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## The Effect of Two Different Doses of Dexmedetomidine Infusion on Oxygenation, Lung Mechanics and Quality of Recovery in Morbidly Obese Patients: A Prospective Randomized Study

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#### Abstract

**Background:** Restrictive lung disease affects the majority of morbidly obese individuals. This study compared the effects of two different doses of dexmedetomidine (Dex) infusion on oxygenation as primary outcome and on lung mechanics, quality of recovery, and postoperative pain relief as secondary outcomes in morbidly obese patients with restrictive lung disease scheduled for laparoscopic abdominal surgery.

**Methods:** Ninety morbidly obese patients were recruited in this prospective randomized trial. Patients were randomly divided into 3 equal groups. Fifteen minutes after intubation, Dex o.3 and Dex 0.6 groups received a bolus dose of  $1\mu$ g/kg over 10 min followed by continuous infusion of 0.3 and 0.6  $\mu$ g/kg/hr for one hour respectively. Control group (C): Patients received comparable volume of normal saline (0.9%).P/F ratio, lung mechanics quality of recovery and perioperative analgesic consumption were recorded.

**Results:** Dex groups resulted in increased P/F ratios, static and dynamic compliance and QoR-15 score compared to control group. Both Dex groups had lower dead space values, lower scores on sedation agitation scale, as well as lower pain scores and perioperative analgesic consumption. However hypotension and bradycardia were more common in the Dex 0.6 groups.

**Conclusions:** Dex infusion at a dose of  $0.3\mu g / kg / hr$  and  $0.6 \mu g / kg / hr$  after a loading dose of  $1 \mu g / kg$  resulted in improvement of oxygenation and lung mechanics lower postoperative pain scores, decreased analgesic consumptions as well as improved quality of recovery in morbidly obese patients with restrictive lung disease undergoing laparoscopic surgery

Keywords: Dexmedetomidine, Oxygenation, morbidly obese

#### Introduction

A significant global health problem is obesity. The reduction in static and dynamic lung volumes is usually related to a condition called restrictive lung disease due to elevated intraabdominal pressure and reduced chest wall compliance <sup>[1]</sup>

In otherwise individuals in good health, atelectasis can appear following the onset of induction of anesthesia and is related to a rise in intrapulmonary shunt that impairs the exchange of gases. In individuals who are severely obese, these effects get worse <sup>[2]</sup>. Obese individuals have a larger reduction in arterial oxygenation (PaO<sub>2</sub>) throughout anesthesia than individuals of a normal weight <sup>[3]</sup>.

Dex is a selective  $\alpha_2$  -receptor agonist with sympatholytic, analgesic, anti-inflammatory, and sedative effects. <sup>[4]</sup>.

Dexmedetomidine has been studied for obstructive lung disease for possible effects on oxygenation and lung mechanics, but its effects in morbidly obese individuals with restrictive lung disease are still under study <sup>[5]</sup>.

Patient satisfaction is closely correlated with the quality of post-operative recovery and anesthesia. In order to evaluate the effectiveness of recovery a number of assessment measures have been created <sup>[6]</sup>. A patient-reported outcome measurement (PROM) of postoperative quality of recovery is the quality of recovery (QoR-15) questionnaire <sup>[7]</sup>

The broader QoR-40, which has been widely used and validated as a measurement of postoperative quality of recovery based on assessments of physical comfort, pain, physical independence, psychological support, and emotional state, served as the basis for its development <sup>[8, 9]</sup> Compared to the QoR-40, the QoR-15 exhibited similar psychometric features, but it was easier to use <sup>[7]</sup>

This study compared the effects of two different doses of dexmedetomidine infusion on oxygenation as a primary outcome, lung mechanics, quality of recovery, and perioperative analgesia as secondary outcomes in morbidly obese patients with restrictive lung disease undergoing laparoscopic abdominal surgery.

