Section: Anaesthesiology

Original Research Article

EFFECT OF INTRAOPERATIVE INFUSION OF LIDOCAINE VS DEXMEDETOMIDINE ON POSTOPERATIVE ANALGESIA AFTER LAPAROSCOPIC CHOLECYSTECTOMY

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Received : 17/07/2023
Received in revised form : 28/07/2023
Accepted : 19/08/2023

Keywords:
Lidocaine, Dexmedetomidine, Postoperative Analgesia, Laparoscopic Cholecystectomy.

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DOI: 10.47009/jamp.2023.5.6.69

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

Int J Acad Med Pharm
2023; 5 (6); 331-335

Abstract

Background: Postoperative pain is most common complaint after laparoscopic cholecystectomy. Perioperative infusion of dexmedetomidine and lidocaine decrease perioperative requirements for analgesics and inhalational anaesthetics. The aim is to study the effects of intraoperative infusion of lidocaine and dexmedetomidine on postoperative analgesia after laparoscopic cholecystectomy. Settings and design is tertiary care hospital, double blinded randomized control study. **Materials and Methods:** Ninety patients of both sex between 20-60 years, posted for elective laparoscopic cholecystectomy were randomly assigned to three groups (n=30 each). The patients in group D received intravenous bolus of dexmedetomidine 1µg/kg followed by continuous infusion of 0.4µg/kg/h. The patients in group L received intravenous bolus of lidocaine 1.5mg/kg followed by continuous infusion of 2mg/kg/h. Group N received normal saline as described for group L. Bolus doses were given 10 minutes before induction of anaesthesia and stopped after removal of trocars. Visual analogue scale (VAS) score, time to first rescue analgesic, total postoperative analgesic consumption and hemodynamic changes were evaluated during 24 hours after surgery. Statistical analysis was Results were analyzed using SPSS software version 15.0, Chi-square test was used for qualitative data. ANOVA and unpaired t test were used for continuous variables. P value of <0.05 was considered as significant. **Result:** Dexmedetomidine had better postoperative analgesia, less VAS score (<4), less requirement of first analgesic demand and total postoperative analgesic consumption when compared to lidocaine (<0.0001). However, both dexmedetomidine and lidocaine were equally effective for better hemodynamic stabilization and smooth emergence when compared to normal saline (<0.05). **Conclusion:** Both dexmedetomidine and lidocaine were effective for hemodynamic stabilization and smooth emergence, but dexmedetomidine had a better analgesic profile. Hence, Dexmedetomidine administered at bolus dose of 1µg/kg followed by infusion of 0.4µg/kg/h serve as an anaesthetic adjuvant of choice in patients undergoing elective laparoscopic cholecystectomy.

INTRODUCTION

Laparoscopic cholecystectomy is a minimally invasive surgical technique. Laparoscopic cholecystectomy has several benefits and many disadvantages like postoperative pain, postoperative nausea, vomiting, pneumo-peritoneum induced stress response and hemodynamic changes.[1] Postoperative pain is the most common complaint after laparoscopic cholecystectomy. Analgesic opioid is effective in reducing pain postoperatively but can cause respiratory depression, nausea, vomiting, postoperative hyperalgesia, prolonged sedation and urinary retention.[2] Dexmedetomidine is a selective α2A receptor agonist. It causes dose dependent sedation and analgesia without respiratory depression.[3] Intravenous lidocaine has analgesic, anti-hyperalgesic and anti-inflammatory effects.[4] Lea A et al in year 2018 showed that dexmedetomidine is a highly selective α2A adrenoceptor agonist and its perioperative intravenous administration is associated with a

ISSN (O): 2687-5365; ISSN (P): 2753-6556

reduction in postoperative pain intensity, analgesic consumption and nausea.[2] The aim of this study was to observe the effects of perioperative infusion of lidocaine and dexmedetomidine on analgesic efficacy, time to first rescue analgesia, total analgesic consumption in 24 hours postoperatively and hemodynamic changes.

