# PHARMACOLOGICAL METHODS TO DECREASE COUGHING ON EMERGENCE FOLLOWING GENERAL ANESTHESIA WITH TRACHEAL INTUBATION IN LOWER ABDOMINAL SURGERIES

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## ABSTRACT:

***Background:*** Emergence from anesthesia and extubation induces variant physiological responses including unwanted circulatory and airway reflexes resulting in hyper circulatory manifestations in the form of tachycardia, hypertension, cough, laryngospasm, and bronchospasm. These events may predispose or induce multiple complications either in the operative site or elsewhere in the body.

***Aim of the Work:*** To explore various pharmacological peri-operative techniques that can be used to achieve a smooth extubation while caring for an uncomplicated patient without significant risk factors for extubation failure.

***Patients and Methods:*** Randomized sample for population who were admitted for lower abdominal surgery under general anesthesia with oral endotracheal intubation in Ain-Shams University Hospitals after Ethical Committee approval and starting from January 2021.

***Results:*** There is clinical evidence to support the use of Dexmedetomidine, Lidocaine and Dexamethsaone to significantly attenuate excessive coughing, hemodynamic shifts, postoperative sedation and prolongation of time during extubation. Patients' characteristics (age and sex), duration of surgery, type of surgery and Oxygen Saturation show non-significant difference between the four groups.

***Conclusion:*** The quality of tracheal extubation was better in Dexmedetomidine, Lidocaine and Dexamethasone groups over control group with Dexmedetomidine group being the most favorable in patients requiring General anesthesia with endotracheal intubation for lower abdominal surgeries, without any adverse effects.

***Keywords:*** *Anesthesia emergence; Endotracheal; General anesthesia; Emergence Coughing, Dexmedetomidine; Lidocaine; Dexamethasone*

## INTRODUCTION:

Physiological responses remain common during anesthesia emergence (AE) and endotracheal (ET) extubation, causing complications including cough, sore throat, laryngospasm, bronchospasm, and tachy-cardia[(1)].

Post-extubation cough has been repeatedly reported to be associated to mechanical irritations such as external pressure, the ET intubation method, ETT cuff, ET tube (ETT) size, and so forth[(2)].

Coughing frequently occurs on emergence from general anesthesia (GA), and it ensues as the effects of anesthesia

retreat. It allows greater peripheral and central nervous system perception of the tracheal irritation caused by the endotracheal tube. In addition to being uncomfortable, coughing has harmful physiological consequences as; increased intrathoracic pressure, decreased venous return to the right atrium, increased intra-abdominal pressures and decreased functional residual capacity[(3)]**.** It increases blood pressure (BP), heart rate (HR) as well as increases the incidence of myocardial ischemia, bronchospasm, and bleeding[(4)]**.** It multiplies the pain caused by surgery and increases intracranial and intraocular pressure in patients with brain involvement or glaucoma[(5)]**.**

Also the physiological sequelae of peri-extubation coughing may lead to significant complications, including neck hematoma after thyroidectomy[(6)]**,** wound dehiscence after laparotomy[(7)]**,** and intracerebral hemorrhage after intracranial surgery. As such, a 'smooth emergence', aiming to minimize coughing and subsequently avoid these complications, has been advocated[(8)]**.**

Given the multitude of publications on various medical strategies to decrease peri-extubation coughing, and the lack of clarity on what is the best evidence based strategy, a more thorough study of the published data is warranted[(8)]**.**

Also, it should be noted that the COVID-19 pandemic has heightened the importance of developing the knowledge of effective techniques to achieve smooth emergence. In an effort to reduce the transmission of COVID-19 to healthcare workers, altered extubation setups have been devised to physically shield workers from aerosol and droplets generated during extubation[(9&10)]**.**

A range of methods is available to reduce post extubation coughing, such as local and IV injection of topical anesthetics[(11)]. Furthermore, IV use of opioids is an alternative to reduce cough at the end of the operation and during ET extubation[(12)]**.** Also, dexamethasone is a potent corticosteroid with analgesic, anti-inflammatory, and antiemetic properties. Preoperative IV dexamethasone has been reported to reduce the incidence of postoperative pain and swelling following surgeries[(13&14)]**.**

Dexmedetomidine (DEX), an $\alpha_2$-adrenoceptor agonist with antinociceptive, sedative, and hypotensive actions, and when infused, it reduces HR, systemic vascular resistance, and BP. Studies found that DEX alone can reduce cough without decrease in respiratory rate[(15)]**.** Furthermore, other studies suggested that DEX and lidocaine, respectively, reduces cough[(16)]**.**

## AIM OF THE WORK:

The goal of this study is to explore various pharmacological perioperative techniques that can be used to achieve a smooth extubation while caring for an uncomplicated patient without significant risk factors for extubation failure.

