

A comparative study on the prophylactic effects of paracetamol and dexmedetomidine for controlling hemodynamics during surgery and postoperative pain in patients with laparoscopic cholecystectomy

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Abstract

Background: Today, the ever-expanding technology is inevitably shadowing on all aspects of human life. This study was aimed to compare the prophylactic effects of paracetamol and dexmedetomidine for controlling hemodynamics during surgery and postoperative pain.

Methods: The study population consisted of 132 patients aged 18 to 70 years and from both genders, who were candidates for emergency cholecystectomy or elective surgery. Group A consisted of 66 patients who received dexmedetomidine, and Group B included 66 patients with paracetamol administration. The amount of postoperative pain was measured on the basis of visual analog scale, arterial blood pressure, as well as heart rate at recovery and 4, 12, and 24 hours after surgery.

Results: The mean age in the 2 groups was similar and almost equal to 52 years; there was no difference in the sex ratios in both groups ($P > .05$). Pain score in the paracetamol group was significantly lower than that in the dexmedetomidine group ($P = .04$); nevertheless, there were no group differences in the mean scores of pain during these hours ($P > .05$). The median opioid use in 24 hours after operation in the paracetamol group was lower when compared with that in the dexmedetomidine group, and the mean duration of analgesia in the paracetamol group was higher when comparing with dexmedetomidine group. Furthermore, in both groups, mean arterial pressure and preoperative PR interval were similar at various times.

Conclusion: The findings demonstrated that both regimens of drugs can control the hemodynamic status of patients during laparoscopic cholecystectomy, which provides effective postoperative analgesia for pain management.

Abbreviations: IRB = Institutional Review Board, MAP = mean arterial pressure, RSS = Ramsay Sedation Score, SVR = systemic vascular resistance, VAS = visual analog scale.

Keywords: dexmedetomidine, laparoscopic cholecystectomy, paracetamol, perioperative vital sign, postoperative pain

1. Introduction

The use of a laparoscope for the removal of gallbladder, as a golden standard and safe treatment, has been accepted worldwide in most patients with gallbladder disease, because it reduces the need for hospitalization and the costs related to hospitalization. Its benefits include faster return to normal activity, less pain and postoperative complications, early onset of oral nutrition, and faster postoperative movement; moreover,

the beauty of the skin is considered as other benefits. Of course, we will be facing complications of this new technique. On one hand, the complications during the procedure include bleeding from the trocar, bile leakage, and injuries to the biliary system. On the other hand, postoperative complications include pain, nausea, and vomiting. In addition to the above-mentioned cases, there are major complaints from patients after surgery.^[1–4] Despite its benefits, the process of laparoscopic surgery is not devoid of side effects, which can disturb the cardiovascular circulation, respiratory status, response to stress, and the acid–base homeostasis of the patient's body.^[4] In this method, CO₂ gas is blown into the abdominal cavity, causing both mechanical (increased intraocular pressure)^[4–9] and neurohormonal changes (secretion of catecholamines and vasopressin).^[6,10] An increase of >10 mm causes significant changes in the hemodynamics of the body, which can exhibit a decrease in cardiac output, an increase in systemic vessel resistance, and an increase in arterial pressure, as well as pulmonary pressure.^[6,11] The heart rate can provide an unchanged level or with a brief increase.^[12] An increase in the mean arterial pressure (MAP) and the systemic vascular resistance (SVR) in response to gas blowing into the peritoneal cavity is due to the involvement of the sympathetic nervous system.^[13–15] It is worth noting that these hemodynamic

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responses are related to the release of two important hormones, namely, catecholamines and vasopressin.^[7,14–16]

