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Research Article

Intratracheal Dexmedetomidine versus Lidocaine for Smooth Tracheal Extubation in Patients Undergoing Eye Surgery: Controlled Randomized Study

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Abstract

Background: Coughing during awakening from general Anesthesia can compromise the outcome of the undergoing eye surgery. **Objectives:** To evaluate and compare the effectiveness and safety of administering intratracheal lidocaine or dexmedetomidine to patients undergoing eye surgery. **Methods:** In this prospective, randomized, double-blinded, controlled trial, 120 American Society of Anesthesiologists (ASA) I and II patients were scheduled for elective keratoplasty and retinal detachment surgery under general Anesthesia. The patients' ages ranged from 18 to 60 of either sex. They randomly divided into three groups, the medication sprayed to patients via their intratracheal tubes, 40 patients in each group: Group D: Received (0.5 µg/kg) of dexmedetomidine diluted in 5 ml saline, Group L: Received (5ml) 2% of lidocaine and Group C: Received 5ml saline. The frequency of coughing in the three groups was the primary finding. The secondary outcomes were awareness time, extubation time, IOP, hemodynamic changes, surgeon satisfaction, and any complication. **Results**: Compared with Group C, cough was significantly reduced in both groups D and L *($P \leq 0.0001$)* with significant increase in cough grade 0 in group D when compared with group L *($P \leq 0.036$)*. The surgeons in groups D and L reported higher satisfaction levels than those in group C. Additionally, intratracheal dexmedetomidine and lidocaine treatment enhanced hemodynamic stability and maintained the IOP without causing any noticeable side effects. **Conclusions:** Intratracheal dexmedetomidine reduced the cough reflex more effectively than lidocaine. However, they both contributed to a smooth extubation and a balanced anesthetic recovery following eye surgery.

Keywords: dexmedetomidine, lignocaine spray, tracheal extubation, coughing, intraocular pressure.

Introduction

The decision to use a certain anesthetic approach during ocular surgery has an important consequence on the patient, the surgeon, and the anesthesiologist[1]. Although local anesthetics are the most common type of ocular Anesthesia, general Anesthesia may be utilized in children and a variety of adult patients, during lengthy complex surgeries and patients with tremor, incapable of keeping a flat position, or claustrophobic[2].

Coughing during awakening from general Anesthesia following ophthalmological surgery can produce a harmful consequence, such as bronchospasm, hemodynamic instability, and increased bleeding at the surgical site[3,4]. Additionally, it induces an increase in the intraocular

pressure, which harms the outcomes of such surgeries as penetrating keratoplasty, vitrectomy, open globe repair. Therefore, several anesthesiologists have been investigating avenues to reduce such laryngeal irritation and facilitating smoother extubation,[5,6] such as intravenous lidocaine[7], dexmedetomidine and remifentanil [8].

The usage of lidocaine has been mentioned in much research for eliminating cough reflex during extubation and facilitating smooth extubation since it is easy to use and has no serious side effects [9]. Lidocaine is administered through a variety of routes, including intravenous injection, topical spray on the laryngeal inlet, in cuff of the endotracheal tube (ETT), and spraying down the ETT[9-12]. Dexmedetomidine, a potent alpha adrenoceptor agonist which attenuates airway-circulatory reflexes, highly beneficial and successful for obtaining better sedation and analgesia [13] and reduced IOP during intubation and extubation[14,15] whatever the methods of administrated such as intramuscular premedication[15], intravenous infusion[8,14], intranasal[13] or Intratracheal[16]. Additionally, Laryngeal reflexes have been reported to be prevented by intratracheal dexmedetomidine instillation due to rapid absorption through the bronchial and alveolar capillary network [16]. However, few trials compare the safety and efficacy of intratracheal dexmedetomidine administration to lidocaine.

This prospective, randomized, double-blinded trial compares the safety and efficacy of intratracheal dexmedetomidine and lidocaine for tracheal extubation in patients undergoing eye surgery.

Methods

This study was approved by the Minia University's Institutional Review Board (identifier ID: 22_2021,), and written informed consent was obtained from all subjects participating in the trial. The trial was registered prior to patient enrollment at clinicaltrials.gov (NCT05291221; https://classic.clinicaltrials.gov/ct2/show/NCT05291221).

