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ANESTHESIOLOGY

Intravenous dexmedetomidine versus intravenous lidocaine in attenuating airway reflexes during recovery of thyroidectomy patients

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ABSTRACT

Background: Cardiac and other airway reflexes are linked to intubation and extubation processes. These hemodynamic and respiratory responses during extubation have previously been attenuated with the use of intratracheal instillation and intravenous administration of lidocaine. In surgical intensive care units, dexmedetomidine, a strong α 2 receptor agonist, considered to make extubation easier. However, its effect on reducing cardiopulmonary reflexes during extubation process under general anesthesia is currently being investigated.

Objective: To evaluate the capability of IV lidocaine or Dexmedetomidine to suppress the coughing reflex during extubation process following thyroid surgery.

Methods: This clinical trial was carried out in the operating rooms of Ain shams university hospitals. It included 140 participants, with 70 patients in each group. NCT05657028 is the clinical trials.gov registration number for this trial.

Results: Showed no statistically significant difference in hemodynamics in both groups regarding MAP and SpO₂. While intraoperative bradycardia has been recorded with the dexmedetomidine group in comparison with lidocaine group, also there was a decrease in the incidence of postoperative cough in dexmedetomidine group in comparison with lidocaine group and no statistically significant difference regarding the pain postoperatively.

Conclusion: Following thyroid surgery, dexmedetomidine was more effective in reducing the cough reflex during the tracheal extubation period. Both intravenous lidocaine and dexmedetomidine achieved acceptable analgesic effect. In terms of hemodynamics, intravenous infusions of dexmedetomidine caused bradycardia,

Keywords: Dexmedetomidine; Lidocaine; Thyroidectomy; cough reflex; Intravenous injection.

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1. INTRODUCTION

The process of intubation and extubation are linked to various cardiac and respiratory reactions¹ Possible causes include uncleared secretions, anesthetic gas, and irritation by endotracheal tube.²

Additionally, bleeding after thyroidectomy is still a major concern and is frequently linked to serious side effects such cardiac arrest, reoperation, and cervical hematoma.³ Deep extubation lowers cardiopulmonary stimulation and lowers the risk of coughing and tube strain.⁴ These hemodynamic and respiratory responses during extubation have previously been attenuated with the use of intratracheal local anesthetic instillation, intravenous lidocaine, opioids like fentanyl, esmolol and labetalol, but with certain restrictions.⁵ Additionally, the "no stimulation" extubation procedure guarantees that extubation only occurs when consciousness is restored, with spontaneous eye opening requiring no stimulation at all during emergence.⁶

Dexmedetomidine, strong $\alpha 2$ receptor agonist, considered to make extubation easier. However, its effect on reducing cardiopulmonary reflexes during extubation process under general anesthesia (GA) is currently being investigated.⁷

Aims of the study

We evaluated and compared the efficacy of intravenous lidocaine and dexmedetomidine to suppress the cough reflex during extubation process following thyroidectomy.

2. METHODOLOGY

This trial was accomplished in operating rooms of Ain Shams University Hospitals, and included 140 participants. The included subjects were ASA I or II, aged 18 to 65, and scheduled for elective thyroidectomy. Patients ASA class III or IV, refusing the procedure or study participation, patients with asthma, chronic cough, or symptoms of an upper respiratory infection prior to surgery, current smokers, those taking ACE inhibitors, those with sinus bradycardia (less than 60 beats per min), and those with a history of heart block or betablockers were excluded.

2.1. Study procedure

Participants were randomly allocated to one of the two groups: Group D (Dexmedetomidine group) and Group L (Lidocaine group).

All subjects underwent a standard preoperative evaluation. Prior to the operation, all individuals fasted for at least six hours. To induce GA, midazolam 0.05 mg/kg, propofol 2 mg/kg, fentanyl 2 μ g/kg, and

cisatracurium 0.15 mg/kg were administrated intravenously. After sufficient muscle relaxation, intubation was done using endotracheal tube of the appropriate size (size 7.5 for males and size 7 for females). Sevoflurane 2% was used to maintain GA, and cisatracurium 0.03 mg/kg was administered every 20 min for controlled ventilation. SpO₂, HR, and MAP were continuously monitored and recorded at the start of operation (time 0) and every 30 min thereafter.

2.2. Group D

Subjects of Group D had a loading dose 0.5 μ g/kg of dexmedetomidine 10 min before induction, followed by infusion @ 0.4 μ g/kg/hour until 30 min prior to the completion of the procedure.

2.3. Group L

Subjects of this group received a loading dose of 1.5 mg/kg lidocaine 2% 10 min before induction. This was followed by infusion of lidocaine @1.5 mg/kg/hour until 30 min prior to completion of the procedure. After the procedure, neostigmine 50 μ g/kg (up to 5 mg) and atropine 10–20 μ g/kg were used to reverse any remaining neuromuscular blockade. As soon as the surgery was finished, sevoflurane was stopped, fresh gas flow was increased, pharyngeal secretions or blood were carefully suctioned out. When the patient was fully conscious, breathing spontaneously, good muscle power, and spontaneous eye opening, extubation was carried out. Following extubation, the patients were moved to the PACU for monitoring.