## **Patients and Methods**

Ninety morbidly obese individuals between the ages of 18 and 50 years with BMI > 40 kg/m<sup>2</sup>, pre-operative pulmonary function tests (FVC <70%), American Society of Anesthesiologists (ASA) II and III, and either gender scheduled for laparoscopic abdominal surgery participated in this prospective randomized controlled study. Following clearance from the Tanta University Hospitals Ethical Committee (33360/09/19), the study was performed between October 2019 and September 2021. All patients provided a written, informed consent.

Patients with FEV1/FVC <0.7, uncontrolled cardiac, respiratory, hepatic, or renal disorders, as well as allergies to the study medication, were excluded from the trial.

Three equal groups of individuals were randomly assigned; the Dex 0.6 and 0.3 groups got a bolus dose of 1  $\mu$ g/kg of dexmedetomidine 15 minutes after endotracheal intubation over a period of 10 minutes, and then received an infusion of 0.6  $\mu$ g /kg/hr for one hour for Dex 0.6 group an 0.3  $\mu$ g /kg /hr for one hour for Dex 0.3 group. The control group got a similar volume of normal saline.

Pre-operative evaluation of baseline pulmonary functions were performed using spirometry [FVC, FEV1in the first second and peek expiratory flow rate (PEFR)] was recorded. The test was repeated three times and the best result was recorded.

#### Anesthetic management

Patients were premedicated with intravenous (IV) ranitidine (50 mg) and metoclopramide (10 mg) upon arrival in the operating room. ECG, non-invasive blood pressure, capnography, and pulse oximetry were used as basic monitoring.

The difficult airway society (DAS) criteria were swiftly followed in the event that direct laryngoscopy proved to be problematic or unsuccessful <sup>[10]</sup>.

With the exception of neostigmine which was calculated on total body weight, lean body weight (LBW) was utilized to determine drug dosage for all medications. James' equation [Men: (1.10 weight) - [128 (weight/height) <sup>2</sup>], Women: (1.07 weight) - [148 (weight/height) <sup>2</sup>] was used to determine LBW.

Fentanyl (2  $\mu$ g/ kg) and propofol (2mg/kg) were used to induce anesthesia .An endotracheal tube was placed using cis-atracurium (0.15 mg/kg). Isoflurane (1–1.5%) and cis-atracurium (0.1 mg/kg/40 min) was used to maintain anesthesia at a ratio of 40:60% O<sub>2</sub> to air, an arterial line was placed in the radial artery to collect arterial blood gases (ABG).

IV fentanyl  $(1\mu g/kg)$  was used to treat any rise in heart rate (HR) or mean arterial blood pressure (MAP) that was 20% or higher than the baseline value. The total fentanyl consumption was calculated. An IV bolus dosage of 10 mg

of ephedrine was used to treat any drop in MAP below 20% of the baseline value. The patient was excluded from the trial if there was no improvement after two further doses of ephedrine. The respiratory rate was adjusted to keep  $EtCO_2$  between 30 and 35 mmHg while the patients were mechanically ventilated using tidal volumes (6-8 ml/kg) and positive end-expiratory pressure (PEEP) (8-10 cmH<sub>2</sub>O).

At the end of surgery, isoflurane was stopped, and neuromuscular block was reversed with neostigmine (0.05 mg/kg) and atropine (0.02 mg/kg) then patients were extubated. All patients received an IV infusion of paracetamol (1 gm.) at the end of the operation, which was repeated every 6 hours. The Riker sedation-agitation scale (SAS) was used to evaluate patients for incidence of emergence agitation after extubation. The scale goes from 1 to 7, with 1 denoting no arousal and 7 denoting hazardous agitation. NRS was assessed immediately after admission to PACU, at 30 min, 1h, 2h, 4h, 6h, 8h, 12h, 18h and 24h post -operatively. IV morphine (0.05mg/kg) was given as rescue analgesia if NRS was  $\geq$  4 and the total dose of rescue analgesia in the 1st 24 post-operative hours was recorded. The following parameters were recorded:

## **Primary outcome**

Intraoperative oxygenation was assessed by P/F ratio ( $PaO_2/Fraction of inspired oxygen$ ).

