Print ISSN: 2321-6379
Online ISSN: 2321-595X

Original Article

Attenuation of Extubation Response in Patients Undergoing Abdominal and Lower-Limb Surgeries under General Anesthesia – A Comparative Study between Dexmedetomidine and Esmolol

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Abstract

Introduction: Laryngoscopy and tracheal intubation cause significant changes in the hemodynamics of patients. Many pharmacological methods have been devised to reduce the extent of hemodynamic events. This study compares the efficacy of two such agents, dexmedetomidine and esmolol, for the attenuation of response to extubation.

Materials and Methods: This study was carried out on 100 patients aged 18–60 years, belonging to the American Society of Anesthesiologists Grades I and II, having no major systemic comorbidities, and undergoing abdominal or lower-limb surgeries under general anesthesia. They were randomly divided into two groups: Group D (dexmedetomidine) and Group E (esmolol). Pre-operative, intraoperative, and post-operative vitals and side effects were monitored.

Results: Both the groups were comparable in terms of demographic variables, physical attributes, and baseline vital parameters. It was observed that dexmedetomidine is better at controlling heart rate and systolic, diastolic, and mean blood pressures during extubation than esmolol. There was no significant respiratory depression. No significant side effects were observed.

Conclusion: Dexmedetomidine is an effective and safe drug to provide stable hemodynamics and protects against the stress response to extubation in patients undergoing abdominal and lower-limb surgeries under general anesthesia.

Key words: Cardiovascular effects, Dexmedetomidine, Esmolol, Extubation, Laryngoscopy, Tracheal intubation

INTRODUCTION

Laryngoscopy and tracheal intubation cause significant changes in the hemodynamics of patients. A similar set of hemodynamic derangements have been noticed by various workers during tracheal extubation.[1] Direct laryngoscopy and endotracheal intubation are almost always associated with hemodynamic changes caused by epipharyngeal and laryngopharyngeal stimulation.[1] This increases sympathoadrenal activity resulting in hypertension, tachycardia, and arrhythmias.[1] This increase in blood pressure (BP) and heart rate (HR) is usually transitory, variable, and unpredictable. Hypertensive patients are more prone to have a significant increase in BP.[2] Transitory hypertension and tachycardia may be hazardous to those with hypertension, myocardial insufficiency, and cerebrovascular diseases.

Many pharmacological methods have been devised to reduce the extent of hemodynamic events with a high dose of opioids, local anesthetics such as lignocaine,[3] alpha[4]- and beta[5]-adrenergic drugs, and vasodilator drugs such as nitroglycerine.[6]

Dexmedetomidine[7] is a selective α2-adrenergic receptor agonist which is known to produce sedation[8] and analgesia

Access this article online

www.ijss-sn.com

Month of Submission : 07-2019
Month of Peer Review : 08-2019
Month of Acceptance : 09-2019
Month of Publishing : 09-2019

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and also has sympatholytic, anesthetic-sparing,[9] and hemodynamic-stabilizing properties without significant respiratory depression. Its sympatholytic effect[10,11] decreases mean arterial pressure and HR by reducing norepinephrine release and hence improves hemodynamic stability during extubation. It has also been documented to decrease post-operative nausea and vomiting[12] after surgery.

Esmolol is an ultra-short-acting β1-adrenoceptor antagonist without any partial agonistic action or local anesthetic action which is known to produce hemodynamic stability during laryngoscopy, intubation, and extubation. It selectively blocks β1-adrenoceptors and competitively reduces receptor occupancy by catecholamines and other β-adrenergic agonists. It has been shown to blunt hemodynamic responses to perioperative noxious stimuli. It also decreases the need for opioids during surgery and recovery.

The present study evaluates the comparative effect of dexmedetomidine and esmolol on the hemodynamic response to extubation in patients undergoing abdominal and lower-limb surgeries.

