acute pain (VAS score ≥5) were brought down to mild or bearable pain (VAS score ~3) within 30 minutes of administration showing a significant change from baseline. However, paracetamol group showed a better efficacy as compared to tramadol group for most of the follow-up intervals being studied. By 18 hour and 24 hour both the groups had pain scores indicative of mild nature of pain (VAS scores ~ 2).

Study done on oral acetaminophen plus IV propacetamol and oral Tramadol plus IV Tramadol, when compared pain management after tonsillectomy [22] found that the side effects of nausea and vomiting were comparable between the two groups, pain relief was higher and need for rescue medication was less in the Tramadol group. In our study only one episode of nausea and vomiting was noticed in Tramadol group and this was not statistically significant.

Given below in the table are the studies comparing different drugs as pain relief measure in patients undergoing surgeries and their outcome [Table/Fig-6].

Author name (year)	Reference no.	Groups compared	Outcome
Hoogewijs et al., (2000)	[23]	Compared intravenous Propacetamol, Pethidine, Tramadol and Diclofenac for pain in patients with peripheral injuries.	No difference between Propacetamol, Pethidine, Tramadol and Diclofenac was found in terms of pain control after single peripheral injuries.
Mustafa Arslan et al., (2013)	[24]	Compared Group I (preemptive) IV Paracetamol 1 g/100 mL 10 min before skin incision and 100 mL of saline solution at the end of the operation; Group II received 100 mL of saline solution 10 min before skin incision and iv Paracetamol 1 g/100 mL at the end of the operation; Group III (placebo) received 100 mL of saline solution 10 min before skin insicision and 100 mL of saline solution at the end of the operation.	Preemptive Iv Paracetamol provided effective and reliable pain control after cholecystectomy surgeries and reduced postoperative pain scores and reduced need for supplementary opioids.
Khaled El-Radaideh et al., (2014)	[25]	Immediately after dissection of the gallbladder, group1 received Paracetamol plus Tramadol- 0.75 mg/kg Tramadol (in normal saline; total volume, 5 mL), followed by 1 g Paracetamol (100 mL) intravenously. Control Group received 5 mL and 100 mL normal saline in the same manner.	IV Paracetamol (1 g) and Tramadol (0.75 mg/kg) had significantly reduced postoperative pain scores, decreased postoperative analgesic requirements, and prolonged the time to first postoperative analgesic.
Mohammed Jawad et al., (2014)	[26]	Comparative study of IV Paracetamol and Tramadol for postoperative pain management in patients undergoing laparoscopic cholecystectomy.	Paracetamol appeared as effective as Tramadol in the management of mild to moderate pain in female patients, while Tramadol seemed to be more effective than Paracetamol in male group.
Aftab Ahmad Khan et al., (2015)	[27]	preemptive use of IV Paracetamol and Tramadol in patients undergoing laparoscopic cholecystectomy.	Paracetamol had significantly lowered total analgesic consumption, postoperative pain and VAS as compared to Tramadol.
Rastogi B et al., (2016)	[28]	Compared preemptive use of Ketorolac & Paracetamol in patients undergoing laparoscopic cholecystectomy.	Ketorolac was found superior in comparison to Paracetamol when given 30 minutes before induction without any significant side effect.
Present study (2016)		Intravenous paracetamol and tramadol for postoperative analgesia following laparoscopic cholecystectomy.	Paracetamol showed significantly lower VAS scores as compared to Tramadol at 1.5 hour, 3 hour, 6 hour, 12 hour and 24 hour follow up intervals.

[Table/Fig-6]: Comparison of results of present study with the previously published similar studies.

In our study, paracetamol proved to be having superior pain control as compared to tramadol in terms of difference in mean VAS scores, however, as far as rescue analgesia was concerned, none of the patients in either group required rescue analgesic. Thus both tramadol and paracetamol were comparable and could be effectively used as postoperative pain management measures in laparoscopic cholecystectomy.

During postoperative follow-up intervals, paracetamol showed significantly lower VAS scores as compared to Tramadol at 1.5 hour, 3 hour, 6 hour, 12 hour and 24 hour follow up intervals, patient's satisfaction was also found more in Paracetamol group.

Paracetamol is antipyretic and analgesic but has little, if any, anti-inflammatory action. Its analgesic efficacy is not more than that of traditional analgesics; however, it has fewer side effects. It has been seen to inhibit COX-3 and at spinal cord level it antagonize neurotransmission by NMDA, substance P, and nitric oxide pathways [29]. Optimal analgesia for moderate to severe postoperative pain cannot be achieved using a single agent alone, but a balanced approach in combination with non-steroidal agents can result in up to a 40 to 50 percent reduction in opioid requirements.