 $\Delta$  P/F ratio = P/F ratio at the end of drug infusion- baseline P/F ratio.

#### Secondary outcomes

#### 1. Lung mechanics

#### Lung compliance

- Dynamic lung compliance = tidal volume/ (peak airway pressure- PEEP).
- Static lung compliance = tidal volume / (plateau pressure –PEEP).
- $\Delta$  compliance = dynamic compliance at the end of the drug infusion baseline dynamic compliance.
- Plateau pressure was calculated by increasing end inspiratory pause to 30-40%

## Physiological Dead space (Vd/Vt)

- It was calculated by Vd/Vt = 1.14 (PaCO<sub>2</sub> -EtCO<sub>2</sub>)/  $PaCO_2$ -0.005
- A dead space (%) = dead space by end of infusion dead space at the base line / dead space by the end of drug infusion %.

## 2-Assessment of post-operative pain was done using the NRS

**3- QoR-15 questionnaire:** It is fifteen questions assess 5 domains of patient reported health status: pain, physical comfort, physical independence, psychological support and emotional state it leads to minimum score of zero (very poor recovery) and maximum score of 150 (excellent recovery). It provides a valid, extensive and efficient evaluation of post-operative QoR. Questionnaire was measured on the day following the surgery after explaining the questionnaire to the patients.

#### Sample size

Based on the results of previous studies, using a SD of 61, at least 28 patients will be needed in each group to detect a difference of 60 in P/F ratio between groups at alpha error of 0.05 and a study power of 90%. We plan to recruit 30 patients in each group to compensate for dropped out cases.

## Statistical analysis

SPSS v27 (IBM©, Chicago, IL, USA) was used for the statistical analysis. Histograms and the Shapiro-Wilks test have been employed to assess the normality of the data distribution. The mean and standard deviation (SD) of quantitative parametric variables were reported, and an ANOVA (F) test with a post hoc test (Tukey) was used to examine them. Quantitative non-parametric variables were provided as median and interquartile range (IQR) and followed by analysis using the Mann Whitney-test and Kruskal-Wallis test. The Chi-square test was used to examine qualitative data, which were reported as frequency and percentage. Statistical significance was defined as a two-tailed P value < 0.05.

## **Results:**

For eligibility 117 individuals were assessed, 21 individuals didn't fulfill the criteria for inclusion, 6 individuals declined to participate. The remaining individuals have been randomly allocated to three groups (30 participants in each) group Dex 0.3; group Dex 0.6 and group C. All of them were followed up to the end of the study. Figure 1

All patients' characteristics were comparable among the three groups. Table 1

After drug infusion, PaO<sub>2</sub> in Dex 0.3 and in Dex 0.6 group was statistically higher than group C (P <0.001), but an insignificant variation existed between group Dex 0.3 and Dex 0.6 (P =0.917). After drug infusion, PaO<sub>2</sub>/FiO<sub>2</sub> (P/F) ratio and  $\Delta$  P/F ratio in Dex 0.3 and in Dex 0.6 group have been statistically higher than group C (P <0.001), but an insignificant variations existed between groups Dex 0.6 and Dex 0.3. Table 2

After drug infusion, static compliance, and dynamic compliance in Dex 0.6 and in Dex 0.3 group was statistically higher than group C (P 0.001), but an insignificant difference existed between group Dex 0.6 and Dex 0.3.  $\Delta$  Static compliance and  $\Delta$  dynamic compliance were significantly increased in Dex 0.3 group and Dex 0.6 group than group C (P<0.001) and were comparable between Dex 0.3 group and Dex 0.6 group. After drug infusion, plateau pressure values in Dex 0.3 and in Dex 0.6 group have been less than group C (P<0.05), but an insignificant variation existed between group Dex 0.3 and Dex 0.6 P1=0.461. After drug infusion, dead space and  $\Delta$  dead space in Dex 0.3 and in Dex 0.6 group were less than group C. Table 2

Time to initial rescue analgesia was significantly increased in both group Dex 0.6 and group Dex 0.3 than group C (P<0.001). Total consumption of postoperative morphine and intraoperative fentanyl were significantly decreased in both Dex 0.6 group and Dex0.3 group than group C (P<0.001). All these variables showed insignificant difference between group Dex 0.6 and Dex 0.3. Table 3

Quality of recovery score (QoR-15) was significantly increased in both groups Dex 0.6 and Dex 0.3 than group C (P<0.001). SAS have been significantly reduced in both Dex 0.6 group and Dex0.3 group than group C (P<0.001). Table 4 NRS is demonstrated in Figure 2.

