European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 09, Issue 04, 2022

Original Research Article

LARYNGOSCOPY INTUBATION AND EXTUBATION ARE AFFECTED BY MELATONIN: A PROSPECTIVE STUDY

[1]Dr. Adithi Devi E, [2]Dr. M Bhawathi, [3]Dr. Pavani Kalyanam, [4]Dr. PV Shiva

[1]Assistant Professor, Department of Anesthesiology, Osmania Medical College, Niloufer Hospital Hyderabad, Telangana, India
[2]Associate Professor, Department of Anesthesiology, Osmania Medical College, Niloufer Hospital Hyderabad, Telangana, India
[3]Professor, Department of Anesthesiology, Osmania Medical College, Osmania General Hospital Hyderabad, Telangana, India
[4]Professor, Department of Anesthesiology, Osmania Medical College, Niloufer Hospital Hyderabad, Telangana, India

Corresponding Author:
Dr. PV Shiva

Abstract

Aim and objectives: Hypertension and increased heart rate are prevalent during laryngoscopy and tracheal intubation. Acute LV failure, dysrhythmias, IC haemorrhage, pulmonary edoema and myocardial infarction are all possible complications. Patients with hypertension had a heightened pressor response, despite being preoperatively normalized with anti-hypertensive medication. The purpose of this research is to see if melatonin is more effective than a placebo at reducing the Haemodynamic reactions to laryngoscopy and endotracheal intubation. Research into the effects of melatonin on extubation response and intraoperative hemostasis is also a goal.

Materials and Methods: This study took place between June 2020 and May 2022 at Public Sector Tertiary care center and the Government Ear, Nose, and Throat Hospital. There were a total of 60 participants in the study. They split up into pairs. Melatonin 6 mg capsules (Group M) and a placebo (Vitamin D3) were given to Group C, both to be taken 120 minutes before to surgery.

Results: The melatonin group had a considerably lower increase in HR compared to the control group during laryngoscopy and intubation (P0.0029). The melatonin group also had considerably decreased heart rate variability during and after extubation compared to the placebo group. After induction, during laryngoscopy and intubation, and for the first 10 minutes after tracheal intubation, systolic blood pressure was considerably lower in the melatonin group. Systolic blood pressure was considerably lower in the melatonin group after surgery. Compared to the placebo group, the SBP of those receiving melatonin prior to, during, and after extubation dropped dramatically. The melatonin group had lower diastolic blood pressure than the placebo group throughout laryngoscopy and intubation, as well as after 1 minute, 5 minutes, and 10 minutes post-intubation. The intraoperative DBP in the melatonin group was substantially lower. DBP was likewise considerably lower in the melatonin group after extubation. As a result, the melatonin group had considerably lower mean arterial pressure (MAP) during the intraoperative time. There was a huge discrepancy between the groups during the extubation process and immediately afterward.

Conclusion: The results of the study show that the hemodynamic reactions to laryngoscopy, intubation, and extubation can be reduced by giving the patient 6 milligrammes of exogenous melatonin orally 120 minutes before intubation. In addition, it aids in keeping intraoperative hemodynamics steady.

Keyword: Haemodynamic, laryngoscopy, intubation, extubation, melatonin, endotracheal

