

A comparative study of the efficacy of intravenous paracetamol and dexmedetomidine alone and in combination on perioperative hemodynamics and post-operative analgesia for patients undergoing laparoscopic cholecystectomy under general anesthesia



Gadde Venkata Harshitha¹, Jitendra Agrawal², Sourabh Shrivastava³, Preeti Goyal⁴

¹Postgraduate Resident, ²Professor, ³Assistant Professor, ⁴Professor and Head, Department of Anaesthesiology, Gajra Raja Medical College, Gwalior, Madhya Pradesh, India

Submission: 08-02-2023

Revision: 30-04-2023

Publication: 01-06-2023

ABSTRACT

Background: With increase in incidence of gallbladder stone disease, the laparoscopic cholecystectomy is most preferred surgical technique. Laryngoscopy and peritoneal gas insufflation leads to hemodynamic stress response and pain during and after the procedure. Multimodal analgesia is recommended to reduce the stress response and prevent the post laparoscopic pain. Intravenous paracetamol and intravenous dexmedetomidine are both effective components in respect of multimodal analgesia. **Aims and Objectives:** The aim of this study was to compare and evaluate the effects of intravenous paracetamol and dexmedetomidine alone and in combination as part of multimodal analgesia on perioperative hemodynamics and post-operative analgesia. **Materials and Methods:** One hundred and five patients between the of age 18–60 years posted for laparoscopic cholecystectomy were randomly assigned to three groups (n=35). Before induction patients in Group D received dexmedetomidine 0.5 µg/kg/h and patients in Group P and Group P+D received 1 g paracetamol infusion over 15 min. Intraoperatively as continuous infusion patients in Group D and Group P+D received dexmedetomidine 0.2 µg/kg/h and Group P received 0.2 mL/kg NS until the removal of gallbladder. Perioperative hemodynamic variables, postoperatively, the need for rescue analgesia and any complications or side effects were recorded, compared, and analyzed. **Results:** Intraoperative hemodynamic variables were significantly higher in Group P compared to Group D and Group P+D (P<0.05). Prolonged rescue analgesia found in Group P+D (9.06 ± 1.16 h) then Group D (5.52 ± 1.22 h) and Group P (4.35 ± 0.99 h), respectively, which was strongly significant among the groups (P<0.0001). **Conclusion:** Our study concluded that the combination of paracetamol and dexmedetomidine maintains the better hemodynamic stability and prolonged the duration of analgesia, with the benefit of high patient satisfaction. In addition, there was significantly less post-operative bradycardia and shivering.

Key words: Dexmedetomidine; Paracetamol; Multimodal analgesia; Laparoscopic cholecystectomy

INTRODUCTION

Laparoscopic cholecystectomy being a minimally invasive procedure has become the standard technique

to remove the gallbladder in symptomatic gallbladder illnesses.¹

Although laparoscopic surgery has many advantages, it also has side effects that can disrupt cardiovascular

Access this article online

Website:

<http://nepjol.info/index.php/AJMS>

DOI: 10.3126/ajms.v14i6.52209

E-ISSN: 2091-0576

P-ISSN: 2467-9100

Copyright (c) 2023 Asian Journal of Medical Sciences



This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

Address for Correspondence:

Dr. Jitendra Agrawal, Professor, Department of Anaesthesiology, Gajra Raja Medical College, Gwalior, Madhya Pradesh, India.

Mobile: +91-9300009942. E-mail: drjagrawal@gmail.com

circulation, respiratory status, stress response, and acid-base homeostasis in the patients body.²

Although laparoscopy provides a significant reduction in post-operative pain, there may be pain as a result of diaphragmatic irritation.³ Hence, effective perioperative pain control may contribute to less morbidity and complications and also improve surgical outcomes, shorter hospital stays, and a decrease risk of developing chronic pain.³⁻⁵

Multimodal analgesia is now recommended to prevent and treat the post-laparoscopic pain.¹⁻⁵ IV paracetamol and IV dexmedetomidine are both effective components in respect of multimodal analgesia.¹¹

Paracetamol is an analgesic which is most commonly used drugs for treatment of mild-to-moderate pain and is also used for treatment of acute pain in perioperative period.^{1-3,12,13}

Dexmedetomidine a highly selective α -2A adrenergic agonist with centrally sympatholytic effect has sedative, analgesic, amnestic, anxiolytic, and opioid saving properties without causing respiratory depression.^{4-6,14,15}

Although intravenous paracetamol and intravenous dexmedetomidine have independently been studied to see their potential in lessening post-operative narcotic requirement and other side effects of laparoscopic cholecystectomy, only few studies have compared them with each other.

