Effects of Ropivacaine with and without Dexmedetomidine on Hemodynamic Responses During Laryngoscopy and Intubation: A Randomized Double-Blind Study

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KEYWORDS

Ropivacaine, Dexmedetomidine, Laryngoscopy

ABSTRACT

Introduction: The study compares the effectiveness of airway nebulization with ropivacaine 0.5% alone and in combination, highlighting the potential benefits of these medications. **Aims:** The study evaluates ropivacaine 0.5% nebulization's effectiveness in reducing pressor response to intubation, assesses potential adverse effects, and compares the dose-sparing effect of propofol and sedation. **Methodology:** A randomized clinical study at Krishna Hospital compared airway nebulism with piroxicam and dexmedetomidine in 60 patients aged 18-60, focusing on treating hypotension and heart rate decline. **Results:** The study compared 60 participants in two treatment groups: RD and R alone, finding no significant difference in age, gender, weight, or ASA status. **Discussion:** The study compared the effectiveness of nebulized ropivacaine alone or combined with dexmedetomidine in reducing pressor response to laryngoscopy and intubation in 60 patients. Results showed that ropivacaine with dexmedetomidine significantly reduced heart rates and systolic blood pressure. **Conclusion:** The study shows that nebulized ropivacaine and dexmedetomidine significantly reduce pressor response during laryngoscopy and intubation, while also enhancing propofol's dose-sparing benefits and increasing sedative effects.

INTRODUCTION

General anesthesia, including laryngoscopy and endotracheal intubation, can trigger significant hemodynamic responses, known as the pressor response, which can lead to hypertension and tachycardia. This can be harmful, especially in patients with compromised cardiovascular systems. The insertion and removal of a breathing tube can elevate catecholamine levels, causing blood pressure changes and potential complications like heart attacks, irregular heart rhythms, and brain bleeding. Medications like propofol and opioids can help dampen tube-induced airway stimulation. [1,2]

After anesthesia, the patient's awakening can trigger the sympathetic nervous system, leading to coughing and blood pressure changes. Various interventions, including α2 agonists, short-acting opioids, local anesthetics, and beta blockers, have been explored to improve perioperative outcomes. However, these medications have different systemic effects, such as decreased

respiratory drive, sedation, and postoperative nausea and vomiting. Direct administration through nebulization is a novel approach with fewer systemic effects, requiring further exploration and research. [3,4]

The duration and intensity of intubation directly affect the body's catecholamine response, which typically starts within 5-10 seconds, peaking at 1-2 minutes, and returning to normal within 5 minutes. This temporary reaction, which usually increases systolic blood pressure, can be tolerated by most healthy individuals without adverse effects, but can pose significant risks for patients with cerebrovascular or cardiovascular conditions. [5]

Ropivacaine, a long-acting amide local anesthetic, has shown promise in anesthesia and postoperative pain management due to its ability to block nociceptive stimuli at peripheral nerves. Researchers are now interested in its topical administration, which can involve nebulization, nerve blocks, intratracheal instillation, or atomization. Using ropivacaine as a local anesthetic during intubation can help mitigate hemodynamic fluctuations and cough responses during extubation due to its longer duration of action. Fang et al. recommend topical instillation of ropivacaine (0.75%) to alleviate stress responses during both intubation and extubation. [6]

Dexmedetomidine, an alpha 2 agonist, has been extensively studied for its ability to suppress hemodynamic stress response. However, it can cause systemic side effects like hypotension and bradycardia. Nebulization offers improved bioavailability, with 65% absorption through the nasal mucosa and 82% through the buccal mucosa. Nebulized dexmedetomidine has a short distribution and elimination half-life, making it a popular premedication in pediatric patients for procedural sedation and premedication. [7,8,9]

Research on the combined effect of ropivacaine and dexmedetomidine when delivered via airway nebulization is limited, as nebulization offers a non-invasive route to deliver drugs directly to the airway mucosa, potentially enhancing efficacy and minimizing systemic side effects.

This study compares the impact of airway nebulization with ropivacaine 0.5% alone and in combination with dexmedetomidine on pressor response to laryngoscopy and intubation in general anesthesia patients, aiming to optimize perioperative management strategies and improve patient outcomes.

AIM & OBJECTIVES

The study aims to evaluate the effectiveness of nebulization with ropivacaine 0.5% alone or in combination with dexmedetomidine in reducing pressor response to intubation.

The study aims to evaluate the effectiveness of nebulized premedication in attenuating pressor response to laryngoscopy and intubation, assess potential adverse effects, and evaluate the dose-sparing effect of propofol and sedation.