## Discussion

In the present study, Dex infusion in both doses improved

oxygenation by decreasing dead space and increasing both static and dynamic compliance with high quality of postoperative recovery. On the other hand, post-operative pain intensity was decreased in patients receiving Dex and the time for the initial rescue of analgesia has been prolonged with low morphine consumption.

These outcomes are in line with results of Hasanin et al. [11] who performed the research on morbidly obese individuals scheduled for bariatric surgery. Ratio of PaO<sub>2</sub>/FiO<sub>2</sub> was significantly improved in the Dex group with greater lung compliance and decreased dead space, compared to control group. Also, Lee et al. <sup>[5]</sup> demonstrated that PaO<sub>2</sub>/FiO<sub>2</sub> ratio was considerably greater in the Dex group with low dead space compared to control group. Dex has been shown to enhance the perfusion of ventilated lungs, decrease oxidative stress, and raise nitric oxide (NO) throughout onelung ventilation (OLV). It also has been shown to protect hypoxic pulmonary vasoconstriction (VC) from the inhibitory effect of inhalational anesthetic drugs. Through activation of alpha-2B receptors in vascular smooth muscles, Dex preserves hypoxic pulmonary VC, which improves ratio of ventilation/perfusion and, as а consequence, increases oxygenation. Dex decreases intrapulmonary shunt by raising the blood concentration of NO. [11].

One work performed by Xia et al. [12] found that management with Dex significantly increased PaO<sub>2</sub> after OLV. They investigated the effect of intravenous infusion of Dex combined with isoflurane inhalation to reduce oxidative stress and potentiate hypoxic pulmonary vasoconstriction during (OLV) in patients undergoing elective thoracic surgery. Patients were randomly allocated to either isoflurane + saline or isoflurane + Dex group and concluded that administration of Dex significantly increased PaO<sub>2</sub> after OLV. In line with our findings, Kernan et al. [13] demonstrated that the amount of expired desflurane needed to keep the bispectral index constant was lower in patients receiving Dex In line with our findings Zhang et al. [14] investigated patients with moderate COPD, In the Dex group, Dex was given as an initial loading dose at 1.0  $\mu/kg$ lasting for 10 min followed by a maintenance dose at 0.5 µg/kg/h while the control group received an equal volume of 0.9% saline. They reported that individuals in the Dex group had a substantially greater index of oxygenation and greater dynamic lung compliance contrasted to individuals within control group. Our results were in line with the findings of Xu B et al. <sup>[15]</sup> who reported that nebulized Dex improved oxygenation.

Against the results of our study Kim *et al.* <sup>[16]</sup> found that infusion of Dex neither improved oxygenation nor lung mechanics.

As regards quality of recovery, our results showed higher quality of recovery scores in both Dex groups contrasted with the control group. Our results confirm the results of Bekker *et al.*<sup>[17]</sup> who suggested that Dex decreases production of inflammatory cytokines.

Our findings were in line with the results of Xin J *et al.* <sup>[18]</sup> who studied the effect Dex infusion for intravenous patient controlled analgesia on the quality of recovery after laparotomy. Patients were randomly allocated into two groups: Dex (group D) and control (group S). Patients in the group D received Dex $0.04 \ \mu/\ kg/\cdot$ h plus sufentanil 0.02 µg /kg/h for 48 h, group S received sufentanil 0.04 µg /kg/h only.Their results showed that within 48 hours following

surgery, group D patients' QoR-15 ratings were considerably greater than those in group S, and group D patients' visual analog scale (VAS) scores were substantially decreased. In accordance with our results, Lee *et al.* <sup>[19]</sup> who performed their study on patients scheduled for video assisted thoracoscopic surgery (VATS) they found that quality of recovery was improved by Dex administration.