The study determines the relative efficacies of Dexmedetomidine IV, Lidocaine IV and Dexamethasone IV in decreasing the incidence of moderate to severe emergence coughing and accomplishment of better quality of emergence from general anesthesia as evidenced by stable mean arterial pressure (MAP), heart rate (HR), without hypotension, delayed recovery, and excessive sedation in lower abdominal surgeries conducted under general anesthesia using endotracheal tube.

## PATIENTS AND METHODS:

- **Type of Study:** Randomized Double-blinded controlled clinical trial.
- **Study Setting:** Randomized sample for population who were admitted for lower abdominal surgery under general

anesthesia with oral endotracheal intubation in Ain-Shams University Hospitals after Ethical Committee approval.

- **Study Period:** Starting from January 2021.
- **Study population:** Patients undergoing lower abdominal surgery under general anesthesia with oral endotracheal intubation.
- **Inclusion Criteria:**

1. Adult Patients (18 years- 50 years).
2. Both sexes.
3. Patients American Society of Anesthesiologists physical status (ASA) Class I.
4. Mallampatti Class I.
5. Patients who are intubated using ETT.
6. Patients who are undergoing elective lower abdominal surgery under general anesthesia.
7. Patients whose surgeries are less than 90 minutes.

- **Exclusion Criteria:**

1- Using nasogastric tube.

2- Patients having contraindication or allergy to any of the study medications and patients on corticosteroid therapy.

3- Pregnant females and addicts.

4- Patients with history of surgery or pathology of larynx and trachea.

5- Patients suffering from lower esophageal sphincter incompetence (reflux).

6- Body mass index >30.

*The exclusion of these cases who were of increased risk of postoperative airway symptoms because of ethical reasons and the potential of bias.*

- **Sampling Method:** Patients were divided by computer-generated simple randomization.
- **Sample Size:** 120 patients divided into 4 groups

Sample size was calculated using PASS 11.0. Based on a study carried out by Tung et al. in 2020[(3)], which showed that emergence coughing after GA affects 40-76% of intubated patients, a sample of 30 patients per group (30 x 4 = 120 in total) achieves 81 % power to detect an odds ratio of 53.545 using two sided McNemar test with significance of 0.05. The odds ratio is equivalent to a difference between two paired proportions of 0.289 which occurs when the proportion in cell 1,2 is 0.295 and the proportion in cell 2,1 is 0.006. The proportion of discordant pairs is 0.30.

- **Ethical Considerations*:*** Approval of the Research and Ethical Committees of Faculty of Medicine, Ain Shams University is obtained and written informed consents are taken from all patients included in the study.
- **Study Procedure: The study included 120 patients fulfilling the inclusion criteria, 30 patients in each group; divided as following:**

  - Group DX: Patients received Dexmedetomidine 0.5 mcg/kg IV at surgery end.
  - Group L: Patients received Lidocaine 1.5 mg /kg IV at the end of surgery.
  - Group D: Patients received Dexamethasone 8 mg IV at the end of surgery.
  - Placebo Group (P): Patients didn't receive any medication.

- **All patients were subjected to the following:**

After hospitalization, thorough history taking from all patients was done with examination (general and respiratory) and

full pre-operative investigations (complete blood count, partial thromboplastin time, prothrombin time, INR, liver and kidney function tests) were done and recorded in their hospital charts.

All patients were assessed preoperatively, and were instructed to fast for 8 hrs. In the preparation room, Intravenous access was established and crystalloid Ringer solution was infused by rate 5 ml/kg. On arrival to the operation theatre, monitors for non-invasive blood pressure, heart rate, electrocardiogram (ECG), end-tidal carbon dioxide ($ETCO_2$), and pulse oximetry ($SpO_2$) were used all the time before induction of anesthesia, throughout surgery, and during ET extubation. All the patients had the same anaesthesia protocol; 1 μg/kg fentanyl, every patient was pre-oxygenated for 3-5 minutes and subsequently, anesthesia unconsciousness was induced with 1 mg/kg propofol and 0.5 mg/kg IV atracurium was given for muscle relaxation and assisted ventilation by bag and mask for 3 minutes was maintained. After confirmation of adequate anesthesia and muscle relaxation, direct laryngoscopy by the same anesthesiologist for all patients via 3 or 4 standard metal Macintosh blade then orotracheal intubation was done using high volume low pressure single use PVC-cuffed endotracheal tube (ETT) with appropriate size for each patient (usually size 7.5 mm and 7.0 mm in male and female patients respectively).

For all groups, one brand of ETTs were used; (PVC, ultramed, Ultra for Medical Products Co., Abnob, Assiout, Egypt). ETT Cuff was inflated till there was no air leak with manual bag ventilation while the ABL valve creating +20 cmH2O, or maximum 7 ml of air. Thus, all participants were in the same condition for irritation by the ETT cuff.

