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THE EFFECT OF LOW-DOSE REMIFENTANIL ON THE HEMODYNAMIC RESPONSES OF ENDOTRACHEAL EXTUBATION

Dr. Natiq D. Shalaan*

Bahrka St, Gulan City, Erbil, Iraq.

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***Corresponding Author: Dr. Natiq D. Shalaan**

Bahrka St, Gulan City, Erbil, Iraq.

ABSTRACT

Background: Emergence from general anesthesia can be associated with coughing, agitation, hypertension, and tachycardia, which may cause bleeding from the surgical site, and an increase in intracranial and intraocular pressure. In addition to respiratory complications, hemodynamic complications such as hypertension, increasing intraocular and intracranial pressure, tachycardia, and dysrhythmia can occur with extubation that can be hazardous in high-risk patients. Remifentanil is an opioid with instant effect and rapid elimination that is not influenced by age or the functions of the liver and kidneys, and does not result in delayed recovery or respiratory depression after a continuous infusion and recently it has been recommended as a promising agent in attenuating hemodynamic and respiratory complications of anesthesia. **Patients and Methods:** This prospective clinical trial, case control study, Including one hundred twenty adult patients undergoing lower abdomen, orthopedics or plastic surgery. All patients received a standard general anesthesia. At the end of surgery, Group A received a bolus dose of remifentanil 0.5 microgram/kilogram (N = forty), Group B received 1microgram/kilogram remifentanil (N= forty) and Group C received placebo (normal saline) (N = forty), when extubation criteria were achieved non- invasive arterial pressure, heart rate and oxygen saturation were measured 1minute before extubation, remifentanil was given over 30 seconds, and tracheal extubation was performed. Non-invasive arterial pressure, heart rate and oxygen saturation also measured 1minute intervals after extubation to fifth minute. **Results:** One hundred twenty patients enrolled the study. 73 of them were male and 47 female, age of 27.47 ± 5.96 years, weight of 75.57 ± 7.96 kg. Patients who developed apnea after endotracheal extubation are (18.33%), 5% of group A and 50% of group B while none of the group C, and P – value was very significant (0.0001). Were no statistically significant associations between different study groups and both of age and weight of the patients, P – values were not significant and more than 0.05. Except for 1 minute before extubation there was statistically significant association between the different study groups and SBP,DBP,MAP and HRreadings before and after extubation follow ups. In all conditions patients from group C had the highest SBP, DBP, MAP and HR readings followed by group A then group B, P – value was significant and less than 0.05. There was no statistically significant association between study groups and SaO_2, P – values were higher than 0.05. **Conclusions:** Patients receiving remifentanil are hemodynamically stable during and after endotracheal extubation in compare with patients receiving normal saline. Patients receiving remifentanil 0.5mcg/kg, hemodynamic measures more close to normal values and less incidence of apnea than patients whose receiving remifentanil 1mcg/kg. No difference in oxygen saturation and no significant associations between different study groups and both of age and weight of the patients among three groups.

KEYWORDS: Remifentanil; Extubation.

AIM OF STUDY

AIM of the study was to examine the effect of optimum bolus low-dose of remifentanil in blunting the hemodynamic responses (blood pressure and heart rate) of tracheal extubation in lower abdomen, orthopedics or plastic surgery.

INTRODUCTION

Emergence from general anesthesia can be associated with coughing, agitation, hypertension, and tachycardia, which may cause bleeding from the surgical site, and an increase in intracranial and intraocular pressure.[1]

The purpose of tracheal intubation is to provide airway patency, ensuring airway protection, to aid ventilation of the lungs and improving surgical access. The endotracheal tube could be withdrawn, when there is no further need to ventilatory assistance and/or protection of the airways.[2] Despite the enormous attention granted to tracheal intubation, especially about the management of the difficult airway[3], little attention has been paid to tracheal extubation and its challenges.[4]

In most patients, extubation is uneventful. However, in a some cases, anatomical and/or physiological problems, technical and human factors can result in morbidity and mortality which occur more commonly among high-risk patients.[2]

The period immediately after extubation is considered as most critical and vulnerable time for the patient that, it is highly recommended for anesthesiologists by American Society of Anesthesiologists (ASA), to have a preplanned strategy for management of potential problems after extubation.[4-5]

In addition to respiratory complications, hemodynamic complications such as hypertension, increasing intraocular and intracranial pressure, tachycardia, and dysrhythmia can occur with extubation that can be hazardous in high-risk patient.[5-6] Remifentanil is an opioid with instant effect and rapid elimination that is not influenced by age or the functions of the liver and kidneys, and does not result in delayed recovery or respiratory depression after a continuous infusion and recently it has been recommended as a promising agent in attenuating hemodynamic and respiratory complications of anesthesia.[7]

The aim of this study was to assess the effects of low-dose Remifentanil injection on the hemodynamic responses of extubation.