We conducted a prospective, randomized, double-blinded study of patients having eye surgery with general anesthesia who were given at Minia University Hospital between the period of March 2021 and March 2022.

Participant: A 120 Participants of either sex, American Society of Anesthesiologists (ASA) I and II with ages ranging from 18 to 60, were scheduled for elective keratoplasty and retinal detachment surgery under general Anesthesia. We excluded patient refused to participate, patients with major organ diseases, significant obesity, body mass index (BMI) >40/m2, known allergies to the study drugs, pregnant, and lactating women.
Randomization was done according to a computer random number table. The participant and the anesthetist who prepared the drug used in the study were blind to the patient group.

Procedure Steps: The same surgeon carried out all procedures to avoid any possible implications of variation in the surgical method used. A detailed medical history was taken, and a general and physical examination included checking the patient's blood pressure, heart rate, respiration rate, chest, and abdomen. Before the procedure, routine, and pertinent examinations such as a detailed electrocardiogram (ECG) analysis, comprehensive blood analysis, coagulation profile, renal and liver function tests, and random blood sugar were done.

ECG, non-invasive blood pressure, and peripheral oxygen saturation monitors began to record when the patients arrived at the operating room and continued until the patient had been discharged from the operating room. A 20 G cannula had been inserted into the hand's dorsum, and a ringer lactate infusion was started at a rate of 5–10 ml per kilogram every hour. Each participant received the same anesthetic strategy; were premeditated by 0.5mg IV

atropine, IV midazolam 0.05mg/kg and fentanyl 1μg/kg. To induction of Anesthesia, 2.5mg/kg of intravenous propofol 2% supplemented, if necessary, with 0.2 mg/kg aliquots until loss of verbal response and tracheal intubation was made by a cuffed endotracheal tube with an internal diameter of 7.0 mm, as well as atracurium 0.5 mg/kg to facilitate tracheal intubation. Atracurium bolus 0.1 mg/kg and inhalational isoflurane (MAC 1-1.5 in O2) were used to maintain Anesthesia. Tidal volume was kept at 6–8 ml/kg and respiratory rate at 12–14 breaths per minute by an anesthetic machine.

We recorded and compared bradycardia, tachycardia, hypertension, and hypotension. We described bradycardia and tachycardia as an HR ≤ 50 or >100 beats/min while hypertension and hypotension as an MBP ≤ 30% or >30% from the baseline reading for 5 min.

Fifteen minutes before the operation's end, 5 ml of tested drug in medical spray bottle was sprayed down the intratracheal tube of all patients. The patients were randomly allocated into three groups according to the drug used; Group D received (0.5 μg/kg) of dexmedetomidine (Precedex, Hospira, vial 200 mcg/2 ml) diluted and completed to 5 ml saline 0.9%, Group L received (5ml) 2% of lidocaine hydrochloride anhydrous (lidocaine hydrochloride- sunny pharmaceutical, vial 50 ml, 20mg/ ml), and Group C received 5ml saline 0.9%.

Metoclopramide (10 mg) was given intravenously to all patients to reduce the incidence of nausea and vomiting, all patients received intravenous infusion 1 g of intravenous paracetamol. Residual neuromuscular blockade was reversed with neostigmine 0.05mg/kg injection and atropine 0.01mg/kg. Anesthetics were discontinued and the O2 flow was increased to 5 L/min to exclude isoflurane. Then, an endotracheal tube was removed (at time of awareness follow verbal commands).

After recovery, all patients were transported to Post Anesthetic Care Unite (PACU) for 2 hours then to the ward where observation was completed for 24 hours.

Outcome Measures

Age, weight, pressure, and the length of the surgery were reported. The primary outcome was the coughing severity in which the postoperative cough was recorded five minutes after extubation till the patient becomes conscious. 0= no cough, 1= little cough (single), 2= moderate cough up to 5 Seconds, and 3= severe cough over 5 Seconds (bucking) [17]. The secondary outcomes included the awareness time (from the end of the surgery to the point at which the patient regained consciousness and the time to extubation (from the end of the surgery to extubation). In addition, the ophthalmologist recorded the Intraocular Pressure (IOP mmHg) before day of operation and 2 hours postoperatively. The HR, MAP, and SaO_2 values were recorded at (M0) 5 min before Anesthesia, (M1) before the administration of drugs (baseline reading) 15 min before end of surgery, (M2) 5 min after the administration of drugs, (M3), 10 min after the administration of drugs, (M4) at the end of surgery, (M5) at the point of awareness (16), (M6) at the point of extubation, (M7) 2 min after extubation, (M8) 5 min after extubation, (M9) 15 min after extubation and (M10) 30 min after extubation. We assessed the surgeon's satisfaction by point Four-point scale: 1 = completely satisfied; 2 = somewhat satisfied. 3 = dissatisfied; and 4 = aborted.

