Original Research Article

Intraperitoneal bupivacaine alone or with dexmedetomidine or tramadol or fentanyl for post operative analgesia following laparoscopic cholecystectomy: A comparative evaluation

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Abstract

Background: Local anaesthetics instilled intraperitoneally have been demonstrated to reduce postoperative discomfort after laparoscopic procedures. In patients having laparoscopic cholecystectomy, it is necessary to compare the antinociceptive effects of intraperitoneal dexmedetomidine, tramadol, or fentanyl coupled with bupivacaine to intraperitoneal bupivacaine alone. **Aim:** Comparative evaluation of Intraperitoneal bupivacaine alone or with dexmedetomidine or tramadol or fentanyl for post operative analgesia following laparoscopic cholecystectomy. **Methods:** This prospective, double-blind, randomised study involved a total of 200 patients. Patients were split into four study groups of equal size (n = 50). Before trocar removal, patients received intraperitoneal bupivacaine 50 ml 0.25 percent +5 ml normal saline (NS) in Group B, bupivacaine 50 ml 0.25 percent + tramadol 1 mg/kg (diluted in 5 ml NS) in Group BT, bupivacaine 50 ml 0.25 percent + fentanyl 1 mg/kg (diluted in 5 ml NS) in Group BF,and bupivacaine 50 ml 0.25% + dexmedetomidine 1 µg/kg, (diluted in 5 ml NS) in Group BD. A visual analogue scale score was used to assess the quality of analgesia (VAS). The time from the first request for analgesia, the total analgesic dose in the first 24 hours, and any adverse effects were all recorded. The Student's ttest and Chisquare test (level of significance P = 0.05) were used in the statistical analysis using Microsoft (MS) Office Excel Software. **Results:** At all occasions, the visual analogue scale in Group BD was statistically substantially lower than in Group BT and Group B. Furthermore, Group BD (2.80±0.36) had a considerably lower overall VAS in 24 hours than Groups BT (4.01±0.48), BF (4.31±0.48), and B (5.50±0.92). However, there was no discernible difference between Groups BT and BF. Group BD took the longest (138±20 minutes) to request analgesia, followed by BT (128±22 minutes), Group BF (129±22 minutes), and Group B (65±18 minutes). Group BD had the lowest total diclofenac intake (55±15 mg) compared to Group BT (95±35 mg), Group BF (97±35 mg), and Group B (185±75 mg). Overall, there were no statistically significant differences in adverse events across the four research groups (P = 5010). When comparing Group BF to Group BT, the incidence of adverse effects was lower in Group BF, and the difference was statistically significant. **Conclusion:** It was concluded that intraperitoneal instillation of bupivacaine in combination with dexmedetomidine is superior to bupivacaine alone and may be better than bupivacaine with tramadol and bupivacaine with fentanyl.

Keywords: Bupivacaine hydrochloride, dexmedetomidine hydrochloride,fentanyl intraperitoneal injection, pain, post-operative, tramadol hydrochloride

Introduction

Laparoscopic surgery is an advanced treatment method that is utilised for cholecystectomy, appendectomy, and hernia repair, among other procedures. This procedure has a lot of advantages, including less pain and bleeding, a shorter recovery time and hospital stay, and lower overall healthcare expenses. The discomfort experienced following laparoscopic surgery differs significantly from that experienced after a laparotomy. Diffuse discomfort in the belly, back, and shoulder is common in patients [1].

The level of pain usually peaks during the first few days after surgery and then gradually decreases over the next few days. The stretching of the intra-abdominal cavity causes pain following laparoscopic surgery and peritoneal inflammation and phrenic nerve irritation caused by residual carbon dioxide (CO2) in the peritoneal cavity.

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Pain can lengthen a patient's stay in the hospital and increase morbidity. Local anaesthetic injections into the peritoneum have been advocated as a way to reduce postoperative pain after laparoscopic surgery [2].Sedation, anxiolysis, analgesia, and sympatholysis are all provided by 2-adrenergic agonists like Dexmedetomidine. Due to its hemodynamic, sedative, anxiolytic, analgesic, neuroprotective, and anaesthetic sparing effects, dexmedetomidine has become one of the most commonly utilised medications in anaesthesia. Dexmedet-omidine's high selectivity for 2-receptors has been used in regional anaesthesia [3].Adjuvants such as fentanyl and tramadol have been demonstrated to extend the duration of postoperative analgesia in peripheral nerve blocks, while synthetic opioids from the phenylpiperidine series, such as pethidine and fentanyl, have a local anaesthetic effect. The duration of analgesia reported exceeds the additive or even synergistic impact of the medications administered, implying preemptive analgesia. Tramadol and fentanyl are synthetic opioids that function by activating pain-inhibitory systems [4].