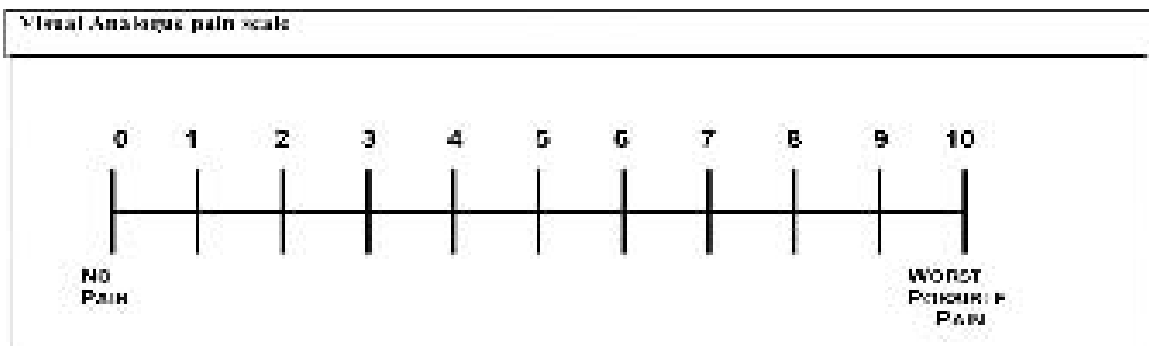
In this regard, changing management during surgery is very important.^[14–16] Various techniques have been proposed to address such changes, including nitroglycerin, beta-blockers, opioids, gabapentin, pregabalin, magnesium sulfate, clonidine, and dexmedetomidine.^[14–16] Dexmedetomidine is a nonopioid drug that is used to control hemodynamic status, which can relieve postoperative pain.^[5,17] Dexmedetomidine is a highly selective alpha 2-adrenoceptor agonist that acts as a general anesthetic adjuvant with central sympathetic effect and helps to stabilize hemodynamic properties. It also has an anesthetic effect that reduces the need for opioids and their complications, as well as this pharmacodynamic profile has many anti-stress actions.^[5,17,18] Dexmedetomidine analgesic properties are less than opioids, indicating the lack of potential for replacement with opiate; however, dexmedetomidine can play a role in multidimensional analgesia. Moreover, it can reduce the required dose during the period of operation.^[5,18]

Paracetamol, also known as intravenous acetaminophen, is a pain reliever, which is typically effective in controlling pain after multiple surgeries, while the least negative effects of this drug on the patient's hemodynamic have been previously observed.^[16,19–21] Therefore, this study was aimed to

Group A included 66 patients receiving laparoscopic cholecystectomy (after anesthesia induction) with dexmedetomidine. Patients in this group received 1 µg/kg stat and then 0.5 µg/kg per hour for up to 6 hours after surgery. In this study, Percedex was used with vials containing 200 µg dexmedetomidine. Group B included 66 patients who received laparoscopic cholecystectomy and paracetamol immediately after injecting anesthesia; patients 1st received 1g paracetamol intraoperative before surgery, and 500mg paracetamol was also prescribed every 6 hours until 24 hours. Both groups underwent laparoscopic cholecystectomy by a surgeon after general anesthesia. In this study, apotel containing 1 g paracetamol was also administered by intravenous infusion. Basic and clinical data were recorded in patient's checklist. The demographic and clinical variables of the patients were as follows: age (years), gender (male/female), operation indication (biliary colic, acute cholecystitis, cholangitis, bile pancreatitis, asymptomatic stone), pain after surgery (abdominal and shoulder pains) according to the visual analog scale (VAS) criteria in different times including recovery (4, 12, and 24 hours after surgery), MAP, pulse rate in 4 steps (immediately after anesthesia induction and 30, 60, and 90 minutes after operation).

It is noteworthy that the VAS criterion includes a 10-cm ruler longitudinally extending between 0 and 10, in which the 0 represents painless and 10 indicates unbearable pain.

VAS (visual analog scale) criterion



compare the effect of these 2 drugs in patients with cholecystectomy.

2. Methods

2.1. Ethics statement

Ethics approval: This study was based on Institutional Review Board (IRB) by Arak University of Medical Sciences, Arak, Iran. The study was approved by the Ethics Committee of our hospitals (reference number: IR.ARAKMU.REC.201701). A written informed consent was obtained from each patient.

