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Research Article

Dexmedetomidine as an adjuvant to Nalbuphine in patient controlled analgesia for post-operative pain in Laparoscopic Cholecystectomy: A preliminary study

Introduction

Postoperative pain control is an important factor affecting patient recovery, return to normal bowel movement, ambulation and daily activity. Intravenous patient-controlled analgesia (IV-PCA) which allows the patient to administer his own pain relief is considered as an efficient tool to control postoperative pain. Safety of IV-PCA relies on the concept of negative feedback control system so that the patient will become too sedated to physically push the button to receive more opioid before reaching a critical point of severe respiratory depression [1].

Although morphine is the most common opioid used for this purpose in PCA due to its short action duration and strong analgesic effect; however, it may induce many adverse events, such as, postoperative pruritus, nausea, vomiting, constipation, decreased blood pressure, respiratory depression, and drowsiness and urinary retention [2-4]. Nalbuphine is an opioid has a ceiling effect in respiratory depression hence, it is considered to be safer than morphine, being mu antagonist and kappa agonist, it has lower incidence of adverse effects in comparison with morphine [5]. Dexmedetomidine is a potent and highly selective α-2 adrenoceptor agonist with sympatholytic, sedative, amnesiac, and analgesic properties. It provides unique "conscious sedation" analgesia, without respiratory depression. It decreases central nervous system (CNS) sympathetic outflow in a dose- dependent manner and has analgesic effects best described as opioid-sparing. There is increasing evidence of its organ protective effects against ischemic and hypoxic injury [6-8].

This study aimed at assessing the role of Dexmedetomidine as an adjuvant to Nalbuphine in patient controlled analgesia for post-operative pain in laparoscopic cholecystectomy.

Patients and Methods

Study design

This study included forty patients scheduled for elective laparoscopic cholecystectomy. It is designed to explore the ability of usage of Dexmedetomidine as an adjuvant to Nalbuphine for post-operative laparoscopic pain. The study was conducted in Theodor Bilharz Research Institute after ethics committee approval of the study protocol. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants at the beginning of the study.

Inclusion criteria involved18-65 years old patients with ASA score I and II and BMI < 30 Kg / m2. Exclusion criteria involved patients older than 65 years or younger than 18 years, history of psychiatric/neurological illness, cardiovascular disease, hypertension, uncontrolled diabetes, morbid obesity, known allergic reaction to any of the study medication, pregnant and nursing women, recent use of sedatives or analgesics, significant laboratory abnormalities and patient's refusal.

Patients were allocated into two equal groups D and P (20 patients each). Both groups received PCA (Accufuser plus M2015M Woo Young Medical CO.LTD) containing 20 mg

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Nalbuphine (Nalufin –Nalbuphine HCl 20mg / 1ml- Amoun Pharmaceutical Co. SAE.) to 100 ml with normal saline over 24 hours. The PCA infuser unit infused at rate of 2 ml.h-1 with lock out time 15 min & bolus of 1 ml per time. Patients in group D received Dexmedetomidine (Precedex – Dexmedetomidine HCl 200 µg/2ml- Hospira, Inc, Lke Forest, IL 60045 USA) (0.5 µg.kg-1 over 10 min followed by 0.2 µg.kg.-1h-1) prepared with 50 ml normal saline as intravenous infusion over 24 hours post-operative. Patients in group P received 50 ml of normal saline as intravenous infusion over 24 hours. Primary outcome measure was Nalbuphine consumption. Secondary outcome measures were visual analogue scale (VAS) for pain control, patient satisfaction and side effects.

Anesthetic technique

Premedication: All patients received Midazolam 0.05 mg kg-1, 4mg Ondansetron and 50 mg Ranitidine intravenously before induction of anesthesia.

Monitoring: Five-lead ECG monitor, NIBP monitor, pulse oximetry, peripheral nerve stimulator, end tidal carbon dioxide (ETCO2) estimation (Capnography) and esophageal thermometer.

