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Incidence of chronic postoperative surgical pain after laparoscopic cholecystectomy: A comparison between dexmedetomidine-fentanyl and propofol-fentanyl based total intravenous anesthesia

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Abstract---Background: The combination of fentanyl to dexmedetomidine or propofol provides complete and balanced anesthesia and has advantages such as high potency, lower dosages, and fewer side effects. The research studies to describe the effect of type of anesthesia on CPSP after laparoscopic cholecystectomy are sparse. Objective: The present study was undertaken to compare the incidence of CPSP after two different types of TIVA using propofol- fentanyl and dexmedetomidine-fentanyl-based anesthesia. Materials and methods: After IEC clearance, 100 patients of ASA I&II undergoing elective laparoscopic cholecystectomy were recruited into the study. They were randomly allocated to group Propofol-fentanyl (P- F) and Group Dexmedetomidine-fentanyl(D-F) where anaesthesia was induced and maintained with propofol (induced with 1.5mg/kg IV and maintained with 3-12mg/kg/h) and dexmedetomidine (induced with 1mcg/kg slow IV over 10 minutes and maintained with 0.3-1mcg/kg). At the end of surgery, time to eye-opening, time to achieve limb lift on command was noted. Modified Aldrete score was assessed every hourly in PACU until score >9. A fixed post-operative analgesic

regimen was standardized in the PACU. After discharge from the hospital each patient was interviewed over telephone at 1st, 2nd, 3rd, month after the surgery. If patients complained of pain at the surgical site after 2nd month, they were considered as candidates of CPSP and were asked to visit the hospital to examine and confirm as a case of CPSP. The patients who visited the hospital fall under CPSP pool and were considered as true incidence of CPSP. Results: The incidence of CPSP as derived from our study over telephonic questionnaire is 31% (pain at 2nd month) and patients who visited to the hospital in total is 24 patients, excluded from CPSP group 1 patient, so the diagnosis of CPSP confirmed in 23 and this is the true incidence of CPSP derived from our study. Recovery profiles of both types of TIVA are comparable in both groups. Conclusion: True incidence of CPSP in laparoscopic cholecystectomy in our study cohort is 23%. The patients in the dexmedetomidine group had less CPSP compared to the propofol group because dexmedetomidine has preemptive analgesic and sympatholytic action which stops firing of neurons even before pain stimulus is given to the patient. The recovery profiles of both types of TIVA are comparable with no adverse effects in the dexmedetomidine group.

Keywords---post-operative surgical pain, anaesthesia, propofol.

Introduction

Open cholecystectomy (OC) has been superseded by laparoscopic cholecystectomy (LC) for the treatment of cholelithiasis. Laparoscopic cholecystectomy gives significantly better results in terms of less postoperative pain, improved pulmonary function, better arterial oxygenation, and shorter hospital stay. [1] Persistent symptoms like abdominal pain, heartburn, flatulence, and nausea after open cholecystectomy occur in up to 40 percent of patients. Severe pain persists in 10% of cases. [2] Patients reported significantly less right upper quadrant pain after laparoscopic than after open cholecystectomy. [2] The incidence of persistent symptoms after laparoscopic cholecystectomy is only 13%. [3] The incidence of chronic post-operative surgical pain (CPSP) after open cholecystectomy is around 3-51%. [4] Laparoscopic cholecystectomy is being carried out as a day-care procedure but very little is known about the actual incidence of CPSP after this procedure.

New insights into the pharmacokinetics and dynamics of intravenous anesthetic techniques, as well as the development of computer technology to facilitate intravenous drug delivery, have greatly enhanced the use of total intravenous anesthesia. Total intravenous anesthesia (TIVA) is better compared to general anesthesia in terms of better hemodynamic stability, recovery profile and lesser incidence of postoperative nausea and vomiting (PONV) and therefore considered as a better technique in daycare surgeries. [5] It also allows early discharge of patients who are well oriented and are fully alert at the time of discharge with fewer complaints of PONV. [5] An ideal intravenous anesthetic regime used in

daycare surgery should provide rapid recovery and early discharge with minimal side effects and should be cost-effective.

