e-ISSN: 0975-5160, p-ISSN: 2820-2651

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2023; 13(1); 186-194

Original Research Article

Effect of Pre-Emptive use of Paracetamol Vs Paracetamol Plus Dexamethasone on Postoperative Analgesia in Laproscopic Appendicectomy: A Comparative Study

Sheetal M Shah[1], Saurin B Panchal[2], Aniket R Aghara[3], Ayushi T Patel[4], Kusum B Bilwal[5]

[1,2]Assistant Professor, Anesthesiology Department, SCL Hospital, NHL Medical College, Ahmedabad.

[3,4,5]Resident Doctor, Anesthesiology Department, SCL Hospital, NHL Medical College, Ahmedabad.

Received: 25-12-2022 / Revised: 15-01-2023 / Accepted: 26-01-2023
Corresponding author: Dr. Ayushi T Patel
Conflict of interest: Nil

Abstract

Postoperative pain has significant impact on health of patients besides delay in discharge. Appropiate methods should be applied as early as possible to control postoperative pain effectively. Pre-emptive analgesia is being widely used nowadays to control postoperative pain. Paracetamol and dexamethasone were used as preemptive analgesic in various surgeries. A total of 90 patients posted for elective laproscopic appendicectomy were randomly divided into three groups. Group A – Inj Normal saline 100 ml iv, Group B – Inj Paracetamol 1gm in 100 ml iv, Group C – Inj Paracetamol 1gm in 100 ml iv + Inj Dexamethasone 8 mg iv. Study drug was given 30 minutes before induction according to groups. Visual analogue score was used to measure postoperative pain at various time intervals in postoperative period. Time for first rescue analgesic, number of rescue doses in first 24 hrs, incidences of postoperative nausea-vomiting and patient satisfaction were noted. There were significant better pain control in paracetamol and paracetamol-dexamethasone group compared to saline group, with least PONV and highest patient satisfaction for paracetamol-dexamethasone group.

Keywords: Dexamethasone, Paracetamol, Preemptive Analgesia.

Introduction:

Pain is defined as an unpleasant emotional and sensory experience with or without actual tissue damage.[1] Postoperative pain may be major cause of patient dissatisfaction after surgery. Postoperative analgesia is still considerable for optimal postoperative care of patient. Postoperative pain control can help early ambulation and hasten recovery thus minimize hospital stay.[2]

Recently preemptive use of drugs has been used to control postoperative pain. Pre-emptive analgesia is defined as administration of drugs before onset of surgical stimulus.[3,4] Pre-emptive analgesia provides optimal postoperative pain control and early discharge from hospital.[5] Opioids (fentanyl, tramodol) and nonopioids drugs (paracetamol, diclofenac, dexamethasone, dexamedetomidine) are commonly used for postoperative analgesia.

Paracetamol, a non-steroidal anti-inflammatory drug, is widely used for postoperative pain control. Paracetamol has wider safety margin and good analgesic property. It acts by inhibition of cyclo-oxygenase pathway and indirectly through serotoninergic pathway.[6,7]

Dexamethasone, a synthetic glucocorticoid, has potent anti-inflammatory activity.[8] It is commonly used for acute and chronic pain control. It acts by inhibiting release of neurotransmitters and decrease transmission in sensory fibres. [9,10]

Both paracetamol and dexamethasone can be used as preemptive medication for postoperative pain control.

Aims and Objectives

Purpose our study was to compare efficacy and safety of paracetamol alone versus paracetamol plus dexamethasone as preemptive analgesic for postoperative pain control in laproscopic appendicectomy. Secondary outcomes measured were number of rescue doses required, incidences of postoperative nausea/vomiting and patient satisfaction.

Material and Methods

A prospective randomized double blind comparative study was carried out on total of 90 patients in our institute from January 2022 to October 2022.Patients of either gender with ASA I or II, aged 20 - 40 years posted for elective laproscopic appendicectomy were selected for our study. Informed consent of patients was taken. Simple randomisation was carried out and patients were divided into three groups, 30 patients each.