Also, the incidence of complications due to increase IOP was recorded such as wound dehiscence, iris prolapses, flat anterior, hyphemia, hypotony, endophthalmitis, suprachoroidal hemorrhage, and expulsive hemorrhage within 24 hours. Also, any other complications such as postoperative nausea and vomiting, dysphagia, sore throat severity, tachycardia, and hypertension were recorded.

Statistical Analysis

Calculation of the sample size using data from a past study, the sample size was determined using the effect of the variation in cough reflex change following administration of dexmedetomidine and lidocaine in each group at a power of 0.80, a confidence interval of 95%, and a significance level of 0.05. To identify this difference, 40 patients in each group, assuming a 20% dropout rate, were sufficient.

The IBM SPSS 20.0 statistical package software was used to analyze the data. For quantitative parametric measurements, data were expressed as mean SD, minimum and maximum range, and number and percentage for category data.

The Chi-square test or Fisher's exact test was used to compare categorical variables, and the analysis of variance (ANOVA) was used to compare independent groups for parametric data. The Kruskal-Walli's test was used for non-parametric quantitative data, followed by the Mann Whitney test to compare the two groups.

Within each group, analyses were conducted using the paired sample t test for parametric quantitative data and the Wilcoxon signed rank test for non-parametric quantitative data. P values of 0.05 or lower were regarded as significant.

Results

In this trial, 134 patients were enrolled; 10 declined to participate in part, and four patients—one patient in group D and three patients in group L—were excluded because the operating technique had changed. As a result, 120 patients were enrolled in the final trial, with 40 patients in each of the three groups (D, L, and C) "Figure 1".

Regarding patient characteristics including age, sex, weight, ASA, kind of surgery, and procedure length, the study groups are compatible, as demonstrated in "Table 1".

There was a significant decrease in cough occurrence in group D when compared to group L ($P \leq 0.036$) at grade 0 and group C *($P \leq 0.0001, 0.004, 0.001$)* at grades 0,1,2 respectively. Also, there was a significant decrease in cough occurrence in group L when compared to group C *($P \leq 0.0001, 0.003$)* at grades 0,2, respectively "Table 2".

The postoperative awareness and extubation times show no significant differences between the three groups. The postoperative IOP was maintained stably in both groups, D and L with no significant difference in comparison to the preoperative readings *($P \leq 0.076, 0.088$),* respectively. In contrast, in group C the postoperative readings were significantly increased *($P \leq 0.0001$)* compared to the preoperative readings. However, the comparison between the three groups, the postoperative IOP showed no significant difference between groups D and L. However, there was significant difference between groups C and both groups D and L *($P \leq 0.0001, P \leq 0.0001$)* respectively "Table 1".

Regarding complications within 24 hours, there was no difference between the study groups that was considered significant, except for sore throat severity at 15 min and 24hrs *($P \leq 0.007$ and 0.045)* respectively. Hypertension was recorded 3(7.5%), 10(25%), and 19(47.5%) in group D, L and C respectively *($P \leq 0.0001$).*

Surgeon satisfaction is demonstrated in "Figure 2", there was no significant difference between group D and L groups where there was a substantial difference between group C and both the D and L groups concerning being completely satisfied *($P \leq 0.0001, 0.0001$)*, somewhat satisfied *($P \leq 0.019, 0.049$),* dissatisfied *($P \leq 0.006$ 0.015)* and aborted *($P \leq 0.027, 0.027$)* respectively.

All values of heart rate (HR) and Mean blood pressure (MBP) in group D were found to be decreased at all-time points compared with baseline readings and in group L it wa comparable at all-time points. In contrast, in group C, there was a significant elevation in all postoperative

values compared to baseline readings. Regarding comparison between groups, heart rate significantly increased in group C *(P ≤ 0.05)* compared with group D and group L from M3 up to M10. Also, there was a significant increase in group L compared with group D from M4 to M7, the change of HR illustrated in "Figs. 3, 4".