Within five min of the extubation, the severity of the cough was assessed using the following criteria: 0 = no cough, 1 = a minor (single) cough, 2 = a moderate (≤ 5 s) cough, and 3 = a severe (> 5 s) cough.²

In this study, our primary outcome was to evaluate the capability of IV dexmedetomidine and lidocaine in attenuating coughing reflex following extubation process post thyroidectomy.

Secondary outcomes included comparing the values of the hemodynamic parameters e.g., SpO₂, HR, and MAP, at the beginning of the operation (time 0) and then every 30 min till the end of the procedure and after extubation, and satisfactory analgesic effect regarding sore throat after surgery using the visual analogue scale.

The study complied with the ethical guidelines set forth by the medical faculty's ethical committee at Ain Shams University. All of the patients who were part of the trial gave their written, informed consent.

2.4. Statistical analysis

Version 27.0 SPSS was used to collect, edit, code, and enter the data. Where applicable, the mean \pm SD or

Table 1: Comparison regarding demographic data								
	Group D (n = 70)	Group L (n = 70)	P-value					
	44.34 ± 12.2	44.87 ± 12.2	0.798 ^t					
Male	12 (17.1%)	18 (25.7%)	0.218 x2					
Female	58 (82.9%)	52 (74.3%)						
Partial	16 (22.9%)	21 (30%)	0.34 x2					
Total	54 (77.1)	49 (70%)						
	Male Female Partial	Group D (n = 70) 44.34 ± 12.2 Male 12 (17.1%) Female 58 (82.9%) Partial 16 (22.9%)	Group D (n = 70) Group L (n = 70) 44.34 ± 12.2 44.87 ± 12.2 Male 12 (17.1%) 18 (25.7%) Female 58 (82.9%) 52 (74.3%) Partial 16 (22.9%) 21 (30%)					

median (IQR) were used to express quantitative data. Frequencies and percentages were used to express the qualitative data. Two means were compared using the t-test of significance. The proportions of two qualitative factors were compared using the chi-square (χ 2) test for significance. Mann Whitney-U test was used for two-group comparisons in non-parametric data.

A 95% confidence interval and a 5% acceptable margin of error were established. Thus, the following P-value was deemed significant: P < 0.05 = significant difference; P > 0.05 = non-significant, and P < 0.01 = highly significant difference.

3. RESULTS

3.1. Demographics

The demographic data (in terms of age, sex, and type of operation) showed no statistically significant difference (Table 1).

3.2. Preoperative hemodynamics

The preoperative hemodynamic in terms of 'MAP', 'HR' and 'SpO2'showed no statistically significant difference (Table 2).

3.3. Intraoperative hemodynamics

The intraoperative hemodynamic in terms of 'MAP', 'HR' and 'SpO2' measured at 30 min after the start of the surgery, showed statistically significant difference between intraoperative heart rates in the two groups (Table 2). There was no difference in the measured MAP and SpO₂ values at this time.

3.4. Postoperative hemodynamics

The postoperative hemodynamic in terms of 'MAP', 'HR' and 'SpO2' showed no statistically significant differences between the two groups (Table 2).

Table 2: Comparison regarding preoperative hemodynamic data							
Parameter	Recoding time	Group D (n = 70)	Group L (n = 70)	P-value ^t			
МАР	Time Zero	81.94 ± 2.1	82.10 ± 2.2	0.669			
	At 30 min	78.11 ± 2.2	78.27 ± 2.2	0.674			
	In PACU	84.80 ± 2.2	85.10 ± 2.4	0.441			
HR	Time Zero	79.14 ± 5.1	79.43 ± 5.1	0.742			
	At 30 min	63.36 ± 5.6	81.63 ± 3.0	< 0.0001*			
	In PACU	74.43 ± 4.5	74.71 ± 4.9	0.719			
SpO ₂	Time Zero	97.26 ± 1.4	97.17 ± 1.5	0.726			
	At 30 min	98.96 ± 0.8	99.03 ± 0.8	0.595			
	In PACU	97.79 ± 1.2	97.70 ± 1.2	0.673			
* Significant P-value							

Table 3: Comparative postoperative complications									
Complication	on Group D (n = 70)			Group L (n = 70)			P- value ^z		
	range	Median	IQR	range	Median	IQR			
Cough score	0-3	1.5	1-2	1-3	2	2-2	0.0003		
Pain score	2-6	2	2-2	2-6	2	2-2	0.6690		

3.5. Postoperative complications

The postoperative cough showed statistically significant difference, but the VAS pain scores were equivalent in both of the groups (Table 3).