Exclusion criteria's

- Patient refusal
- Allergy to nonsteroidal anti-inflammatory drugs
- Liver dysfunction
- Renal dysfunction
- History of treatment on NSAIDS or steroids
- Severe uncontrolled comorbities like diabetes, hypertension

Visual Analogue Score (VAS) was used to grade intensity of pain in postoperative period. Patients were given information about VAS score grading preoperatively. VAS is pain measurement tool ranging from 0-10, 0- no pain, 10- most severe pain. All patients were applied baseline monitoring and preoperative vitals were recorded. Patients were given study drug according to group 30 minutes before induction of general anesthesia.

Group A – Inj Normal saline 100 ml iv
Group B – Inj Paracetamol 1gm in 100 ml iv
Group C – Inj Paracetamol 1gm in 100 ml iv + Inj Dexamethasone 8 mg iv

Premedication was given in form of inj midazolam 0.5 mg before induction. All patients of three groups were induced with general anesthesia with inj sodium pentothal 6 mg/kg and inj succinylcholine 1.5 mg/kg. All patients were given inj fentanyl 1 mcg/kg. Anesthesia was maintained with oxygen, sevofluarne 1 MAC and inj atracurium. Laproscopy surgery was initiated 10 minutes after induction. At the end of surgery, patients were reversed from neuromuscular blockade with inj glycopyrrolate 8 mcg/kg and inj neostigmine 0.05 mg/kg. Hemodynamic parameters were recorded intraoperatively and immediate postoperative period up to 8 hrs. Postoperative pain was measured using VAS score in immediate postoperative period, 15 min, 30 min, 1 hr, 2 hr, 4 hr, 6 hr, 8 hr, 12 hr, 18 hr and 24 hr. VAS score > 3 at any time was noted and rescue drug in form of inj diclofenac 1.5 mg/ kg iv slowly was given.VAS score at different time interval and time for first rescue analgesic were recorded. Number of rescue doses in first 24 hrs in postoperative period and incidences of postoperative nausea/vomiting were also recorded. Patient satisfaction score at 36 hrs was also recorded using patient satisfaction scale (0-

4), 0-poor to 4 - excellent. Person taking follow up in postoperative period was blind to study drug administered.

All data were collected as mean ± standard deviation. Data were analysed using SPSS software (version 17) and appropriate statistical methods (t test, chi square test) were applied accordingly. Significance value of was set at $p < 0.05$.

Results

All patients of three groups were considered for study without any dropout and level of significance was calculated using p value.

Table 1: Demographic characteristics

	Group A (Saline)	Group B (PCM)	Group C (PCM +Dexona)	P value
Age	30.12 ± 8.56	28.87 ± 10.49	30.13 ± 7.65	> 0.05
Sex(M/F)	22/8	24/6	22/8	> 0.05
ASA I / II	26/4	28/2	25/5	> 0.05
Weight	65.54 ± 15.54	60.35 ± 18.34	62.45 ± 15.27	> 0.05
Duration of surgery	45.12 ± 10.35	48.25 ± 14.26	46.24 ± 14.25	> 0.05

Patients from all three groups were comparable in regards to demographic data like age, sex, weight, ASA grading and duration of surgery, difference is not statistically significant.

Table 2: VAS score in postoperative period

	0 min	15 min	30 min	1 Hr	2 Hr	4 Hr	6 hr	8 Hr	12 hr	18 Hr	24 hr
Group A (Saline)	2.06 ± 0.34	2.10 ± 0.56	2.17 ± 0.34	2.67 ± 0.98	2.00 ± 0.37	2.10 ± 0.43	2.64 ± 0.23	2.20 ± 0.54	2.45 ± 0.46	2.10 ± 0.77	2.59 ± 0.33
Group B (PCM)	1.78 ± 0.34	2.15 ± 0.26	2.10 ± 0.67	2.14 ± 0.56	2.30 ± 0.45	2.89 ± 1.13	2.11 ± 0.87	2.08 ± 0.65	2.34 ± 0.54	2.13 ± 0.56	2.56 ± 0.34
Group C (PCM+ Dexona)	1.89 ± 0.56	2.25 ± 0.39	2.30 ± 0.45	2.27 ± 0.56	2.10 ± 0.66	2.76 ± 0.97	2.23 ± 0.65	2.13 ± 0.64	2.23 ± 0.54	2.10 ± 0.87	2.63 ± 0.31

There was no significant difference is VAS score up to 1 hr among all groups A, B and C ($P > 0.05$).There was significant difference is VAS score from 1 hr to 6 hrs for group A and B ($P < 0.05$) and also for group A and C ($P < 0.05$).There was no difference in VAS score for group B and group C at all time except at 1 to 6 hrs. Postoperative period 1 hr to 6 hr, VAS score was slightly higher for group B compared to group C, but difference is not significant. VAS score was comparable for all three groups at 8, 12, 18 and 24 hrs.