MATERIALS AND METHODS

This study was a hospital based prospective, randomized, double blinded, comparative study. Ninety patients of both sex between 20-60 years age, American Society of Anaesthesiologists I and II, were posted for elective laparoscopic cholecystectomy under general anaesthesia. The exclusion criteria were weight >60 kg, significant cardiovascular, hepatic, renal, neurological or psychiatric diseases, ASA grade III, IV or emergency services, patients on chronic analgesic medication, opioid use, treatment with anti-platelet agents, antihypertensive medication, steroids, β blockers or calcium channel blockers, pregnant or lactating women, any contraindications to NSAIDS, drug or alcohol abuse, preoperative hypotension (MAP<60mmHg) and bradycardia (HR<60/minutes).

Patients with group D received intravenous dexmedetomidine (100µg/1ml), patients with group L received intravenous lidocaine (2%, 400mg/20ml). Group N patients received normal saline 0.9%. In group D, patients received dexmedetomidine bolus of about 1 µg/kg diluted in normal saline up to 10ml and continuous intravenous infusion of 0.4 µg/kg diluted in normal saline up to 6ml given in 1 hour. In group L, patients received lidocaine bolus of about 1.5mg/kg diluted in normal saline up to 10ml and continuous intravenous infusion of 2mg/kg diluted in normal saline up to 6ml given in 1 hour. In group N, patients received a normal saline bolus of 10ml and continuous infusion at 6ml/hour.

The patients were randomly allocated into above mentioned three groups of 30 patients each.

To ensure double blind study, study medications were prepared by an anaesthesiologist who was blinded to the study and label free drug was administered. All persons involved in surgery were not aware of patient group assignment.

A thorough preoperative evaluation of each patient was done. At the time of this checkup, they were acquainted with the Visual Analogue Scale (VAS) for pain scoring. Intravenous cannula was secured. Ringer Lactate was started at 4ml/kg/h. Study drug boluses were given followed by infusion, according to the allocated group. Ten minutes after bolus dose, infusion was started; patients were given inj. Midazolam 1mg IV and inj. Glycopyrrolate 0.2mg as premeditation. Before induction patients were pre-oxygenated with 100% Oxygen for three minutes. Induction was carried with Inj. Fentanyl (2.0µg/kg) intravenously and Inj. Propofol (2mg/kg) intravenously. After giving Inj. Atracurium (0.3mg/kg) intravenously for muscle relaxation and ventilating the patient with oxygen for 3minutes, intubation was facilitated, and anaesthesia was maintained with isoflurane and oxygen with controlled ventilation using circle system to keep EtCO2 between 35 and 40mmHg. Intra-abdominal pressure was maintained up to 15mmHg throughout the laparoscopic procedure. Drug infusion and anaesthetic agents were stopped at the end of surgery. Neuromuscular blockade was reversed with Inj. Neostigmine (0.05mg/kg) and Inj. Glycopyrrolate (0.01mg/kg). At the end of the surgery, patients were extubated when adequate spontaneous ventilation (tidal volume > 4ml/kg), ability to open the eyes, and patient response to anaesthesiologist verbal commands were established.

All the patients were observed for vital parameters like HR and MBP at regular intervals. After surgery, parameters were recorded every hour for the first 6 hours, then at 12 hours and 24 hours postoperatively. HR, MBP, time to first rescue analgesic demand, VAS score and total postoperative analgesic requirement in 24 hours were noted and recorded.

Pain was assessed by VAS score. When pain reported by patient is ≥ 4 on visual analogue scale. Inj. Tramadol 100mg intravenous was used as rescue analgesic and repeated thereafter whenever the VAS score became ≥ 4. VAS < 3 was taken as satisfactory pain relief.

Ethics: Ethical approval from institutional ethical committee was obtained [No.F.3 Acad/Ethical Clearance/2020/07].