MATERIALS AND METHODS

This was a prospective, randomized, open-label, double-blind study. Prior approval of the Institutional Ethics Committee was taken. A total of 100 patients aged 18–60 years, belonging to the American Society of Anesthesiologists (ASA) Grades I and II, and undergoing abdominal or lower-limb surgeries under general anesthesia were included in the study. Any patient refusing to give consent, pregnant and lactating women, morbidly obese patients or patients having any systemic comorbidity (uncontrolled asthma or chronic obstructive pulmonary disease despite treatment, acute cholecystitis, and severe hepatic and renal diseases), and patients on beta-blockers were excluded from the study. Written informed consent was taken from all the patients.

Preoperatively, the patients were kept nil by the mouth for the last 10–12 h prior to surgery. All the necessary pre-operative investigations such as complete blood count, serum biochemistry, random blood sugar, and urine tests were done as per standard protocol.

The patients were, then, randomly divided into two groups as (CONSORT 2010 Flow Diagram):

- Group "D": In this group, patients will receive an intravenous bolus of 0.5 μg/kg dexmedetomidine starting 10 min before extubation.
- Group "E": In this group, patients will receive an intravenous bolus of 1 mg/kg esmolol starting 2 min before extubation.

Pre-operative vitals were recorded in the form of baseline pulse, electrocardiogram, SpO_2, and BP. Venous cannulation was done. Premedications were given. All patients received 500 ml of lactated Ringer's solution prior to induction. Induction was done with propofol, and vecuronium was used as a muscle relaxant. Patients were intubated with appropriate-sized polyvinyl chloride endotracheal tubes. Anesthesia was maintained by nitrous oxide in oxygen 50:50, and HR was maintained at a rate of 60–90 beats/min and systolic BP at 110–140 mmHg and diastolic BP at 70–100 mmHg. Any decrease in HR (<45 beats/min) was treated with injection atropine 0.001 mg/kg and injection glycopyrrolate 0.004 mg/kg. Anesthesia was reversed with injection Neostigmine 0.05 mg/kg and injection glycopyrrolate 0.008 mg/kg.

HR, systolic and diastolic BPs, respiratory rate, and SpO_2 were monitored preoperatively, at the time of bolus dose (10 min before extubation for Group D and 2 min before extubation for Group E), at extubation and up to 15 min after extubation. Patients were also observed for any complication.

Statistical Analysis

The analysis was done by SPSS. Quantitative data were analyzed using Student's *t*-test, and qualitative data were analyzed using Chi-square test. *P*-value of <0.05 was considered statistically significant.

RESULTS

Both the groups were comparable in terms of demographic variables (age and gender), physical attributes such as weight, ASA grade, and SpO_2.

There was also no statistically significant difference in the baseline HRs of both the groups. However, there was a statistically significant but clinically insignificant decrease (compared to baseline) in HR after extubation. However, HR remained more in Group E than Group D, even after 15 min [Table 1].

Similar were the trends of systolic BP [Table 2], diastolic BP [Table 3], and mean arterial pressure [Table 4]. All of these parameters remained higher in Group E than Group D from extubation till after 15 min, and this difference was statistically significant ($P < 0.05$).

The incidence of side effects (hypotension and bradycardia) is as per Table 5. The incidence and difference were not statistically significant ($P = 0.14$).