In consistent with our results, Ge *et al.* <sup>[20]</sup> who investigated whether abdominal hysterectomy individuals who receive intraoperative Dex benefit from postoperative analgesia and recovery, concluded that the quality of recovery questionnaire showed higher recovery scores in the Dex group.

As regards emergence from anesthesia, our results showed lower scores on the Riker sedation agitation scale in both Dex groups contrasted with control group. Our study confirms the results of Kim *et al.*<sup>[21]</sup>, who compared Dex to placebo, and discovered that individuals receiving Dex were more at ease when they emerged.

Also, Kim *et al.* <sup>[22]</sup> investigated the effect of the intraoperative utilization of Dex for the avoidance of post-operative delirium and emergence agitation among individuals having thoracoscopic lung excision surgery. Patients were randomly allocated to Dex sevoflurane group or the sevoflurane group they discovered that the Dex sevo group had emergence agitation less often than the Sevo group.

In line with our findings, Yang *et al.* <sup>[23]</sup> concluded that Dex decreased the emergence agitation risk, post-operative vomiting and nausea frequency, and requirement of rescue analgesics.

Our findings are in line with Jun *et al.* <sup>[24]</sup> who performed their work to evaluate the effects of intranasal Dex premedication in children and concluded that when contrasted alternative premedication methods, intranasal Dex produced more satisfying sedation during parent separation, decreased the requirement for rescue analgesics, and prevented vomiting and nausea following surgery.

Our results confirm the results of Yang *et al.* <sup>[23]</sup> who concluded that Dex decreased the emergence agitation risk, post-operative nausea and vomiting frequency, and requirement of rescue analgesic.

One study performed by Abdel-Rahman *et al.* <sup>[25]</sup> to demonstrate, the impact of two various Dex dosages on the frequency of emergence agitation following strabismus surgery. Patients received 0.5  $\mu$ g/.kg of Dex in high Dex group, 0.25  $\mu$ g /kg of Dex in low Dex group, or normal saline in the placebo group. The incidence of agitation was significantly lower in high Dex group compared to other groups and it was significantly lower in low Dex group compared to placebo group This study is consistent with our results from one side as our study showed reduced scores on SAS scale in both Dex groups contrasted to control group without substantial variation among Dex groups. On the other hand, this work showed that the frequency of agitation was substantial decreased in the high Dex group contrasted to lower Dex group and control group.

Our results showed reduced intraoperative fentanyl consumption in both Dex groups contrasted to control

group. In agreement with our result, DeX infusion throughout laparoscopic bariatric surgeries was evaluated by Tufanogullari *et al.* <sup>[26]</sup>, who came to the conclusion that concomitant utilization of an intraoperative Dex infusion (0.2-0.8  $\mu$ g/ kg /h) reduced the consumption of antiemetic and fentanyl medication.

AS regard to NRS, post-operative morphine consumption and time to 1st rescue analgesia, our results showed lower post-operative pain intensity scores, prolonged time for 1st request of analgesia and lower morphine consumption in both Dex groups compared to control group. In consistent with our findings, Hall *et al.* <sup>[27]</sup> they revealed that Dex groups had significantly lower morphine requirements than control group throughout the initial 24 hours following surgery.

In consistent with our results Khademi *et al.* <sup>[28]</sup> Dex was used during simple mastectomy to reduce pain, delay the need for analgesia for the first 24 hours after surgery, and assess the impacts of intraoperative infusion of Dex on both chronic and acute postoperative pain following simple mastectomy. They concluded that Dex resulted in significant difference in the occurrence of chronic pain compared to placebo. Also, Gurbet *et al.* <sup>[29]</sup> concluded that continuous intravenous Dex after surgery on the abdomen produced efficient postoperative analgesia and decreased the need for morphine without enhancing the likelihood of adverse effects. However, McQueen *et al.* <sup>[30]</sup> found no opioid sparing benefit for individuals receiving Dex in the PACU or during laparoscopic surgeries in women.