Aims and objectives

The primary objective of study was comparing the analgesic effect of IV paracetamol and IV dexmedetomidine alone and in combination in post-operative period.

The secondary objective of the study is to study the efficacy of paracetamol and dexmedetomidine alone and in combination in terms of perioperative hemodynamic changes and any side effects or complications.

MATERIALS AND METHODS

The present prospective, double-blinded, and randomized controlled study was conducted after obtaining approval from the Institutional Ethical Committee (No:69/IEC-GRMC/2020). A total of 105 ASA grade I and II patients aged between 20 and 60 years undergoing laparoscopic cholecystectomy were enrolled in the study.

Sample size

$$n = \frac{(S_1^2 + S_2^2) (Z_{\alpha/2} + Z_{1-\beta})^2}{\mu_1 - \mu_2}$$

From the study done Swaika et al.,³ it was observed that mean VAS score at 16 h in paracetamol group was 1.53 ± 0.93 and for the group dexmedetomidine was 2.03 ± 0.50 .

Where $\mu_1=1.53$, $\mu_2=2.03$, $S_1=0.93$, $S_2=0.5$, $Z_{\alpha/2}=1.96$, $Z_{1-\beta}=0.84$, at 5% level of significance, and 80% power of test.

Putting all these values in the formula, we obtained $n=33$, that is, approximate to 35. Hence, 35 patients were assigned under each group, so total sample size required for the study was 105.

Two investigators participated in the study, first investigator prepared the drugs and second investigator did monitoring and data collection and was blinded to the study. Patients were subsequently randomized into three groups of 35 each by close envelope method.

- i. Group P (n=35) patients received loading dose of IV paracetamol 1 g in 100 mL over 15 min before induction of anesthesia and 0.2 mL/kg/h 0.9% normal saline as continuous infusion during intraoperative period
- ii. Group D (n=35) patients received loading dose of IV dexmedetomidine 0.5 μ g/kg in 100 mL NS over 15 min before induction of anesthesia and 0.2 μ g/kg/h by continuous infusion during intraoperative period
- iii. Group P+D (n=35) patients received I/V paracetamol 1 g in 100 mL over 15 min before induction of anesthesia and IV dexmedetomidine 0.2 μ g/kg/h by continuous infusion during intraoperative period.

Inclusion criteria

Patients giving consent, between age 20 and 60 years and belonging to ASA grade 1 and 2, were included in the study.

Exclusion criteria

Patients who are uncooperative or not able to understand pain assessment test, pregnant and lactating women, or any significant pulmonary, cardiovascular, neurological, hepatorenal, psychiatric, metabolic diseases, bleeding disorders, and with history of any previous allergy to paracetamol or dexmedetomidine were excluded from the study.

Pre-anesthetic assessment was done; informed consent was obtained from all patients included in the study. All patients were kept nil orally for at least 8 h before the procedure.

On the day of the surgery, after arrival of the patient in operation theatre, routine monitors were attached. An intravenous access of 18G or 20G cannula was achieved