2.2. Study subjects and patients

The present randomized clinical trial was performed at Valiasr and Amiralmomeini Hospitals on subjects scheduled to undergo emergency cholecystectomy or elective surgery. The study population included patients aged 18 to 70 years old from both sexes who entered the study after obtaining informed consent based on the inclusion and exclusion criteria. Finally, 132 patients were randomly divided into 2 groups; it should be noted that the patients in both groups were matched for age and sex.

2.3. Sample size calculation and statistical analysis

Sample size calculations were performed in this study by using Power and Sample Size (PS) Calculation (version 3.1.2). Therefore, the sample size for each group was calculated as 66 to determine a study power of 80% with an α value of 0.05. Finally, the statistical analysis was conducted using IBM SPSS Statistics V21.0. Data were presented as mean \pm SD or percentage. Furthermore, the parametric variables were evaluated based on the use of the Student *t* test, whereas nonparametric variables were analyzed using the Mann–Whitney test. In addition, a *P*-value of $<.05$ was considered statistically significant.

2.4. Inclusion criteria

Patients 18 to 70 years of age, both sexes, patients scheduled to undergo emergency laparoscopic or elective laparoscopic cholecystectomy, obtaining informed consent in clinical study.

2.5. Exclusion criteria

The need of conversion from laparoscopic surgery to open surgery, partial cholecystectomy, gangrenous gallbladder, abscess, major bile duct injuries.

Table 1**Comparison of mean age, sex in patients with laparoscopic cholecystectomy in 2 groups of apotel and dexmedetomidine.**

Groups	Apotel group; mean \pm SD		Dexmedetomidine group; mean \pm SD		P-value
Average age, yr	53/3/-3/8		51/4 \pm 4/2		.05
Frequency of sex, %	Male	Female	Male	Female	.05
	55/2	44/8	55/5	44/5	

SD=standard deviation.

3. Results

Based on the data presented herein, there was no significant difference between the 2 groups in terms of mean age; therefore, the mean age was found to be similar in both groups (52 years, $P \geq .05$). Furthermore, there was no difference in the sex ratios in both groups ($P > .05$), that is the percentage of disease in the 2 groups was almost the same (Table 1).

With regards to Table 2, there was a significant difference between the 2 groups in terms of mean scores of pain during recovery. As a matter of fact, the scores of pain in the apotel group were significantly lower than that of the dexmedetomidine group ($P = .04$). However, the mean scores of pain at 2nd, 4th, 8th, 12th, and 24th hour after surgery were not significantly different between the 2 groups, that is, the scores of pain in patients were similar in both the groups ($P \geq .05$) (Fig. 1).

As shown in Table 3, there was a significant difference between the 2 groups in terms of the amount of opioids consumed in 24 hours after operation and the mean duration of analgesia. As a matter of fact, the average drug used in 24 hours after surgery in the apotel group was significantly lower than in the dexmedetomidine group, whereas the mean duration of analgesia in the apotel group was greater than that in dexmedetomidine group ($P = .01$; $P = .02$) (Fig. 2).

The results revealed that there was no significant difference between the mean blood pressure of patients with laparoscopic cholecystectomy during the pre- and postoperative periods in both the apotel and dexmedetomidine groups (Table 4; $P \geq .05$).

With regards to Table 5, there was no significant difference in the mean heart rate of patients at different times in either groups, which was the same in both groups at different times of the MAP ($P \geq .05$).

4. Discussion

One of the concerns of anesthesiologists and general surgeons is finding an appropriate drug combination for controlling

Table 2

Pain score in patients with laparoscopic cholecystectomy at 2th, 4th, 8th, 12th, and 24th hour after surgery and during recovery in both groups of apotel and dexmedetomidine; values are expressed as medians (mean \pm SD).