1- Tracheal extubation and hemodynamic responses

Most often, extubation should be performed when a patient is either deeply anesthetized or awake. In either case, adequate recovery from neuromuscular blocking agents should be established prior to extubation. If neuromuscular blocking agents are used, the patient has at least a period of controlled mechanical ventilation and likely must be weaned from the ventilator before extubation can occur.[10]

This may take place with the patient supine if the anaesthetist is satisfied that airway patency can be maintained by the patient in this position and there is no risk of regurgitation. In patients at risk of regurgitation and potential aspiration, the lateral position is preferred. Return of respiratory reflexes is signified by coughing and resistance to the presence of the tracheal tube. Tracheobronchial suction via the tracheal tube is carried out using a soft sterile suction catheter with an external diameter less than half the internal diameter of the tube. Pharyngeal suction is performed best under direct vision, avoiding trauma to the pharyngeal mucosa, uvula or epiglottis.[8]

Oxygen 100% replaces the anaesthetic gas mixture before extubation to avoid the potential effects of diffusion hypoxia and to provide a pulmonary reservoir of oxygen in case breath-holding or coughing occurs. Tracheal extubation is performed preferably during inspiration when the larynx dilates; the cuff is deflated and the tube is withdrawn along its curved axis, as careless withdrawal in a straight line may damage laryngeal structures.[8] The tube is withdrawn in a single smooth motion[10] Extubation during a light plane of anesthesia (ie, a state between deep and awake) is avoided because of an increased risk of laryngospasm. The distinction between deep and light anesthesia is usually apparent during pharyngeal suctioning: any reaction to suctioning (eg, breath holding, coughing) signals a light plane of anesthesia, whereas no reaction is characteristic of a deep plane.

Similarly, eye opening or purposeful movements imply that the patient is sufficiently awake for extubation.[10]

Extubating an awake patient is usually associated with coughing (bucking) on the Tracheal tube. This reaction increases the heart rate, central venous pressure, arterial blood pressure, intracranial pressure, intra abdomen pressure and intraocular pressure.[10] It may also cause wound dehiscence and increased bleeding.

The presence of a Tracheal tube in an awake asthmatic patient may trigger bronchospasm. Some practitioners attempt to decrease the likelihood of these effects by administering 1.5 mg/kg of intravenous lidocaine 1–2 min before suctioning and extubation; however, extubation during deep anesthesia may be preferable in patients who cannot tolerate these effects (provided such patients are not at risk of aspiration and/or do not have airways that may be difficult to control after removal of the Tracheal tube). A deep extubation and good postoperative analgesia (without respiratory acidosis) may also help prevent the onset of arrhythmias.[10]

Regardless of whether the tube is removed when the patient is deeply anesthetized or awake, the patient's pharynx should be thoroughly suctioned before extubation to decrease the potential for aspiration of blood and secretions.[10]

Deep extubation (before airway reflexes return) reduces bronchospasm on emergence. Lidocaine as a bolus (1.5–2 mg/kg) may help obtund airway reflexes during emergence.

After extubation, the patient's ability to maintain the airway is ensured, the ability to cough and clear secretions is assessed and an oropharyngeal airway is inserted if required. Administration of oxygen is

continued by face mask.[8]
Problems that may occur include the following

- Cardiovascular response: similar to that on tracheal intubation but usually of reduced magnitude.(hypertensive response: associated with sympathetic activity and tachycardia, may increase intracranial pressure and intraocular pressure, particularly undesirable in patients with hypertension and ischemic heart disease).
- Coughing and laryngospasm: the latter is especially likely to occur at light planes of anaesthesia and in children.
- Regurgitation and aspiration of gastric contents.
- Airway obstruction.
- Laryngeal trauma caused by the cuff if still inflated.[9]

At the end of surgery, the timing of extubation should balance the risk of bronchospasm with that of respiratory failure, but evidence suggests that early extubation (in the operating room) is beneficial. Successful extubation at the end of the procedure depends on multiple factors: adequate pain control, reversal of neuromuscular blockade, absence of significant bronchospasm and secretions, absence of significant hypercapnia and acidosis, and absence of respiratory depression due to residual anesthetic agents. Patients with an FEV below 50% may require a period of postoperative ventilation, particularly following upper abdominal and thoracic operations.[10]

2- Remifentanil

2-1-Structure– synthetic anilinopiperidine opioid with amethyl ester linkage.[11]

Remifentanil is a potent ultra short-acting synthetic opioid. The chemical name of Remifentanil hydrochloride is 1-(2-methoxycarbonyl-ethyl)- 4-(phenylpropionyl-amino) -piperidine-4-carboxylic acid methyl ester hydrochloride. The structural formula is given figure 2.[12]

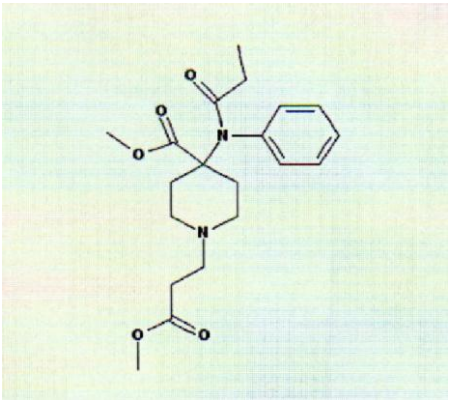

Figure 1: the structural formula of remifentanil.