Propofol is commonly used as an intravenous anesthetic agent for daycare surgery and is widely used as a component of TIVA. [6] Propofol has a pharmacokinetic profile that favors its use as a continuous infusion for the maintenance of general anesthesia. [7] Fentanyl is used in TIVA along with intravenous induction agents. It belongs to an opioid group of drugs. It is a hundred times more potent analgesic than morphine and is a part of balanced anesthesia. [8] Dexmedetomidine is an alpha-2 adrenergic receptor agonist (A2ARA) used for sedation and analgesia and as an adjunct in anesthesia to reduce anesthetic requirements in procedures requiring total intravenous anesthesia (TIVA). [9] The combination of fentanyl to dexmedetomidine or propofol provides complete and balanced anesthesia and has advantages such as high potency, provides dosages, and fewer side effects. The research studies to describe the effect of type of anesthesia on CPSP after laparoscopic cholecystectomy are sparse. Hence, the present study was undertaken to compare the incidence of CPSP after two different types of TIVA using propofol-fentanyl and dexmedetomidine-fentanyl-based anesthesia.

Materials and Methods

Study setting

The present study was conducted at the tertiary care teaching hospital after obtaining approval from the Institutional Ethics Committee (IEC).

Study design

The present study was a prospective, randomized double-blind clinical trial.

Study participants

A total of a hundred male and female, willing patients were recruited during the study period from October 2020-March 2022. The following are the criteria for the recruitment of the participants.

Inclusion criteria

Willing male and female patients within the age group 18-60 years, scheduled for elective laparoscopic cholecystectomy, American Society of Anesthesiologists Physical Status grade I & II were included in the study.

Exclusion criteria

Patients with chronic opioid use, pre-existing pain syndrome, severe complications, inability to communicate and understand NRS (Numerical rating scale), and pregnant and nursing mothers were excluded from the study. After

recruitment, they were randomly assigned to two groups with 50 participants in each group.

Group Propofol-fentanyl (P-F, n=50)

Induction with injection propofol 1.5mg/kg IV and maintenance with 3-12mg/kg/hr propofol infusion along with fentanyl infusion at a rate of 1mcg/kg/hr.

Group Dexmedetomidine-fentanyl(D-F, n=50)

Induction with injection dexmedetomidine 1mcg/kg slowIV over 10 minutes and maintenance with 0.3-1mcg/kg dexmedetomidine along with fentanyl infusion at a rate of 1mcg/kg/hr. In both the groups tracheal intubation was facilitated with injection vecuronium 0.1mg/kg IV with top up doses of 1mg. All patients were ventilated with 40% oxygen in nitrous oxide during induction and maintenance of anaesthesia. Drug infusion rates in both the groups were titrated to maintain BIS around 40-50 and or to maintain haemodynamic variables within 20% of baseline.

Pre-operative visit

All patients were visited in the pre-anesthesia check-up clinic. General and systemic examination of the cardiovascular system, central nervous system, gastrointestinal system & respiratory system was done. All patients have explained the study protocol and how to use a 10 cm numerical rating scale NRSto indicate their pain perception identifying 0 as no pain and 10 as the worst imaginable pain. Telephone number and contact address were taken for subsequent communications. Demographic data like age, sex, weight, Body mass index (BMI), ASA grade, and socioeconomic status were recorded. All patients received tablet alprazolam 0.5mg orally 1 hour before sleep and tablet ranitidine 150 mg orally on the night before surgery.

Post-Surgery

All patients were operated on by the same surgical team with the standard number of port placement and surgical steps. Before discharge from the hospital patients were informed of the long-term pain they might continue to experience at the end of two and four months. Each patient was interviewed over the telephone by an investigator in 1st, 2nd, 3rd, months after the surgery.

Statistical analysis

Data was analyzed using SPSS 19.0 version. Continuous data was analyzed with Student's t-test or Mann-Whitney U test as appropriate. Categorical data was analyzed with proportion, Chi-square test or Fisher's exact test as appropriate. A p value less than 0.05 was considered statistically significant.

Results

Table 1 presents the comparison of demographic data between the study groups. Demographic parameters were not statistically significant between the groups. Figure 1 presents the comparison of the duration of pain episodes before surgery between the study groups. The parameters were not statistically significant. Figure 2 presents the comparison of the number of episodes of pain before surgery between study groups. Figure 3 presents the Postoperative pain scores for 1st month. Figure 4 presents the Postoperative pain scores 2nd month. Figure 5 presents the Postoperative pain scores 3rd month.