ETT position was confirmed and secured. Mechanical ventilation using tidal volume of 8 ml/kg was adjusted to maintain end tidal carbon dioxide between 30 and 35 mmHg. Anesthesia was continued through isoflurane (MAC 1.2), oxygen 100%, top up doses of atracurium (maintenance dose) every 20 minutes and opioid when needed as standard procedure keeping heart rate (HR) and mean arterial pressure (MAP) within 20% of preoperative baseline values.

- ***Study intervention:***

The intervention is a pharmacological method. Medications include Dex-medetomidine 0.5 mcg/kg, Lidocaine 1.5 mg /kg and Dexamethasone 8 mg. Each drug was given to the patient at the end of surgery intravenously over 10 minutes with the intent of smoothing emergence or decreasing coughing on extubation.

Participants were randomly assigned to one of the four groups at the end of surgery. At the beginning with subcutaneous wound closure, the inhaled isoflurane was titrated to MAC 1% and patients received either dexmedetomidine 0.5 μg/kg, lidocaine 1.5 mg/kg or dexamethasone 8 mg intravenous and no medication in the last group, respectively, in a 10 mL volume (for each) over 10 min in their corresponding groups. The patients were kept blinded to the group they were assigned.

At the end of the operation after completion of skin closure, inhalational anesthetic was discontinued, the residual neuromuscular block was antagonized with neostigmine 0.05 mg/kg and atropine 0.02 mg/kg and 100% Oxygen was administrated at 6 L/min till extubation. The patients were stimulated gently with intermittent verbal requests to open their eyes. The tracheal tube cuff was deflated and extubation was done by the same anesthesiologist after clearing any secretions from the upper airway by gentle suctioning, following adequate spontaneous respiration and full consciousness of the patients confirmed by eye opening in response to stimuli. All patients received oxygen through face mask

after extubation and in post anesthesia care unit (PACU).

Heart rate, MAP, and $SpO_2$ were recorded before anesthesia, after drug administration, 0 minutes after tracheal extubation and every 10 minutes after extubation during recovery up to 30 minutes.

A cough was considered real when the patient spontaneously and quickly exhaled, whereas the sound of a cough was heard. Coughing incidence and severity were recorded by an assessor anesthiologist, blinded to the intervention group drugs, from the time that isoflurane was discontinued until five minutes after extubation and then was graded according to the modified Minogue scale ***(Minogue and Ralph, 2004)*** [17].

Also, the time from discontinuation of isoflurane to extubation was recorded (Extubation time). In addition, the patient's postoperative (PO) level of sedation was assessed according to Rasmay sedation scale (RSS).

Patients were observed for any complications for 24 hours which were managed by an attending anesthesiologist.

- ***The primary Outcome is to evaluate:***

  ✓ ***Extubation quality:*** Extubation quality was rated depending on the coughing grade **according to the modified Minogue scale [17]*:***

  - Grade 1 (none) = No coughing or muscle stiffness.
  - Grade 2 (mild) = Coughing once or twice or transient cough response to removal of tracheal tube that resolved with extubation.
  - Grade 3 (moderate) ≤ 3 coughs lasting 1 to 2 seconds or total duration of cough less than 5 seconds.
  - Grade 4 (severe) ≥ 4 coughs with each lasting > 2 seconds or total coughing duration > 5 seconds.

- ***The secondary outcomes were:***

  1. **Postoperative sedation level:** it will be rated using **Ramsay Sedation Scale [18]*:***

  - Score 1 = Anxious, agitated and restless.
  - Score 2 = Cooperative, oriented and tranquil.
  - Score 3 = Responsive to commands only.
  - Score 4 = Brisk response to light glabellar tap or loud auditory stimulus.
  - Score 5= Sluggish response to light glabellar tap or loud auditory stimulus.
  - Score 6 = No response to light glabellar tap or loud auditory stimulus.

  2. **Extubation time:** which is the time from end of inhalational anesthesia administration until extubation**.**

## RESULTS:

This double blinded randomized controlled trial was conducted on 120 people divided into 4 groups; Group DX: 30 patients received 0.5 mcg/kg dexmedetomidine i.v., Group L: 30 patients received 1.5 mg/kg i.v., Group D: 30 patients received 8 mg dexamethasone i.v. and Group P: 30 patients didn't receive any medication, in a 10 mL volume (for each) over 10 min before extubation in their corresponding groups.

### A. Demographic data and patients' characteristics:

Table 1 shows insignificant difference between the 4 groups as regard to patients' characteristics (age and sex), duration of surgery and type of surgery (P> 0.05).