As regards intraoperative and postoperative side effects, intraoperative hypotension occurred in 9 patients in group Dex 0.6 compared to 8 patients in group Dex 0.3, and 1 patient in control group. Intraoperative bradycardia occurred in 10 patients in group Dex 0.6, compared to 8 patients in group Dex 0.3 and 1 in control group. Postoperative nausea and vomiting occurred in1 patient in group Dex 0.6, 2 patients in group Dex 0.3, and 13 patients in control group.

Turgut *et al.* <sup>[31]</sup> came to the same conclusion as the current research that patients having elective spinal laminectomy have frequent vomiting and nausea following surgery while using propofol-fentanyl medications as opposed to propofol-Dex. Furthermore, Salman *et al.* <sup>[32]</sup> who compared Dex with remifentanil in desflurane-based gynecologic laparoscopic surgeries found that postoperative vomiting, nausea, and analgesic needs had been lower in the Dex group than in the remifentanil group.

Our findings, however, did not agree with those of Bakhamees *et al.* <sup>[33]</sup> They investigated adult individuals scheduled for elective laparoscopic gastric bypass surgeries allocated randomly into two study groups: D or P. Group D obtained Dex in loading dose at  $0.8\mu g/kg$  and maintenance dose of  $0.4\mu g/kg/hr$ . along with fentanyl and propofol, while group P obtained normal saline at the same rate and volume. They discovered that there was no variance among the two groups in the frequency of vomiting and nausea following surgery.

**Limitations**: Our study had some limitations. In addition to the relatively small sample size, we did not assess the serum level of Dex.

		Group Dex 0.6	Group Dex 0.3	Group C	P value	
	Age (Year)	$33 \pm 8.5$	$35.5 \pm 8.5$	$34 \pm 8.6$	0.473	
Corr	Male	18 (60%)	16 (53%)	17 (56%)	0.987	
Sex	Female	12 (40%)	14 (47%)	13 (43%)	0.987	
	Weight (kg)	$136 \pm 13.4$	$138 \pm 13.4$	$140\pm14.2$	0.656	
	Height (cm)	$166 \pm 3.7$	$168 \pm 4.2$	$167 \pm 4.3$	0.375	
	BMI (kg/m <sup>2</sup> )	$49\pm4.6$	$51 \pm 4.4$	$51 \pm 4.7$	0.129	
	Duration of surgery (min)	$110 \pm 13.9$	$110 \pm 16.2$	$112 \pm 14$	0.232	
	Laparoscopic sleeve gastrectomy	16 (53%)	13 (43%)	11 (37%)		
Type of surgery	Laparoscopic cholecystectomy	9 (30%)	6 (20%)	$\begin{array}{r} 34\pm 8.6\\ 17\ (56\%)\\ 13\ (43\%)\\ 140\pm 14.2\\ 167\pm 4.3\\ 51\pm 4.7\\ 112\pm 14\\ \end{array}$	7%) 0.421	
	Laparoscopic mini gastric bypass	14 (47%)	9 (30%)	7 (23%)		

**Table 1:** Patients' characteristics among the three groups

Data are presented as mean ± SD or frequency (%). BMI: body mass index value <0.05 indicates statistical significance.