Statistical Analysis: Based on minimum mean difference of 25% in parameters (mean heart rate and mean blood pressure) with α =0.01 and β =0.20, sample size for each group is estimated to be 30. The results were tabulated and statistically analyzed using SPSS software version 15.0. Chi-square test was used for qualitative data. HR, MBP were compared within three groups using ANOVA t test. ANOVA test was used for three group comparisons of continuous variables. Two groups were compared using unpaired t test. The results were expressed as mean ± standard deviation. P>0.05 was considered insignificant, P<0.05 as significant and highly significant if P<0.001.

RESULTS

There was no statistically significant difference between all three groups regarding to age (group D: 41.96±12.96 years, group L: 41.5±11.65 years and group N: 41.46±12.93 years), weight (group D: 57.06±2.65 Kgs, group L: 56.63±2.78 Kgs and group N: 56.73±2.81 Kgs) and height (group D: 159.4±5.98 Cms, group L: 158.93±5.34 Cms and group N: 158.93±5.65 Cms) in all three groups (P>0.05). Other factors like sex, ASA grade, duration of surgery (group D: 87.83±8.37 min, group L: 87.7±7.59 min

ISSN (O): 2687-5365; ISSN (P): 2753-6556

and group N: 87.36±7.85 min) were also comparable in all three groups (P >0.05).

Hemodynamic effects: The three groups were comparable in baseline HR and MBP. In group D, baseline HR was 78.75±6.02 bpm. After bolus dose, it decreased to 69.21±6.23 (i.e. -9.54 bpm). When the mean Heart Rate (HR) at different time points was compared in all three groups, significant decrease was found 10 minutes after giving bolus dose in group D when compared to group L and group N (P<0.05). After that mean HR showed insignificant change in group D and remained between 69.60 to 72.39 bpm for entire intraoperative period. In group L, mean HR showed insignificant change and remained between 76.56 to 77.33 bpm after bolus dose and infusion intraoperative. In group N, baseline HR was 78.53±6.54, it decreased to 74.43±6.78 (i.e. -4.1 bpm), increased to 91.23±6.24 (i.e. +12.7 bpm) and 92.26±5.58 (i.e. +13.73 bpm) after intubation and extubation respectively when compared to group D and group N (P<0.05) [Table 1].

In group D, baseline MBP was 81.94±2.42. 10 minutes after bolus dose, it decreased to 75.47±2.35 (i.e. -6.47 mmHg). When the mean Mean Blood Pressure (MBP) at different time points was compared in all three groups, significant decrease was found after giving bolus dose in group D compared to group L and group N (P<0.05). After that mean MBP showed insignificant change in group D and remained between 74.97 to 76.1 mmHg in entire intraoperative period. In group L, mean MBP decreased to 79.09±2.19 (i.e. -2.64 mmHg) after induction, after that mean MBP showed insignificant change and remained between 79.09 to 80.77 mmHg intraoperative. In group N, the mean MBP decreased to 76.78±2.22 (i.e. -5.13 mmHg) after induction and increased to 83.43±2.52 (i.e. +1.52 mmHg), 83.86±2.20 (i.e. +1.95 mmHg) and 85.52±2.42 (i.e. +3.61 mmHg) at the time of intubation, after creating pneumo-peritoneum and after extubation respectively when compared to group D and group L (P<0.05) [Table 2].

The difference in mean HR and mean MBP were statistically insignificant in postoperative period in all three groups (P>0.05).

Pain (VAS) score: Comparing the mean VAS score between the three groups, the mean VAS score was less in group D (<4) and group L when compared to group N at all points of time. In group L, it was >4 at 6 hours and 12 hours postoperative and in group N, it was >4 at 6, 12 and 24 hours (P<0.05) [Table 3].

Time to first analgesic demand: The mean postoperative time to first analgesic demand in group N was 1.3 hrs which was much earlier when compared to group D (4.83hrs) and group L (2.46 hrs.) (P<0.0001). The mean postoperative time to first analgesic demand in group L was earlier when compared to group D, the difference was highly significant (P<0.0001).