2-2-Presentation– lyophilised white powder as 1, 2 or 5 mg vials for reconstitution, which forms a clear colourless solution containing 1 mg ml−1 remifentanil hydrochloride. Further dilution to a concentration of 50µgml−1 recommended for general anaesthesia. Reconstituted solution is stable for 24 hours at room temperature.[11]

2-3-Dose–IV–bolus at induction 1µgkg−1 over not less than 30 s, maintenance infusion 0.05–2 µgkg−1 min−1 titrated to desired level. For spontaneous ventilation, starting dose 0.04µgkg−1 min−1, with range of 0.025–0.1 mg kg −1 min−1 titrated to effect.[11]

2-4-Pharmacokinetics of Remifentanil

2-4-1- Absorption: it is administered as an intravenous infusion. Blood concentrations of remifentanil are proportional to the dose administered throughout the recommended dose range. Unlike other fentanyl analogues, the duration of action does not increase with prolonged administration.[12]

2-4-2- Distribution: The central volume of distribution is 100ml/kg, and the steady-state volume of distribution is 350ml/kg. Remifentanil is approximately 70% bound to plasma proteins.[12]

2-4-3- Metabolism and excretion: Remifentanil is an esterase metabolized opioid. It is rapidly and extensively metabolized by non-specific esterases in blood and tissues to the carboxylic acid derivative, GR90291. This metabolite in healthy adults is 2 hours. Approximately 95% of remifentanil is recovered in the urine as the carboxylic acid metabolite. Following administration of the recommended doses of remifentanil, the effective biological half-life is 3-10 minutes due to redistribution. The terminal half-life of the unchanged is 10-20 minutes.[13]

2-5- Pharmacodynamics of Remifentanil

Remifentanil is a potent, selective, 4-anilidopiperidine µ-opioid agonist with pharmacological action typical of this class of compound. It is distinguished from other 4-anilidopiperidines (fentanyl analogues) by its rapid onset and very short duration of action. The µ-opioid activity of remifentanil is antagonized by naloxone. Remifentanil in humans has a rapid blood-brain equilibration half-time of 1 minute and a rapid onset of action. Blood concentration decreases 50% in 3 to 6 minutes after a 1-minute infusion or after prolonged continuous infusion due to rapid distribution and elimination process and is independent of duration of drug administration. Recovery from the effects of remifentanil occurs rapidly (within 5 to 10 minutes). Rapid onset of action (~1 min) and rapid offset of action following discontinuation of a continuous infusion (~3-10 min).[13]

2-6- Clinical effects of Remifentanil

2-6-1- Central Nervous System–potent opioid receptor agonist; analgesic potency comparable to fentanyl; rapid onset and recovery even after several hours' infusion.[11]

2-6-2- Cardiovascular System– haemodynamically very stable; rarely bradycardia and hypotension.[11]

2-6-3- Respiratory System– respiratory rate and volume reduced, response to hypercarbia reduced; muscle rigidity, related to dose and rate of administration.[11]
2-6-4- Other– nausea and vomiting, no histamine release.[11]
2-6-5- Contraindications– concurrent administration with monoamine oxidase inhibitors.[11]

PATIENTS AND METHODS

After consent of patients a prospective clinical trial case control study was conducted with the approval of the Scientific committee of Iraqi consul.

Study conducted in Erbil Teaching Hospital and West Erbil Hospital from September to November 2015.

Inclusion criteria: One hundred twenty patients male and female, ages of 18-40 years, ASA physical status I-II according to the ASA's classification system. who were scheduled for lower abdomen, orthopedic or plastic surgery.

Exclusion criteria: Patients under long term treatment with sedatives, antitussives, or angiotensin converting enzyme inhibitors, patients with chronic cough, asthma, chronic diseases or predicted difficult intubation.

Participant patients were classified randomly into three groups (two case and one control).

All patients received standard general anesthesia, 5ml/kg serum ringer given to maintain intravascular volume and pre induction intravenous 1mg Midazolam and 100mcg Fentanyl. Anesthesia was induced using Propofol sedation 1.5-2mg/kg. Atracurium 0.6 mg/kg was administrated to facilitate intubation, 100% oxygen with flow of 6 liter/minute. Maintenance with inhalant 1-1.5% Isoflurane and Atracurium.

Patients monitoring during surgery were heart rate, arterial blood pressure, oxygen saturation and Temperature. At the end of surgery, after discontinuing Isoflurane, we used the combination of Atropine and Neostigmine to antagonize the remaining effects of non-depolarizing neuromuscular blocking agents and mechanical ventilation was continued with 100% oxygen. In this time, oropharyngeal suction was preformed genteelly, and then the extubation was considered in a standard manner when the patients achieved criteria of extubation when they're able to open their eyes, swallowing, spontaneous respirations.

1minute before extubation non-invasive arterial pressure, heart rate and oxygen saturation recorded for all patient groups then the case group A received bolus 0.5 mcg/kg intravenous remifentanil, case group B received bolus 1 mcg/kg intravenous remifentanil over 30seconds, whilst the control group C received similar amount of saline solution as placebo. Non-invasive arterial pressure (systolic (SBP), diastolic (DBP) and mean (MAP)), heart rate (HR), the oxygen saturation (SaO_2) and Development of Apnea were recorded 1 minute intervals to 5th minute post- extubation.

Data were analyzed via Chi square and ANOVA Test using SPSS statistical software ver16.

Demographics and Statistical analysis

A questionnaire designed to collect data. These collected data were processed via Microsoft office Excel and SPSS v.19 computer program. Data from each parameter were expressed as mean ± standard deviation. ANOVA test at p value < 0.05 was the measure for statistical signific.