Table 3: Postoperative rescue dose requirement

	Group A	Group B	Group C	P value
Time for first rescue dose	78.34±30.67	346.45±54.87	380.45±69.54	<0.001(A & B) <0.001(A &C) 0.13 (B & C)
Number of rescue doses in 24 hrs	2.10±0.56	1.34±0.37	1.44±0.45	<0.001(A & B) <0.001(A & C) 0.35 (B & C)

Time for first rescue analgesic is significantly shorter in group A(Saline Group) compared to group B(Paracetamol Group) and C(Paracetamol+Dexona Group). Number of rescue doses in first 24 hrs were more in group A compared to other two groups. But there is no significant

difference for time for first rescue analgesic requirement and number of rescue doses for group B and group C.

Table 4: Postoperative rescue dose requirement

Rescue dose	Group A	Group B	Group C
1-4 hrs	24(80%)	0(0%)	0(0%)
4-6 hrs	5(16.7%)	26(86.7%)	22(73.4%)
6-12 hrs	1(3.3%)	4(13.3%)	8(26.6%)

Rescue dose requirement was higher in group A(Saline group) compared to other two groups in first 1-4 hr ($p < 0.05$). During 4-6 hrs and 6-12 hrs, rescue dose requirement were comparable for groups B(Paracetamol Group) and C(Paracetamol +Dexona Group) ($p > 0.05$).
There was no significant difference in hemodynamic parameters in all three groups at preoperative period, immediate after incision and immediate postoperative period.($p > 0.05$)

Table 5: PONV and Patient satisfaction scale

	Group A	Group B	Group C	P value
Nausea /vomiting (First 24 hrs)	18(60 %)	8(26.7%)	1(3.3%)	0.001(A & B) 0.001(A & C) 0.01 (B & C)

	Group A	Group B	Group C	P value
Patient satisfaction scale (At 36 hrs)	1.12 ± 0.67	2.27± 0.48	3.08 ±0.46	0.001(A & B) 0.001(A & C) 0.001(B & C)

Incidences of PONV were high with group A(Saline Group) compared to group B(Paracetamol Group) and C(Paracetamol + Dexona group).PONV were higher for group B compared to group C, difference was statistically significant ($p < 0.05$).

Patient satisfaction were higher with group B and C compared to Group A. There was significant difference for level of patient satisfaction for group B and C, higher satisfaction with Group C ($p < 0.05$).

Discussion

Pain is a protective mechanism of body to potentially injurious stimulus. Individual variations in response to pain may be influenced by age, gender, genetic makeup and type of surgery.[11,12] Approximately 80 -90 % surgical patients experience moderate to severe pain postoperatively.[13,14] Pain due to surgical trauma is nociceptive acute pain which if untreated can result into chronic postoperative pain.

Postoperative pain is major cause of postoperative morbidity. Inadequate pain control has serious health impacts on cardiovascular and respiratory system, like hypertension, tachycardia, inadequate coughing, basal atelectasis, deep vein thrombosis, insomnia. Besides this, it delays hospital discharge and affects patient satisfaction.[15,16] So efforts should be always towards early and effective control of postoperative pain.

Various drugs like, opioids and nonopiods drugs has been used to effectively control postoperative pain. Opioids hold important place in postoperative analgesic but associated with side effects like sedation, respiratory depression, vomiting. Non opioids drugs commonly used are dexamethasone, dexmedetomidine,

paracetamol, diclofenac and other nonsteroidal anti-inflammatory drugs. These drugs are usually effective for mild to moderate pain control. However postoperative pain control is still demanding in first 24 hrs. Effective control of postoperative pain by multimodal approach may be necessary.