CONSORT 2010 Flow Diagram

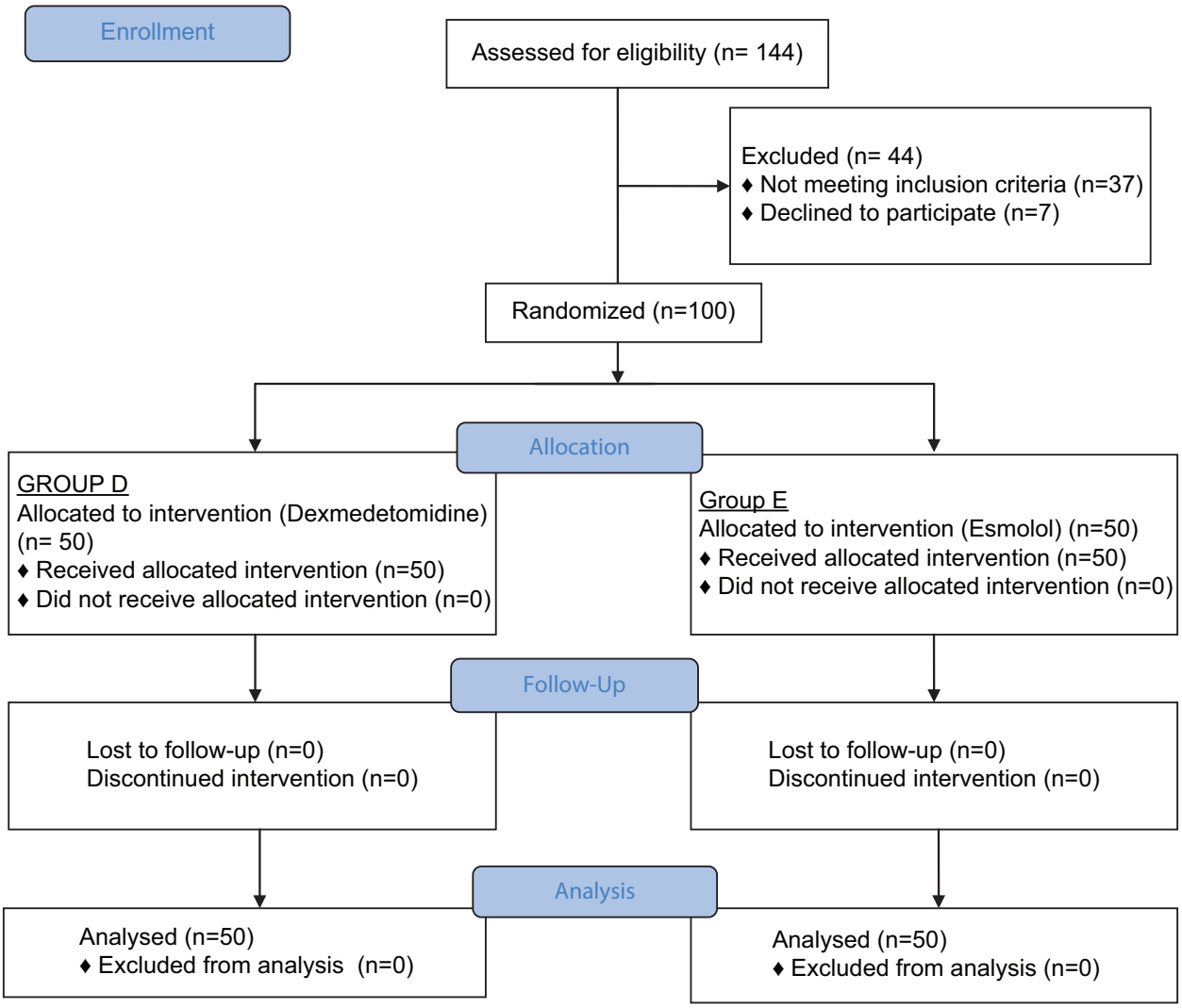

Table 1: Comparison of heart rate in Group D and Group E

Event	Mean heart rate (beats/min)		*P*-value	Significance
	Group D	Group E		
Pre-operative	78.680±9.861	80.880±6.997	0.201	Not significant
At the time of bolus dose	87.52±10.62	90.60±9.26	0.12	Not significant
At extubation	76.60±8.48	81.020±9.52	0.016	Significant
1 min	70.74±9.46	76.6±9.83	0.03	Significant
3 min	66.82±9.94	74.52±8.28	<0.001	Significant
5 min	65.30±8.28	73.46±6.73	<0.0001	Significant
10 min	63.78±5.68	71.94±6.94	<0.0001	Significant
15 min	62.32±4.37	70.64±5.92	<0.0001	Significant