DATA COLLECTION PAPER

The Effect of Low-Dose Remifentanil on the Hemodynamic Responses of Endotracheal Extubation

Case No……
□ Group A (0.5mcg/kg remifentanil)
□ Group B (1mcg/kg remifentanil)
□ Group C (Control Group) Age:…..…years Sex: □ Male, □ Female Apnea: □Yes, □No, Weight: ……kg. Date of operation:……/… /2015

Blood Pressure

1minute before extubation:	SBP……...mmHg,	DBP……...mmHg,	MAP……..
1st minute after extubation:	SBP…….mmHg,	DBP……...mmHg,	MAP ……..
2nd minute after extubation:	SBP…..….mmHg,	DBP……...mmHg,	MAP……..
3rd minute after extubation:	SBP…….mmHg,	DBP……...mmHg,	MAP ……..
4th minute after extubation:	SBP…….mmHg,	DBP……...mmHg,	MAP ……..
5th minute after extubation:	SBP…….mmHg,	DBP……...mmHg,	MAP ……..

Heart Rate:	SaO_2:
1minute before extubation..... bpm	:……%
1st minute after extubation..... bpm	:……%
2nd minute after extubation..... bpm	:……%
3rd minute after extubation: .....bpm	:……%
4th minute after extubation: .....bpm	:……%
5th minute after extubation: .....bpm	:……%

RESULTS

One hundred twenty patients enrolled the study. 73 of them were male and 47 were female (Figure 2) with mean ±S.D age of 27.47 ± 5.96 years, and mean ±S.D weight of 75.57 ± 7.96 kg (Table 1).

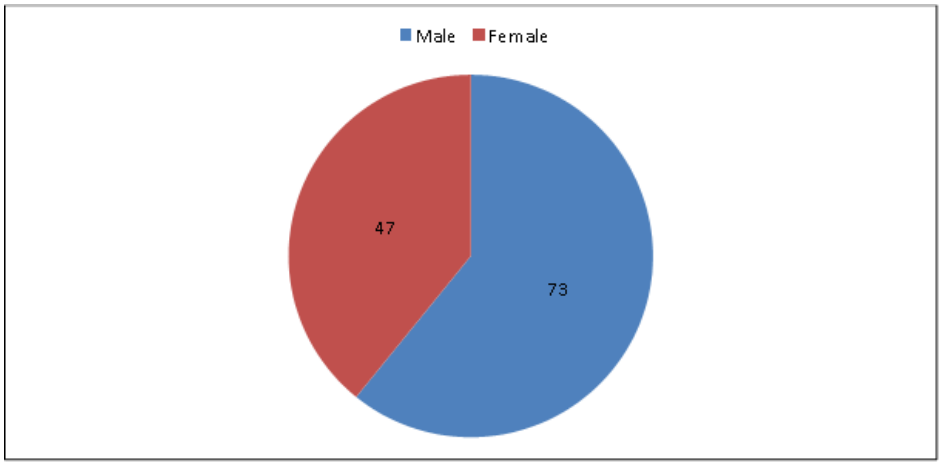

Figure 2: Gender distribution of participants.

Table 1: Descriptive data of participants.

Measure	N	Range	Minimum	Maximum	Mean	S.D
Age	120	22	18	40	27.47	5.963
Weight	120	46	50	96	75.57	7.968

The results of Table (2) show that 18.33% patient all patients developed post operative apnea, there was a significant statistical association between the study samples (groups A, B, C) and apnea. Only 5% of group A and 50% of group B developed apnea while none of the group C developed that. Chi square test was done and P – value was very significant (0.0001). See (Figure 3).

Table 2: Association between study groups and apnea (P=0.0001).

Apnea	Groups			Total
	A	B	C	
No	38 95%	20 50%	40 100%	98 81.76%
Yes	2 5%	20 50%	0 0%	22 18.33%
Total	40 100%	40 100%	40 100%	120 100%

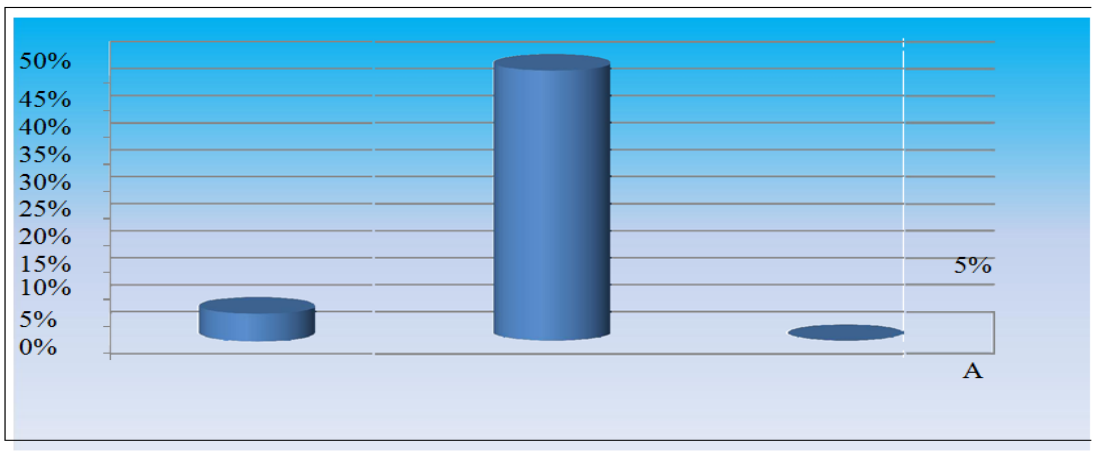

Figure 3: Distribution of apnea between study groups.