Groups	Apotel group; mean \pm SD	Dexmedetomidine group; mean \pm SD	P-value
Postoperative VAS			
VAS Recovery	1/8 \pm 0/63	2/55 \pm 0/85	.04
2h	1/69 \pm 0/54	1/52 \pm 0/48	.12
4h	1/51 \pm 0/46	1/70 \pm /60	.32
8h	1/58 \pm 0/33	1/84 \pm 0/28	.28
12h	1/30 \pm 0/48	1/53 \pm 0/36	.67
24h	1/12 \pm 0/18	1/53 \pm 0/38	.42

SD=standard deviation, VAS=visual analog scale.

postoperative pain in patients with laparoscopic cystitis, where laparoscopic cholecystectomy is a most common surgical procedure.

Uncontrolled postoperative pain may lead to complications such as insomnia, anxiety, depression, and dissatisfaction in patients. Various methods for controlling postoperative pain in patients with laparoscopic cholecystectomy have been suggested, of which paracetamol is the most commonly used drug in these patients as an injectable type of acetaminophen.^[19-21] The aim of this study was to investigate the effect of paracetamol (or appendix) and dexmedetomidine on pain and hemodynamic control of patients with laparoscopic cholecystectomy.

The findings of this study showed that the mean score of pain in recovery was lower in the apotel group over dexmedetomidine group, whereas no significant difference was observed at 2nd, 4th, 12th, and 24th hour after surgery.

In terms of opioid prescription, the average narcotic use was significantly lower in the apotel group when compared with that in the dexmedetomidine group. Moreover, the mean duration of analgesia per hour in the apotel group was higher than that in the dexmedetomidine group. Overall, the apotel drug as a prophylactic drug was more effective in reducing the median consumption of opioid in 24 hours after operation and the mean duration of postoperative analgesia.

The results of previous studies are relatively consistent with the results of our study. A study has been conducted to investigate the effects of paracetamol IV and dexmedetomidine on postoperative analgesia among patients undergoing laparoscopic cholecystectomy surgery. The results of this study revealed that the mean score of pain in the paracetamol group was lower than that in the dexmedetomidine group at 8th, 16th, and 24th hour after surgery,^[16] where the results were quite similar and consistent with the present study.

In this study, the duration of analgesia in the apotel group was higher than that in the dexmedetomidine group and opioid use was archived to be lower in the apotel group when compared with that in the dexmedetomidine group, indicating better efficacy of apotel or paracetamol. However, no difference was noted in the hemodynamic parameters during postoperative period. Meanwhile, Swaika et al^[16] reported that heart rate, diastolic blood pressure, and moderate blood pressure were similar in both groups, but systolic blood pressure in the dexmedetomidine group was further decreased, which contradicts with the result of our study.

Another study by Sharma et al^[22] has been performed to evaluate the quality and duration of analgesia with dexmedetomidine and paracetamol based upon the use of the VAS among patients undergoing laparoscopic cholecystectomy surgery. They reported that postoperative analgesic significantly decreased in both groups. The percentage of opioid consumed after surgery was significantly lower in the paracetamol group when compared with that in the dexmedetomidine group. Overall, they indicated reduced level of postoperative pain with a decreased score on

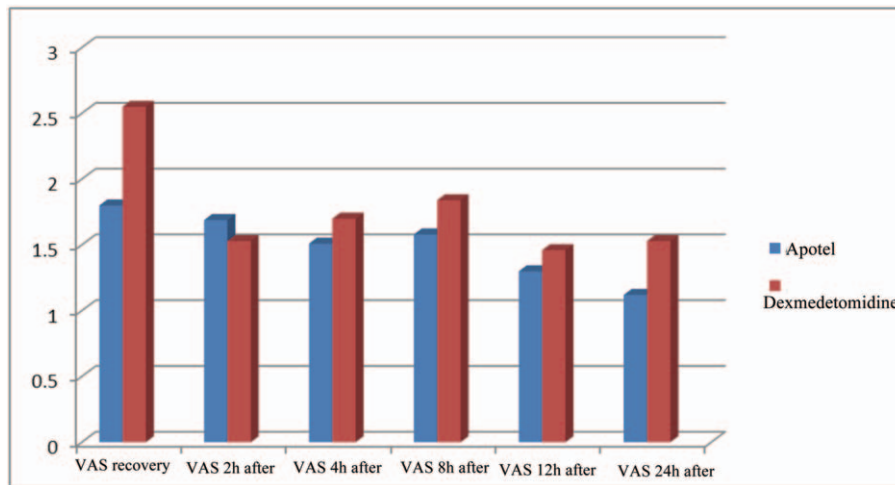


Figure 1. Score of pain in patients at 2th, 4th, 8th, 12th, and 24th hour after operation and in recovery in 2 groups of apotel and dexmedetomidine.