Induction of anesthesia: Both D and P groups received (Ringer Acetate) infusion at a rate of 3–6mlkg-1h-1 for supplying fluid maintenance and deficit. After pre-oxygenation, anesthesia was induced with 1.5–2mg kg-1 Propofol and 2µg kg-1 Fentanyl. Neuromuscular blockade was achieved with 0.5mg kg-1 Atracurium followed by tracheal intubation. Anesthesia was maintained with Isoflurane administered in fresh gas flow oxygen /air 40% at a rate of 1L.min1. Neuromuscular blockade was achieved with intermittent doses of Atracurium 10mg when Train of Four (TOF) ratio reached 25% and ventilation was adjusted to obtain end-tidal carbon dioxide of 30-35 mm Hg. The mean arterial blood pressure was maintained within 20% above or below pre-anesthetic level. Atropine IV 0.5 mg increments was used to control bradycardia (<50beat min-1) while hypotension (less than 20% of pre-anesthetic level) was managed by increasing fluid infusion rate or incremental IV 5mg doses of ephedrine. In case of hypertension and tachycardia increment dose of 50 µg Fentanyl was given. Reversal of neuromuscular blocker was achieved by intravenous administration of Neostigmine 0.05 mg kg-1 and atropine 0.02 mg kg-1 guided by TOF guard 4:1 ratio 0.9.Normothermia was maintained by means of a warm blanket, humidifier, and warm intravenous fluids. At the end of the procedure,2 mg Nalbuphine was injected IV for all patients as loading analgesic dose in post-operative care unit followed by repeated boluses of 1 mg each aiming to reach VAS score 40mm Then all patients monitored for 24 hours:

Post-operative pain was evaluated every 6 hours using Visual Analogue Scale (VAS): no pain (0–4mm), mild pain (5–44mm), moderate pain (45–74 mm), and severe pain (75– 100 mm) [9].

Nausea and vomiting was recorded every 6 hours on a four-point scale: (0 = no nausea; 1 = mild nausea; 2= severe nausea requiring antiemetic; and 3 = retching and/or vomiting) [10].

Sedation score was recorded every 6 hours on a four-point scale: (0 = fully awake; 1 = drowsy, closed eyes; 2 = asleep, easily aroused with light tactile stimulation or a simple verbal command; 3 = asleep, arousal only by strong physical stimulation; and 4 = un-arousal) [11].

Vital signs including heart rate , blood pressure , peripheral capillary oxygen saturation (SpO2)&respiratory rate were recorded every 5 min for 30 min then every 30 min for 3 hours then every 2 hours till the end of the 24 hours .

Patient satisfaction score: was assessed at the end of 24 hours about their satisfaction concerning pain control using pain treatment satisfaction scale (PTSS, 0= no satisfaction to 10= complete satisfaction) [12].

Nalbuphine consumption: Nalbuphine consumed by the accufuser was calculated and recorded at the end of 24 hours for all patients.

Sample size

As no previous study evaluating the effect of Dexmedetomidine on Nalbuphine consumption in patient controlled analgesia for post-operative pain of laparoscopic surgeries was available to calculate number of participants included, we considered this research as a pilot study and 20 patients in each group were suitable.

Statistical analysis

Results were expressed as mean ± standard deviation (SD) or number (percent). Comparison between categorical data [number (%)] was performed using Chi square test. According to test of normality, comparison between different variables in the two groups was performed using either unpaired t test or Mann-Whitney U test whenever it was appropriate. In normality distributed data, pair-wise comparison (baseline versus different times of measurements] for the same variable was performed using repeated measure ANOVA followed by Bonferroni test if significant results was recorded with corrected p value= 0.401. In not normality distributed data, pair-wise comparison was performed using Friedman ANOVA followed by Wilcox on Signed Ranks test. Statistical Package for Social Sciences (SPSS) computer program (version 19 windows) was used for data analysis. P value ≤ 0.05 was considered significant.

Results

The age, gender, height and weight of patients were comparable in both studied groups with no significant difference (Table 1). Post-operative pain as evaluated using Visual Analogue Scale (VAS); group D showed significant low VAS value compared to group P during all times selected (Table 2, Figure 1) . Nalbuphine consumption in the two studied groups showed significant decrease in group D compared to group P by 36.74 % while patient satisfaction score over 24 hours showed significant increase in group D compared to group P by 51.24 % (Table 3, Figures 2, 3) . As regard nausea and vomiting score at different selected times in the two studied groups showed significant decrease in group D compared to group P (Table 4,5 & Figure 4). Sedation score at different selected times in

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the two studied groups showed significant increase in group D compared to group P (Table 6,7 & Figure 5).