Table (1): patients' data in the three groups.

Variables	Group D (n=40)	Group L (n=40)	Group C (n=40)	P value all		
				D vs L	*D vs C*	*L vs C*
Age (year)	38.2±10.8	40.5±11.9	43.2±12.9	0.280		
				0.077	0.090	0.379
Sex: n (%)						
Male	27(67.5%)	21(52.5%)	25(62.5%)	0.376		
Female	13(32.5%)	19(47.5%)	15(37.5%)	0.171	0.639	0.366
Weight (kg)	83.9±9.1	85.3±7.1	86.3±10.4	0.577		
				0.547	0.657	0.298
ASA: n (%)				0.219		
ASA I	29(72.5%)	25(62.5%)	32(80%)	0.340	0.431	0.084
ASA II	11(27.5%)	15(37.5%)	8(20%)			
Type of Surgery:				0.270		
n (%)	12(30%)	10(25%)	11(27.5%)	0.679	0.210	0.300
Keratoplasty RD	28(70%)	30(75%)	29(72.5%)			
Operation time (min)	87.56±10.89	87.01±10.07	87.40±10.44	0.971		
				1.00	1.00	1.00
Awareness Time (min)	8.40±120	8.39±1.30	8.25±1.13	0.827		
				1.000	1.000	1.000
Extubation Time (min)	8.75±1.51	8.79±1.27	8.64±1.58	0.887		
				1.000	1.000	1.000
Preoperative IOP(mmHg)	17.75±0.78	17.74±0.95	17.94±0.85	0.498		
				1.000	0.939	0.903
Postoperative IOP(mmHg)	17.94±0.74	17.95±0.78	22.54±1.85#	0.0001*		
				1.000	0.0001*	0.0001*

ASA, American Society of Anesthesiologists, RD, Retinal detachment. Group D: dexmedetomidine, Group L: lidocaine and Group C: control. Variables are presented as Mean ± SD, Data were analyzed using ANOVA test with post hoc test (Bonferroni), or number and percentage (n %) using chi-square. *P is significant at ≤0.05.

Table (2): The incidence of postoperative cough in the studied groups.

Variables	Group D (n=40)	Group L (n=40)	Group C (n=40)	P value		
				all		
				D vs L	*D vs C*	*L vs C*
No cough (0)	35 (87.5%)	28 (70%)	11(27.5%)	0.0001*		
				0.036*	0.0001*	0.0001*
Minimal Cough (1)	5 (12.5%)	11 (27.5%)	16 (40%)	0.002*		
				0.060	0.004*	0.095
Moderate cough (2)	0%	1 (2.5%)	10 (25%)	0.0001*		
				0.500	0.001*	0.003*
Severe cough (3)	0%	0%	3 (7.5%)	0.035*		
				----	0.120	0.120

Group D: dexmedetomidine, Group L: lidocaine and Group C: control. Variables are presented as number and percentage (n %) data analyzed using chi-square. *P is significant at ≤0.05.