Postoperative total rescue analgesic: The mean postoperative total doses of rescue analgesic were much higher in group N (mean 4.0 doses that was inj. Tramadol 400mg)) when compared to group D (mean 1.53 doses that was inj. Tramadol 153mg) and group L (mean 3.4 doses that was inj. Tramadol 340mg) (P<0.0001). While postoperative total doses of rescue analgesic were much less in group D when compared to group L, the difference was highly significant (P<0.0001).

Table 1: Comparison of intraoperative and postoperative Heart rate (bpm) in all groups

Time Intervals	Group D† HR (bpm)‖ (mean±SD)	Group L‡ HR (bpm)‖ (mean±SD)	Group N§ HR (bpm)‖ (mean±SD)
Before Bolus	78.75±6.02	78.46±6.72	78.53±6.54
10 min after bolus *	69.21±6.23	76.56±6.80	77.16±7.56
1 min after induction*	69.60±6.24	75.83±7.17	74.43±6.78
1 min after intubation*	70.10±7.45	78.03±7.31	91.23±6.24
5 min after intubation*	69.53±8.38	76.4±6.94	87.9±5.97
1 min after pneumoperitoneum*	69.71±9.32	77.9±7.22	77.9±7.22
15 min*	68.85±8.87	77±6.76	76.93±6.72
30 min*	68.71±9.59	76.53±7.09	76.53±7.09
45 min*	69.82±8.76	77.4±7.51	77.4±7.51
Before release of pneumoperitoneum*	70.71±7.99	77.53±6.94	77.33±7.20
After release of pneumoperitoneum*	71.32±6.54	76.2±6.45	76.46±6.44
Before extubation*	72.03±6.54	76.93±7.33	76.5±7.07
After extubation*	72.39±5.52	77.33±7.16	92.26±5.58
1 hour	77.93±5.10	77.8±5.29	78.6±6.47
2 hour	78.46±5.66	78.26±5.81	78.13±6.93
3 hour	77.73±6.87	77.53±7.04	77.9±6.53
4 hour	77.03±7.27	76.76±6.42	77.73±6.87
5 hour	78.13±6.93	78.23±6.81	77.93±5.13
6 hour	77.9±6.53	77.9±6.53	77.03±7.27
12 hour	78.6±6.47	78.33±6.49	78.33±6.54
24 hour	78.26±6.59	77.56±5.84	78.46±5.66

**P<0.05, † Group Dexmedetomidine, ‡ Group Lidocaine, § Group Normal saline, ‖ Heart rate (beats per minute)*

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 2: Comparison of intraoperative and postoperative Mean Arterial Blood Pressure (MBP mmHg) in all groups

Time Intervals	Group D† MBP (mmHg)‖ (mean±SD)	Group L‡ MBP (mmHg)‖ (mean±SD)	Group N§ MBP (mmHg)‖ (mean±SD)
Before Bolus	81.94±2.42	81.73±1.91	81.91±2.55
10 min after bolus*	75.47±2.35	80.48±2.16	82.17±2.47
1 min after induction*	74.97±2.23	79.09±2.19	76.78±2.22
1 min after intubation*	75.09±2.08	80.19±1.83	83.43±2.52
5 min after intubation*	73.38±2.79	80±2.12	82.65±2.49
1 min after pneumoperitoneum*	75.28±2.65	80.41±2.19	83.86±2.20
15 min*	75.2±2.23	80.1±2.11	82.92±1.92
30 min*	74.9±2.48	80.69±2.23	82.51±1.79
45 min*	74.79±2.36	80.52±1.93	82.45±1.85
Before release of pneumoperitoneum*	75.24±2.12	80.34±2.13	80.93±2.20
After release of pneumoperitoneum*	75.25±2.28	80.56±2.01	80.05±2.22
Before extubation*	75.5±2.27	80.58±1.98	80±1.86
After extubation*	76.1±2.15	80.77±1.84	85.52±2.42
1 hour	77.58±2.75	78.83±2.49	77.73±2.83
2 hour	78.07±2.82	77.77±2.47	77.28±2.74
3 hour	77.47±2.35	77.28±2.74	78.11±2.47
4 hour	77.63±2.08	78.11±2.51	78.75±2.27
5 hour	77.94±2.67	77.63±2.08	77.69±2.70
6 hour	78.11±2.51	78.75±2.79	78.13±2.33
12 hour	78.75±2.27	78.27±2.32	77.93±2.67
24 hour	78.03±2.35	78.11±2.51	77.67±1.99