MATERIALs& METHODS

A randomized, double-blind clinical study was conducted at Krishna Hospital, KVV, to compare the effect of airway nebulism with piroxicam alone and dexmedetomidine on pressor response to laryngoscope and intubation in patients.

The study involved 60 patients, randomly divided into two groups of 30 each. The sample size was calculated using two parameters: heart rate and mean arterial pressure. The study used a sealed envelope method for double blinding, and patients were anesthetized and intubated. Two groups received nebulization: Group R, which received 10 ml of ropivacaine 0.5% mixed with

normal saline, and Group RD, which received 10 ml of ropivacaine 0.5% mixed with dexmedetomidine. Patients were included based on inclusion and exclusion criteria.

INCLUSION CRITERIA: Patients with Mallampati class I and II, both genders, undergoing elective surgery under general anesthesia with endotracheal intubation, with ASA physical status I and II, aged 18-60 years.

EXCLUSION CRITERIA: The study excludes patients not consenting, known drug allergies, Mallampati class III and IV patients with difficult airway, ASA III and above patients, those with a history of disorders, those on anti-depressants/anti-psychotics, and those with a BMI over 30 kg/m2.

The study involved a detailed history, physical examination, and routine investigations for all patients. Patients were informed about the procedure, potential complications, and informed consent was obtained. Pulse oximeters, noninvasive blood pressure monitors, and electrocardiographic monitors were connected to the patient, and baseline vital parameters were recorded. A separate intravenous line was started, and Ringer Lactate solution was preloaded before general anesthesia. Drug was administered as aerosol through nebulization using a piston compressor nebulizer. After nebulization, the patient was shifted into the operation theater, and vital parameters were recorded. Sedation score was assessed using the Ramsay Sedation Scale.

The patient underwent a procedure where they were premedication, preoxygenated, sedated, and induced with propofol and cisatracurium. After 3 minutes of bag and mask ventilation, a direct laryngoscopy and intubation were performed by an experienced anesthesiologist. Vital parameters were recorded at various time points post-intubation, and the procedure was standardized for all patients.

The study focuses on the treatment of a patient with a hypotension and a decrease in heart rate. Atropine is administered if the heart rate decline is less than 50 bpm or greater than 20% of the baseline heart rate, or whichever is lower. Mephentermine is administered if the blood pressure decline is less than 90/60 mmHg or greater than 20% from the baseline heart rate. The data was analyzed using SPSS version 20 for Windows, with a p-value of < 0.05 considered statistically significant.

OBSERVATION & RESULTS

Table 1: Age distribution in both the groups

GROUP	**N**	**Age (years)**	
		Mean	Std. Deviation
RD	30	35.60	8.665
R	30	34.77	7.758
Total	30	35.18	8.165
T test applied, t value- 0.39, p value- 0.69, non-significant			

The table shows the mean age of study subjects in two groups: RD and R alone. The RD group had a mean age of 35.60 years, while the R group had a mean age of 34.77 years. The overall mean age was 35.18 years. A t-test showed no significant difference in mean age between the groups.

Table 2: Gender distribution in both the groups

		GROUP		Total
		RD	R	
Gender	F	13	11	24
	M	17	19	36
Total		30	30	60
Chi-sq value- 0.27, p value- 0.59, non-significant				

The table shows gender distribution in two groups: RD and R. The RD group has 13 females and 17 males, while the R group has 11 females and 19 males. The total number of subjects is 60, with no significant difference in gender distribution, indicating comparable distribution.

Table 3: Weight distribution in both the groups

Group	N	Weight (kg)				
		Mean	SD	Minimum	Maximum	p-value
RD	30	57.97	8.57	40	68	0.2518
R	30	60.33	7.21	46	70	

The table compares weights of participants in the RD and R treatment groups. The RD group has 30 participants with a mean weight of 57.97 kg, ranging from 40 to 68 kg, while the R group has 30 participants with a mean weight of 60.33 kg, indicating no statistically significant difference.

Table 4: ASA distribution in both the groups

			Group		Total
			RD (N=30)	R (N=30)	
ASA Physical Status	I	Frequency	26	20	46
		Percent	86.7%	66.7%	76.7%
	II	Frequency	4	10	14
		Percent	13.3%	33.3%	23.3%
Total		Frequency	30	30	60
		Percent	100.0%	100.0%	100.0%
Pearson Chi-Square $X^2 = 3.354$ p = 0.067					

The study found no significant association between ASA physical status (I and II) and treatment group (RD and R) in 60 participants, indicating that ASA status does not significantly influence participant distribution between the two treatment groups.