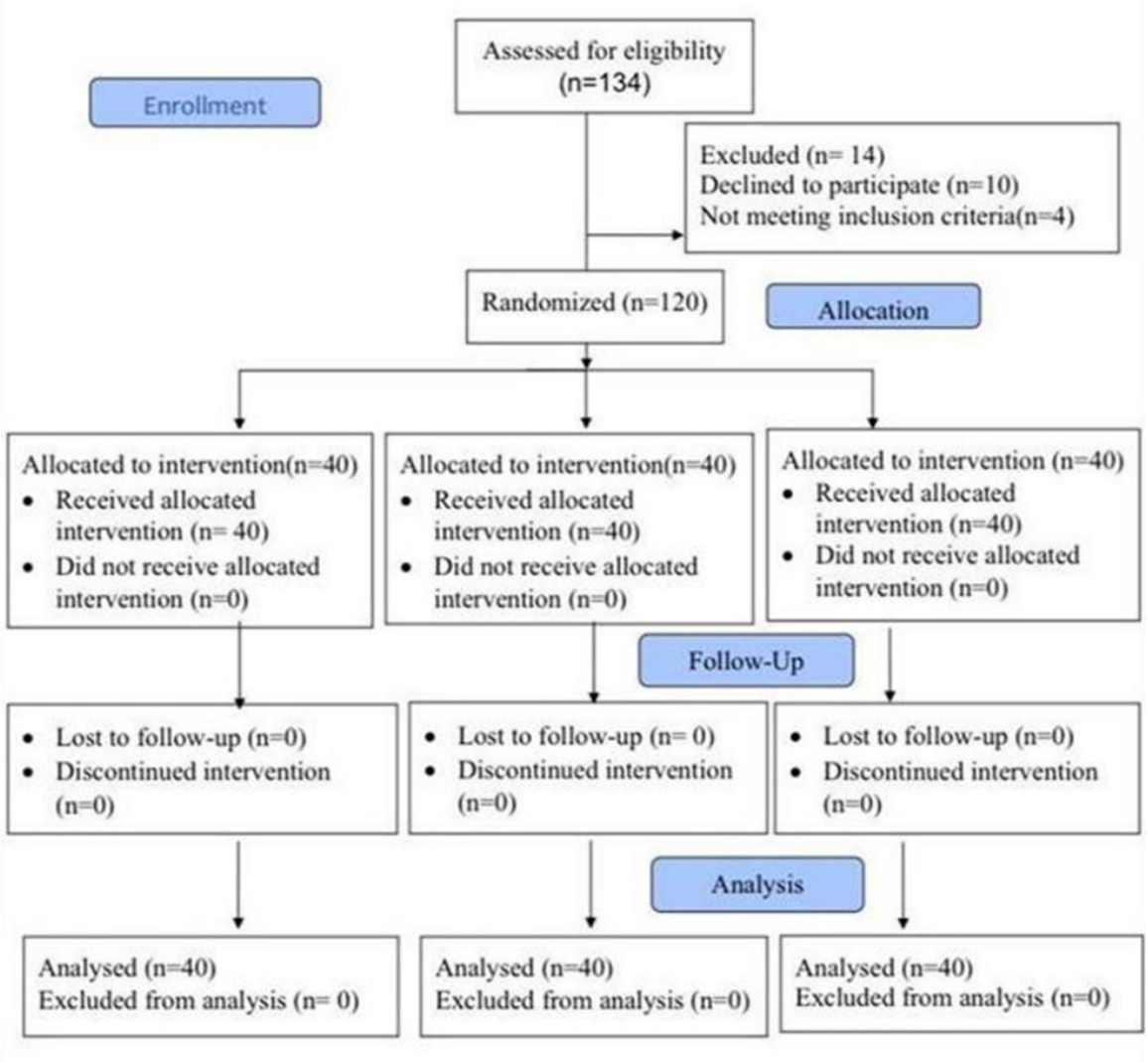

Figure (1): Flowchart

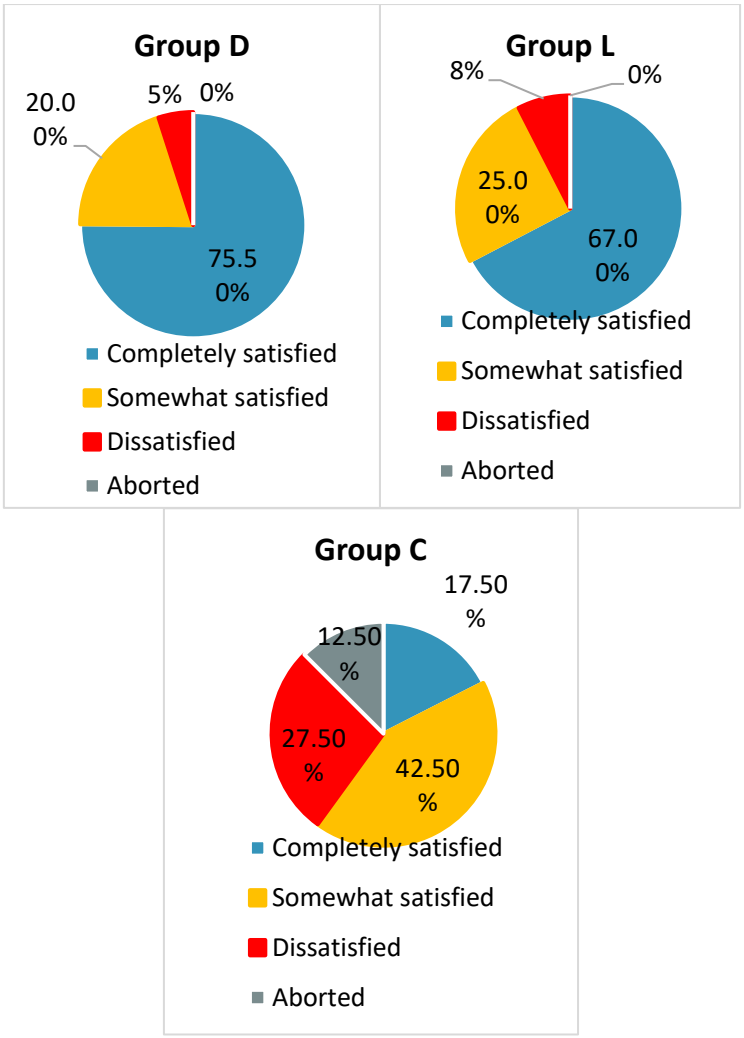

Figure (2): Surgeon Satisfaction in the three groups. Variables are presented as number and percentage (n %), data analyzed using chi-square. Group D: dexmedetomidine, Group L: lidocaine and Group C: control.

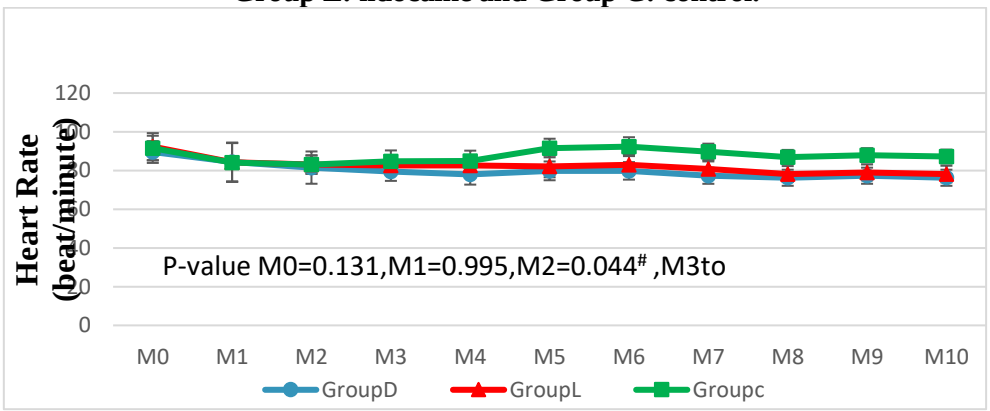

Figure (3): Heart Rate (beat/minute) changes in the studied groups. Variables are presented as Mean ± SD, data were analyzed using ANOVA test with post hoc test (Bonferroni). **Group D=** dexmedetomidine; **Group L=** lidocaine; **Group C=** control; **M0=** 5 min before Anesthesia; **M1=** before the administration of drugs; **M2=** 5 min after the administration of drugs; **M3=** 10 min after the administration of drugs; **M4=** at the end of surgery; **M5**= at the point of awareness; **M6=** at the point of extubation; **M7=** 2 min after extubation; **M8=** 5 min after extubation; **M9=** 15 min after extubation; **M10=** 30 min after extubation.