**P<0.05, † Group Dexmedetomidine, ‡ Group Lidocaine, § Group Normal saline, ‖ Mean arterial blood pressure (mmHg)*

Table 3: Comparison of Postoperative pain (VAS Score) in all groups

Time Intervals	Group D† VAS‖ (mean±SD)	Group L‡ VAS‖ (mean±SD)	Group N§ VAS‖ (mean±SD)
1 hour*	1.93±0.69	2.3±0.70	3.9±0.95
2 hour*	2.2±0.66	3.63±0.99	3.1±1.21
3 hour*	2.76±0.43	3.16±1.41	2.33±0.66
4 hour*	3.26±1.11	2.4±0.56	2.63±0.49
5 hour*	3.8±1.09	2.9±0.54	3.3±0.91
6 hour*	2.73±0.86	4.13±0.93	4.03±1.18
12 hour*	3.26±0.63	4.36±0.61	4.5±0.50
24 hour*	3.33±0.60	3.76±0.67	4.33±0.47

**P<0.05, † Group Dexmedetomidine, ‡ Group Lidocaine, § Group Normal saline, ‖ Visual analogue scale score.*

DISCUSSION

Postoperative pain is the most common complaint. Usually, postoperative pain is less intense in laparoscopic cholecystectomy compared with open cholecystectomy.[4] Both pneumoperitoneum secondary to raised intra-abdominal pressure and carbon dioxide causes adverse cardiovascular effects. Dexmedetomidine binds the α2A receptors of locus ceruleus and spinal cord and causes dose dependent sedation and analgesia respectively without respiratory depression. Pretreatment with dexmedetomidine attenuates hemodynamic responses to intubation, decreases plasma catecholamine concentration, decreases perioperative requirement for inhaled anaesthetic agents and analgesics. Intravenous lidocaine has analgesic, anti -hyperalgesic and anti-inflammatory effects. Lidocaine blocks Na+ current, thereby reducing excitability of neuronal, cardiac or central nervous system tissue.

In this study in group Dexmedetomidine, mean HR and mean MBP remained decreased at all point of time compared to group Lidocaine. The observations made in our study coincides with the study conducted by Mohammed N S et al,[5] (2020) that, at 10, 15, 30 and 60 min, the MBP and HR significantly decreased in group D, received inj. Dexmedetomidine compared to group X, received inj. Lidocaine.

In this study we observed statistically significant differences in MAP changes between group Dexmedetomidine, Lidocaine and Normal saline (P<0.05). A study conducted by Ahmed I MA et al,[6] (2020) also noted that, regarding MAP changes, statistically significant differences were observed between the three groups (magnesium sulfate, dexmedetomidine, and lignocaine) and control group all over the study (P<0.05). The differences in MAP changes between each of magnesium, dexmedetomidine, and lignocaine during the study were statistically significant (P<0.05).