Paracetalmol with its safety profile can prove to be an asset in managing perioperative pain, especially of mild to moderate severity [29].

IV Propacetamol (1g), a prodrug of acetaminophen, has been shown to be as efficacious as intramuscular morphine (10 mg) following dental extractions [30] and as effective as intramuscular Ketorolac (30 mg) following lower limb arthroplasty [31].

Given the mild to moderate profile of laparoscopic cholecystectomy pain after 24 hours, the utility of analgesics capable of controlling the postoperative pain to that level and up to the required period of time, but with fewer side effects is a promising finding. In the present study, except three cases, none of the cases had VAS pain score above 3 after initial dose of analgesia with either of the two drugs in the 24 hour interval and no side effect was reported in Paracetamol group.

The findings in the present study will pave way for further work on the issue. More studies on use of drugs with less side effects and optimum analgesic efficacy are recommended.

LIMITATION

Limitations of our study was small sample size, lack of placebo arm, and these were reasons we could not draw further conclusion.

CONCLUSION

On the basis of present study both Paracetamol and Tramadol were found to be safe and comparable in postoperative pain management though Paracetamol showed better results in terms of significantly lower mean VAS pain scores for most of the postoperative follow-up intervals. Thus intravenous infusion of Paracetamol can safely and effectively be recommended for postoperative pain relief in patients undergoing laparoscopic cholecystectomy.

REFERENCES

[1] Kum CK, Wong CW, Goh MY, Ti TK. Comparative study of pain level and analgesic requirement after laparoscopic and open cholecystectomy. *Surg Laparosc Endosc*. 1994;4:139-41.

[2] Michaloliakou C, Chung F, Sharma S. Preoperative multimodal analgesia facilitates recovery after ambulatory laparoscopic cholecystectomy. *Anesth Analg*. 1996;82:44–51.

[3] Ure BM, Troidl H, Spangberger W, Dietrich A, Lefering R, Neugebauer E. Pain after laparoscopic cholecystectomy. *Surgical Endoscopy.* 1994;8(2):90-96.

[4] Joris J, Cigarini I, Legrand M, et al. Metabolic and respiratory changes after cholecystectomy performed via laparotomy or laparoscopy. *Br J Anaesth.* 1992;69:341-45.

[5] Lepner U, Goroshina J, Samarütel J. Postoperative pain relief after laparoscopic cholecystectomy: a randomised prospective double-blind clinical trial. *Scandinavian Journal of Surgery*. 2003;92:121–24.

[6] Sachs CJ. Oral analgesics for acute nonspecific pain. *Am Fam Phys*. 2005;71:913–18.

[7] Hyllested M, Jones S, Pedersen JL, Kehlet H. Comparative effect of paracetamol, NSAIDs or their combination in postoperative pain management: a qualitative review. *Br J Anaesth*. 2002;88:199–214.

[8] Saliho glu Z, Yildirim M, Demiroluk S, Kaya G, Karatas A, Ertem M, et al. Evaluation of intravenous paracetamol administration on postoperative pain and recovery characteristics in patients undergoing laparoscopic cholecystectomy. *Surg Laparosc Endosc Percutan Tech*. 2009;19(4):321-23.

[9] Choudhari AH, Uppal R. A comparison between intravenous paracetamol plus fentanyl and intravenous fentanyl alone for postoperative analgesia during laparoscopic cholecystectomy. *Anesthesia Essays and Research*. 2011;5(2):196-200.

[10] Dejonckheere M, Desjeux L, Deneu S, Ewalenko P. Intravenous tramadol compared to propacetamol for postoperative analgesia following thyroidectomy. *Acta Anaesthesiol Belg*. 2001;52(1):29-33.