Table (1): Comparison of mean±standard deviation of age, sex, surgery and surgery duration.

| | | Group DX | Group L | Group D | Group P | Test value | P-value | Sig. |
|---|---|---|---|---|---|---|---|---|
| | | No. = 30 | No. = 30 | No. = 30 | No. = 30 | | | |
| Age (y) | Mean ± SD | 38.63 ± 5.87 | 38.80 ± 6.72 | 38.43 ± 7.22 | 38.97 ± 8.17 | 0.032• | 0.992 | NS |
| | Range | 25 – 48 | 23 – 49 | 25 – 50 | 22 – 50 | | | |
| Sex | Female | 15 (50.0%) | 13 (43.3%) | 16 (53.3%) | 12 (40.0%) | 1.339* | 0.720 | NS |
| | Male | 15 (50.0%) | 17 (56.7%) | 14 (46.7%) | 18 (60.0%) | | | |
| Surgery type | Appendectomy | 19 (63.3%) | 19 (63.3%) | 17 (56.7%) | 15 (50.0%) | 1.509* | 0.680 | NS |
| | Hernioplasty | 11(36.7%) | 11 (36.7%) | 13 (43.3%) | 15 (50.0%) | | | |
| Surgery duration (min) | Mean ± SD | 80.00 ± 4.55 | 80.50 ± 4.42 | 81.67 ± 3.03 | 81.17 ± 4.29 | 0.949• | 0.419 | NS |
| | Range | 70 – 85 | 70 – 85 | 75 – 85 | 70 – 85 | | | |

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS) *:Chi-square test; •: One Way ANOVA test

**B. Hemodynamic changes and monitoring:**

**1- HR:**

Table 2 shows significant difference between the 4 groups as regard to heart rate at all examined timings after drug administration (P value<0.01).

At T1 lower HR observed in the DX and L than the D and P groups (P<0.01). Also, according to Post Hoc analysis, the HR was significantly lower in DX group than L group (P1 = 0.000).

At T2 the stress response to extubation was suppressed at DX group and L group than D group and P group, depending on the heart rate (P<0.01). And based on Post Hoc analysis HR was the least in DX group compared to L group (P1=0.000), D group (P2=0.000) and P group (P3=0.000). Yet HR was lower in D group than P group (p6=0.042).

Table (2): Comparison of Heart Rate at different study timings in the four groups.

| HR (bpm) | | Group DX | Group L | Group D | Group P | Test value | P-value | Sig. |
|---|---|---|---|---|---|---|---|---|
| | | No. = 30 | No. = 30 | No. = 30 | No. = 30 | | | |
| Before anesthesia (T0) | Mean ± SD | 80.50 ± 5.08 | 81.23 ± 4.08 | 81.77 ± 3.24 | 81.97 ± 3.83 | 0.762• | 0.518 | NS |
| | Range | 70 – 89 | 74 – 89 | 75 – 88 | 76 – 88 | | | |
| After drug administration (T1) | Mean ± SD | 74.27 ± 3.06 | 83.73 ± 3.87 | 85.37± 1.47 | 85.83 ± 4.01 | 83.114• | 0.000 | HS |
| | Range | 70 – 79 | 77 – 90 | 82 – 88 | 80 – 95 | | | |
| After extubation | | | | | | | | |
| 0 min (T2) | Mean ± SD | 75.27 ± 3.81 | 88.97 ± 3.86 | 96.40 ± 2.13 | 99.07 ± 8.18 | 135.212• | 0.000 | HS |
| | Range | 71 – 83 | 81 – 96 | 92 – 100 | 89 – 122 | | | |
| 10 min (T3) | Mean ± SD | 79.77 ± 4.54 | 91.10 ± 3.35 | 102.50 ± 1.78 | 104.23 ± 2.50 | 376.006• | 0.000 | HS |
| | Range | 72 – 88 | 84 – 97 | 100 – 105 | 100 – 110 | | | |
| 20 min (T4) | Mean ± SD | 81.40 ± 4.22 | 93.07 ± 3.13 | 89.33 ± 2.06 | 91.77 ± 4.70 | 60.788• | 0.000 | HS |
| | Range | 75 – 88 | 87 – 98 | 85 – 97 | 85 – 101 | | | |
| 30 min (T5) | Mean ± SD | 83.90 ± 3.99 | 93.93 ± 2.88 | 85.03 ± 1.45 | 92.07 ± 4.53 | 64.361• | 0.000 | HS |
| | Range | 77 – 90 | 89 – 97 | 82 – 87 | 86 – 101 | | | |
| Post Hoc analysis by LSD | | | | | | | | |
| | | P1 | P2 | P3 | P4 | P5 | P6 | |
| After drug administration (T1) | | 0.000 | 0.000 | 0.000 | 0.055 | 0.014 | 0.581 | |
| 0 min after extubation (T2) | | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.042 | |
| 10 min after extubation (T3) | | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.039 | |
| 20 min after extubation (T4) | | 0.000 | 0.000 | 0.000 | 0.000 | 0.173 | 0.012 | |
| 30 min after extubation (T5) | | 0.000 | 0.202 | 0.000 | 0.000 | 37.000 | 0.000 | |