Due to impact on health and patient outcome, pain management should be started prior to pain initiation. This has brought about concept of preemptive analgesia. Preemptive analgesia is antinociceptive drug given before start of surgery to interrupt altered afferent signals from surgical site.[17] It acts by preventing or reducing establishment of central sensitization of surgical stimulus. Various studies has shown that preemptive analgesic provide better postoperative pain control, minimize hospital stay and improve patient satisfaction.[3,4]

Preemptive analgesic has tendency to be more efficacious than a similar drug given after initiation of surgery, resulting better postoperative pain control.[18] The agents commonly used for preemptive analgesia are nonsteroidal antiinflammatory, opioids, ketamine, and dexamethasone.[19]

Paracetamol, non-opioid analgesic, is used due to wider safety margin and better analgesic profile. It acts centrally via inhibition of cyclooxygenase and prostaglandin synthesis and also via peripheral anti-inflammatory mechanisms. Action on serotoninergic pathway has been demonstrated in some studies.[20] Various studies has shown that paracetamol in dose of 1 gm is effective for postoperative pain control.[5,21,22,23] So we had used paracetamol in single iv dose of 1gm. Maximum recommended dose for adults is 1 gm in 24 hrs.[12] It has been shown that analgesic effect of paracetamol 1 gm start within 5 min and lasts 4-6 hrs.[24]

Dexamethasone, a synthetic glucocorticoid with minimal mineralocorticoid activity, is widely used as anti-inflammatory drug and also for postoperative nausea/vomiting. When combined with other analgesics it can be useful for postoperative pain control.[25,26] It acts by inhibiting release of interleukins, bradykinin and prostaglandins synthesis. It may also affect impulse transmission in C type sensory fibers.[27] Various studies has shown that single dose of 8 mg dexamethasone is effective for postoperative pain control.[8,9,10]

So in our study we had used dose of paracetamol 1 gm and dose of dexamethasone 8 mg for preemptive analgesia for postoperative pain control.

VAS sore in postoperative period

In our study, there was comparable pain score for all three groups during early postoperative period up to 1 hr, that might due to intraoperative use of opioids. During 1 to 4 hrs, there was significant higher pain score in saline group compared to paracetamol and paracetamol-dexamethasone group. VAS score was comparable for paracetamol and paracetamol-dexamethasone group with no significant difference, revealing that preemptive analgesia was better for pain control in 1 to 4 hrs postoperative period. Both paracetamol and paracetamol-dexamethasone are nearly equal effective for pain control in 1 to 4 hr postoperatively. Ahmad khan et al[14] revealed that VAS score were significantly lower in paracetamol group compared to saline group in early postoperative period. Chaudhari et al[28] found that preemptive paracetamol 1 gm significantly reduced pain score in postoperative period compared to saline group. In contrast to our findings, Gousheh SM et al[12] revealed that 1 gm paracetamol could give pain relief but not suitable for moderate pain in postoperative period. Lakhan et al[29] also revealed in their study that single dose preoperative dexamethasone decreased postoperative pain in tonsillectomy patients.

Time for first rescue analgesic and number of rescue doses

There was significant longer time for first rescue analgesic requirement in paracetamol and paracetamol-dexamethasone group. Our findings were indicating that preemptive use of paracetamol alone or in combination with dexamethasone had capable of better postoperative pain control for longer duration of action.

Number of rescue doses in first 24 hrs in postoperative period was higher for saline group. Our findings revealed that paracetamol and paracetamol-dexamethasone group had better quality of pain control for longer duration than saline group.

In their studies, Salihoglu et al[30] and Arici et al[31] also found that patients with preemptive use of paracetamol had decreased requirement of rescue dose in postoperative period. Giannoni et al[32] and Lachance et al[33] had demonstrated that dexamethasone failed to control pain effectively.

Rescue doses at various time interval

In our study, rescue doses requirement was earlier in saline group. Paracetamol and paracetamol-dexamethasone group had rescue dose requirement in 4 – 6 hrs postoperative period indicating that paracetamol and dexamethasone were useful for delay pain sensation and minimizing threshold for pain. A study done by Ahmad khan et al[14] found that preemptive intravenous paracetamol 1 gm significantly decreased postoperative pain and rescue analgesic doses.