VAS, relatively excellent patient satisfaction, where Ramsay Sedation Score ranges from 3 to 5 in the paracetamol group. On the other hand, they demonstrated that the rate of nausea, vomiting, hypotension, and bradycardia in the dexmedetomidine group was lower when compared with that in the paracetamol group. In other words, hemodynamic changes were less in the dexmedetomidine group, where had greater stability.^[22] These results were also found to be consistent with the results of our study, which highlighted that postoperative pain and the mean score of pain in recovery were lower in the apotel group over the other group. Furthermore, the need for opiate was lower in the paracetamol group at 24th hour and the mean duration of analgesia in mentioned group was higher; however, in terms of hemodynamic, we were getting inconsistent results when comparing findings of Sharma et al^[22] for aforementioned terms. On the basis of our data presented herein, no significant difference was noted in the hemodynamic responses in the 2 groups. The dosages of paracetamol and dexmedetomidine used in both studies were similar, but the reason for the difference need further comprehensive studies to determine whether there are significant differences in the hemodynamic parameters and what is the cause of the difference? In another study, the analgesic effect of dexmedetomidine injection has been investigated during laparoscopic cholecystectomy surgery based upon the use of multimodal analgesia.^[23] The results of abovementioned study revealed a reduction in VAS and pain score in the dexmedetomidine group after laparoscopic cholecystectomy,^[23] and is in agreement with the present study, where clearly reduced

postoperative pain in the paracetamol and dexmedetomidine groups. However, the effect of apotel was higher and the mean pain score in the apotel group was reported to be lower as compared to other group. Furthermore, the effect of dexmedetomidine and morphine on postoperative pain management in patients undergoing major inpatient surgery was evaluated by Arain et al in 2004; the findings indicated the efficacy of dexmedetomidine vs morphine for the postoperative pain. In the mentioned study, dexmedetomidine was combined with morphine as an adjuvant, whereas in the 2nd group only morphine was used. The use of dexmedetomidine in the form of adjuvant with morphine has reduced the amount of postoperative pain and the need for postoperative analgesic drug after surgery. Moreover, hemodynamics of patients treated with dexmedetomidine was much more stable than those who only use morphine.^[24] The results of the aforementioned study were similar to the findings of our study, indicating the effects of dexmedetomidine on reducing postoperative pain and the need for postoperative opioids.

Gurbet et al^[18] examined the effects of dexmedetomidine infusion in controlling perioperative analgesic requirements. They found that dexmedetomidine had an effective analgesic effect in patients, where can reduce perioperative morphine needs. It is noteworthy that these findings were also in line with the current research. In a double-blind clinical trial, the analgesic effect of two repeated doses of acetaminophen was evaluated in comparison with placebo group over 24 hours. The findings demonstrated that each of intravenous acetaminophen (1000 mg q6 h and 650 mg q4 h, administration) had a significant analgesic effect in patients with laparoscopic abdominal surgery compared to placebo.^[25]

Sinatra et al^[26] reported the analgesic effect and the effectiveness of intravenous acetaminophen (1g, administration) compared with propacetamol and placebo over 24 hours after major orthopedic surgery, indicating its benefit for pain management.

Table 3

Percentage of opioids consumption at 24th hour after operation and mean analgesia per hour in patients with laparoscopic cholecystectomy in both apotel and dexmedetomidine; values are indicated as medians (mean ± SD).

Groups	Apotel group; mean ± SD	Dexmedetomidine group; mean ± SD	P-value
Opioids consumption, mg	28/69 ± 12/4	53/14 ± 22/6	.01
Mean duration of analgesia, h	4/76 ± 0/79	2/90 ± 0/48	.02

SD = standard deviation.