Table 5: Comparison of heart rate variation in both the groups

Time Interval	Heart Rate (bpm)				
	RD		R		p-value
	Mean	SD	Mean	SD	
Before nebulisation	84.27	16.52	85.5	9.37	0.7233
After nebulisation at 1 minute	69.4	9.51	86.33	9.55	<.0001
After intubation 1 minute	68.37	11.08	88.87	11.32	<.0001
After intubation 3 minutes	67.33	10.55	84.43	10.05	<.0001

After intubation 5 minutes	68.77	10.29	84.73	10.63	<.0001
After intubation 10 minutes	73.67	12.57	96.1	10.4	<.0001
After intubation 15 minutes	93.37	12.13	123.17	11.92	<.0001
After intubation 20 minutes	86.2	10.8	109.73	10.51	<.0001
After intubation 30 minutes	84.8	15.44	100.3	10.72	<.0001

The study found that patients receiving ropivacaine with dexmedetomidine (RD) had significantly lower heart rates compared to those receiving ropivacaine alone after nebulization and intubation. The RD group showed a more stable and controlled heart rate response, requiring no intervention. No significant changes were observed in the ropivacaine group before and after nebulization, and heart rate remained stable during and after intubation. However, 15 minutes post intubation, there was a slight increase in HR.

Table 6: Comparison of systolic blood pressure variation in both the groups

Time interval	**Systolic Blood Pressure (mmHg)**				
	RD		R		p-value
	Mean	SD	Mean	SD	
Before nebulisation	127.23	13.64	128.57	6	0.6258
After nebulisation at 1 minute	115.73	10.07	127.8	5.83	<.0001
After intubation 1 minute	113	11.17	128.33	5.21	<.0001
After intubation 3 minutes	112.83	10.46	127.1	5.36	<.0001
After intubation 5 minutes	111.9	9.96	131.7	5.94	<.0001
After intubation 10 minutes	111.73	9.31	118.47	21.06	<.0001
After intubation 15 minutes	128.77	12.55	157.87	4.88	<.0001
After intubation 20 minutes	110.17	15.09	139.03	8.11	<.0001
After intubation 30 minutes	104.87	13.16	129.2	7.12	<.0001

The table compares systolic blood pressure (SBP) between Group RD and Group R during nebulization and intubation. No significant difference in SBP was found before nebulization. However, Group RD consistently had lower SBP post-intubation and after nebulization. Most patients in Group RD showed lower SBP but did not require intervention. The RD combination was more effective in attenuating pressor response to intubation compared to R alone.

Table 7: Comparison of diastolic blood pressure variation in both the groups

Time Interval	**Diastolic Blood Pressure (mmHg)**				
	RD		R		p-value
	Mean	SD	Mean	SD	
Before nebulisation	79.5	9.41	78.53	5.89	0.634
After nebulisation at 1 minute	72.03	10.41	75.73	5	0.0847
After intubation 1 minute	71.4	11.28	74.73	6.46	0.1656
After intubation 3 minutes	70.63	11.08	76.13	5.33	0.0173
After intubation 5 minutes	70.67	11.02	76.53	4.7	0.0095
After intubation 10 minutes	73.07	12.71	76.97	8.14	0.1623
After intubation 15 minutes	87.97	14.33	98.73	5.98	0.0004

After intubation 20 minutes	67.73	14.38	85.87	8.21	<.0001
After intubation 30 minutes	65.17	12.89	80.53	7.61	<.0001

The study compared diastolic blood pressure (DBP) between ropivacaine with dexmedetomidine (RD) and ropivacaine alone. Before nebulization, DBP was similar. After nebulization and intubation, RD had generally lower DBP. Significant differences were observed at different time intervals after intubation. The addition of dexmedetomidine to ropivacaine led to more stable DBP. Patients in the ropivacaine group showed minimal changes post-nebulization and intubation.