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS) , •: One Way ANOVA test

**2- MAP:**

Table 3 shows significant difference between the 4 groups as regard to mean arterial pressure at all examined timings after drug administration (P value<0.01)

At T1 MAP was lower in the DX and L than the D and P groups (P<0.01). According to Post Hoc analysis, the MAP was insignificantly lower in DX group than L group (P1 = 0.167), but was significantly lower than D group (P2=0.000) and P group (P3=0.000). MAP was significantly lower in D group than P group as well (P6=0.000).

At T2 the MAP increase during extubation was significantly suppressed the most at DX group compared to L group, D group and P group (P<0.01). And based on Post Hoc analysis MAP was the least in DX group in comparison to L group (P1=0.000), D group (P2=0.000) and P group (P3=0.000).

Table (3): Comparison of mean Blood pressure at different study timings in the four groups.

| MAP (mmHg) | | Group DX | Group L | Group D | Group P | Test value | P-value | Sig. |
|---|---|---|---|---|---|---|---|---|
| | | No. = 30 | No. = 30 | No. = 30 | No. = 30 | | | |
| Before anesthesia (T0) | Mean ± SD | 88.80 ± 3.07 | 87.30 ± 4.26 | 87.07 ± 4.14 | 88.50 ± 3.63 | 1.537• | 0.209 | NS |
| | Range | 85 – 98 | 80 – 95 | 79 – 98 | 83 – 97 | | | |
| After drug administration (T1) | Mean ± SD | 86.57 ± 1.87 | 87.83 ± 3.86 | 91.10 ± 2.51 | 95.53 ± 5.02 | 38.549• | 0.000 | HS |
| | Range | 85 – 90 | 80 – 98 | 89 – 96 | 86 – 100 | | | |
| After extubation | | | | | | | | |
| 0 min (T2) | Mean ± SD | 89.83 ± 1.39 | 98.63 ± 7.81 | 96.80 ± 1.94 | 110.07 ± 6.30 | 79.454• | 0.000 | HS |
| | Range | 88 – 94 | 90 – 120 | 92 – 100 | 100 – 120 | | | |
| 10 min (T3) | Mean ± SD | 88.83 ± 4.24 | 91.63 ± 1.40 | 103.00 ± 5.64 | 112.17 ± 6.11 | 155.676• | 0.000 | HS |
| | Range | 80 – 95 | 90 – 95 | 94 – 112 | 100 – 120 | | | |
| 20 min (T4) | Mean ± SD | 86.67 ± 1.40 | 94.63 ± 1.88 | 105.57 ± 5.39 | 111.67 ± 3.30 | 327.994• | 0.000 | HS |
| | Range | 85 – 90 | 92 – 100 | 95 – 115 | 100 – 115 | | | |
| 30 min (T5) | Mean ± SD | 82.40 ± 1.85 | 104.50 ± 4.02 | 95.03 ± 1.25 | 108.40 ± 4.97 | 350.808• | 0.000 | HS |
| | Range | 80 – 86 | 100 – 110 | 92 – 97 | 100 – 116 | | | |

| Post Hoc analysis by LSD | | | | | | |
|---|---|---|---|---|---|---|
| | P1 | P2 | P3 | P4 | P5 | P6 |
| After drug administration (T1) | 0.167 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| 0 min after extubation (T2) | 0.000 | 0.000 | 0.000 | 0.171 | 0.000 | 0.000 |
| 10 min after extubation (T3) | 0.023 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| 20 min after extubation (T4) | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| 30 min after extubation (T5) | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS). •: One Way ANOVA test

**3- $SaO^2$:**

Table 4 shows insignificant difference between the 4 groups as regards Oxygen Saturation at all examined timings (P value>0.05).

Table (4): Comparison of Oxygen saturation at different study timings in the four groups.