Local anaesthetics such as bupivacaine, alone or in combination with opioids such as fentanyl and tramadol, ∝-2 agonists such as clonidine and dexmedetomidine are injected intraperitoneally to reduce post-operative pain following laparoscopic cholecystectomy [5].

The aim of this study was to compare the antinociceptive effects of intraperitoneal dexmedetomidine or tramadol or fentanyl combined with bupivacaine to intraperitoneal bupivacaine alone in patients undergoing laparoscopic cholecystectomy.

Methods

Before surgery, all patients signed written informed consent after receiving permission from the Institutional Ethical Committee. This prospective, randomised, double-blind trial comprised 200 patients with American Society of Anaesthesiologists (ASA) physical status I-II, both sexes, aged 18 to 60 years, who were undergoing laparoscopic cholecystectomies between November 2019 and August 2020.

Patients who were allergic to the local anaesthetic and study medicines, those who had acute cholecystitis, those who had serious cardiac, pulmonary, and neurological problems, those who had to have the procedure converted to an open cholecystectomy, and those who had to have an abdominal drain were excluded from the study.

All of the patients were taken to the operating room without being given any medicine beforehand. An 18 gauge intravenous (IV) catheter was inserted upon arrival in the operating room, and 6 ml/kg/h crystalloid was administered intraoperatively. Electrocardiography, noninvasive blood pressure, and oxygen saturation (SpO2) monitoring were commenced, and baseline values were recorded. Three minutes of preoxygenation with 100 percent oxygen (O2) were performed. To assist orotracheal intubation, general anaesthesia was produced using IV fentanyl 1.5 g/kg, propofol 2.0–2.5 mg/kg, and succinyl choline 2 mg/kg. A cuffed orotracheal tube of sufficient size, lubricated with lidocaine jelly 2 percent, was used to intubate the trachea. 60 percent N2O in oxygen with 0.5–1% isoflurane was used to maintain anaesthesia. Muscle relaxation was achieved by intermittent boluses of vecuronium bromide. The end tidal carbon dioxide [EtCO2] was monitored and minute ventilation was adjusted to maintain normocapnia (between 34 and 38 mm Hg). A suitable sized nasogastric tube was implanted.

Hypotension/hypertension were defined as a drop/rise in systolic blood pressure of more than 20% from baseline values, and bradycardia/tachycardia as a drop/rise in pulse rate of more than 20% from baseline values. Variations in haemodynamic pressure had to be controlled correspondingly. Patients were placed in a reverse Trendelenberg posture of 15-20 degrees.

Intraabdominal pressure was maintained at 12-14 mm Hg during laparoscopy. At the end of the treatment with open trocar, the CO2 was carefully evacuated by manual compression of the abdomen.

Using a table of randomization, patients were assigned to one of four groups: Group B (n = 50): Group BT (n = 50): Intraperitoneal bupivacaine 50 ml 0.25 percent + tramadol 1 mg/kg (diluted in 5 ml NS), Group BD (n = 50): Intraperitoneal bupivacaine 50 ml 0.25 percent + dexmedetomidine1 g/kg (diluted in 5 ml NS), Group BF (n = 50): Intraperitoneal b (diluted in 5 ml NS). An anaesthesiologist who was not involved in the study prepared the study medicines. Until the end of the trial, the anesthesiologist and surgeon who saw the patient were uninformed of the study group. The research solution was injected intraperitoneally at the end of the surgery before the trocar was removed in Trendelenberg's position, into the hepatodiaphragmatic area, on the gall bladder bed, and near and above the hepatoduodenal ligament. The trachea was extubated after the neuromuscular blockade was reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg. The patient was transported to a postanaesthesia care facility after the nasogastric tube was withdrawn (PACU).