Table 1: Comparison of demographic data between the study groups

Variables	Group P-F (n=50)	Group D-F (n=48)	p-value
Age (years)	46.0±11.9	43.1±10.9	0.220
Sex (Male/Female)(n)	32/18	31/17	1.000
BMI(kg/m ²)	24.69±3.7	23.81±4.5	0.290
Duration of surgery (minutes)	91.4±31.2	92.0±36.2	0.920
ASA grade I/II(n)	39/11	37/11	1.000
Socioeconomic class*(n)			0.550
Upper	9	9	
Upper middle Lower	15	8	
middleUpper lower	9	9	
Lower	7	11	
	10	11	

Figure 1: Comparison of duration of pain episode before surgery between the study groups

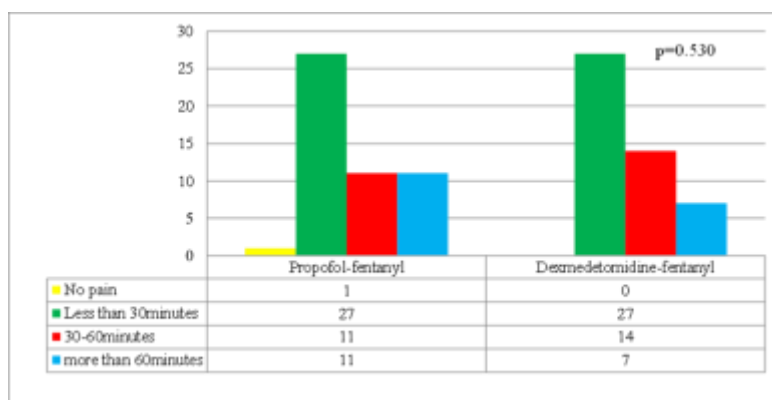


Figure 2: Comparison of number of episodes of pain before surgery between study groups