Some studies demonstrated that paracetamol as preemptive analgesic was no more effective than other drugs, but they had used low dose paracetamol up to 500 mg.[34,35]In their study, Jose l et al[36] revealed in their studies that preemptive analgesic effect of dexamethasone and diclofenac was comparable for third molar surgery.

PONV

There were increased incidences of PONV in saline group compared to other group. This might be due to better postoperative pain control in paracetamol group and paracetomol-dexamethasone group. Incidences of PONV were higher for paracetamol group compared to paracetamol-dexamethsaone group. This might be due to antiemetic effect exerted by dexamethasone. In a study done by Sreenivasulu et al[37] and Apfel et al[38], they revealed that preemptive paracetamol significantly reduced chances of PONV. In a study done by Vosdoganis et al[39] also revealed that intravenous dexamethasone significantly reduced incidence of postoperative vomiting. In their study, Junnkon et al[40] also demonstrated that preemptive low dose dexamethasone had lower chances of PONV after total knee arthroplasty. These findings were similar to our study.

SS Unal et al[5] revealed that preemptive paracetamol 1gm was safe and effective for postoperative pain control following nephrectomy. Lakhan et al[29] revealed that single dose of intravenous dexamethasone 8 mg given preoperatively had no any adverse effect despite better pain control.

Patient satisfaction

Highest patient satisfaction was seen in paracetamol-dexamethasone group compared to other groups. This was may be due to better quality of pain control, less number of rescue doses and least incidences of PONV. Some studies revealed that intravenous paracetamol as preemptiveanalgesic had better pain control, early discharge and better patient satisfaction compared to saline group.[21,41] Mckean S et al[42] also revealed that single dose dexamethasone preoperatively decreased incidences of PONV and had better patient satisfaction.

Limitation

There are several studies showing efficacy of paracetamol and dexamethasone as preemptive analgesic in various surgeries. There were few limitations of our study. Relatively small sample size was important limitation of study. We had used VAS score for postoperative pain assessment, alternatively other pain score could provide stronger evidences for same. We had not recorded incidences of wound infection in follow-up period if any.

Conclusion

Both, paracetamol alone or in combination with dexamethasone, were useful as preemptive analgesic for postoperative analgesia. Paracetamol and paracetamol-dexamethasone combination were nearly equally efficacious in controlling postoperative pain. In addition to that, paracetamol-dexamethasone combination had least incidences of PONV and highest patient satisfaction, so preferred as preemptive analgesic in laproscopicappedicectomy.

References

1. Merskey H, Bogduk N. Classification of chronic pain second edition.Seatttle: IASP Task Force on Taxonomy, IASP Press: 1994.
2. Lee RM, Tey JBL, Chua NHL. Postoperative pain control for total knee arthroplasty: Continuous femoral nerve block versus intravenous patient controlled analgesia. Anesth Pain. 2012;1(3):184-186.
3. Wang Y, Zhang HB, Xia B, Wang GM, Zhang MY.Preemptive analgesic effects of flurbiprofen axetil in patients undergoing radical resection of esophageal carcinoma via the left thoracic approach. Chin Med J. 2012;125:579-582.
4. Trabulsi EJ, Patel J, Viscusi ER, Gomella LG, LallasCD.Preemptive multimodal pain regimen reduces opioid analgesia for patients undergoing robotic assisted laproscopic radical prostatectomy. Urology. 2010;76:1122-1124.
5. Unal SS, Aksoy M, Ahiskaliogu A, Erdem AF, AdanurS.The effect of intravenous preemptive paracetamol on postoperative fentanyl consumption in patients undergoing open nephrectomy: A prospective randomized study. Niger J Clin Pract. 2015;18:68-74.
6. Sinatra RS, Jahr JS, Reynolds LW, Viscusi ER, Groudine SB, Payen-Champenois C. Efficacy and safety of single and repeated administration of 1 gm intravenous acetaminophen injection for pain management after major orthopedic surgery. Anesthesiology. 2005;102:822-831.
7. Remy C, Marret E, Bonnet F. State of art of paracetamol in acute pain therapy. Curr Opin Anesthesiol 2006;19:562-565
8. Allen TK, Jones CA, Habib AS. Dexamethasone for the prophylaxis of postoperative nausea and vomiting associated with neuraxial morphine administration: a systemic review and meta-analysis. Anesth Analg. 2012;114:813-822.
9. De Oliveira Almeida MD, Benzon HT, McCarthy RJ. Perioperative single dose systemic dexamethasone for postoperative pain. Anesthesiology. 2011;115:575-588.
10. De Oliveira GS, Ahmad S, Fitzgerald PC et al. Dose ranging study on the effect of preoperative dexamethasone on postoperative quality of recovery and opioid consumption after ambulatory gynaecological surgery.Br J Anaesth. 2011;107:362-371.
11. Hosseini Jahromi SA, Sadeghi Poor S, Hosseini Valami SM, Javadi A. Effects of suppository acetaminophen, bupivacaine wound infiltration and caudal block with bupivacaine on postoperative pain in pediatric inguinal herniorrhaphy. Anesth Pain. 2012; 1(4):243-247.
12. Gousheh SM, Nesioonpour S, Javaher Foroosh F, Akhondzadeh R, Sahafi SA,