After surgery, all patients were kept in the PACU for 2 hours. The pain (visual analogue scale [VAS]) score was the major outcome variable. The time to the first request for analgesia in the postoperative phase, the total dose of analgesic utilised in a 24-hour period (postoperative), and any adverse/side effects were the secondary outcomes. At 0.5, 1, 2, 4, 6, 12, 24 hours after surgery, and over all VAS score, the intensity of postoperative pain was measured for all patients (mean of all VAS scores). Before induction of anaesthesia, all study subjects were taught how to utilise the VAS score (VAS score 0 = no pain, VAS score 10 = greatest possible pain). Patients with a VAS of 3 or above were administered 75 mg diclofenac intramuscularly as a rescue analgesic. Patients were also monitored for nausea and vomiting after surgery. Ondansetron 4 mg IV was given to patients who had nausea or vomiting. Over a 24-hour period, the time to the first request for analgesia (regarding extubation as time 0), total dose of analgesia, and unfavourable or side effects were recorded.

Using the Power and Sample size calculator (PS version 3.0.0.34), a total sample size of 200 patients (n = 50 each for four groups) was computed, assuming a 30% increase in pain scores with a 0.05 error and an 80 percent power. A total of 235 patients were included in the study for a sample size of 200, but 35 individuals were excluded due to exclusion criteria.

Microsoft (MS) Office Excel Software was used to conduct the statistical analysis (Microsoft Microsoft Excel, Redmond, Washington: Microsoft 2003, Computer software). The average, standard deviation, number, and percentage were used to represent the findings (percent). The post hoc analysis approach was used to examine the data. The unpaired Student's ttest was used to examine normally distributed data (for comparison of parameters among groups). The Chisquare (2) test was used to do the comparison, with a P value reported at a 95% confidence level. P = 0.05 was utilised as the level of significance.

Results

There was no statistically significant difference in age, sex, weight, ASA physical status, operation duration, or anaesthetic time [Table 1]. Four patients were removed from the research due to conversion to open surgery in the BT group and common bile duct damage in one patient in the BD group. No patient, however, was excluded from the study due to intolerable pain, a cardiac episode, or intolerance.

At all occasions, the visual analogue scale in Group BD was statistically substantially lower than in Group BT, Group BF and Group B [Table 2]. Furthermore, Group BD (2.800.36) had a considerably lower overall VAS in 24 hours than Groups BT (4.01±0.48), BF (4.31±0.48), and B (5.5±0.92). However, there was no discernible difference between Groups BT and BF. (See Table 3)

Group BD took the longest (138±20 minutes) to request analgesia, followed by BT (128±22 minutes), Group BF (129±22 minutes), and Group B (65±18 minutes). Group BD had the lowest total diclofenac consumption (55±15 mg) compared to Group BT (95±35 mg), Group BF (97±35 mg), and Group B (185±75 mg) [Table 3]. Comparative analysis showed that adverse events were not statistically significantly different in all the four study groups (*P* = 5010) [Table 4].The incidence of side effects was low in Group BF as compared to Group BT and the the difference was statistically significant.

Table 1: Demographic characteristic of patients, operative data in studied groups (mean±SD)

Variable	Group B (*n*=50)	Group BT (*n*=50)	Group BD (*n*=50)	Group BF(n=50)	P value
Age (years)	37.71±8.96	39.43±9.01	38.21±7.57	39.47± 4.32	0.7890* 0.917[#] 0.867[σ] 0.534[ł] 0.698[a] 0.321[b]
Sex					
Males	19 (50)	18 (50)	19 (50)	18 (50)	0.860

Females	31 (50)	32 (50)	31 (50)	32 (50)	
Weight (kg)	61.20±8.22	60.41±9.96	63.90±9.60	62.50±8.96	0.9115* 0.873♯ 0.863 σ 0.771 I 0.665a 0.887b
ASA$					
I	33 (50)	32 (50)	32 (50)	32 (50)	0.8582
II	17 (50)	18 (50)	18 (50)	18 (50)	
Duration of surgery (min)	53.56±10.94	54.00±10.89	55.96±9.80	57.00±10.89	0.757* 0.754♯ 0.8468 σ 0.531 I 0.612a 0.561b
Anaesthesia time (min)	64±11.40	63.00±10.90	64.00±11.00	63.00±10.90	0.741* 0.784♯ 0.4510 σ 0.746 I 0.692a 0.432b