As regard hemodynamic parameters; mean values of systolic and diastolic blood pressure at different selected times in the two studied groups showed significant decrease in group D compared to group P (Table 8,9). The mean blood pressure at different selected times in the two studied groups showed significant decrease in group D compared to group P (Table 10, Figure 6). Mean values of heart rate at different selected times in the two studied groups showed significant decrease in group D compared to group P (Table 11, Figure 7). However, mean values of peripheral capillary oxygen saturation (SpO2) at different selected times in the two studied groups showed no significant difference between both groups (Figure 8).

Discussion

Few randomized clinical trials compared the efficacy of Dexmedetomidine as an adjuvant to different opioids (e.g. morphine & Fentanyl) in minimizing their consumption and side effects. However, there was no single study evaluating such effect as regarding Nalbuphine which is the drug of choice in this study. Lin et al. [13], studied whether Dexmedetomidine added to intravenous PCA morphine could improve analgesia while reducing opioid related side-effects. They found that

Table1: Demographic features of different studied groups.

	Group P (n= 20)	Group D (n= 20)	p value
Age(yrs.)	37.65 ± 10.83	38.90 ± 10.65	0.715
Gender (F:M)	17:3 (85%:15%)	17:3 (85%:15%)	1.000
Height (cm)	164.50 ± 7.45	162.50 ± 6.16	0.361
Weight (kg)	72.80 ± 6.52	72.95 ± 5.49	0.938

Data were expressed as mean ± SD or number (%).
P> 0.05= not significant.

Table 2: Comparison between mean values of VAS at different selected times in Placebo and Dexmedetomidine Groups.

	Group P (n= 20)	Group D (n= 20)	p value
6 hrs.	37.25 ± 9.80	20.50 ± 9.31	0.001
12 hrs.	35.25 ± 8.96	14.75 ± 8.96	0.001
18 hrs.	31.00 ± 10.83	5.00 ± 6.07	0.001
24 hrs.	26.00 ± 8.97	4.00 ± 5.98	0.001

Data were expressed as mean ± SD.
P< 0.05= significant.

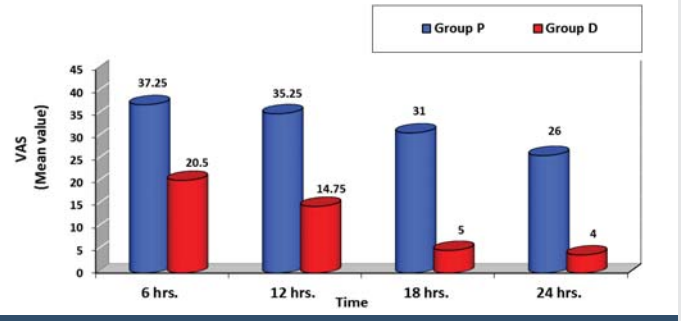

Figure 1: Comparison between mean values of VAS at different selected times in Placebo and Dexmedetomidine Groups.

Table 3: Comparison between mean values of total Nalbuphine consumption and patient satisfaction score measured over 24 hours in Placebo and Dexmedetomidine Groups.

	Group P (n= 20)	Group D (n= 20)	Percent change (%)	p value
Total Nalbuphine consumption over 24 hrs.	16.44 ± 1.71	10.40 ± 0.44	36.74↓↓	0.001
Patient satisfaction score over 24 hrs.	6.05 ± 1.19	9.15 ± 0.67	51.24↑↑	0.001

Data were expressed as mean ± SD.
P< 0.05= significant.

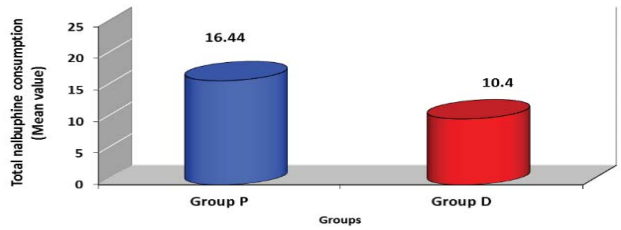

Figure 2: Comparison between mean values of total Nalbuphine consumption over 24 hours in Placebo and Dexmedetomidine Groups.