and premedicated with Inj. Glycopyrrolate 0.2 mg IV and Inj. Midazolam 1 mg IV. After recording base line readings of heart rate (HR), systolic blood pressure (SBP) diastolic blood pressure (DBP) and mean arterial pressure (MAP) blood pressures, and oxygen saturation, loading dose of study drug Inj. Paracetamol 1 g infusion over 15 min for Group P and Group P+D was given and Inj. Dexmedetomidine 0.5 µg/kg in 100 mL NS over 15 min for Group D was given. General anesthetic induction was done by preoxygenation with 100% oxygen, Inj. Pentazocine 0.5 mg/kg and Inj. Propofol 2 mg/kg followed by Inj. Succinylcholine 2 mg/kg IV which facilitates tracheal intubation after 1 min using appropriate size cuffed endotracheal tube and connected to anesthesia work station. Maintenance of anesthesia was achieved with nitrous oxide+Oxygen (67:33) along with intermittent inhalation anesthetic agent (isoflurane) and muscle relaxant (Inj. Atracurium) on body weight basis for loading (0.25 mg/kg) and maintenance (0.1 mg/kg) doses and controlled ventilation was done to maintain normocapnia (ETCO₂ between 35-45 mmhg). During intraoperative period, study drug Inj. Dexmedetomidine 0.2 µg/kg/h infusion for Group D and Group P+D was given and infusion was stopped after the removal of gallbladder. After completion of procedure, patients were completely reversed with Inj. Neostigmine 0.05 mg/kg+Inj. Glycopyrrolate 0.01 mg/kg and extubated (once extubation criteria were met) and oxygenated for 10 min. Hemodynamic variables were noted after intravenous infusion of study drugs, after induction, intubation, and then at 15, 30, 60, 90, and 120 min. Postoperatively, patients were monitored and hemodynamic variables and side effects were recorded at 15, 30, 60, 90, 2 h, 3 h, 4 h, 6 h, 8 h, 10 h, and 12 h. Rescue analgesia Inj. Tramadol 100 mg IV was given when the patient complains of pain and the time for rescue analgesia (TRA1) was noted in all the groups.

FOLLOW-UP: Up to 12 h.

Statistical analysis

- The statistical analysis was done using IBM SPSS 22.0 software
- One-way analysis of variance test is used to test the significance of difference in hemodynamic variables in all the three groups
- Where $P < 0.05$ is statistically significant and $P > 0.05$ is statistically insignificant and $P < 0.01$ is statistically highly significant.

RESULTS

As shown in Table 1, age, weight, gender, and ASA grading were comparable between the groups ($P > 0.05$) which were

statistically insignificant. Moreover, female patients were predominantly higher than male's in all the groups.

Intraoperative parameters

Figure 1 shows that intraoperative pulse rate was higher in Group P from induction to 120 min as compared to Group D and Group P+D ($P < 0.0001$).

Figure 2 shows statistically significant increase in intraoperative MAP in Group P from induction to 120 min compared to Group D and Group P+D ($P < 0.0001$).

Post-operative parameters

Figure 3 shows significant decrease in post-operative pulse rate in Group P+D until 12 h compared to Group P and Group D ($P < 0.0001$).

Figure 4 shows statistically significant decrease in post-operative MAP in Group P+D until 12 h as compared to Group P and Group D ($P < 0.0001$).

As shown in Table 2, there was prolonged TRA1 in Group P+D (9.06 ± 1.16 h) as compared to Group D (5.52 ± 1.22 h) and Group P (4.35 ± 0.99 h) and also shows prolonged TRA1 in Group D as compared to Group P.

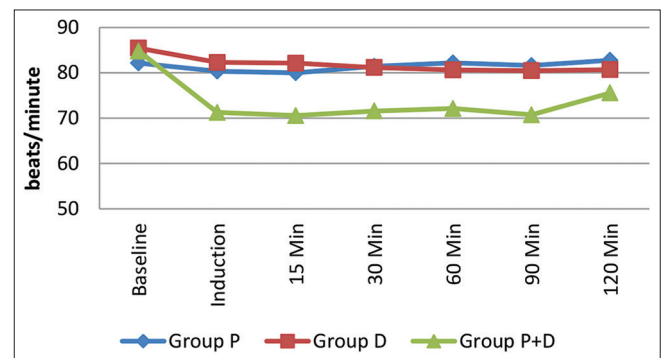


Figure 1: Intraoperative pulse rate

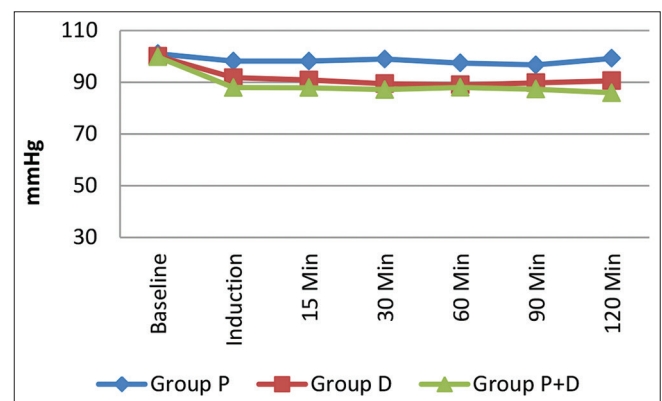


Figure 2: Intraoperative mean arterial pressure (MAP)