Alizadeh Z. Intravenous paracetamol for postoperative analgesia in laproscopic cholecystectomy. Anesth Pain Med. 2013;3(1):214-218.
13. Wils VL, Hunt DR. Pain after laproscopic cholecystectomy. Br J Surg. 2000;87:273.
14. Ahmad khan,Shabir Ahmad Sofi, Farhana Bashir, Mustaq Ahmad Rather.A comparative study showing efficacy of preemptive intravenous paracetamol in reducing postoperative pain and analgesic requirement in laparoscopic cholecystectomy. J of Evol Of Med And Dent Sci. 2015;4(62):10771-10777.
15. Imani F, Rahimzadeh P, Faiz SHR. Comparison of the efficacy of adding clonidine, chlorpromazine, promethazine and midazolam to morphine pumps in postoperative pain control of addicted patients. Anesth Pain. 2011;1(1):10-14.
16. Shoar S, Esmaeili S, Safari S. Pain management after surgery: A brief review. Anesth Pain. 2012;1(3):184-186.
17. Shen X, Wang F, Xu S,Ma L, Liu Y, Feng S et al. Comparison of the analgesic efficacy of preemptive and preventive tramodol after lumpectomy. Pharmacol Resp. 2008;60:415-421.
18. Woolf CJ, Chong MS. Preemptive analgesia-treating postoperative pain by preventing the establishment of central sensitization. Anesth Analg. 1993; 77:362-379.
19. Anderson DA, Gentry C, Alenmyr L, Killander D, Lewis SE et al. TRAP 1 mediates spinal antinociception induced by acetaminophen and cannabinoid 9-tetrahydrocannabiorcil. Nat Commun. 2011;2:551.
20. Pickering G, Loriot MA, Libert F, Eschalier A, Beaune P, Dubray C. Analgesic effect of acetaminophen in humans: First evidence of a central serotonergic mechanism. Clin Pharmacol Ther. 2006;79:371-378.
21. Saikat M, Das A, Kunda R, Dipankar. Intravenous paracetamol infusion: Superior pain management and earlier discharge from hospital in patients undergoing palliative head-neck cancer surgery. Perspect Clin Res. 2014; 5(4): 172-177.
22. Swati Choughle, Jyotsna Paranjpe, Ashwini kumar Patil. Comparative evaluation of preemptive use of intravenous paracetamol and intramuscular diclofenac on postoperative analgesia in lower abdominal surgeries done under spinal anesthesia. Med Pulse-International Medical Journal. 2017;4(4):457-461.
23. Hossam Ibrahim Eldersuky Ali Hassan. Perioperative analgesic effects of intravenous paracetamol : Preemptive versus preventive analgesia in elective cesareansection. Anesth Essays Res. 2014;8(3):339-344.
24. Bjune K, Stubhaug A, Dodgson MS, Breivik H. Additive analgesic effect of codeine and paracetamol can be detected in strong, but not moderate pain after caesarean section. Baseline pain intensity is a determinant of assay sensitivity in a postoperative analgesic trail. Acta Anaesthesiol Scand 1996;40:399-407.
25. Jackobsson J. Preoperative single dose intravenous dexamethasone during ambulatory surgery: update around benefit versus risk. Curr Opin Anesthesiol. 2010;23:682-686.
26. Allen K. Dexamethasone: anall purposeagent? Australasian Anaesthesia. 2007:65-70.
27. Valdivia-Sanchez CG, Prieto-Duarte ML.Effectiveness of dexamethasone as an adjuvant in preemptive analgesia for postoperative pain in paients undergoing abdominal surgery. Gac Med Mex. 2017;153(3):390-396.
28. Choudhari AH, Uppal R.A comparison between intravenous paracetamol plus fentanyl and intravenous fentanyl alone for postoperative analgesia during