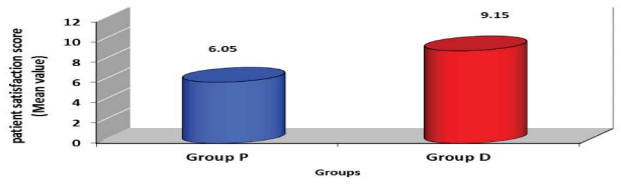

Figure 3: Comparison between mean values of patient satisfaction score over 24 hours in Placebo and Dexmedetomidine Groups.

patients in Dexmedetomidine and morphine group required significantly less PCA morphine than those from morphine alone group at all times in the study. During the 0–24 h postoperative period, cumulative PCA morphine use was 29% less in Dexmedetomidine group than in morphine group [23.3 ±10 vs. 32.8 ±12.4 mg, P<0.01]. Their results were in consistence with the results of the current study in reduction of cumulative PCA Nalbuphine usage by 36.74 % in group D in comparison with group P in which we use Nalbuphine alone without Dexmedetomidine [10.4 ±0.44 vs. 16.44 ±1.44 mg, P<0.05]. Also, Kim et al. [12], studied the efficacy of Dexmedetomidine in the reduction of Fentanyl consumption and opioid related side effects during intravenous PCA during post-procedure 24 h. They found that patients in Dexmedetomidine group required less Fentanyl during first 6 h after procedure (P < 0.001), but Fentanyl consumption was not significantly different between the two groups after 6 h. The cumulative Fentanyl consumption at 24 h was 28% less in Dexmedetomidine group compared with placebo group (729 ± 342 µg vs1017 ± 363 µg, P = 0.006). This was similar to our study as mentioned before as regard Nalbuphine consumption with significant P value in our study <0.05, but the difference was we found decrease in Nalbuphine consumption all through the 24 hours.

As regard pain control; Lin et al. [13], found that pain was significantly lower in Dexmedetomidine and morphine group

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Table 4: Nausea and vomiting score at different selected times in Placebo and Dexmedetomidine Groups.

	Group P (n= 20)				Group (n= 20)			
	6 hrs	12 hrs	18 hrs.	24 hrs.	6 hrs	12 hrs	18 hrs.	24 hrs.
No nausea (0)	6 (30.0%)	2 (10.0%)	7 (35.0%)	8 (40.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)	20 (100.0%)
Mild nausea (1)	7 (35.0%)	10 (50.0%)	10 (50.0%)	12 (60.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Severe nausea	4 (20.0%)	4 (20.0%)	2 (10.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Retching and/or vomiting (3)	3 (15.0%)	4 (20.0%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table 5: Comparison between median values of nausea & vomiting score at different selected times in Placebo and Dexmedetomidine Groups.

	Group P (n= 20)	Group D (n= 20)	p value
6 hrs. #	1 (0-3)	0 (0-0)	0.001
12 hrs. #	1 (0-3)	0 (0-0)	0.001
18 hrs. #	1 (0-3)	0 (0-0)	0.001
24 hrs. #	1 (0-1)	0 (0-0)	0.001

Data were expressed as median (minimum-maximum).
#= non parametric statistics.
P< 0.05= significant.

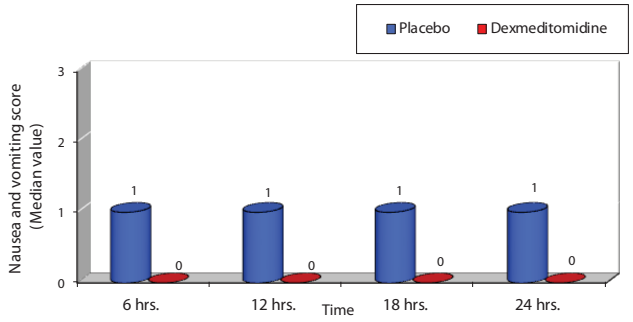

Figure 4: Comparison between median values of nausea & vomiting score at different selected times in Placebo and Dexmedetomidine Groups.

Table 6: Sedation scores at different selected times in Placebo and Dexmedetomidine Groups.