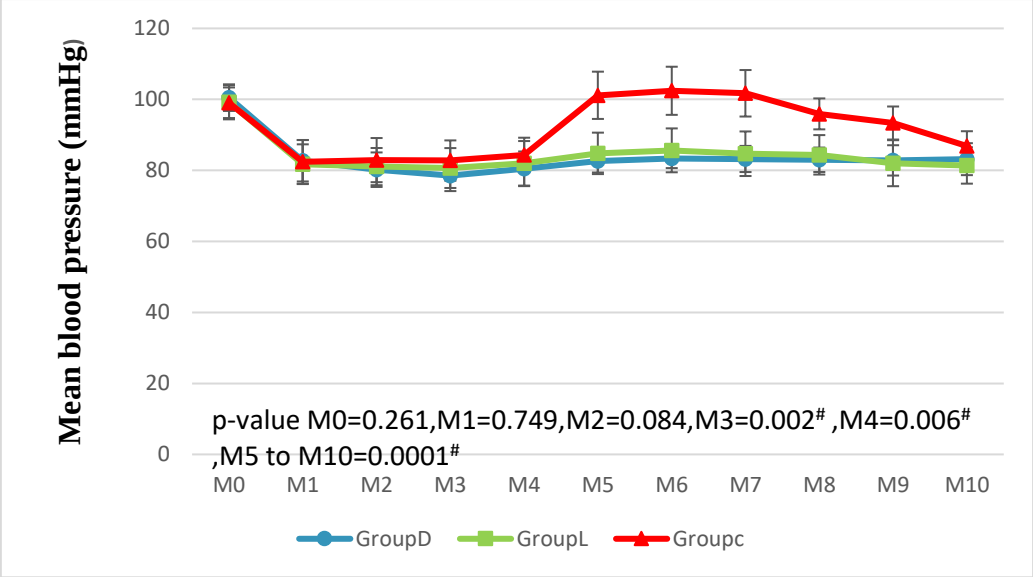

Figure (4): Mean blood pressure (mmHg) changes in the studied groups. Variables are presented as Mean ± SD, data were analyzed using ANOVA test with post hoc test (Bonferroni). **Group D=** dexmedetomidine; **Group L=** lidocaine; **Group C=** control; **M0=** 5 min before Anesthesia; **M1=** before the administration of drugs; **M2=** 5 min after the administration of drugs; **M3=** 10 min after the administration of drugs; **M4=** at the end of surgery; **M5=** at the point of awareness; **M6=** at the point of extubation; **M7=** 2 min after extubation; **M8=** 5 min after extubation; **M9=** 15 min after extubation; **M10=** 30 min after extubation.

Discussion

The most important goals of Anesthesia during ophthalmic surgery are preventing ETT-induced cough [18], maintaining stable cardiovascular function, and controlling IOP [14]. Coughing may cause an elevation of IOP up to 50 mmHg[19]. The sudden elevation of venous pressure produced mainly by the Valsalva effect following coughing may lead to vessel wall rupture and suprachoroidal hemorrhage [20].

The lung is an organ that absorbs substances quickly and can already be accessed by a wide range of medications. Consequently, proteins and peptides, both hydrophilic and hydrophobic, may pass the pulmonary epithelium at a molecular weight-dependent flow [21]. So, it has been suggested that intratracheal medication can efficiently reach systemic circulation in an emergency when intravenous administration is not an option[22]. Numerous studies have shown that intratracheal administration has successfully been used to deliver a wide range of drugs in various therapeutic settings, including lidocaine sprays during tracheal intubation and extubation [12,23-25]. Lidocaine has been applied locally and intravenously to reduce coughing during emergence from general Anesthesia. It is well known that intravenous lidocaine can suppress cough because it depresses the central nervous system [7] or simply because it has local anesthetic effects on the mucosa of the airways [26]. Dexmedetomidine can therefore be successfully administered intratracheally as an alternative technique in cases where it is impossible to set up an intravenous line, which is easier and more useful [16].

This research aimed to assess and compare the attenuating effects of a single dose of dexmedetomidine, and lignocaine spray administered endotracheally on the cough reflex, IOP, and hemodynamics during extubation in patients undergoing eye surgery.

The results of this study demonstrated that the extent of cough was significantly

reduced in both groups D and L more than the control group. Nonetheless, group D reveals a higher percentage of patients (87.5%) with postoperative cough grade zero which is superior to group L (70%) with significant *(P≤0.036)*. Furthermore, intratracheal dexmedetomidine and lignocaine administration improved stability in hemodynamics and IOP with no significant side effects. Additionally, the patients in either group D or L have better surgeon satisfaction than the control group.

In accordance with our findings, research by Jee and Park [12] found that, lignocaine injected through the ETT is more effective than IV injection at suppressing cough when administered around 5 minutes before extubation. They hypothesized that this method would have a local mucosal effect. Furthermore, Shabnum et al.,[27] discovered that intravenous and intra-tracheal lignocaine effectively reduces the hemodynamic response when administered within 20 minutes after removing the skull pin and extubation.

Furthermore, Hong et al., [28] and Artawan et al.,[29] demonstrated that intratracheal lidocaine administered just before intubation or just before extubation significantly reduced the incidence of cough during extubation and sore throat on the first and sixth hours after surgery when compared with placebo in the post-tonsillectomy procedure.