	Group Dex 0.6	Group Dex 0.3	Group C	P value	Post hoc P	95% CI
		PaO <sub>2</sub> values (m				
Baseline	$151 \pm 4.2$	$151 \pm 4.6$	$152 \pm 6.0$	0.327		
End of drug infusion	164 ± 4.1 *	164 ± 5.1*	153 ± 6.2		P1=0.917	(-6.44; 9.78)
				< 0.001	P2<0.001	(20.32; 36.54)
					P3<0.001	(18.66;34.88)
		<b>P/F</b> ratio and $\Delta$ <b>P/F</b> i				
Baseline	$377 \pm 10.5$	379 ± 11.5	$382 \pm 15.1$	0.317		
End of drug infusion	412± 10.2*	$410 \pm 12.8*$	$383 \pm 15.5$	<0.001	P1==0.917	(-6.44; 9.78))
					P2<0.001	(20.32;36.54)
					P3<0.001	(18.66;34.88)
$\Delta P/F$	$34.4\pm8.4$	31.1± 6.6	1.0±7.6	< 0.001	P1=0.277	(51;7.91
					P2< 0.001	(24.26;32.68)
					P3<0.001	(20.56;28.98)
	Static complia	nce and $\Delta$ static comp	<mark>liance values (</mark> 1	mL/cmH <sub>2</sub> O)		
Baseline	$48 \pm 3$	47± 2.8	$47.4 \pm 3.2$	P=0.443		
	53 ± 2.5*			< 0.001	P1=0.421	(2.70;83)
End of drug infusion		$52 \pm 2.9*$	$46.5 \pm 3.2$		P2< 0.001	(4.778; 8.30)
	55 ± 2.5	$52 \pm 2.7$	40.5 ± 5.2	<0.001	P3<0.001	(3.48;7.36)
	5.4± 2.3	5.5 ± 1.9			P1=0.997	(-1.79; 0.46)
$\Delta$ static			$-0.8 \pm 0.9$	< 0.001	P2<0.001	(3.17; 5.43)
					P3<0.001	(3.84; 6.09)
		<u>nce and ∆ dynamic co</u>			2 <b>O</b> )	
Baseline	$38 \pm 2.5$	$37.6 \pm 2.5$	$38 \pm 2.4$	P=0.577		
	44.9 ± 2.7*	44 ± 2.5*	37± 2.5	<0.001	P1=0.389	(70: 2.43)
End of drug infusion					P2< 0.001	(6.13; 9.27)
					P3<0.001	(5.27; 8.40)
	6.6 ± 1.9	6 ± 1.9	1±.9	<0.001	P1=0.377	(44: 1.57)
∆ Dynamic					P2=0.001	(4.56: 6.57)
					P3=0.001	(3.99: 6.01)
		Plateau pressure valu			-	
Baseline	$22 \pm 1.5$	$22 \pm 1.4$	$21 \pm 2.1$	P=0.423		
	sion $20 \pm 1.2^*$	21.1 ± 1.3*	21.4 ± 1.7	<0.001	P1=0.461	(-2.29;0.24)
End of drug infusion					P2 =0.002	(-0.42; -2.18)
					P3=0.045	(-0.02; -1.78)
		ad space values (ml)				
Baseline	$22.1 \pm 1.27$	$22.8 \pm 1.8$	$22 \pm 1.4$	0.091		
	18.1 ± 1.2 *		23 ±1.6*	< 0.001	P1=0.496	(-0.69: 0.96)
End of drug infusion		18.6 ± 1.3 *			P2<0.001	(-4.59; 2.94)
					P3<0.001	(-4.72; 3.08)
	-3.9 ± 1.2	-4.2 ± 1.42	1.0 ±.9	<0.001	P1=0.6	(-1.51:0.09)
$\Delta$ dead space :/					P2<0.001	(2.09: 3.51)
					P3<0.001	(2.89: 4.31)

Table 2: Comparison of P/F ratio and lung mechanics among the three studied groups

Data are presented as mean  $\pm$  SD. CI: Confidence interval. \*Indicates significance of end of drug infusion compared to baseline values in each group. P presents the comparison among the three groups. P < 0.05 indicates statistical significance. P1 presents the comparison between group Dex 0.6 and group Dex 0.3. P2 presents the comparison between group Dex 0.6 and group C. P3 presents the comparison between group Dex 0.3 and group C.