	Group P (n= 20)	Group D (n= 20)
6 hrs.		
Fully awake (0)	20 (100.0%)	2 (10.0%)
Drowsy with closed eye (1)	0 (0.0%)	18 (90.0%)
12 hrs.		
Fully awake (0)	20 (100.0%)	3 (15.0%)
Drowsy with closed eye (1)	0 (0.0%)	15 (75.0%)
Arowsed with verbal stimulus (2)	0 (0.0%)	2 (10.0%)
18 hrs.		
Fully awake (0)	20 (100.0%)	6 (30.0%)
Drowsy with closed eye (1)	0 (0.0%)	14 (70.0%)
24 hrs.		
Fully awake (0)	20 (100.0%)	10 (50.0%)
Drowsy with closed eye (1)	0 (0.0%)	10 (50.0%)

compared to morphine group from the 2nd postoperative hour onwards and throughout the study. In addition, two patients in morphine group reported insufficient analgesia and received adjunctive analgesics. In our study, pain was significantly decreased in group D compared to group P with [P<0.05] at 6,12,18,24 hours postoperatively.

As regard sedation; Kim et al. [14], found that the level of sedation was higher in Dexmedetomidine group compared with placebo group (P < 0.001). Also in this point there was similarity with our study as we found that sedation was higher in group D compared to group P with significant P value <0.05 at 6. 12, 18 & 24 hour's post-operative. This confirm that Dexmedetomidine had a clear sedative effect on all patients all through the 24 hours post-operative with no or minimal affection on their oxygen saturation which was compared between the two group and showed no significant difference between both groups with P value >0.05. Degree of Sedation had a great role in assessment of patient satisfaction at the end of 24 hours. Group D showed significant increase in patients satisfaction score compared to group P with P value <0.05 with mean value 9.15 ±0.67 for group D compared to mean value 6.05 ±1.19 for group P.

As regard nausea and vomiting Lin et al. [13], found that the incidence of nausea during the 4–24 h period was significantly lower in Dexmedetomidine group compared to morphine group

Table 7: Comparison between median values of sedation scores at different selected times in Placebo and Dexmedetomidine Groups.

	Group P (n= 20)	Group D (n= 20)	p value
6 hrs. #	0.0 (0.0-0.0)	1.0 (0.0-1.0)	0.001
12 hrs. #	0.0 (0.0-0.0)	1.0 (0.0-2.0)	0.001
18 hrs. #	0.0 (0.0-0.0)	1.0 (0.0-1.0)	0.001
24 hrs. #	0.00 ± 0.00	0.5 (0.0-1.0) [a]	0.001

Data were expressed as median (minimum-maximum).
#= non parametric statistics.
P< 0.05= significant.
[a] p< 0.05 relative to 6 hrs)Within the same group).

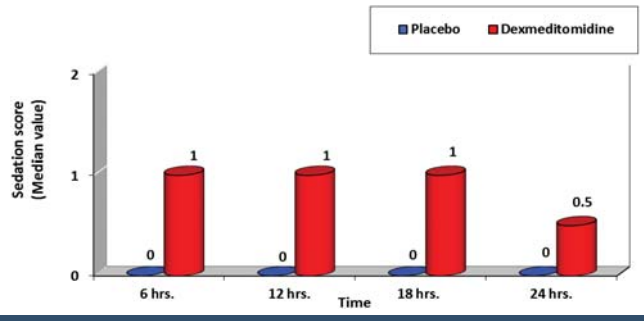

Figure 5: Comparison between median mean values of sedation scores at different selected times in Placebo and Dexmedetomidine Groups.

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(34% vs. 56.3%, P<0.05). Furthermore, the overall incidence of severe nausea was significantly lower in Dexmedetomidine group than in morphine group (6% vs. 20.8%, P<0.05). However, the incidence of vomiting during 4–24 h (18% vs. 33%, P=0.106) and the overall incidence of severe vomiting (6% vs. 17%, P=0.117) were lower in Dexmedetomidine group than in morphine group, but the differences were not significant. In contrast to our study which showed significant decrease in nausea and vomiting in group D compared to group P with P value <0.05 at all different selected times (6, 12, 18 & 24 h) post-operatively. There was no incidence of nausea or vomiting all through 24 hours in group D while in group P at 6h postoperatively 35 % of patients had mild nausea , 20% had severe nausea required anti-emetics and 15% had vomiting. Furthermore, at the end of 24 hours 60% of patients in group P experienced mild nausea.