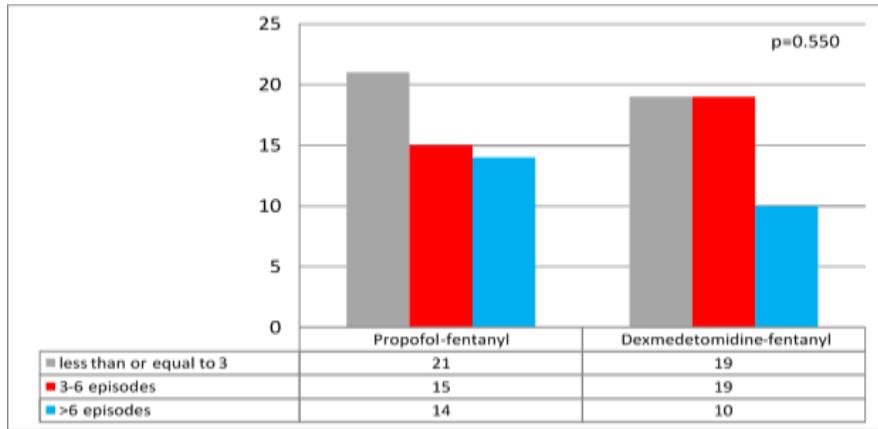


Figure 3: Postoperative pain 1st month

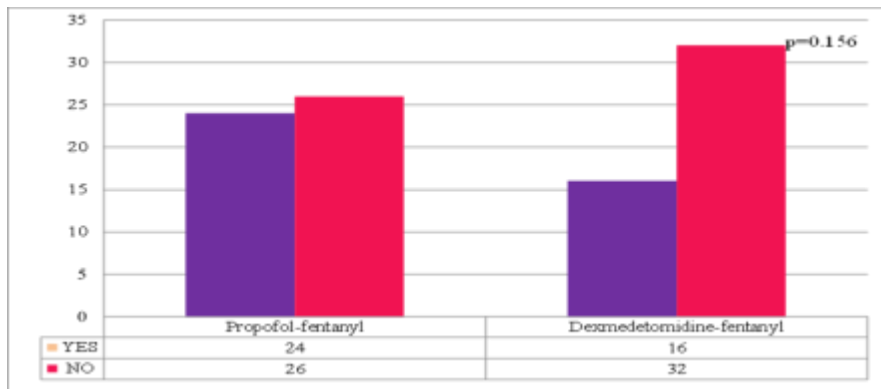


Figure 4: Postoperative pain 2nd month

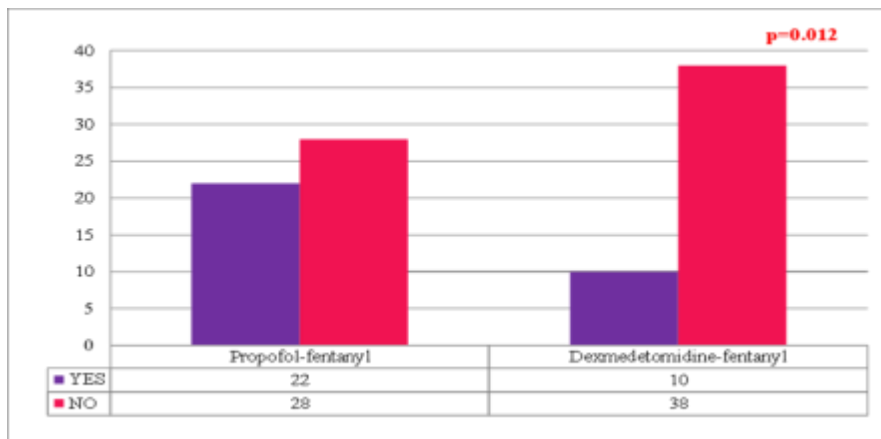
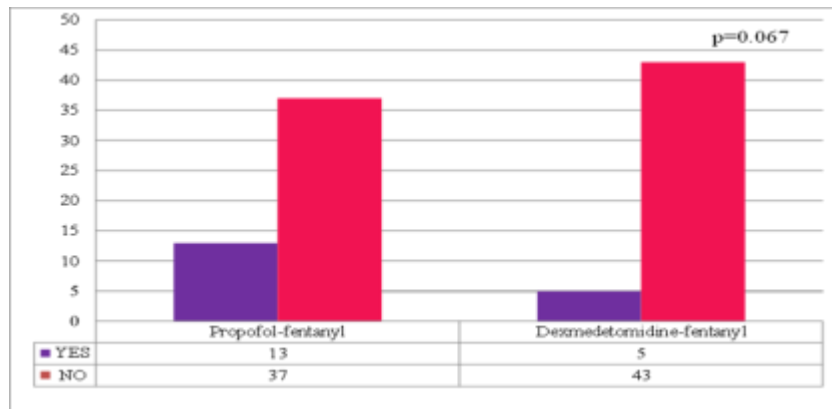


Figure 5: Postoperative pain 3rd month

Discussion

Laparoscopic cholecystectomy (LC) has become a popular alternative to open cholecystectomy (OC) in the treatment of acute cholecystitis (AC). Laparoscopic cholecystectomy is now considered the gold standard of therapy for symptomatic cholelithiasis and chronic cholecystitis in view of low rate of complications, shorter hospital stay and offers the patient a more comfortable postoperative period than OC. [9] Cholecystectomy is a difficult area to investigate because most patients have bouts of pain before surgery and in many patients problems persist after cholecystectomy. Chronic pain after cholecystectomy is common in 3% to 51% of patients. [9] Typically around 40% of patients still complain of problems related to pain. Despite improvements in methods of providing acute pain control since the 1990s, there have been no dramatic improvements in the incidence of CPSP. On the other hand, patients are led to believe by their doctors that their symptoms will be relieved by the operation. [10]

Kock et al have suggested that chronic post-surgical pain can be caused by a hypervigilant state. Fear of surgery and anxiety might also be factors. [11] Katz et al concluded that preoperative anxiety is a risk factor in the development of pain for up to 30 days following breast surgery. [12] The incidence of acute postoperative pain is affected by catastrophization (exaggerated negative beliefs and response). There have only a few studies on the influence of psychosocial factors on chronic pain following surgery, the results of which are contradictory. [13] Katz et al studied depression and anxiety in patients with or without pain following thoracotomy and concluded that preoperative assessment may affect the results. [14] The surgical approach appears to make no significant difference in overall complaints. Nicholl et al in a randomized controlled trial noted that patients randomized to lithotripsy had more complications related to biliary colic whereas patients randomized to open cholecystectomy had more complaints of scar pain and diarrhea. They did not report pain incidence data. There appears to be no difference in chronic abdominal pain when laparoscopic cholecystectomy is compared with open cholecystectomy. [15] All the patients responded to telephonic questionnaire of which 41 complained of pain over telephonic questionnaire at the end of first month and 32 patients at the end of 2nd

month. Out of 32 patients, 24 patients visited the hospital all but one patient satisfied the criteria of CPSP (True incidence 23%). We did not find any difference in the incidence of CPSP between the two groups except at the end of 2nd month ($p=0.012$). We did not find any difference in the recovery profile between the two groups. The time to eye opening ($p=0.579$), time to limb lift on command ($p=0.651$), modified Aldrete score ($p=0.471$). So, we conclude that CPSP do occur in patients undergoing LC and the incidence of CPSP in our study cohort is 23%. Dexmedetomidine based TIVA may be a better choice to reduce the incidence of CPSP because of its preemptive analgesic effect.

Conclusion

True incidence of CPSP in laparoscopic cholecystectomy in our study cohort is 23%. The patients in the dexmedetomidine group had less CPSP compared to the propofol group because dexmedetomidine has preemptive analgesic and sympatholytic action which stops firing of neurons even before pain stimulus is given to the patient. The recovery profiles of the types of TIVA are comparable with no adverse effects in the dexmedetomidine group.

Conflicts of interest: None-declared

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