The findings of Table (3) indicate that there were no statistically significant associations between different study groups and both of age and weight of the patients. ANOVA test was done to compare between the averages of the study groups regarding their age and weight which were very close in the different groups A, B and C. In all circumstances P – values were not significant and more than 0.05. See (Figure 4).

Table 3: Relationship between study groups and age and weight.

Measures	Groups	N	Mean	S.D	P-value	ANOVA
	A	40	26.73	6.110		
Age	B	40	27.55	5.510	0.57	Non-significant
	C	40	28.13	6.309		
	Total	120	27.47	5.963		
	A	40	75.58	6.563		
Weight	B	40	75.93	9.054	0.92	Non-significant
	C	40	75.20	8.272		
	Total	120	75.57	7.968		

Figure 4: Relationship between study groups and age and weight.

The data from Table (4) prove that (except for SPB 1 minute before extubation) there was statistically significant association between the different study protocols or groups and SBP readings. In all conditions patients from group A tended to have a normal SBP while group B had lower blood pressure in contrast to group C participants who had higher SBP. ANOVA test was performed to find the relationship and P – value was significant and less than 0.05. See (Figure 5).

Table 4: Relationship between study groups and SBP.

Measures	Groups	N	Mean	S.D	P-value	ANOVA
	A	40	145.95	9.500		
SBP1min	B	40	146.93	14.165	0.23	Non-significant
before	C	40	144.68	11.292		
	Total	120	145.18	12.347		
	A	40	125.33	12.158		
SBP1 min	B	40	117.00	14.882	0.0001	Significant
After	C	40	144.55	10.013		
	Total	120	128.96	16.974		
	A	40	117.33	10.319		
SBP2 min	B	40	108.30	14.902	0.0003	Significant
After	C	40	152.58	67.799		
	Total	120	126.07	44.521		
	A	40	114.35	10.436		
SBP3 min	B	40	102.53	17.548	0.0002	Significant
After	C	40	134.65	9.380		

	Total	120	117.18	18.518		
	A	40	118.15	8.660		
SBP4 min	B	40	102.03	19.074	0.0001	Significant
After	C	40	127.85	9.046		
	Total	120	116.01	16.883		
	A	40	122.88	7.405		
SBP5 min	B	40	106.93	17.620	0.0002	Significant
After	C	40	121.23	8.322		
	Total	120	117.01	13.934		

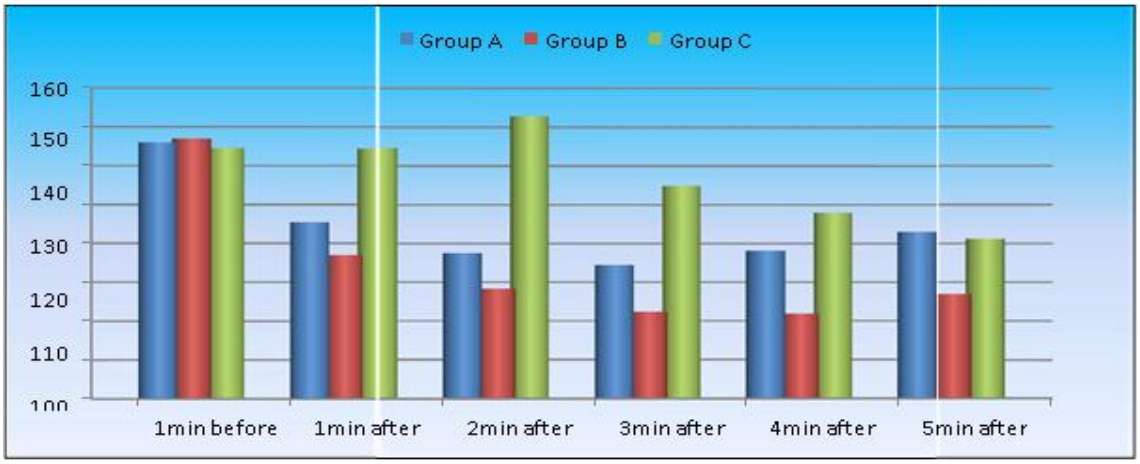

Figure (5): Relationship between study groups and SBP.

The data of Table (5) show that there was a statistically significant association between study groups and DBP in all occasions except for the "one minute before extubation". In all conditions ANOVA test was done to compare between the averages and S.D of different study groups. Group A patients mostly experienced normal DBP while group B participants had hypotensive and group C hypertensive readings in almost all instances. In all circumstances P – values were highly significant and less than 0.05. See (Figure 6).

Table 5: Relationship between study groups and DBP.