Table 2: Comparison of systolic blood pressure in Group D and Group E

Event	Mean systolic blood pressure (mmHg)		*P*-value	Significance
	Group D	Group E		
Pre-operative	123.74±12.57	123.74±11.79	0.82	Not significant
At the time of bolus dose	125.62±10.45	129.02±9.42	0.09	Not significant
At extubation	110.58±6.89	117.92±8.04	<0.001	Significant
1 min	103.92±7.001	114.64±7.13	<0.0001	Significant
3 min	99.62±7.94	112.48±6.12	<0.0001	Significant
5 min	99.98±6.50	110.14±6.207	<0.0001	Significant
10 min	98.82±4.66	109.62±6.25	<0.0001	Significant
15 min	96.84±4.04	108.28±6.76	<0.0001	Significant

DISCUSSION

Significant hemodynamic fluctuations can occur during laryngoscopy and during intubation and extubation which can especially be detrimental in patients with reduced cardiopulmonary reserve. Various pharmacological agents have been studied to counteract these adverse hemodynamic changes during tracheal extubation.

Table 3: Comparison of diastolic blood pressure in Group D and Group E

Event	Mean diastolic blood pressure (mmHg)		*P*-value	Significance
	Group D	Group E		
Pre-operative	75.76±8.19	76.28±8.39	0.761	Not significant
At the time of bolus dose	79.12±10.14	78.74±9.80	0.849	Not significant
At extubation	68.88±5.72	73.88±6.46	<0.001	Significant
1 min	62.80±6.99	71.92±6.68	<0.0001	Significant
3 min	60.50±7.23	70.46±6.24	<0.0001	Significant
5 min	60.04±5.41	67.88±7.003	<0.0001	Significant
10 min	58.58±4.94	67.62±6.88	<0.0001	Significant
15 min	57.82±4.78	67.440±6.50	<0.0001	Significant

Table 4: Comparison of mean arterial pressures in Group D and Group E

Event	Mean arterial pressure (mmHg)		*P*-value	Significance
	Group D	Group E		
Pre-operative	91.78±9.24	91.98±9.29	0.914	Not significant
At the time of bolus dose	94.66±9.23	95.52±9.00	0.638	Not significant
At extubation	82.76±5.65	88.627±6.74	<0.0001	Significant
1 min	76.52±6.65	86.34±6.39	<0.0001	Significant
3 min	73.56±7.05	84.44±5.78	<0.0001	Significant
5 min	73.36±5.36	81.94±6.29	<0.0001	Significant
10 min	72.08±4.31	81.500±6.31	<0.0001	Significant
15 min	70.80±3.902	81.08±6.24	<0.0001	Significant

Table 5: Comparison of adverse effects

Event	Group D (%)	Group E (%)	*P*-value	Statistical significance
Hypotension	3 (6)	2 (6.66)	0.14	Not significant
Bradycardia	2 (4)	0		

In the present study, two such agents were studied: Dexmedetomidine and esmolol.

Both the groups were comparable in terms of demographic variables, physical attributes, ASA grades, and SpO_2. The baseline values of HR and BP (systolic, diastolic, and mean) were also comparable in both the groups.

HR

During extubation, HRs were higher in Group E than in Group D, which were statistically significant. This difference in HRs during extubation could be attributed to the termination of action of esmolol due to its very short half-life.

There was also a clinically insignificant decrease in HRs in both the groups after extubation. However, HRs remained more in Group E compared to Group D, which were statistically significant.

This difference could be attributed to the early start of dexmedetomidine bolus (10 min before extubation) as the bolus has to be administered over 10 min; whereas, esmolol is administered over 2 min before extubation.

Thus, the control of HR was significantly better in Group D than in Group E from extubation to 15 min after extubation.

BP

The trend of systolic BP, diastolic BP, and mean arterial pressure followed similar trends as discussed with HR above.

Thus, the control of BP (systolic BP, diastolic BP, and mean arterial pressure) was significantly better in Group D than in Group E from extubation to 15 min after extubation.