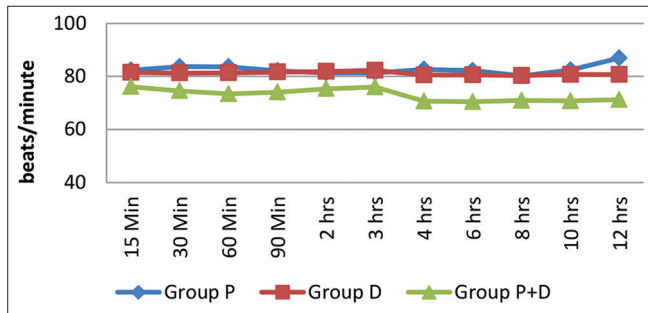


Figure 3: Post-operative pulse rate

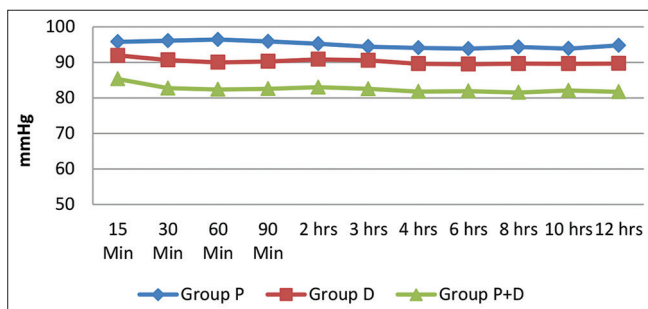


Figure 4: Post-operative MAP

Side effects among the three groups

Side effects such as shivering were noticed in three patients in Group P. We found bradycardia in 4 and sedation (Ramsay sedation scale 3) in three patients in Group D. We also found bradycardia and hypotension in one patient each in Group P+D. On statistical comparison of side effects, we found no statistically significant difference among three groups.

DISCUSSION

The use of laparoscope for the removal of gallbladder becomes gold standard, acceptable, and safe treatment in patients with gallbladder disease.⁴ Laparoscopy has benefits like faster return to normal activity, early onset of nutrition, post-operative mobility, and less post-operative complications. Labile hemodynamics are brought on by changes in the patient's position during laparoscopic surgery due to surgical stress, particularly after pneumoperitoneum. For upper abdominal laparoscopic surgery, general anesthesia with muscle relaxation, tracheal intubation, and intermittent positive pressure ventilation is the technique of choice.

One of the major concerns of anesthesiologists is finding an appropriate drug combination to control and maintain exaggerated intraoperative hemodynamic responses and for relieving post-operative pain in laparoscopic cholecystectomy patients. Poorly controlled post-operative pain may lead to anxiety, depression, and dissatisfaction in patients.¹⁻⁴ The ideal post-operative analgesic treatment should also have a low incidence of side effects, minimal

impact on major organ systems, and no significant interaction with other pharmacologic agents. It should also offer quick and efficient pain relief. Multimodal post-operative pain management with synergic and additive drugs aims to provide adequate analgesia with less side effects. As a part of multimodal analgesia IV paracetamol a cyclooxygenase inhibitor with analgesic as well as anti-inflammatory effects and an α_2 adrenoreceptor agonist dexmedetomidine with sedative, sympatholytic, anxiolytic, and analgesic effects were used in this study to minimize the known adverse effects of opioids.

In the present study, demographic parameters such as age, weight, gender, and ASA grading were comparable between the three groups and were statistically insignificant, $P > 0.05$ (Table 1) and found that female patients were predominantly higher than male in all the groups.