Measures	Groups	N	Mean	S.D	P-value	ANOVA
	A	40	95.05	5.747		
DBP1min	B	40	97.35	9.286	0.31	Non-significant
Before	C	40	96.35	8.381		
	Total	120	96.58	8.439		
	A	40	85.10	8.599		
DBP1min	B	40	73.73	12.760	0.0001	Significant
After	C	40	94.03	8.731		
	Total	120	91.03	75.614		
	A	40	77.55	9.072		
DBP2min	B	40	64.50	12.766	0.0001	Significant
After	C	40	92.60	8.488		
	Total	120	78.22	15.392		
	A	40	73.20	10.699		
DBP3min	B	40	58.08	13.016	0.0002	Significant
After	C	40	88.03	8.402		
	Total	120	73.10	16.338		
	A	40	74.75	8.079		
DBP4min	B	40	59.05	12.856	0.0001	Significant
After	C	40	83.65	6.608		
	Total	120	72.48	13.934		
	A	40	75.93	6.399		
DBP5min	B	40	63.10	12.516		Significant
After	C	40	79.18	7.476	0.0002	

	Total	120	72.73	11.474		

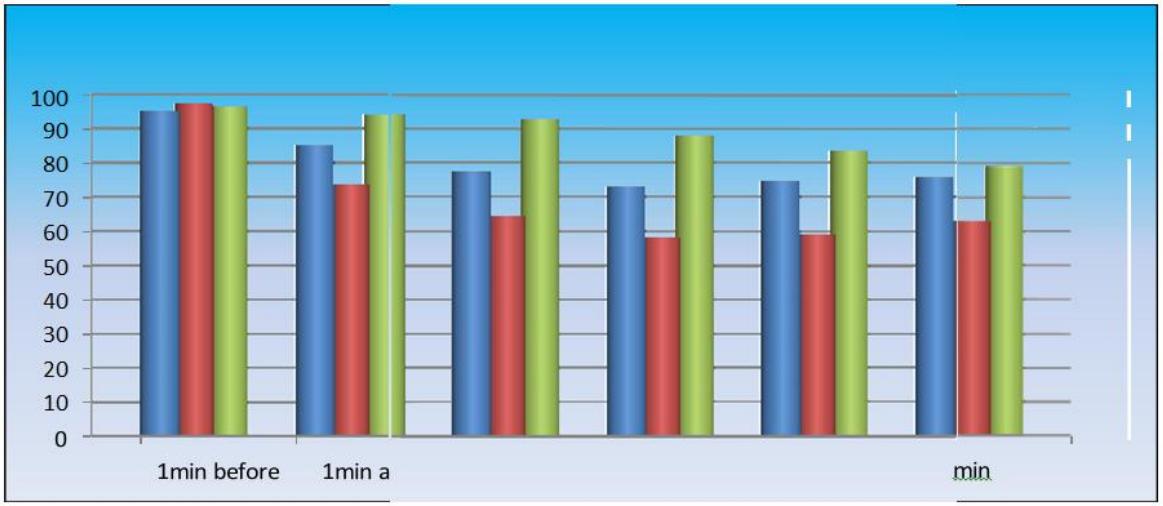

Figure 6: Relationship between study groups and DBP.

The data of Table (6) indicate that (except for MAB 1 minute before extubation) there was statistically significant association between the different study groups and MAP readings before and after extubation follow ups. In all conditions patients from group C had the highest MAP readings followed by group A then group B. ANOVA test was performed to find the relationship and P – value was significant and less than 0.05. See (Figure 7).

Table 6: Relationship between study groups and MAP.

Measures	Groups	N	Mean	S.D	P-value	ANOVA
	A	40	115.13	6.438		
MAP1min	B	40	114.98	10.134	0.071	Non-significant
Before	C	40	113.10	9.347		
	Total	120	113.73	9.311		
	A	40	98.20	8.228		
MAP1min	B	40	88.13	13.011	0.0001	Significant
After	C	40	110.73	7.984		
	Total	120	99.02	13.592		
	A	40	90.68	8.965		
MAP2min	B	40	78.95	12.940	0.0001	Significant
After	C	40	108.35	8.580		
	Total	120	92.66	15.893		
	A	40	86.30	10.266		
MAP3min	B	40	72.80	14.298	0.0002	Significant
After	C	40	103.88	6.386		
	Total	120	87.66	16.677		
	A	40	89.13	7.927		
MAP4min	B	40	73.50	14.516	0.0001	Significant
After	C	40	98.28	6.365		
	Total	120	86.97	14.437		
	A	40	91.25	6.058		
MAP5min	B	40	77.20	13.497		Significant
After	C	40	95.93	17.898	0.0002	
	Total	120	88.13	15.510		

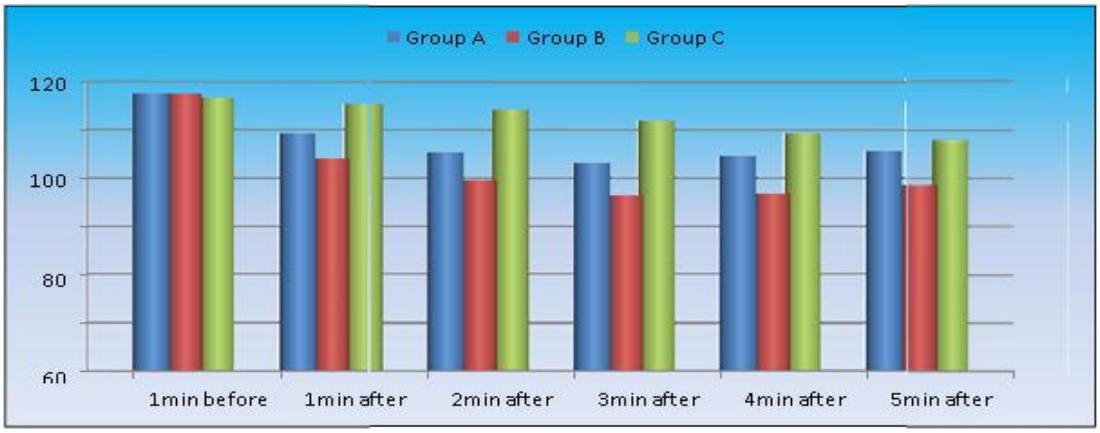

Figure 7: Relationship between study groups and MAP.