Table 8: Comparison of mean arterial pressure variation in both the groups

Time Interval	**Mean Arterial Pressure (mmHg)**				
	RD		R		p-value
	Mean	SD	Mean	SD	
Before nebulisation MAP	94.73	11.54	92	3.17	0.2159
After nebulisation at 1 minute	85.9	9.56	91.27	4.12	0.0065
After intubation 1 minute	85	11.98	91.13	3.4	0.0091
After intubation 3 minutes	84.5	11.5	91.2	3.97	0.0038
After intubation 5 minutes	83.73	10.33	91.93	3.39	0.0001
After intubation 10 minutes	86.4	11.56	85.7	8.15	0.7873
After intubation 15 minutes	102.1	12.71	117.67	5.82	<.0001
After intubation 20 minutes	82.03	15.52	102.83	7.6	<.0001
After intubation 30 minutes	79.4	13.26	96.57	6.6	<.0001

The study compares mean arterial pressure (MAP) between patients of the RD group and R group during nebulization and intubation. The RD group shows a significant reduction in MAP after nebulization, continuing at 1, 3, and 5 minutes post-intubation. No significant difference is observed at 10 minutes post-intubation. From 15 minutes to 30 minutes post-intubation, the RD group consistently shows lower MAP without intervention. The ropivacaine group showed minimal change in MAP post nebulization and intubation.

Table 9: Comparison of post nebulisation Ramsay sedation score in both the groups

Group	**N**	**Ramsay Sedation Score**					
		Normal range	Mean	SD	Minimum	Maximum	p-value
RD	30	1-6	3.13	0.57	2	4	<.0001
R	30	1-6	2.63	0.49	2	3	

The table reveals a significant difference in sedation levels between two groups: RD and R. Group RD achieved a higher sedation score of 3.13 post-nebulisation, while group R achieved a score of 2.63. This indicates a significant difference in sedation levels.

Table 10: Comparison of induction dose requirement of propofol in both the groups

Group	N	Propofol requirement (mg)			
		Mean	Std. Deviation	Std. Error Mean	p-value
R	30	94.1400	14.64973	2.67466	0.006

RD	30	84.0517	12.42377	2.26826	

The table compares propofol dose requirements for induction between patients receiving R alone and those receiving RD. The RD group had a significantly lower mean propofol requirement (84.05 mg) compared to the R group (94.14 mg), indicating dexmedetomidine's significant reduction in anaesthesia induction.

Table 11: Comparison of side effects observed in both the study groups

		GROUP		
		RD	R	**Total**
SIDE EFFECT	Bradycardia	3	1	4
	Hypotension	2	1	3
	Nil	25	28	53
Total		30	30	60
Chi-sq value- 1.50, p value- 0.47, non-significant				

Table 11 shows no significant differences in side effects between RD and R groups. Bradycardia and hypotension were self-resolving and did not require treatment. Most patients experienced no side effects in both groups. The chi-square test showed no significant association between drug group and side effects, with a non-significant p-value of 0.47.

DISCUSSION

Pharmacological techniques were used to attenuate the pressor response to airway instrumentation, including selective beta-adrenergic antagonists, hypotensive agents like sodium nitroprusside, nitroglycerine, calcium channel blockers, and opioids. Intranasal nitroglycerine blocks the hypertensive response, while glossopharyngeal and superior laryngeal nerve blocks and topical analgesia may also be effective.

Nebulization offers a non-invasive method for drug delivery to the airway mucosa, potentially improving efficacy and minimizing side effects. While ropivacaine and dexmedetomidine have been studied individually, limited research exists on their combined effect when delivered via airway nebulization.

The study aimed to determine the efficacy of nebulized ropivacaine alone or in combination with dexmedetomidine in blunting the pressor response to laryngoscopy and intubation in 60 patients divided into two groups. The patients were given 10 ml of ropivacaine 0.5% mixed with 1 ml of normal saline and 1 ml of dexmedetomidine (1mcg/kg, not more than 50 mcg) as nebulization for 10 to 12 minutes before induction.

The study found that the mean age of participants in Group RD was 35.60 ± 8.66 years, while in Group R it was slightly lower at 34.77 ± 7.76 years. This suggests a fairly balanced age distribution, allowing for equitable comparisons in treatment outcomes. The close age ranges across all three groups suggest age-related biases are unlikely to affect the study's outcomes, enhancing the reliability of the findings. The study also reported mean ages of 38.66 ± 13.907 years for Group D and 39.28 ± 14.475 years for Group C. [10,11]

The study involved 60 participants, divided into two groups: Group RD (13 females and 17 males) and Group R (11 females and 19 males). A chi-square test showed no significant differences in gender representation. The mean weight of participants in Group RD was 57.97 ± 8.57 kg, while in Group R it was 60.33 ± 7.21 kg. This suggests a balanced weight distribution,

preventing weight-related biases from confounding the study's outcomes. Studies by Kumar et al [12](2020) and Shiriastava et al[11] (2022) also found no significant difference in weight between the groups, indicating a balanced distribution that does not act as a confounding variable in the analysis.

Misra et al's[13] 2021 study found no significant weight difference between Group D and Group C, highlighting the importance of maintaining comparable weight distributions in clinical research to minimize potential biases and enhance the robustness and generalizability of findings.