In the present study, intraoperative hemodynamic variables (HR, SBP, DBP, and MAP) (Figures 1 and 2) were found to be considerably more with the use of paracetamol than with the use of dexmedetomidine and paracetamol-dexmedetomidine combination at all-time points starting from induction to 120 min in the perioperative period ($P < 0.05$).

In accordance with our study, intraoperative hemodynamic variables (HR, SBP, DBP, and MAP) were also higher in paracetamol group in studies done by Swaika et al.,³ and Kumar.⁹

Study done by Sharma et al.,⁴ also confirms the findings of our study, where patients received infusion with intravenous PCM 1g and dexmedetomidine 1 μ g/kg as bolus followed by infusion of 0.5 μ g/kg/h, respectively, in two groups. Their study observed stable hemodynamics in both the groups and did not found any considerable difference between the groups.

Another study Talke et al.,¹⁰ who used continuous infusion of dexmedetomidine at variable rates (targeting plasma concentration in the range of 0.15 ng/mL–0.45 ng/mL) found that dexmedetomidine is effective in attenuating the rise in HR and plasma norepinephrine concentrations during emergence from anesthesia which supports the hemodynamic findings in our study.

Dexmedetomidine is capable of decreasing HR and blood pressure by a gradual decrease in sympathetic outflow and circulating catecholamine levels by a vagal mimetic effect.¹⁶⁻¹⁹ An initial loading dose of dexmedetomidine can result in hypotension immediately after tracheal intubation and can be avoided by a slower infusion rate over 20 min. The observations in our study correlate with available literature on the hemodynamic effects of dexmedetomidine.^{3,20}

Table 1: Demographic parameters

Demographic variables	Group P (n=35)	Group D (n=35)	Group P+D (n=35)	P-value
Age (years)	41.37±11.76	39.22±10.91	37.94±9.11	0.399
Weight (kg)	56.51±6.23	56.22±7.21	56.20±5.88	0.975
Gender				
Male	3 (8.57%)	2 (5.71%)	2 (5.71%)	0.858
Female	32 (91.42%)	33 (94.28%)	33 (94.28%)	
ASA grade				
Grade I	0	0	0	1.000
Grade II	35 (100%)	35 (100%)	35 (100%)	

Table 2: Time for first rescue analgesia (TRA)

Time for rescue analgesia	Group P (n=35)	Group D (n=35)	Group P+D (n=35)	P-value
Time for first rescue analgesia (h)	4.35±0.99	5.52±1.22	9.06±1.16	<0.0001

The present study observation shows that there was considerable reduction of all post-operative hemodynamic variables (HR, SBP, DBP, and MAP) (Figures 3 and 4) with the use of combination of paracetamol-dexmedetomidine than the use of either the drugs alone. Our study was supported by the studies done by Swaika S et al.,³, Sharma R et al.,⁴, Sarkar M et al.,⁷ and Guru K et al.⁸

The study done by Kamali et al.,² concluded that there was no significant difference in mean blood pressure of patients during the pre- and post-operative periods in both the apotel (paracetamol) and dexmedetomidine groups (P>0.05).

In the present study, considerable prolongation was observed regarding the “TRA1” (Table 2) with the use of dexmedetomidine-paracetamol combination compared with dexmedetomidine or paracetamol alone (about 9 h, 5.5 h, and 4 h, respectively). Our findings are in concordance with study done by Kumar⁹, in which the time to administration of the first dose of rescue analgesia for the PCM group was 79.25±50.85 min, while it was 143.63±137.17 min for dexmedetomidine group.

In the present study, side effects like shivering were noticed in three patients in Group P. Bradycardia in 4 and sedation in three patients in Group D. We also noticed bradycardia and hypotension in each patient in Group P+D. There was no statistically significant difference among three groups. Sharma et al.,⁴ have found that incidence of nausea and vomiting and other side effects such as hypotension and bradycardia were comparable in both the groups.

Limitations of our study

The present study has certain limitations. First, formal sample size calculation was not performed and instead a convenient sample was considered by recruiting 35 patients

in each group for study. Second, pregnant and lactating mothers and patients with significant compromise in cardiovascular, pulmonary and hepatorenal functions were not included. Furthermore, the patients who were suffering from any bleeding diathesis or psychiatric illness were not considered for the present study. Hence, caution should be exercised during generalization of the present study findings.