| SaO2 (%) | | Group DX | Group L | Group D | Group P | Test value | P-value | Sig. |
|---|---|---|---|---|---|---|---|---|
| | | No. = 30 | No. = 30 | No. = 30 | No. = 30 | | | |
| Before anesthesia (T0) | Mean ± SD | 98.03 ± 0.72 | 98.23 ± 0.82 | 98.20 ± 0.96 | 98.43 ± 0.82 | 1.165• | 0.326 | NS |
| | Range | 97 – 99– | 97 – 100 | 97 – 100 | 97 – 100 | | | |
| After drug administration (T1) | Mean ± SD | 99.20 ± 0.71 | 99.37 ± 0.61 | 99.50 ± 0.68 | 99.40 ± 0.67 | 1.032• | 0.381 | NS |
| | Range | 98 – 100 | 98 – 100 | 98 – 100 | 98 – 100 | | | |
| After extubation | | | | | | | | |
| 0 min (T2) | Mean ± SD | 97.23 ± 0.94 | 97.30 ± 0.92 | 97.27 ± 1.05 | 97.17 ± 0.95 | 0.105• | 0.957 | NS |
| | Range | 96 – 99 | 96 – 99 | 96 – 99 | 96 – 99 | | | |
| 10 min (T3) | Mean ± SD | 97.63 ± 0.49 | 97.70 ± 0.75 | 97.53 ± 0.51 | 97.30 ± 1.09 | 1.640• | 0.184 | NS |
| | Range | 97 – 98 | 97 – 99 | 97 – 98 | 96 – 99 | | | |
| 20 min (T4) | Mean ± SD | 98.43 ± 0.63 | 98.50 ± 0.63 | 98.37 ± 0.61 | 98.23 ± 0.73 | 0.917• | 0.435 | NS |
| | Range | 97 – 99 | 97 – 99 | 97 – 99 | 97 – 99 | | | |
| 30 min (T5) | Mean ± SD | 99.33 ± 0.61 | 99.23 ± 0.73 | 99.13 ± 0.78 | 99.13 ± 0.82 | 0.507• | 0.678 | NS |
| | Range | 98 – 100 | 98 – 100 | 98 – 100 | 98 – 100 | | | |

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS) •: One Way ANOVA test

## C. Outcomes:

### 1- The Primary Outcome is Extubation quality depending on coughing grade:

In our study, the results showed in Table 5 revealed that a statistically significant difference was observed in emergence coughing grade according to modified Minogue scale among the 4 groups (P < 0.05). The moderate to severe (Grade 3 & 4) emergence coughing was significantly decreased in group DX than in group L, group D and group P where it was the highest ratio (3.3%, 10%,16.7 and 26.7%. respectively).

### 2- PO sedation level:

Given the results in Table 5, a statistically significant difference was seen in RSS among the 4 groups (P<0.01). The RSS level 3 was significantly higher in group DX than in group L compared to group D and group P where there was no RS level 3.

### 3- Extubation Time:

Comparing Extubation Time among 4 groups in table 5 showed that, no significant difference was observed among groups (P>0.05).

Table (5): Outcomes, Data are presented as number of patients.

| | | Group DX | Group L | Group D | Group P | Test value | P-value | Sig. |
|---|---|---|---|---|---|---|---|---|
| | | No. = 30 | No. = 30 | No. = 30 | No. = 30 | | | |
| Coughing grade according to modified Minouge scale (1-6) | Grade 1 | 23 (76.7%) | 20 (66.7%) | 16 (53.3%) | 11 (36.7%) | 12.711* | 0.047 | S |
| | Grade 2 | 6 (20.0%) | 7 (23.3%) | 9 (30.0%) | 11 (36.7%) | | | |
| | Grade 3+4 | 1 (3.3%) | 3 (10.0%) | 5 (16.7%) | 8 (26.7%) | | | |
| PO sedation level according to Rasmey Sedation score(1-4) | Level 1 | 2 (6.7%) | 6 (20.0%) | 18 (60.0%) | 18 (60.0%) | 38.568* | 0.000 | HS |
| | Level 2 | 20 (66.7%) | 21 (70.0%) | 12 (40.0%) | 12 (40.0%) | | | |
| | Level 3 | 8 (26.7%) | 3 (10.0%) | 0 (0.0%) | 0 (0.0%) | | | |
| Extubation time (min) | Mean ± SD | 9.70 ± 1.37 | 9.07 ± 1.87 | 8.77 ± 2.01 | 8.70 ± 1.51 | 2.134• | 0.100 | NS |
| | Range | 7 – 13 | 5 – 12 | 5 – 12 | 5 – 11 | | | |

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS). *:Chi-square test; •: One Way ANOVA test

**DISCUSSION:**

There have been various reported frequencies of cough during emergence from anesthesia. It is reported that they occur in 30-70% patients after extubation. Such cough responses occur from the chemically or mechanically sensitive ascending vagus nerve **(19)**.

The physiological and morbid consequences of emergence coughing have led to multiple studies examining different medications to decrease peri-extubation coughing. However, prior systematic reviews were limited in scope regarding medications covered**(3)**.

Also, in addition to emergence coughing, recovering from anesthesia results in elevated catecholamine concentration following anesthetic withdrawal which is further aggravated by laryngeal manipulation occurring during extubation**(20)**.