The data of Table (7) reveal that there was a statistically significant association between study groups and HR of the patients in all occasions except for the "one minute before extubation". In all conditions ANOVA test was done to compare between the averages and S.D of different study groups. Patients from groups A and B mostly experienced normal HR while group C participants had higher HR and even reached tachycardia. In all circumstances P – values were highly significant and less than 0.05. See (Figure 8).

Table 7: Relationship between study groups and HR.

Measures	Groups	N	Mean	S.D	P-value	ANOVA
	A	40	119.45	15.381		
HR1 min	B	40	119.00	14.024	0.431	Non-significant
Before	C	40	115.48	15.414		
	Total	120	117.98	14.934		
	A	40	95.83	14.016		
HR1 min	B	40	87.73	13.510	0.0001	Significant
After	C	40	116.63	14.653		
	Total	120	100.06	18.546		
	A	40	90.18	7.742		
HR2 min	B	40	82.00	10.593	0.0001	Significant
After	C	40	113.50	13.771		
	Total	120	95.23	17.268		
	A	40	87.30	7.261		
HR3 min	B	40	81.60	10.330	0.0002	Significant
After	C	40	108.83	11.578		
	Total	120	92.58	15.323		
	A	40	87.25	5.628		
HR4 min	B	40	81.90	10.551	0.0001	Significant
After	C	40	99.70	10.620		
	Total	120	89.61	14.934		
	A	40	87.75	5.062		
HR5 min	B	40	82.68	9.882	0.0002	Significant
After	C	40	92.28	8.370		
	Total	120	87.57	8.881		

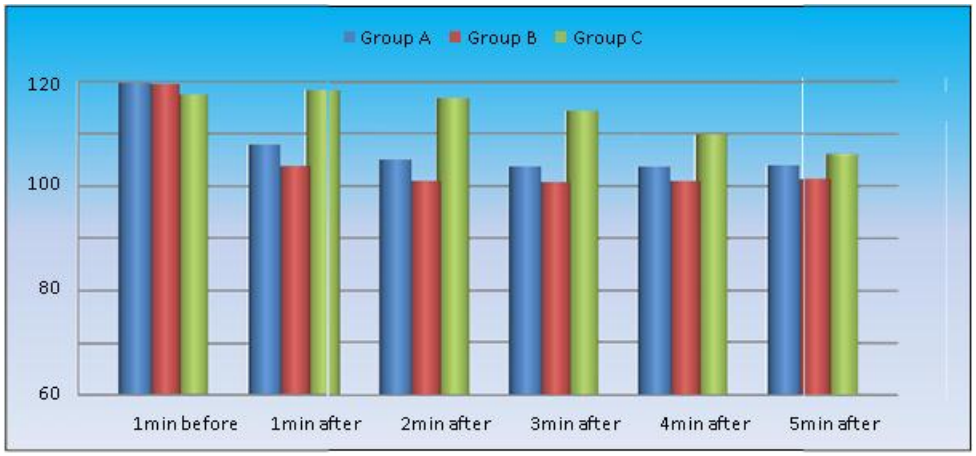

Figure 8: Relationship between study groups and HR.

The findings of Table (8) indicate that there was no statistically significant association between study groups and SaO_2. The mean oxygen saturation of all groups and in all occasions was very close to each other and approximately 99%. ANOVA test was done to compare between the averages of all groups, there was no statistical difference between them. P – values were higher than 0.05. See (Figure 9).

Table 8: Relationship between study groups and SaO_2.

Measures	Groups	N	Mean	S.D	P-value	ANOVA
$SaO_2$1 min Before	A C Total	40 40 120	99.45 99.33 99.36	0.552 0.730 0.605	0.498	Non-significant
	A	40	99.25	0.870		
$SaO_2$1 min	B	40	99.45	0.504	0.058	
After	C	40	99.03	0.920		Non-significant
	Total	120	99.24	0.799		
	A	40	99.13	1.017		
$SaO_2$2 min	B	40	99.20	0.608	0.658	Non-significant
After	C	40	99.03	0.891		
	Total	120	99.12	0.852		
	A	40	99.25	0.899		
$SaO_2$3 min	B	40	99.53	0.554	0.123	Non-significant
After	C	40	99.13	1.114		
	Total	120	99.30	0.894		
	A	40	99.38	0.868		
$SaO_2$4 min	B	40	99.28	0.640	0.347	Non-significant
After	C	40	99.10	1.008		
	Total	120	99.25	0.853		
	A	40	99.43	0.712		
$SaO_2$5 min	B	40	99.38	0.705	0.095	Non-significant
After	C	40	99.08	0.888		
	Total	120	99.29	0.782		