In our study we found that all patients in group D experienced bradycardia which was within the clinically accepted range (>50 BPM) as there was significant decrease in HR in group D compared to group P at all different selected times allover 24 hours post-operatively with [P<0.05] all

Table 8: Comparison between mean values of SBP at different selected times in Placebo and Dexmedetomidine Groups.

	Group P (n= 20)	Group D (n= 20)	p value
Immediate after reaching VAS 40	137.55 ± 10.10	133.80 ± 7.84	0.198
30 min.	136.85 ± 13.15	116.75 ± 11.83 [a]	0.001
1 hr.	132.90 ± 10.50	116.85 ± 10.70 [a]	0.001
2 hrs.	132.50 ± 11.20	114.35 ± 10.16 [a]	0.001
4 hrs.	131.50 ± 8.36	110.10 ± 11.04 [a]	0.001
6 hrs.	128.20 ± 10.60 [a]	108.45 ± 9.79 [a]	0.001
8 hrs.	129.25 ± 10.43 [a]	111.85 ± 8.68 [a]	0.001
12 hrs.	131.15 ± 9.28	112.65 ± 8.01 [a]	0.001
18 hrs.	129.85 ± 8.69	108.85 ± 10.07 [a]	0.001
24 hrs.	128.20 ± 7.80	106.35 ± 8.40 [a]	0.001

Data were expressed as mean ± SD.
P> 0.05= not significant. P< 0.05= significant.
[a]p< 0.05 relative to immediate after reaching VAS 40 within the same group.

Table 9: Comparison between mean values of DBP at different selected times in Placebo and Dexmedetomidine Groups.

	Group P (n= 20)	Group D (n= 20)	p value
Immediate after reaching VAS 40	80.45 ± 6.50	78.80 ± 4.19	0.346
30 min.	78.95 ± 7.98	69.20 ± 8.12 [a]	0.001
1 hr.	79.55 ± 6.51	69.50 ± 7.27 [a]	0.001
2 hrs.	77.55 ± 8.91	69.60 ± 7.37 [a]	0.004
4 hrs.	77.00 ± 10.02	65.30 ± 7.92 [a]	0.001
6 hrs.	74.60 ± 9.65	62.25 ± 7.60 [a]	0.001
8 hrs.	75.95 ± 9.18	63.95 ± 7.25 [a]	0.001
12 hrs.	77.80 ± 10.22	68.00 ± 6.91 [a]	0.001
18 hrs.	77.70 ± 11.16	65.20 ± 6.53 [a]	0.001
24 hrs.	73.10 ± 10.13	62.75 ± 6.89 [a]	0.001

Data were expressed as mean ± SD.
P> 0.05= not significant. P< 0.05= significant.
[a]p< 0.05 relative to immediate after reaching VAS 40 within the same group.

Table 10: Comparison between mean values of MBP at different selected times in Placebo and Dexmedetomidine Groups.

	Group P (n= 20)	Group D (n= 20)	p value
Immediate after reaching VAS 40	99.15 ± 6.78	96.70 ± 4.99	0.201
30 min.	97.80 ± 9.66	86.75 ± 8.72 [a]	0.001
1 hr.	96.55 ± 8.95	86.00 ± 6.09 [a]	0.001
2 hrs.	994.30 ± 8.53	886.15 ± 7.94 [a]	00.003
4 4hrs.	93.80 ± 8.69	81.00 ± 9.26 [a]	0.001
6 hrs.	91.25 ± 8.77 [a]	78.90 ± 8.23 [a]	0.001
8 hrs.	92.85 ± 8.02	80.20 ± 8.16 [a]	0.001
12 hrs.	95.50 ± 8.62	83.10 ± 6.41 [a]	0.001
18 hrs.	94.10 ± 9.62	80.45 ± 5.64 [a]	0.001
24 hrs.	90.40 ± 8.17 [a]	78.30 ± 6.66 [a]	0.001

Data were expressed as mean ± SD.
P> 0.05= not significant. P< 0.05= significant.
[a]p< 0.05 relative to immediate after reaching VAS 40 within the same group.