Several studies tried to investigate the perioperative hemodynamic variables of PCM alone compared to dexmedetomidine alone, but, in our study, we added the combination group of PCM and dexmedetomidine as part of multimodal analgesia.

CONCLUSION

The combination of dexmedetomidine and paracetamol has better hemodynamic stability and prolonged the duration of analgesia with benefit of high patient satisfaction and minimum postoperative side effects when compared to paracetamol and dexmedetomidine used alone. In addition, there was a significant decline in the incidence of post-operative bradycardia and shivering in the combination group.

ACKNOWLEDGMENT

We are grateful to the patients and their family undergoing laparoscopic cholecystectomy for their co-operation in the study. Besides this, the entire team of the Department of Anesthesiology, Gajra Raja Medical College helped a lot in this research work.

REFERENCES

- Chilkoti GT, Karthik G and Rautela R. Evaluation of postoperative analgesic efficacy and perioperative hemodynamic changes with low dose intravenous dexmedetomidine infusion in patients undergoing laparoscopic cholecystectomy-a randomised, double-blinded, placebo-controlled trial. *J Anaesthesiol Clin Pharmacol.* 2020;36(1):72-77. https://doi.org/10.4103/joacp.JOACP_184_17
- Kamali A, Ashrafi TH, Rakei S, Noori G and Norouzi A.