In our study we found that Dexmedetomidine (4.83±0.64 hrs.) has a better sparing effect on intraoperative anesthetic consumption and longer time to the first postoperative analgesic demand than that of lidocaine (2.46±0.50 hrs.). Menshawi M A et al,[7] (2019) in their study also observed that, the time to the first postoperative analgesic requirement was significantly longer in group D (69.38min) and L (43.67min) when compared with group C (24.85min); it was also significantly longer in group D when compared with group L.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

In our study we observed, higher postoperative analgesic doses in group L (3.4±0.56) and time to first analgesic demand (2.46±0.50 hrs.) compared to group D in which postoperative analgesic doses were 1.53±0.50 and time to first analgesic demand was 4.83±0.64 hrs. The VAS score was significantly higher in group C compared to group D and group L. On comparing group D and group L, VAS score was significantly higher at 1, 2, 3, 6, 12, 24 hours in group L. Mohammed N S et al,[5] (2020) also noted that, there was significantly higher numeric rating scale in group X (received Lidocaine) compared to group D (received dexmedetomidine) postoperatively. Request of the first analgesia was earlier in group X (124.78min) when compared to group D (159.64min), and higher dose of postoperative analgesia paracetamol in group X (751.39mg) when compared to group D (430.34mg).

In our study, the mean VAS score in group D was 1.93, group N was 3.9 and in group L was 2.3 at 1 hour. Krishna Murthy TK et al,[8] (2018) in their study noted that, at 1 hour mean VAS score was 4.38 in group received normal saline and 1.17 in group received Lidocaine. The findings in their study coincide with our study.

The findings in our study were in agreement with the findings of various above-mentioned investigators in that dexmedetomidine and lidocaine bolus followed by infusion intraoperative decreases VAS score of postoperative pain significantly than normal saline. Dexmedetomidine has a better effect on decreasing VAS score postoperative than lidocaine.

Like other studies in our study Dexmedetomidine bolus of 1 µg/kg and continuous intravenous infusion of 0.4 µg/kg/hour reduces rise in heart rate and mean blood pressure associated with laryngoscopy and intubation, creation of pneumoperitoneum and extubation during laparoscopic cholecystectomy. After bolus dose heart rate and mean blood pressure decreased and then remained sustained for entire intraoperative period. Dexmedetomidine decreases VAS score, provides postoperative analgesia, decreases requirement of first analgesic demand and reduces total postoperative analgesic consumption. Lidocaine bolus of 1.5 mg/kg and continuous intravenous infusion of 2mg/kg/hour reduces rise in heart rate and mean blood pressure associated with laryngoscopy and intubation, creation of pneumoperitoneum and extubation during laparoscopic cholecystectomy. After bolus dose and infusion heart rate and mean blood pressure remained sustained for entire intraoperative period. Lidocaine also decreases VAS score, provides postoperative analgesia, decreases requirement of first analgesic demand and total postoperative analgesic consumption. The mean postoperative total doses of rescue analgesic were much higher in group Normal saline (mean 4.0 doses that was inj. Tramadol 400mg) when compared to group Dexmedetomidine (mean 1.53 doses that was inj. Tramadol 153mg) and group Lidocaine (mean 3.4 doses that was inj. Tramadol 340mg).

Both dexmedetomidine and lidocaine are equally effective for better hemodynamic stabilization and smooth emergence when compared to normal saline. Dexmedetomidine had better postoperative analgesia, less VAS score, decrease requirement of first analgesic demand and total postoperative analgesic consumption when compared to lidocaine.

Hence, we conclude that Dexmedetomidine administered as bolus dose of 1 µg/kg followed by infusion of 0.4 µg/kg/hour serve as anaesthetic adjuvant of choice in patients undergoing laparoscopic cholecystectomy under general anaesthesia with time to first rescue analgesic demand at 4.83 hours and reduced doses of postoperative rescue analgesic mean inj. Tramadol requirement 153mg in comparison to 400mg in control group.

CONCLUSION

Both dexmedetomidine and lidocaine were effective for hemodynamic stabilization and smooth emergence, but dexmedetomidine had a better analgesic profile. Hence, Dexmedetomidine administered at bolus dose of 1µg/kg followed by infusion of 0.4µg/kg/h serve as an anaesthetic adjuvant of choice in patients undergoing elective laparoscopic cholecystectomy.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556