5. Conclusions

Our findings revealed that both regimes of dexmedetomidine and paracetamol were capable of controlling the postoperative pain and hemodynamic status of patients undergoing laparoscopic

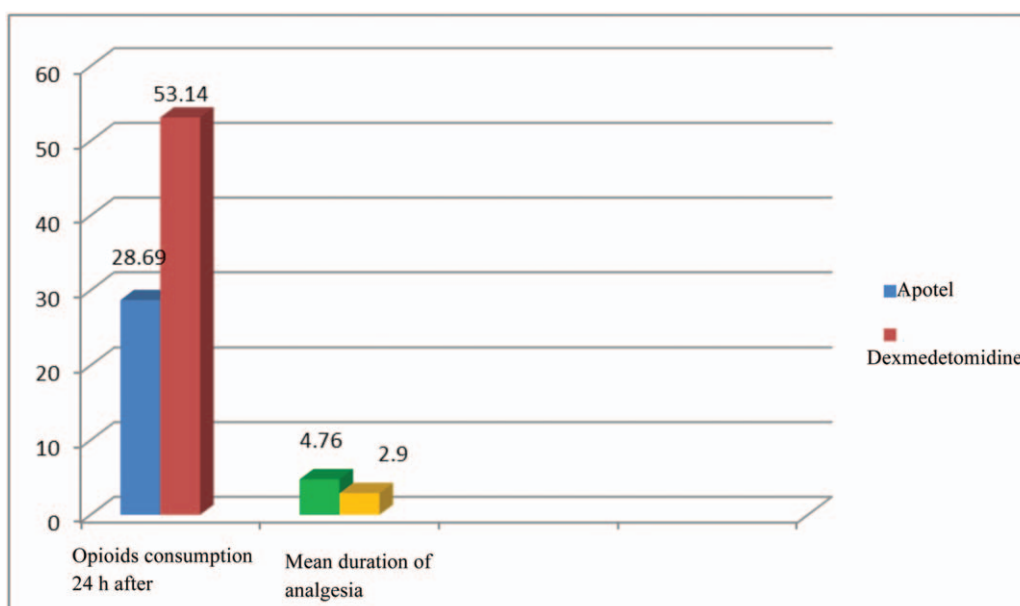


Figure 2. The mean of consumed narcotics in 24hours after operation and mean analgesia in terms of hours in patients.

Table 4

The mean blood pressure of patients undergoing laparoscopic cholecystectomy in pre- and postoperative periods in both apotel and dexmedetomidine; all values are expressed as medians (mean ± SD).

Groups	Apotel group; mean ± SD	Dexmedetomidine group; mean ± SD	P-value
Postoperative MAP	-25/1 ± 87/2	85/2 ± 27/2	.12
30 min	80/4 ± 22/2	82/1 ± 23/4	.73
60 min	77/6 ± 19/7	75/7 ± 18/7	.65
90 min	80/1 ± 31/1	82/4 ± 27/5	.71
Recovery	82/1 ± 18/8	84/1 ± 30/6	.84

MAP=mean arterial pressure, SD=standard deviation.

Table 5

The mean heart rate of patients undergoing laparoscopic cholecystectomy in pre- and postoperative periods in 2 groups of apotel and dexmedetomidine; values are expressed as medians (mean ± SD).

Groups	Apotel group; mean ± SD	Dexmedetomidine group; mean ± SD	P-value
Preoperative PR interval	70/3 ± 10/5	72/1 ± 11/2	.74
30 min	72/2 ± 12/6	77/8 ± 22/1	.68
60 min	71/6 ± 11/4	74/7 ± 18/7	.48
90 min	72/6 ± 15/4	76/2 ± 19/2	.69
Recovery	78/4 ± 12/2	84/5 ± 15/6	.71

SD=standard deviation.

cholecystectomy, while the effect of apotel was greater than that of dexmedetomidine.

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