Shruthi and his coworkers[30] proved that intravenous dexmedetomidine administered at a dosage of 0.5mg/kg before extubation suppressed hemodynamic responses during emergence from Anesthesia without overly sedating the patient, but prolonged time to extubation. In their investigation, coughing was less common in the dexmedetomidine group (D) than in the control group (C) *(P <0.001)*. However, Group D took longer to extubate and open their eyes than Group C *(P <0.001)*. The dissimilarity from our findings is since dexmedetomidine was only given in a small dose via the endotracheal tube.

Network meta-analysis of RCTs to assess the relative effectiveness of the drugs in reducing moderate to severe emerging coughing after general Anesthesia. Study drugs included fentanyl, dexmedetomidine, remifentanil, and lidocaine (i.v., intracuff, topical, or tracheal administration). They established that all study drugs reduced moderate to severe emerging cough better than a placebo or no drug, with dexmedetomidine coming out on top [17].
Jafarzadeh et al., [31] evaluated the effectiveness of intravenous dexmedetomidine and lidocaine on cough suppression during tracheal extubation therapy, which is consistent with our results. They discovered that during tracheal extubation following thyroid surgery, lidocaine and dexmedetomidine were equally efficient at reducing cough and hemodynamic abnormalities. However, compared to lidocaine and ordinary saline, intravenous infusions of dexmedetomidine caused bradycardia and prolonged the time to awareness. Intratracheal medications brought on this deviation from our findings.

In line with the findings of Dutta et al.'s study[26], emergence and extubation hemodynamic response is attenuated more effectively by intravenous dexmedetomidine (0.3 mcg/kg) than lignocaine spray (1.5 mg/kg). It also allows for smooth extubation and easy recovery without any postoperative sedative effects. Furthermore, In line with what we discovered Saidie et al., [32] studied 120 patients who were divided into three groups at random and received 10 mL of normal saline, 1.5 mg of intravenous lidocaine, and 0.5 mcg of intravenous dexmedetomidine 10 min before Anesthesia. They proved that dexmedetomidine decreased cough frequency and seems a safe medication for managing cough during the emergence from Anesthesia.

The efficiency of intratracheal dexmedetomidine injection in avoiding the laryngeal reaction during gynecological laparoscopic surgery was examined by

Wang et al., [16] contrary to our results. They found that intratracheal dexmedetomidine administration maintains hemodynamic stability with no obvious negative effects.

Dexmedetomidine can attenuate the extubation reaction and lessen emergence agitation in pediatric patients following vitreoretinal surgery. However, it did not affect IOP, according to Lili et al., [33] study, which is comparable to ours in terms of IOP.
Conversely, Banga et al.,[34] demonstrated that a single intravenous dosage of the premedication drug dexmedetomidine (0.5 µg /kg) significantly reduced the IOP and hemodynamic response to suxamethonium administration and tracheal intubation. Furthermore, Jaakola et al., and Ayoglu et al.,[14,35] demonstrated that dexmedetomidine decreased IOP and inhibited the sympathoadrenal reactions related to laryngoscopy and intubation. Also, in a double-blind, randomized research with 90 patients undergoing day-case cataract surgery under regional Anesthesia, Virkkilä et al., [15] proved that an intramuscular injection of dexmedetomidine 0.5 µg/kg - 45 minutes before the peri-ocular block, reduced IOP before, during, and after surgery. This result varies from ours because, contrary to previous studies, we assessed the IOP two hours after extubation and utilized a lower dose of dexmedetomidine.

In line with our research, Yoo et al., [36] study on forty-four patients scheduled for elective retinal surgery under sub-tenon's Anesthesia, in which intravenous dexmedetomidine or 0.9% saline via infusion pump was continuously administered to the dexmedetomidine or control group, respectively. They found that the dexmedetomidine group was more satisfied than the control group with the surgical procedure *(P<0.002)*.

This study has a variety of limitations that must be considered. First, further research is still needed to fully understand the absorption properties, pharmacokinetics, and pharmacodynamics of intratracheal dexmedetomidine delivery. Second, we should have compiled our patients' smoking histories. Future studies should focus on smoking because past smoking habits may influence the circumstances and timing of extubation. Finally, because our sample size was small, more people will need to participate in future studies to confirm the results.

We concluded that giving dexmedetomidine or lidocaine intratracheally 15 minutes prior to the procedure's conclusion was more effective at reducing cough, facilitating a smooth extubation, and encouraging a balanced anesthetic recovery. Dexmedetomidine was also more effective at reducing the cough reflex.

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