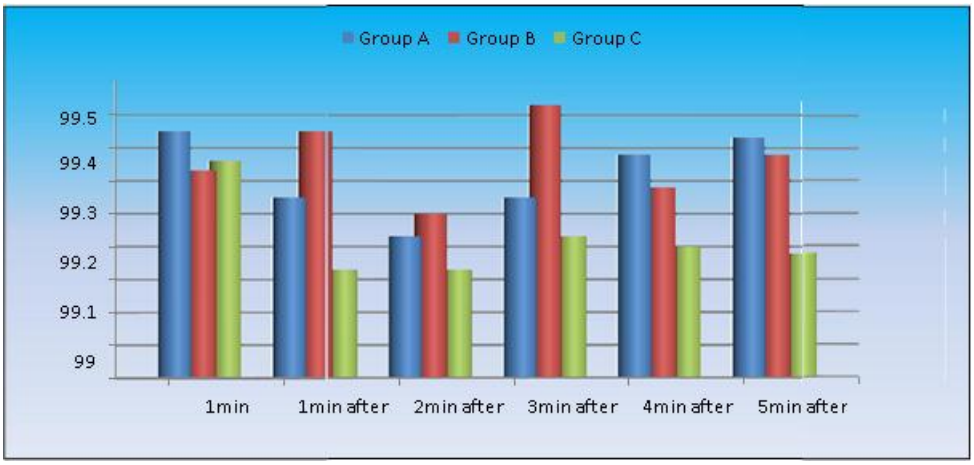

Figure 9: Relationship between study groups and SaO_2.

DISCUSSION

Emergence from anesthesia and tracheal extubation accompanied by hemodynamic instability so we intended to examine the effect of bolus low-dose remifentanil on the hemodynamic response to the emergence from anesthesia and tracheal extubation and compare three groups (two case groups and one control group participants are one hundred twenty adult patients (age: 18-40years old) both sex, undergoing lower abdomen, orthopedics or plastic surgery, Patients under long term treatment (with sedatives, antitussives, angiotensin converting enzyme inhibitors), patients with chronic diseases, or predicted difficult intubation were excluded from the study. All patients received a general anesthesia comprising Propofol, Atracurium and 1% Isoflurane. At the end of surgery, Group A received a bolus dose of remifentanil 0.5 mcg/kg (N = forty), Group B received 1mcg/kg remifentanil (N= forty) and Group C received placebo (normal saline) (N = forty) 90 seconds before extubation. Systolic, diastolic, mean arterial pressure (non-invasively) , heart rate and SaO_2 were measured,1minute before and 1minute interval after extubation to fifth minute after extubation. All patients were ASA physical status I-II according to the ASA's classification system.

In our study Remifentanil decrease in the systolic, diastolic, mean arterial pressure (non-invasively) and heart rate after extubation compared to the control group, the decrease in blood pressure and heart rate more in group B than in group A,

In the study of Aouad et al. remifentanil administration was associated with slower heart rates during extubation in patients who underwent nasal surgery[14], and also in the study of Lee.[15]

Hall and Thomson found remifentanil as an effective agent in hemodynamic stabilization during intubation and anesthesia.[16-17]

Wu et al assessed the efficacy and safety of low-dose remifentanil for attenuating cardiovascular response to tracheal extubation.[18] They (Wu et al.,) reported that remifentanil at the optimal dose of 0.10 μg/kg/min can effectively prevent cardiovascular response (change of systolic and diastolic blood pressure and heart rate) to tracheal extubation.

Nho et al., also found similar results in their study.[19] Shajar et al., reported in their trial that remifentanil attenuated both mean arterial pressure and heart rate during extubation.[20]

In the study of Nishina administration of 1-2 μg/kg remifentanil attenuated cardiovascular changes during extubation in patients who underwent gynecologic surgery and it did not prolong the recovery.[21]

In our study, apnea in group A occurs in 2 patients (2%), in group B occurs in 20 patients (50%), on apnea occur in group C, In present study, Oxygen saturation levels never decreased to less than 97% in neither of the three groups. There were no significant associations between different study groups and both of age and weight of the patients. Considering the findings of this study in association with the literature, the administration of 0.5mcg/kg bolus remifentanil before extubation, seems to be effective in reducing hemodynamic responses after extubation and better than the dose 1mcg/kg which there is high incidence of apnea and more decrease in blood pressure. There were no difference in oxygen saturation among the three groups and never decrease below 97% and no significant association between the groups and both age and weight of the patients.

CONCLUSIONS

1- Patients receiving remifentanil are hemodynamically stable during and after endotracheal extubation in compare with patients receiving normal saline.
2- Patients receiving remifentanil 0.5mcg/kg, hemodynamic measures more close to normal values than patients whose receiving remifentanil 1mcg/kg.
3- Apnea incidence more in patients receiving 1mcg/kg, than in patients receiving 0.5mcg/kg,
4- No difference in oxygen saturation among the three

groups.

5- There were no significant associations between different study groups and both of age and weight of the patients.

RECOMMENDATIONS

We recommend that patients undergoing surgery with endotracheal tube is better to receive low-dose remifentanil 0.5mcg/kg prior to extubation for abolishing hemodynamic response of endotracheal extubation.

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