Table 2: Post-operative VAS score (mean±SD) in studied groups

Time (h)	Group B (*n*=40)	Group BT (*n*=40)	Group BD (*n*=40)	Group BF (n=40)	*P*
0.5	5.10±1.60	4.60±0.96	3.10±0.84	4.39±0.86	0.041* 0.003♯ 0.000 σ 0.000 I 0.0001a 0.432b
1	6.90±0.09	4.62±1.01	3.02±0.26	4.42±1.01	0.031* 0.002♯ 0.000 σ 0.000 I 0.0001a 0.332b
2	6.02±1.00	4.11±0.96	3.06±0.90	4.31±0.96	0.021* 0.005♯ 0.000 σ 0.000 I 0.0003a 0.132b
4	5.46±1.20	3.80±1.80	2.84±0.22	3.60±1.80	0.041* 0.003♯ 0.000 σ 0.000 I 0.0001a 0.432b
6	5.12±0.90	3.78±1.22	3.02±0.20	3.98±1.22	0.011* 0.002♯ 0.000 σ 0.000 I 0.0006a 0.632b
12	6.00±0.80	3.60±0.92	2.61±0.50	3.80±0.92	0.021* 0.003♯ 0.000 σ 0.000 I 0.0001a 0.432b
24	4.00±0.86	3.50±0.84	2.06±0.81	3.70±0.84	0.011* 0.003♯ 0.000 σ 0.000 I 0.0001a 0.432b

Table 3: Post-operative overall VAS score and analgesic requirements (mean±SD) in studied groups

Variable	Group B (*n*=50)	Group BT (*n*=50)	Group BD (*n*=50)	Group BF (*n*=50)	*P*
Over all VAS over 24 h post-operatively	5.5±0.92	4.01±0.48	2.80±0.36	4.31±0.48	0.000* 0.0000♯ 0.000 σ 0.0000 I 0.0000a 0.132b
Time to first request of analgesia in postoperative period (min)	65±18	128±22	138±20	129±22	0.000* 0.0000♯ 0.046 σ 0.0000 I 0.0000a 0.232b
Total dose of diclofenac (mg) in 24 h	185±75	95±35	55±15	97±35	0.000* 0.0000♯ 0.000 σ 0.0000 I 0.0000a 0.132b

Table 4: Post-operative adverse/side effects (%) in studied groups

Variable	Group B (%)	Group BT (%)	Group BD (%)	Group BF (%)	*P*
Nausea	18.5	13.6	4	12.5	χ=7.20, df=7, *P*=0.5010
Vomiting	6	4	1	4	
Shoulder pain	72	18	06	17	
Pruritis	0	7	0	8	

statistical difference between Group B and Group BT= *, statistical difference between Group B and Group BD= #,statistical difference between Group B and Group BF= σ, statistical difference between Group BD and Group BT = I, statistical difference between Group BD and Group BF=a,statistical difference between Group BT and Group BF = b

Discussion

In comparison to open cholecystectomy, laparoscopic cholecystectomy had a better surgical outcome in terms of postoperative discomfort, morbidity, and recovery time [6-7].

The three types of postoperative pain after laparoscopic cholecystectomy are visceral, parietal, and referred shoulder pain, which differ in intensity, latency, and duration. Previous research has suggested that parietal pain is the most common cause of pain, but many other studies have found that visceral pain is the most common cause of pain in the early stages of recovery [8]. This is because, in comparison to small incisions and minimal trauma to the abdominal wall, the surgical manipulation and tissue destruction in visceral organs is much more. To lower overall discomfort and improve postoperative circumstances in patients undergoing laparoscopic procedures, multimodal efforts such as parenteral opioids, nonsteroidal antiinflammatory medications, and local wound infiltration have been used. Regardless of their effectiveness, all parenteral drugs have side effects [9].

Intraperitoneal instillation of local anaesthetic drugs has become a significant strategy for controlling postoperative pain, nausea, vomiting, and reducing hospital stay in this modern era of surgery. Peritoneal inflammation and neuronal rupture occur during laparoscopic procedures due to gas insufflations and higher intraperitoneal pressure. Hence, we chose intraperitoneal route because it blocks the visceral afferent signals and modifies visceral nociception [10].

Antinociception is achieved via influencing neuronal membrane related proteins, as well as reducing the generation and action of prostaglandins, which excite nociceptors and promote inflammation. We used 0.25 percent bupivacaine intraperitoneally to generate effective analgesia, and then added either dexmedetomidine or tramadol to compare the antinociceptive efficacy when coupled with bupivacaine. Dexmedetomidine's antinociceptive actions occur at the dorsal root neuron level, where it inhibits the release of substance P in the nociceptive pathway and increases conductance through potassium channels by acting on inhibitory G protein [11].