The main purpose of this study was to test the hypothesis that intravenous administration of dexmedetomidine, lidocaine and Dexamethasone before extubation would reduce the incidence and severity of post-extubation cough with safe hemodynamic changes or complications in patients undergoing lower abdominal surgery with general anesthesia using orotracheal intubation.

This randomized controlled trial was conducted over 120 eligible people undergoing general anesthesia using endotracheal intubation for lower abdominal surgery, divided randomly into 4 groups; Group DX: 30 patients received dexmedetomidine 0.5 mcg/Kg i.v., Group L: 30 patients received 1.5 mg/kg lidocaine i.v., Group D: 30 patients received 8 mg dexamethasone i.v. and Group P: 30 patients didn't take any drug, in a 10 mL volume (for each) over 10 min before extubation in their corresponding groups.

As regards patients' characteristics, to avoid potential confounding factors that may affect the incidence and severity of postoperative cough, we selected patients with close ages as seen in Table 1, and near the same weight, ASA and Mallampati classification. Also we used the same type of endotracheal tube between the groups, minimized surgical excision to decrease the requirement of postoperative analgesics, and used a surgical site distal to the airway structures.

No statistically significant difference was observed among the 4 groups regarding to age, gender, Duration of surgery, type of surgery and $SaO_2$, as was found in Table 1 and Table 4.

As regard emergence coughing, this study demonstrated that all medications studied (dexmedetomidine, lidocaine i.v. and Dexamethasone) significantly decreased the incidence of moderate to severe periextubation coughing in comparison with placebo (Group P).

Our study showed that Dexmedetomidine i.v. (Group DX) had the highest cumulative likelihood of ranking first with respect to significantly decreasing the incidence of moderate and severe emergence coughing, followed by lidocaine i.v. (Group L) and then dexamethasone i.v. (Group D).

Dexmedetomidine, a potent alpha-adrenoceptor agonist, has become one of the used drugs in the anesthetic armamentarium, along with routine anesthetic drugs, because of its hemodynamic, sedative, anxiolytic, analgesic, neuroprotective, and anesthetic sparing effects. The α1 to α2 ratio of 1: 1600 makes it a highly selective α2 agonist compared with clonidine, thus reducing the unwanted side effects involving α1 receptors **(20)**.

Lidocaine, the first aminoamide local anesthetic, also acts for inhibition of cough or strain associated with tracheal extubation that could cause hypertension and tachycardia through attenuation of the activity in afferent C fibers from the larynx. In addition, lidocaine may act centrally to

increase the depth of anesthesia. The valuable effect of lidocaine on suppressing the hemodynamic perturbations to extubation may be because of its direct cardiac depression and peripheral vasodilatation as it could significantly depress all excitable membranes including the heart **(21).**

In agreement with our results, Bindu et al. demonstrated that IV infusion of 0.5 microgram per kilogram (mcg/kg) of dexmedetomidine 15 minutes before the end of surgery reduced the amount of coughing upon emergence **(22).**

Also, Rajendram and colleagues' meta-analysis determined lidocaine i.v. to be the least effective at preventing emergence coughing, among other drugs including dexmedetomidine and remifentanil **(3).**

In contrast to our study, another previous study showed that Intravenous dexmedetomidine did not effectively reduce straining or coughing associated with extubation compared with lidocaine and that was because of using a different methodology in that previous study which was using a higher intravenous lidocaine dose of 2 mg/kg, also another timing which was 1 min before extubation and a different population including both children and adults**(21).**

Also Contrary to our study, in a previous study lidocaine combined with dexamethasone did not reduce the incidence of postoperative cough compared with dexamethasone alone. Although the reason is unclear, the controversy may be due to the dose of lidocaine, in that previous study, insufficiency to additionally suppress coughing that has already been suppressed by intravenous dexamethasone, in addition to the difference of criteria for study inclusion and exclusion**(23).**

Other considerations should be taken into account when selecting a pharmacological intervention to decrease emergence coughing, such as hemodynamic effects, perioperative patients' oxygen saturation, postoperative sedation level, extubation times, and adverse events.

For hemodynamic effects and adverse events of the study Medications, Our study showed that all the study groups (DX, L and, D) are associated with a significant and comparable Difference in HR and MAP (but still within normal ranges) after administration of the study drugs compared to group P ($P< 0.05$), according to One Way ANOVA test. Based on Post Hoc analysis by LSD, the highest significant difference was found in comparing group DX to each one of the 3 groups (P1, P2 and $P3 < 0.01$).

As Regards the results in Table 2 and Table 3, a temporary decrease was seen in HR and MAP among Group DX after drug administration. At (T1) HR and MAP were the least in group DX then higher in group L and group D and the highest in group P. This decrease in HR and MAP was through 10 min interval after drug administration (T1), but within the normal range and without respiratory depression, hypoxemia (No $SaO_2$<95%) or adverse effects. None of the patients sustained bradycardia or hypo-tension sufficient to require pressor or sympathomimetic drugs after extubation. No arrhythmia, evidence of myocardial ischemia, or hypoxemia was observed within the 4 groups over the indicated study times.