laproscopic cholecystectomy. Anesth Essays Res. 2011;5:196-200.
29. Lakhan MS, Ramlan S, Somayaji G. Efficacy of single dose preoperative intravenous dexamethasone for postoperative pain relief in tonsillectomy patients. Int J Otorhinolaryngol Head Neck Surg. 2017;3:323-326.
30. Salihoglu 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 laproscopic cholecystoctemy. Surg Laprosc Endosc Percutan Tech. 2009;19:321-323
31. Arici S, Gurbet A, Turker G, Yavascaoglu B, Sahin S. Preemptive analgesic effects of intravenous paracetamol in total abdominal hysterectomy. Agri Dergisi 2009;21:54-61.
32. Giannoni C, White S, Enneking FK. Does dexamethasone with preemptive analgesia improve pediatric tonsillectomy pain? Otolaryngol Head Neck Surg. 2002;126(3):307-315.
33. Lachance M, Lacroix Y, Audet N, Savard P, Thuot F. The use of dexamethasone to reduce pain after tonsillectomy in adults: A double blind prospective randomized trial. Laryngosccope. 2008;118(2):232-236.
34. Khalili G, Janghorbani M, Saryazdi H, Emaminejad A. Effect of preemptive and preventive acetaminophen on postoperative pain score: A randomized double blind trial of patients undergoing lower extremity surgery. J Clin Anesth. 2013; 25:188-192.
35. Kashefi P, Honarmand A, Safavi M. Effects of preemptive analgesia with celecoxib or acetaminophen on postoperative pain relief following lower extremity orthopedic surgery. Adv Biomed Res. 2012;1:66.
36. Simon JL, Jorge WA, Horliana AC, Canaval TG, Tortamano IP. Comparative analysis of preemptive analgesic effect of dexamethasone and diclofenac following third molar surgery. Braz Oral Res. 2013;27(3):266-271.
37. Sreenivasulu A, Prabhavathi R, Kumar GC, Reddy PN, Prasad GV, Sujit TR. Effect of preemptive intravenous paracetamol on postoperative analgesic requirements in patients undergoing laproscopic surgeries. Int J Sci Stud. 2015;3(8):92-96.
38. Apfel CC, Turan A, Souza K, Pergolizzi J, Hornuss C. Intravenous acetaminophen reduces postoperative nausea and vomiting: A systemic review and metaanalysis. Pain. 2013;154:677-689.
39. Vosdoganis F, Baines D. The effect of single dose intravenous dexamethasone in tonsillectomy in children. Anaesth Intensive Care. 1992;27(5):489-492.
40. Koh IJ, Chang CB, Lee JH, Jeon YT, Kim TK. Preemptive low dose dexamethasone reduces postoperative emesis and pain after TKA: a randomized controlled study. Clin Orthop Relat Res. 2013.471(9):3010-3020.
41. Sharma R,Gupta R, Choudhary R, Singh Bajwa SJ. Postoperative analgesia with intravenous paracetamol and dexmedetomidine in laproscopic cholecystectomy surgeries: A prospective randomized comparative study. Int J App Basic Med Res. 2017;7:218-222.
42. McKean S, Kochilas X, Kelleher R, Dockery M.Use of intravenous steroids at induction of anaesthesia for adult tonsillectomy to reduce postoperative nausea and vomiting and pain:a double blind randomized controlled trial. Clin Otolaryngol. 2006;31(1):36-40.