- A comparative study on the prophylactic effects of paracetamol and dexmedetomidine for controlling hemodynamics during surgery and postoperative pain in patients with laparoscopic cholecystectomy. *Medicine (Baltimore)*. 2018;97(51):e13330. <https://doi.org/10.1097/MD.00000000000013330>
3. Swaika S, Parta N, Chattopadhyay S, Bisui B, Banarjee SS and Chattarjee S. A comparative study of the efficacy of intravenous paracetamol and dexmedetomidine on peri-operative hemodynamics and post-operative analgesia for patients undergoing laparoscopic cholecystectomy. *Anesth Essays Res*. 2013;7:331-335. <https://doi.org/10.4103/0259-1162.123225>
 4. Sharma R, Gupta R, Choudhary R and Bajwa SJ. Postoperative analgesia with intravenous paracetamol and dexmedetomidine in laparoscopic cholecystectomy surgeries: A prospective randomized comparative study. *Int J Appl Basic Med Res*. 2017;7(4):218-222. https://doi.org/10.4103/ijabmr.IJABMR_25_17
 5. Tang C and Xia Z. Dexmedetomidine in perioperative acute pain management: A non-opioid adjuvant analgesic. *J Pain Res*. 2017;10:1899-1904. <https://doi.org/10.2147/JPR.S139387>
 6. Kaye AD, Chernobylsky DJ, Thakur P, Siddaiah H, Kaye RJ, Eng LK, et al. Dexmedetomidine in enhanced recovery after surgery (ERAS) protocols for postoperative pain. *Curr Pain Headache Rep*. 2020;24(5):21. <https://doi.org/10.1007/s11916-020-00853-z>
 7. Sarkar M, Desai P, Pawaskar S and Sarkar S. Comparative study of intravenous dexmedetomidine versus paracetamol for postoperative pain relief in laparoscopic surgery. *Indian J Clin Anaesth*. 2016;3(1):44-47.
 8. Guru K, Adinarayanan S, Krishnan B, Parida S, Hemavathi B, Bidkar PU, et al. Comparative evaluation of IV paracetamol versus IV dexmedetomidine in inpatient oral and maxillofacial surgery: A double-blinded randomized controlled study. *J Maxillofac Oral Surg*. 2020;19:394-400. <https://doi.org/10.1007/s12663-019-01264-3>
 9. Kumar S, Kadlimatti DV, Iqbal SM, Lincia R and Harsoor SS. Intravenous paracetamol versus dexmedetomidine in patients undergoing laparoscopic cholecystectomy: Hemodynamic changes. *Eur J Mol Clin Med*. 2022;9(2):1436-1444.
 10. Talke P, Chen R, Thomas B, Agarwal A, Gottlieb A, Thorborg P, et al. The hemodynamic and adrenergic effects of perioperative dexmedetomidine infusion after vascular surgery. *Anesth Analg*. 2000;90(4):834-839. <https://doi.org/10.1097/0000539-200004000-00011>
 11. Kundu M, Ahmed F and Rathor P. Comparison of intravenous dexmedetomidine and paracetamol for postoperative analgesia in abdominal hysterectomy under general anaesthesia. *IJSR*. 2020;9(8):25-27.
 12. Ong CK, Seymour RA, Lirk P and Merry AF. Combining paracetamol with nonsteroidal anti-inflammatory drugs: A qualitative systematic review of analgesic efficacy for acute postoperative pain. *Anesth Analg*. 2010;110(4):1170-1179. <https://doi.org/10.1213/ANE.0b013e3181cf9281>
 13. Salihoglu Z, Yildirim M, Demiroglu 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):321-323. <https://doi.org/10.1097/SLE.0b013e3181b13933>
 14. Kataria AP, Attri JP, Kashyap R and Mahajan L. Efficacy of dexmedetomidine and fentanyl on pressor response and pneumoperitoneum in laparoscopic cholecystectomy. *Anesth Essays Res*. 2016;10(3):446-450. <https://doi.org/10.4103/0259-1162.17640>
 15. Manne GR, Upadhyay MR and Swadia VN. Effects of low dose dexmedetomidine infusion on haemodynamic stress response, sedation and post-operative analgesia requirement in patients undergoing laparoscopic cholecystectomy. *Indian J Anaesth*. 2014;58(6):726-731. <https://doi.org/10.4103/0019-5049.147164>
 16. Alimian M, Pournajafian A, Kholdebarin A, Ghodrati M, Rokhtabnak F and Yazdkhasti P. Analgesic effects of paracetamol and morphine after elective laparotomy surgeries. *Anesth Pain Med*. 2014;4(2):e12912. <https://doi.org/10.5812/aapm.12912>
 17. Savitha KS, Dhanpal R and Kothari AN. The effect of multimodal analgesia on intraoperative morphine requirement in lumbar spine surgeries. *Anesth Essays Res*. 2017;11(2):397-400. <https://doi.org/10.4103/0259-1162.194553>
 18. Feld JM, Hoffman WE, Stechert MM, Hoffman IW and Ananda RC. Fentanyl or dexmedetomidine combined with desflurane for bariatric surgery. *J Clin Anesth*. 2006;18(1):24-28. <https://doi.org/10.1016/j.jclinane.2005.05.009>
 19. Park JK, Cheong SH, Lee KM, Lim SH, Lee JK, Cho K, et al. Does dexmedetomidine reduce postoperative pain after laparoscopic cholecystectomy with multimodal analgesia? *Korean J Anesthesiol*. 2012;63(5):436-440. <https://doi.org/10.4097/kjae.2012.63.5.436>
 20. Tufanogullari B, White PF, Peixoto MP, Kianpour D, Lacour T, Griffin J, et al. Dexmedetomidine infusion during laparoscopic bariatric surgery: The effect on recovery outcome variables. *Anesth Analg*. 2008;106(6):1741-1748. <https://doi.org/10.1213/ane.0b013e318172c47c>

Authors Contributions:

GVH- Literature survey, prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation and submission of article; **JA**- Concept and design of the study, clinical protocol and manuscript preparation, editing, manuscript revision and supervision; **SS**- Concept, coordination, statistical analysis and interpretation; **PG**- Proofreading and revision of manuscript.

Work attributed to:

Gajra Raja Medical College, Gwalior - 474 001, Madhya Pradesh, India.

Orcid ID:

Gadde Venkata Harshitha - <https://orcid.org/0009-0003-8416-2962>

itendra Agrawal - <https://orcid.org/0009-0001-2470-4761>

Sourabh Shrivastava - <https://orcid.org/0009-0004-0828-4092>

Preeti Goyal - <https://orcid.org/0000-0002-6057-4781>

Source of Support: Nil, **Conflict of Interest:** None declared.