The cardiovascular effects of dexmedetomidine may be attributed to stimulation post-synaptic alpha-receptors leading to direct vasoconstriction and nitric oxide-mediated vasodilation.[13] Central sympatholysis also leads to hypotension and bradycardia.[14] There is a considerable decrease in myocardial work and myocardial O_2 consumption, and it has been found to decrease adverse cardiac events perioperatively.[15]

These results were in accordance with the study by Ghodki *et al.*,[16] an observational study on dexmedetomidine as an anesthetic adjuvant in laparoscopic surgery using entropy monitoring, which observed that extubation was smooth in all patients with minimal change in hemodynamics. Furthermore, in the study by Ornstein *et al.*,[17] demonstrating the effect of esmolol on HR, mean arterial pressure, and plasma renin activity, it was found that the control of mean arterial pressure was delayed, which may, in part, be related to the gradual decline in the plasma renin activity.

In another study by Uysal *et al.*,[18] comparing the effects of dexmedetomidine, esmolol, and sufentanyl, the hemodynamic responses to extubation were suppressed in the dexmedetomidine group. It was hypothesized to be due to dexmedetomidine being a highly selective alpha-2-agonist.

In another study, Ibraheim *et al.*[19] found that both esmolol and dexmedetomidine, when added to anesthetic regimen, provided an effective and well-tolerated method to reduce the amount of blood loss in patients undergoing scoliosis surgery, which may be attributed to attenuated hemodynamic responses.

Similarly, in the study by Kol *et al.*,[20] it was concluded that both esmolol and dexmedetomidine, combined

with desflurane, provided an effective and well-tolerated method of achieving controlled hypotension to limit the amount of blood in the surgical field in these adult patients undergoing tympanoplasty. Another study by Shams *et al.*,[21] comparing dexmedetomidine and esmolol with sevoflurane for induction of hypotension for functional endoscopic sinus surgery, had a similar conclusion. They concluded that both dexmedetomidine and esmolol with sevoflurane were safe agents for controlled hypotension and were effective in providing ideal surgical field during functional endoscopic sinus surgery.

Adverse Effects

In the present study, two patients (4%) had bradycardia (HR < 45 bpm) in Group D while no patients in Group E had bradycardia (statistically insignificant). However, clinically significant hypotension (defined as <20% of basal map sustained for 2 or more readings) was found in 3 (6%) patients in Group D and 2 (6.66%) patients in Group E.

This was similar to the study by Wiest,[22] which studied the therapeutic efficacy and pharmacokinetic characteristics of esmolol. The principal adverse effect of esmolol was noted to be hypotension (incidence of 0 to 50%), which was frequently accompanied by diaphoresis. The incidence of hypotension appeared to increase with doses exceeding 150 μg/kg/min and in patients with low baseline BP. Hypotension infrequently required any intervention other than decreasing the dose or discontinuing the infusion. Symptoms generally resolved within 30 min after discontinuing the drug. They concluded that in surgical and critical care settings, the pharmacokinetic profile of esmolol allows the drug to provide rapid pharmacological control and minimizes the potential for serious adverse effects.

In another study, Aho *et al.*[7] showed that dexmedetomidine causes bradycardia at a dose of >2.4 mcg/kg. Wiest,[22] in the study, demonstrated that esmolol causes bradycardia at a dose of 150 mcg/kg/min.

Limitations

The study was limited to the outpatient department attendance and indoor admission of the patients undergoing abdominal or lower-limb surgeries under general anesthesia. Therefore, the results may not be generalized.

CONCLUSION

It can be effectively concluded that although both, dexmedetomidine and esmolol, are safe and efficacious in attenuating the hemodynamic stress response during extubation, dexmedetomidine is better at controlling HR and systolic, diastolic, and mean BPs during extubation than esmolol. Thus, dexmedetomidine is an effective and safe drug to provide stable hemodynamics and protects against the stress response to extubation in patients undergoing abdominal and lower-limb surgeries under general anesthesia.

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How to cite this article: Mamde R, Chhallani VP, Jaiswal AV. Attenuation of Extubation Response in Patients Undergoing Abdominal and Lower-Limb Surgeries under General Anesthesia – A Comparative Study between Dexmedetomidine and Esmolol. Int J Sci Stud 2019;7(6):22-27.

Source of Support: Nil, **Conflict of Interest:** None declared.