Golubovic et al investigated the analgesic effects of intraperitoneal instillation of bupivacaine and/or tramadol in patients undergoing laparoscopic cholecystectomy, concluding that intraperitoneal instillation of bupivacaine or tramadol, or a combination of both, is an effective method for managing pain after laparoscopic cholecystectomy, significantly reducing postoperative analges On the contrary, we discovered that bupivacaine plus tramadol (Group BT) had a significantly lower VAS score at all time points and overall VAS score, as well as statistically poorer postoperative analgesia than Group B [12].

In paediatric cleft lip repair, a prospective, randomised, double-blind trial was conducted to examine the efficacy, duration, and safety of intraoral nerve block using bupivacaine alone or in combination with fentanylor pethidine on post-operative pain relief. The addition of fentanyl or pethidine to bupivacaine for Bilateral Intraoral Infraorbital Nerve Block prolongs analgesia with no side effects and can be used safely in paediatric patients, according to the findings [13-14]

Memis et al. investigated the effects of tramadol or clonidine combined with intraperitoneal bupivacaine on postoperative pain in total abdominal hysterectomy and discovered that the combination of tramadol or clonidine with intraperitoneal bupivacaine was more effective than bupivacaine alone [15-16]. In terms of efficacy, there was no significant difference between the tramadol and clonidine groups, although dexmedetomidine had much superior efficacy than tramadol in combination with bupivacaine. The considerable effect of dexmedetomidine could be attributed to its higher efficacy in our study and clonidine's higher efficacy in Memis et al study.There are very less studies in the literature which analysed the analgesic effects of ά-2 agonists intraperitoneally [17].

Our findings are consistent with those of Ahmed et al., who found that intraperitoneal instillation of mepiridine or dexmedetomidine in combination with 0.25 percent bupivacaine significantly reduces postoperative analgesic requirements and shoulder pain in patients

undergoing laparoscopic gynaecological surgeries. In the postoperative period, time to first request analgesia was considerably delayed in Group BD compared to Group B (P = 0.000). Memis et al. discovered no difference between tramadol and clonidine groups, while the tramadol group took considerably less time than the dexmedetomidine group (P = 0.03) in this investigation [18].

We found that Group B required statistically higher doses of diclofenac in the postoperative period than Group BD or Group BT , which was in agreement with Memis et al. and Ahmed et al., but Memis et al. found higher doses in the clonidine group than the tramadol group in their study [19].

In our investigation, there was no statistically significant difference between the four study groups in terms of unfavourable effects (P = 0.5010).Incidence of shoulder pain was also lower in dexmedetomidine group in study done by Ahmed *et al* [20-21]

The postoperative discomfort, which is a subjective sensation that might be difficult to define objectively and evaluate when comparing various treatment choices, is a limitation of the current study. Because there have been few studies on the addition of dexmedetomidine to intraperitoneal bupivacaine in the past, more research is needed with different doses of dexmedetomidine, timing, concentrations of local anaesthetics, and routes of administration to provide the most benefit in terms of postoperative pain relief with the fewest side effects after laparoscopic surgeries.

Conclusion

We conclude that intraperitoneal instillation of dexmedetomidine 1 µ/kg in combination with bupivacaine 0.25% in elective laparoscopic cholecystectomy significantly reduces the post-operative pain and significantly reduces the analgesic requirement in post-operative period as compared to bupivacaine 0.25% alone and may be better than bupivacaine combined with tramadol and bupivacaine combined with fentanyl