4. DISCUSSION

Given that dexmedetomidine a known $\alpha 2$ receptor agonist used in perioperative sympatholysis, and preservation of respiratory function, this study evaluated the efficacy of intravenous lidocaine (Group L) and dexmedetomidine (Group D) in reducing coughing reflex and hemodynamic changes in patients undergoing thyroid surgery.⁸ However, lidocaine has also been demonstrated to lessen post-operative sore throat and coughing during extubation. It can be injected intravenously, administered locally to the airway before intubation, or infused into the ETT cuff.⁹

Our primary endpoint showed that postoperative coughing was less in the dexmedetomidine group; where only 5 patients experienced severe cough, compared to the lidocaine group where 15 patients had severe cough. This can be correlated to dexmedetomidine's sympatholytic properties, analgesic and sedative properties of $\alpha 2$ agonistic effect. Moreover, dexmedetomidine also modulate the inflammatory process, responsible for airway hyperactivity by decreasing the levels of IL-6 and TNF– α and attenuating tracheal ring contraction caused by exogenous acetylcholine and the C-fiber mediated contraction.¹⁰

In agreement with our study, Xu et al.¹¹ found postoperative cough less in dexmedetomidine cohort in comparison with midazolam cohort after partial and total laryngectomy. Also, Aksu et al.¹² and Fan et al.,¹³ who compared fentanyl with dexmedetomidine, found the prevalence of cough is lower with dexmedetomidine suggesting that dexmedetomidine was more effective in smooth emergence extubation. Moreover Guler et al. stated that postoperative coughing was markedly less in the dexmedetomidine arm compared to the placebo arm.¹⁴

Conversely, Kim et al. showed no differences between the remifentanil and dexmedetomidine in attenuation of cough reflex after craniotomy surgery.¹⁵

Regarding the preoperative and post-operative hemodynamics, our clinical trial showed no statistically significant difference between both arms. Additionally, intraoperative hemodynamics in terms of MAP and SpO₂ showed no statistical significance. However, there was significant difference regarding heart rate, where 8 patients of the dexmedetomidine group had bradycardia (HR < 60 beats/min), two of them received atropine (0.04 mg/kg). Dexmedetomidine reduces the production of norepinephrine, which in return lower catecholamine release from nerve endings and central sympatholytic effect, leading to decreases in HR and blood pressure.

In line with our research, Hu et al. reported that 35 patients had bradycardia (HR 60 beats/min), and one patient's HR in the dexmedetomidine group was 40 beats/min, compared to the lidocaine and control groups in patients having thyroid surgery.² Additionally, Kim et al. discovered that the MAP and heart rate were considerably greater in the remifentanil group than in the dexmedetomidine group when they compared the two medications in patients having craniotomies.¹⁵

Additionally, Elmasry et al. discovered that the "no stimulation" method and dexmedetomidine groups experienced considerably fewer variations in vital data during emergence extubation than the Standard awake extubation group.⁵ This could be explained as airway-related events during removal of the endotracheal tube using the "no stimulation" technique, was more efficient than standard awake extubation in inhibiting catecholamine release. Additionally, dexmedetomidine, reduces sympathetic outflow and noradrenergic activity, which counteracts hemodynamic fluctuation that occurs during extubation.

In our investigation, there were no statistically significant differences between the groups regarding the postoperative pain or analgesic intake. This can be explained by the analgesic qualities of both dexmedetomidine and lidocaine. Moreover, in both myelinated A and unmyelinated C nerve fibers, lidocaine reduces spike activity, amplitude, and conduction time. Our results came in harmony with Hu et al. that found both lidocaine and dexmedetomidine achieved satisfactory analgesic effect post thyroidectomy.² Also, Kim et al. showed no difference between remifentanil and dexmedetomidine in postoperative pain score after craniotomy.

Conversely, Xu et al. stated that the pain scores postoperatively were markedly lower in dexmedetomidine group compared to the midazolam group at departure from PACU.¹¹

5. LIMITATIONS

First, ASA 3 and 4 patients were excluded, so the findings of this study cannot be applied to ASA 1 and 2 patients. Further, the incidence of post-operative bleeding was not recorded.

Finally, this clinical trial was a single-center clinical trial, hence larger sample, multicenter studies are still required to support the findings, and draw universally applicable conclusions.

6. CONCLUSION

Following thyroid surgery, both intravenous infusions of lidocaine and dexmedetomidine achieved acceptable analgesic effect. In terms of hemodynamics, intravenous infusions of dexmedetomidine caused bradycardia, although it was more effective in reducing the cough reflex during the tracheal extubation period.

7. Data availability

The numerical data generated during this research is available with the authors.

8. Ethical considerations

Ain Shams University Hospitals ethical committee approved the trial. Written permission was obtained from all participating patients.

9. Study Registration

The study was registered with clinicaltrials.gov under registration number NCT05657028

10. Conflict of interest

The study utilized the hospital resources only, and no external or industry funding was involved.

11. Authors' contribution

ONHZ: Conducted the study MMK: Drafting and editing the manuscript HNAH: Literature search MMAZ: Statistical analysis; Revision of the manuscript RHAH: Literature search

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