It was found that HR and MAP increased immediately after tracheal extubation (T2) in Group P, Group D, to lesser extent in Group L and the least increase was in Group DX ($P<0.05$). This increase remained for 1 minute in group DX, 3 minutes in Group L, 5 minutes in Group D and 9 minutes in group P, then started to fade 10 minutes after extubation becoming stable during the indicated study period. Therefore, dexmedetomidine likely reduced the sympathetic response to extubation which is favorable over lidocaine and dexamethasone.

As regard Rasmay sedation score (RSS) for PO sedation as in Table 5, a statistically significant difference was seen in RSS among the groups (P<0.05). After arrival in PACU, the Rasmay Sedation Score was significantly higher in the DX group and L group (level 1, 2 and 3) compared to D group and P group (level 1 and 2 only). However, all patients in all groups were arousable and responded to oral commands in the PACU and in the ward.

Lastly, based on our results, no significant differences were recorded in extubation time between the groups (P> 0.05) and so there's no statistically significant prolongation of the recovery in either group.

The limitations of our study should be noted. First, the large degree of heterogeneity in medication dosage. We attempted to delineate this effect by using high-quality dose-finding studies related to the effect of the study's drugs on peri-extubation coughing. Another limitation is that cough and coughing severity may be a subjective interpretation of the participant's actions, raising the issue of inter-observer variability and bias so we used a blinded anesthesiologist for coughing assessment. Lastly, the sample size enrolled in our study was limited to adult patients, and hence, it cannot predict the coughing suppression effect of the studied drugs during emergence in pediatric patients receiving the same doses scheduled in our study, so further investigations are needed on wider population with different ages in order to concur our results, to confirm their safety, and to support the absence of any complication.

**Conclusion:**

The quality of tracheal extubation was better in Dexmedetomidine, Lidocaine and Dexamethasone groups over P group with Dexmedetomidine group was the most favorable in patients requiring General anesthesia with endotracheal intubation for lower abdominal surgeries, without any adverse effects.

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# الطرق الدوائية لتقليل السعال عند الصحو من التخدير الكلي مع التنبيب الرغامي في العمليات الجراحية بالجزء السفلي من البطن

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**الخلفية:** يستحث الصحومن التخدير ونزع الأنبوب الرغامي استجابات فسيولوجية متباينة بما في ذلك ردود الفعل غير المرغوب فيها في الدورة الدموية والمجرى الهوائي مما يؤدي إلى مظاهر فرط الدورة الدموية في شكل تسرع القلب وارتفاع ضغط الدم والسعال والتشنج الحنجري والتشنج القصبي. قد تؤهب هذه الأحداث أو تسبب مضاعفات متعددة إما في موقع الجراحة أو في أي مكان آخر من الجسم.

**الهدف من البحث:** لاستكشاف تقنيات دوائية مختلفة محيطة بالجراحة يمكن استخدامها لتحقيق نزع الأنبوب الرغامي السلس أثناء رعاية مريض بدون مضاعفات و بدون عوامل خطر كبيرة لفشل نزع الأنبوب..

**المرضى والطرق:** في هذه الدراسة، قمنا بمقارنة ثلاث تقنيات دوائية لتسهيل نزع الأنبوب الرغامي السلس : تشمل الأدوية ديكسميديتوميدين ٠.٥ ميكروجرام / كيلوجرام، ليدوكايين ١.٥ ميلي جرام لكل كيلوغرام و ديكساميثازون ٨ ميلي جرام. تم إعطاء كل دواء للمريض في نهاية العملية الجراحية عن طريق الوريد على مدار ١٠ دقائق لتقليل السعال المتوسط إلى الشديد عند الصحو من التخدير الكلي مع التنبيب الرغامي في جراحات أسفل البطن، بهدف تجنب السعال و مضاعفاته.

**النتائج و الإستنتاج:** قد يُنظر إلى ديكسميديتوميدين، مثل ليدوكايين وديكساميثازون، كخيار دوائي لتقليل ظهور السعال ولتسهيل نزع الأنبوب الرغامي، نظرًا لقلة الآثار الجانبية. ومع ذلك، من المعقول أن يكون ديكسميديتوميدين هو الأفضل لهذا الغرض بناءً على النتيجة التي توصلنا إليها.

بالإضافة إلى ذلك، دعمت نتيجة هذه الدراسة استخدام هذه الأدوية لتخفيف و تقليل التغيرات في الدورة الدموية، والتقرح في الحلق، والإفراط في الكحة وإطالة الوقت أثناء نزع الأنبوب الرغامي.