The study found that 86.7% of participants in the RD group had grade I ASA, while 13.3% had grade II. In contrast, 66.7% of participants in the R group had grade I ASA, and 33.3% had grade II. Both groups had no statistical difference. Previous studies reported that all participants in the RD group had grade I, while the control group had 96% ASA I and 4% ASA II. Both studies showed comparable ASA grades, minimizing potential biases. [12]

The study found that patients receiving ropivacaine with dexmedetomidine (Group RD) had significantly lower heart rates compared to those receiving ropivacaine alone during and after nebulization and intubation. Heart rates were stable and did not require intervention from 1 minute after nebulization through 30 minutes post-intubation. No significant changes were observed in the ropivacaine group before and after nebulization, but a slight increase in heart rate was observed 15 minutes post-intubation, but not statistically significant. The combination of dexmedetomidine and ropivacaine showed a more controlled and stable heart rate for a longer period post-intubation.

The study by Shrivastava et al[11] (2022) found that dexmedetomidine significantly reduced heart rate in group D after nebulisation, laryngoscopy, intubation, one minute, five minutes, and ten minutes. Thangavelu et al [14](2018) found ropivacaine effective in reducing HR after intubation compared to saline. Saxena et al (2024) consistently found both drugs to significantly reduce HR and SBP at intubation.

The study found that the group RD combination significantly lowers systolic blood pressure (SBP) compared to the ropivacaine group after nebulization and multiple time points post-intubation. This suggests that the RD combination is more effective in attenuating pressor response to intubation compared to ropivacaine alone. Most patients in the RD group showed lower SBP after nebulization but did not require intervention. Studies by Shrivastava et al [11](2022) and Saxena et al[10] (2024) also found significant differences in SBP post-nebulization. Moreover, Thangavelu et al [14](2018) found that ropivacaine 0.25% was effective in reducing SBP post-intubation when compared to saline. Overall, the RD combination was found to be more effective in attenuating pressor response to intubation.

The study found that diastolic blood pressure (DBP) was not significantly different between groups before and after nebulization and intubation. However, after intubation, the DBP was significantly lower in the RD group compared to the R group. The addition of dexmedetomidine to ropivacaine led to a more pronounced reduction and stability in DBP during and after the intubation process. Patients in the ropivacaine group did not show much change post nebulisation and intubation, but a minimal rise in DBP was observed 15 minutes after intubation. Similar studies found significant differences in mean DBP before, after, one minute, five minutes, and 10 minutes of intubation. The drug ropivacaine was found to be effective in reducing DBP at intubation compared to saline. [10,14]

The study found no significant difference in mean arterial pressure (MAP) between the two groups before nebulization. After nebulization, the group RD showed a significantly lower MAP,

which continued at 1, 3, and 5 minutes post-intubation. No significant difference was observed at 10 minutes post-intubation. However, from 15 minutes to 30 minutes post-intubation, the group RD consistently showed significantly lower MAP, not requiring any intervention. The RD combination significantly reduced MAP compared to R alone at most time points measured. There was not much change in MAP in the ropivacaine group post nebulisation and intubation. In comparison to other studies, both group R and D showed a statistically significant reduction in MAP at intubation, after intubation, and extubation. Nebulised ropivacaine was found to be effective in reducing MAP after intubation when compared to saline.
The study found that patients in the RP group were mildly sedated after nebulisation, with a mean sedation score of 3.13. The addition of dexmedetomidine to ropivacaine had an additional advantage of mildly sedating the patient. The incidence of adverse effects, specifically bradycardia and hypotension, was not statistically significant in the RP group. However, bradycardia and hypotension were self-resolving and did not require intervention.

The study also found that patients in the RP group required a normal dose of propofol at induction, while in the RD group, the dose was significantly lower. This suggests that the addition of dexmedetomidine effectively reduces the dose of propofol at induction of anesthesia.

Research by Shrivastava et al (2022) [11]and Kumar et al (2020)[12] also showed a substantial decrease in propofol requirements. Misra et al (2021)[13] also found that the induction dose of propofol was significantly less in the dexmedetomidine group versus the saline group.

Overall, the consistent results across these studies underscore the efficacy of the dexmedetomidine combination in reducing propofol requirements, which can benefit patient outcomes and resource utilization.

CONCLUSION

The research demonstrates that the combination of nebulized ropivacaine and dexmedetomidine markedly diminishes the pressor response during laryngoscopy and intubation, while also enhancing the dose-sparing benefits of propofol and increasing sedative effects.

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