 Table 3: Total intraoperative fentanyl consumption, postoperative morphine consumption and time to 1st rescue analgesia among the three studied groups

	Group Dex 0.6	Group Dex 0.3	Group C	P value	Post hoc P	95% CI
					P1= 0.376	(-2.59: 9.25)
Intraoperative fentanyl consumption (mic)	137.7±13.31	$138.2 \pm 13.4$	280±28.8	< 0.001	P2<0.001	(-75.42 -63.58)
					P3<0.001	(-78.75 -66.91)
					P1=0.63	(-0.67: 0.93)
Postoperative morphine consumption(mg)	$12\pm4.1$	15± 3.6	$30.8 \pm 8.7$	< 0.001	P2<0.001	(-4.59: -2.63)
					P3<0.001	(-5.72: -3.51)
	344± 80.5				P1=0.982	(-6. 24:9.88)
Time to 1st rescue analgesia(min)		$340.7 \pm 89.8$	$75 \pm 28.1$	< 0.001	P2<0.001	(39.32;43.54)
					P3<0.001	(40.61;46.88)

Data presented as mean  $\pm$  SD, CI; confidence interval. P < 0.05 indicates statistical significance P presents the comparison among the three groups. P1 presents the comparison between group Dex 0.6 and group Dex 0.3. P2

presents the comparison between group Dex 0.6 and group C. P3presents the comparison between group Dex 0.3 and group C.

Table 4: Quality of recovery score and sedation agitation scale among the three studied groups

	Group Dex 0.6	Group Dex 0.3	Group C	P value	Post hoc P	95% CI
Quality of recovery score	138.6± 2.5	139.3±2	116. ± 2.8	<0.001	P1=0.513	(-2.21: 0.81)
					P2<0.001	(21.06;24.08)
					P3<0.001	(21.76; 24.78)
					P1= 0. 146	(46; 2.57)
SAS scale	$2.27 \pm 0.5$	$2.1 \pm 0.5$	$5.1 \pm 0.5$	< 0.001	P2<0.001	(4.58; 6.73)
					P3<0.001	(3.64; 5.01)

Data presented as mean  $\pm$  SD, CI; confidence interval. SAS: sedation agitation scale. P < 0.05 indicates statistical significance P presents the comparison among the three groups. P1 presents the comparison between group Dex 0.6 and group Dex 0.3. P2 presents the comparison between group Dex 0.6 and group C. P3 presents the comparison between group Dex 0.3 and group C.

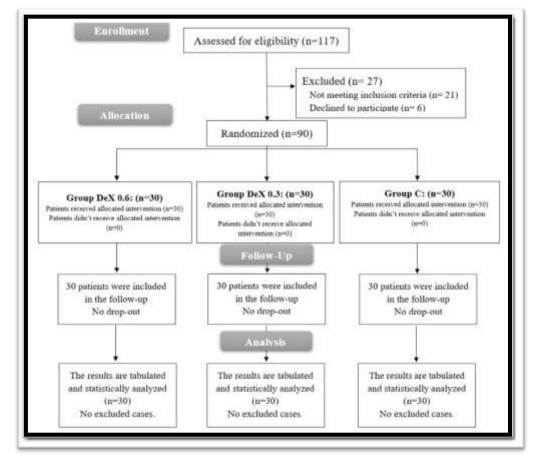


Figure 1: The CONSORT flow diagram, including enrolment, intervention, allocation, and analysis.

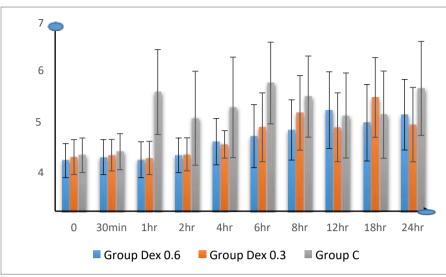


Figure 2: NRS among the three groups.

#### **Conclusions:**

Dex infusion at a dose of  $0.3 \ \mu g \ /kg \ /hr$  and  $0.6 \ \mu g \ /kg \ /hr$  after a loading dose of  $1 \ \mu g \ /kg$  resulted in improvement of oxygenation and lung mechanics lower postoperative pain scores, decreased analgesic consumptions as well as improved quality of recovery in morbidly obese patients with restrictive lung disease undergoing laparoscopic surgery

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