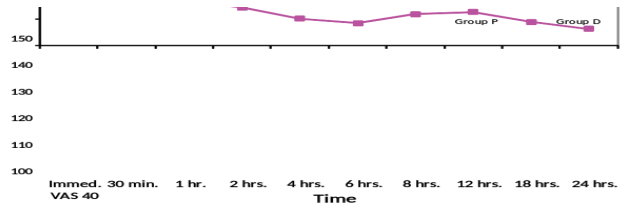

Figure 6: Comparison between mean values of SBP at different selected times in Placebo and Dexmedetomidine Groups.

Table 11: Comparison between mean values of HR at different selected times in Placebo and Dexmedetomidine Groups.

	Group P (n= 20)	Group D (n= 20)	p value
Immediate after reaching VAS 40	81.40 ± 12.89	77.30 ± 12.95	0.322
30 min.	79.65 ± 14.24	70.60 ± 11.55 [a]	0.033
1 hr.	78.45 ± 10.95	67.75 ± 8.01 [a]	0.001
2 hrs.	80.00 ± 12.24	66.50 ± 8.64 [a]	0.003
4 hrs.	83.75 ± 8.71	69.35 ± 9.51	0.001
6 hrs.	83.70 ± 12.39	66.85 ± 9.72	0.001
8 hrs.	83.50 ± 9.60	67.95 ± 11.49	0.001
12 hrs.	86.50 ± 12.55	68.20 ± 10.96	0.001
18 hrs.	85.75 ± 11.05	68.05 ± 10.06	0.001
24 hrs.	84.95 ± 9.05	68.50 ± 10.18	0.001

Data were expressed as mean ± SD.
p> 0.05= not significant. p< 0.05= significant.
[a]p< 0.05 relative to immediate after reaching VAS 40 within the same group.

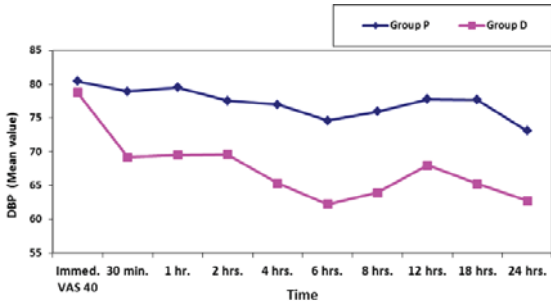

Figure 7: Comparison between mean values of DBP at different selected times in Placebo and Dexmedetomidine Groups.

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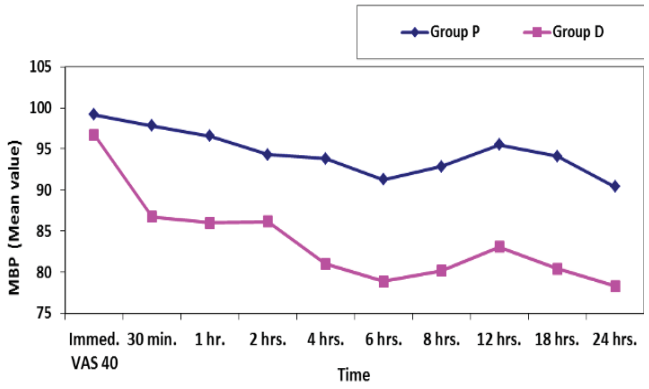

Figure 8: Comparison between mean values of MBP at different selected times in Placebo and Dexmedetomidine Groups.

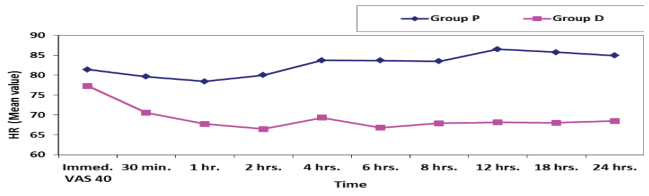

Figure 9: Comparison between mean values of HR at different selected times in Placebo and Dexmedetomidine Groups.