References

1. Kim TH, Kang HK, Park JS, Chang IT, Park SG. Intraperitoneal ropivacaine instillation for postoperative pain relief after laparoscopic cholecystectomy. J Korean Surg Soc 2010; 79: 130-6.
2. Bisgaard T, Kehlet H, Rosenberg J. Pain and convalescence after laparoscopic cholecystectomy. Eur J Surg 2001;167:84-96.
3. Hernandez-Palazon J, Tortosa JA, Nuño de la Rosa V, Gimenez-Viudes J, Ramírez G, Robles R. Intraperitoneal application of bupivacaine plus morphine for pain relief after laparoscopic cholecystectomy. Eur J Anaesthesiol 2003;20:891-6.
4. Esmat ME, Elsebae MM, Nasr MM, Elsebaie SB. Combined low pressure pneumoperitoneum and intraperitoneal infusion of normal saline for reducing shoulder tip pain following laparoscopic cholecystectomy. World J Surg 2006;30:1969-73.
5. El-Labban GM, Hokkam EN, El-Labban MA, Morsy K, Saadl S, Heissam KS. Intraincisional vs intraperitoneal infiltration of local anaesthetic for controlling early post-laparoscopic cholecystectomy pain. J Minim Access Surg 2011;7:173-7.
6. Ahmed B, Elmawgoud AA, Dosa R. Antinociceptive effect of (ά-2 adrenoceptor agonist) dexmedetomidine vs meperidine, topically, after laproscopic gynecologic surgery. J Med Sci 2008;8:400-4.
7. Golubovic S, Golubovic V, Cindric-Stancin M, Tokmadzic VS. Intraperitoneal analgesia for laparoscopic cholecystectomy: Bupivacaine versus bupivacaine with tramadol. Coll Antropol 2009;33:299-302.
8. Memis D, Turan A, Karamanlioglu B, Tükenmez B, Pamukçu Z. The effect of tramadol or clonidine added to intraperitoneal bupivacaine on postoperative pain in total abdominal hysterectomy. J Opioid Manag 2005;1:77-82.
9. Verma GR, Lyngdoh TS, Kaman L, Bala I. Placement of 0.5% bupivacaine-soaked Surgicel in the gallbladder bed is effective for pain after laparoscopic cholecystectomy. Surg Endosc 2006; 20:1560-4.
10. Cantore F, Boni L, Di Giuseppe M, Giavarini L, Rovera F, Dionigi G. Pre-incision local infiltration with levobupivacaine reduces pain and analgesic consumption after laparoscopic cholecystectomy: A new device for day-case procedure. Int J Surg 2008;6 Suppl 1:S89-92.
11. Karaaslan D, Sivaci RG, Akbulut G, Dilek ON. Preemptive analgesia in laparoscopic cholecystectomy: A randomized controlled study. Pain Pract 2006;6:237-41.
12. Pappas-Gogos G, Tsimogiannis KE, Zikos N, Nikas K, Manataki A, Tsimoyiannis EC. Preincisional and intraperitoneal ropivacaine plus normal saline infusion for postoperative pain relief after laparoscopic cholecystectomy: A randomized double-blind controlled trial. Surg Endosc 2008;22:2036-45.
13. Papadima A, Lagoudianakis EE, Antonakis P, Filis K, Makri I, Markogiannakis H, *et al.* Repeated intraperitoneal instillation of levobupivacaine for the management of pain after laparoscopic cholecystectomy. Surgery 2009;146:475-82.
14. Tobias JD. Pain management following laparoscopy: Can we do better? Saudi J Anaesth 2013;7:3-4.
15. Abdulla S, Eckhardt R, Netter U, Abdulla W. A randomized, double-blind, controlled trial on non-opioid analgesics and opioid consumption for postoperative pain relief after laparoscopic cholecystectomy. Acta Anaesthesiol Belg 2012;63:43-50.
16. 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 laparoscopic cholecystectomy. Surg Laparosc Endosc Percutan Tech 2009;19:321-3.
17. Kahokehr A, Sammour T, Soop M, Hill AG. Intraperitoneal local anaesthetic in abdominal surgery-A systematic review. ANZ J Surg 2011;81:237-45.
18. Bharadwaj N, Sharma V, Chari P. Intraperitoneal bupivacaine instillation for postoperative pain relief after laparoscopic cholecystectomy. Indian J Anaesth 2002;46:49-52.
19. Liu SS, Hodgson PS. Local anaesthetics. In: Barash PG, Cullen BF, Stoelting RK, editors. Clinical Anaesthesia. 4th ed. Philadelphia: Lippicott Williams and Wilkins; 2001. p. 449-69.
20. Kamibayashi T, Maze M. Clinical uses of alpha2-adrenergic agonists. Anesthesiology 2000;93:1345-9.
21. Golubovic S, Golubovic V, Tokmadzic VS. Intraperitoneal analgesia for laproscopic cholecystectomy. Periodicum Biologorum 2009;3:263-6.

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