[11] Alexander JI. Pain after laparoscopy. *Br J Anaesth*. 1997;79:369–78.
[12] Jackson SA, Laurence AS, Hill JC. Does post laparoscopy pain relate to residual carbon dioxide? *Anaesthesia.* 1996;51:485–87.
[13] Comyn DJ. Minimizing pain after laparoscopy. Proceedings of the 9th World Congress of Anesthesiologists. Washington, DC, May 1988; A4.
[14] Lehmann KA. Tramadol in acute pain. *Drugs*. 1997;53 Suppl 2:25-33.
[15] Le Blanc-Louvry I, Coquerel A, Koning E, Maillot C, Ducrotté P. Operative stress response is reduced after laparoscopic compared to open cholecystectomy: the relationship with postoperative pain and ileus. *Dig Dis Sci*. 2000;45(9):1703-13.
[16] Hashmi ZA, Bashir G, Shah SA. Tramadol hydrochloride in postoperative analgesia: clinical comparison with diclofenac sodium. *Gomal J Med Sc*. 2004;2(2):47-49.
[17] Kiliçaslan A, Tuncer S, Yüceaktas A, Uyar M, Reisli R. The effects of intravenous paracetamol on postoperative analgesia and tramadol consumption in cesarean operations. *Agri*. 2010;22(1):7-12.
[18] Launo C, Bassi C, Spagnolo L, Badano S, Ricci C, Lizzi A, et al. Preemptive ketamine during general anesthesia for postoperative analgesia in patients undergoing laparoscopic cholecystectomy. *Minerva Anestesiol*. 2004;70(10):727-34; 734-38.
[19] Akinci SB, Ayhan B, Aycan IO, Tirnaksiz B, Basgul E, Abbasoglu O, et al. The postoperative analgesic efficacy of intraperitoneal tramadol compared to normal saline or intravenous tramadol in laparoscopic cholecystectomy. *Eur J Anaesthesiol*. 2008;25(5):375-81.
[20] Ali M, Khan FA. Comparison of analgesic effect of tramadol alone and a combination of tramadol and paracetamol in day-care laparoscopic surgery. *Eur J Anaesthesiol.* 2009;26(6):475-79.
[21] Shabbir SA, Saleem B, Hakim A, Hashia AM. Postoperative analgesia in laparoscopic cholecystectomy: a comparative study using bupivacaine instillation and infiltration versus parenteral analgesia (tramadol). *The Internet Journal of Anesthesiology*. 2011;29(2).
[22] Pendeville PE, Von Montigny S, Dort JP, Veyckemans F. Double-blind randomized study of tramado vs. paracetamol in analgesia after day-care tonsillectomy in children. *Eur J Anesthesiol*. 2000;17:576-82.
[23] Hoogewijs J, Diltoer MW, Hubloue I, Spapen HD, et al. A prospective randomized, open-lable, single bind study comparing four analgesics in the treatment of peripheral injury in the emergency departent. *Eur J Emerg Med*. 2000;7(2):119-23.
[24] Arslan M, Celep B, Çiçek R, Kalender HU, Yılmaz H. Comparing the efficacy of preemptive intravenous paracetamol on the reducing effect of opioid usage in cholecystectomy. *J Res Med Sci*. 2013;18(3):172–77.
[25] El-Radaideh K, Alhowary A, Hani DB, Bataineh A, Hani MB. Analgesic efficacy of intravenous paracetamol plus tramadol combination for pain after laparoscopic cholecystectomy: a doubleblind, randomized, placebocontrolled trial. *Analg Resusc: Curr Res*. 2014;3:3. http://dx.doi.org/10.4172/2324-903X.1000120.
[26] Jawad M, Jebur MA. A comparative study of intravenous paracetamol and tramadol for postoperative pain management in patients undergoing laparoscopic cholecystectomy. *Medical Journal of Babylon*. 2014;11(2):335-42.
[27] Khan AH, Sofi SA, Bashir, Rather MA. A comparative study showing efficacy of preemptive intravenous paracetamol in reducing postoperative pain and analgesic requirement in laparoscopic cholecystectomy. *Journal of Evolution of Medical and Dental Sciences*. 2015;4(62):10771-77.
[28] Rastogi B, Singh VP, Gupta K, Jain M, Singh M, Singh I. Postoperative analgesia after laparoscopic cholecystectomy by preemptive use of intravenous paracetamol or ketorolac: A comparative study. *Indian Journal of Pain*. 2016;30(1):29-33.
[29] Vadivelu N, Mitra S, Narayan D. Recent advances in postoperative pain management. *Yale J Biol Med*. 2010;83(1):11–25.
[30] Van Aken H, Thys L, Veekman L, Buerkle H. Assessing analgesia in single and repeated administrations of propacetamol for postoperative pain: comparison with morphine after dental surgery. *Anesth Analg*. 2004;98(1): 159-65.
[31] Zhou T, Tang J, White P. Propacetamol versus ketorolac for treatment of acute postoperative pain after total hip or knee replacement. *Anesth Analg*. 2001;92(6):1569–75.

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