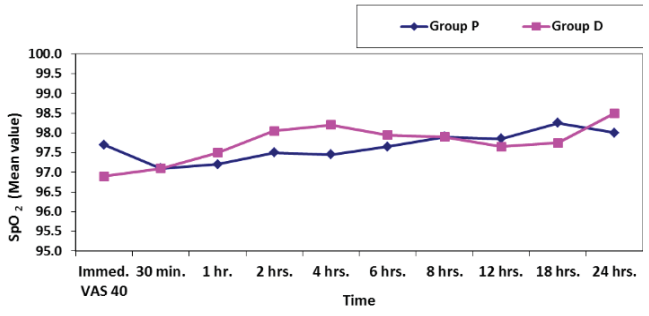

Figure 10: Comparison between mean values of SpO2 at different selected times in Placebo and Dexmedetomidine Groups.

through these selected times with the least mean value 66.5 ±8.64 at 2 hours post-operative. Systolic, diastolic and mean blood pressure showed significant decrease in group D compared to group P. As well as, peripheral capillary oxygen saturation (SpO2) at different selected times in the two studied groups showed no significant difference between both groups. Thus, hemodynamic parameters was within the clinically accepted range with no harm on patients

Studies of effect Dexmedetomidine alone for intravenous PCA in comparison with Fentanyl and not as an adjuvant ; nausea found that the incidence of the incidence of postoperative and vomiting was less than Fentanyl while the VAS scores and sedation scale were not significantly different [11,15]. This study was similar to our study in illustration that Dexmedetomidine alone can minimize incidence of nausea and vomiting when compared to opioids (. However, its effect as a sole agent in the previous study can't cause more pain control or more sedation compared to Fentanyl. Thus, it differs from our study as they used Dexmedetomidine alone in comparison with Fentanyl and not as an adjuvant. Dexmedetomidine offers a unique ability of providing both sedation and analgesia without respiratory depression. It is a new agent with a wide safety margin, excellent sedative capacity and moderate analgesic properties [16-18]. Our study demonstrated that usage of Dexmedetomidine as an adjuvant to Nalbuphine was effective as evidenced by decreased total Nalbuphine consumption and its side effects. Dexmedetomidine also improved pain control as assessed by VAS and patient satisfaction.

From surgical point of view; Although LC results in less pain than open cholecystectomy; it is not a pain free procedure. Many methods of analgesia for pain after laparoscopy have been evaluated involving non-steroidal anti-inflammatory drugs, wound and intraperitoneal local anesthetics, intraperitoneal saline, low-pressure gas and nitrous oxide pneumo-peritoneum have been shown to reduce pain after LC however, The clinical significance of this pain reduction is questionable. Pain after LC is multifactorial. Studies demonstrate that visceral pain accounts for most of the pain experienced after LC in the postoperative first day which is causes more discomfort than abdominal wall pain and pain referring to shoulder. It was linked to operative time and extent of tissue trauma caused by surgery [19,20]. Also, the intensity of pain after LC depends on pneumoperitoneum pressure, speed of insufflation and the residual gas volume [21]. In order to eliminate all these variables the procedure was performed by the same surgical team in similar durations in this study. After laparoscopic surgery was introduced to many surgical fields, IV-PCA became the standard modality for postoperative pain control. The advantages of reduced pain intensity, lower need for analgesics and reduced occurrence of nausea and vomiting must be weighed against some disadvantages such as an increased rate of urinary retention and restriction of mobility.

Patients were allocated into two equal groups D and P (20 patients each) using sealed envelope technique at the beginning of the study and personnel included in the postoperative pain management did not know in which study group D or P patient belong. Age, gender and CPT class distribution was comparable in both groups of the study. LC procedure was performed by the same surgical team with almost similar operative time and pneumoperitoneum pressure in this study. However, the randomization was biased by the fear of addition of Dexmedetomidine in some of the cases against the closed envelope choice if there is a worry about over sedation. So, this study became a prospective cohort analysis. Age, gender and CPT class distribution was comparable in both groups of the study. LC procedure was performed by the same surgical team with almost similar operative time and pneumoperitoneum pressure in this study. This was the main limitation of the study.

Conclusion

Dexmedetomidine could be used as a good adjuvant to Nalbuphine decreasing its consumption, improving its analgesic effect, providing good sedation and good patient satisfaction in patient controlled analgesia for post-operative pain in laparoscopic cholecystectomy. Although there was a significant decrease in BP and HR with usage of Dexmedetomidine, yet it was within the clinically accepted range. There was no significant difference in oxygen saturation by its usage.

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