Introduction

Hypertension and increased heart rate are prevalent during laryngoscopy and tracheal intubation [1]. The extent to which haemodynamic changes are detected may depend on variables such as the patient's level of anaesthesia, the precautions taken before any airway manipulation, the type of anaesthetic used, and the time it takes to perform laryngoscopy and intubation. It is thought that an increase in catecholamine activity is the primary mechanism underlying hypertension and tachycardia [2]. The vast majority of patients already had reflex tachycardia and hypertension before to intubation, and these symptoms were frequently exacerbated by the procedure. The rise in HR and BP is temporary, sporadic, and hard to anticipate. It is possible that the systolic pressure will average out at +45 mm Hg. Pulse rate fluctuations, most notably sinus tachycardia but also ventricular tachycardia, are common side effects [3]. In healthy people, occasional spikes in blood pressure or heart rate probably won't cause any lasting damage. Hypertension, myocardial insufficiency, cerebrovascular disease, elevated intracranial pressure, and aneurysmal vascular disease are all conditions that could be made worse by either. Acute left ventricular failure (LVF), dysrhythmias, intracranial haemorrhage, pulmonary edoema, and myocardial infarction are all possible complications of the cardiovascular system as a result of laryngoscopy and intubation [4-6]. Patients with hypertension had a heightened pressor response, despite being preoperatively normalized with antihypertensive treatment. Nodal rhythm, atrial and ventricular extrasystoles, and pulsus alternans are the most prevalent dysrhythmias; multifocal extrasystoles, pulsus bigeminy, and atrial fibrillation occur less frequently [7-10]. There have been many attempts to mitigate this reaction in high-risk populations. Despite the best efforts of anesthesiologists, intubating a patient with an endotracheal tube elicits a circulatory response that cannot be reliably suppressed by IV anaesthetic induction medications [11-14]. Additional pharmacological measures have included the use of volatile anaesthetics, topical and IV lidocaine, opioids like fentanyl, alfentenyl, calcium channel blockers like verapamil, diltiazem, sympatholytics like clonidine, dexmedetomidine, methyldopa, beta blockers like esmolol, propranolol, benzodiazepine like mid Respiratory depression, hypotension, tachycardia, bradycardia, rebound hypertension, and allergic reaction are some of the side effects that can occur with any given drug [15-18]. The search for a more effective agent, therefore, predates modern times. Pineal gland secretes the hormone melatonin (N-Acetyl-5-methoxytryptamine), which regulates sleep. Its hypnotic effects are the reason it is so well-known among both doctors and patients [19-22]. Also, it effectively relieves pain. Unlike BZD, it does not lead to the unpleasant aftereffects of a hangover and does not cause addiction or dependence in the user. It reduces inflammation, protects cells from free radical damage, and lowers blood pressure [23, 24]. When combined with melatonin, the dosage of IV propofol used to induce anaesthesia can be reduced [25]. While melatonin has shown promise as a premedicant in anaesthetics, there is still just a small body of research on its use. Injecting yourself with melatonin from the outside helps you fall asleep faster and sleep better. In contrast to BZD and its derivatives, it does not cause cognitive impairment and instead promotes sleep patterns more similar to those of the natural world. Premedication with this substance has been tested across a wide range of doses in both adults and children [26-32].

Materials and Methods

Following the receipt of approval from the hospital ethics committee and the informed consent of the study's participants, this prospective randomised control trial was carried out. This was carried out at Public Sector Tertiary care center. The research was carried out between the periods June 2020 to May 2022. The research was carried out on sixty patients who were either male or female and were between the ages of 20 and 45. All of the patients were scheduled to have elective surgical procedures under general anaesthesia. This research was carried out on individuals who had undergone a variety of surgical procedures, including those pertaining to the ear, nose, and throat (ENT), the head and neck (H&N), urology (PCNL), and neurosurgery (Laminectomy, etc.).

Inclusion criteria

ASA physical status Grade I and Grade II, respectively, Weight between 40 and 65 kg, Age between 20 and 45 years old, either male or female Surgical procedure that must be performed under general anaesthesia and must last for at least two hours.

Exclusion criteria

Diseases such as diabetes, hypertension, and mental illnesses Consumption of antipsychotics, sedatives, anxiolytics, and antiepileptic medications; sleep disorders; obesity; and Drug Allergy, Intubation was expected to be challenging, Intubation that requires more than one try or more than 20 seconds for laryngoscopy, pregnancy, or lactation; abnormalities on the electrocardiogram; intubation complications. Clinical evaluations were performed on all of the patients. It was determined that there was neither a medical condition present, nor was there a history of drug use. Patients who had a history of chest pain, palpitations, syncope, or difficulties with their respiratory system, liver, or kidneys were not allowed to participate in the trial. Assessments of the patient's airway were performed to rule out the possibility of difficult intubation.

Results

Age, gender distribution, weight, ASA status, and surgical time were all the same in both research groups. Significant difference between two groups is implied by a P value of less than 0.05. No significant difference between the two groups is implied by a P value > 0.05. When compared to the control group, the melatonin group's increase in HR was considerably lower during laryngoscopy (P = 0.0029), at 1 minute (P = 0.046), and at 10 minutes following intubation (P value 0.0042). At 30 minutes (P 0.0001), 60 minutes (P 0.0004), 90 minutes (P 0.0069), and 120 minutes (P 0.0001) during the perioperative time, HR was considerably lower in the melatonin group compared to the placebo. During extubation, the HR increased in the melatonin and placebo groups alike. However, the melatonin group's increase in HR was noticeably lower during extubation (P 0.0013). At one minute (P 0.0007), three minutes (P 0.0001), and five minutes (P 0.0001) following extubation (table 1).

Table 1: Different variables

Variable	Group C	Group M
Age (in years) Mean	30.8	29.9
Weight (in Kg) Mean	56.8	55.03
Surgery Duration (Mean Hrs)	2.2	2.49
ASA Grade 1/2	28/2	27/3

Table 2: Systolic Blood Pressure at various time points

Sr. No.	Time	Melatonin Mean	Melatonin Mean	Placebo Mean	SD	t-Value	P-Value
1.	Baseline	119.87	119.87	115.30	8.06	1.4662	0.1227
2.	120 Mins After Drug	122.13	122.13	127.77	15.82	1.5576	0.1028
3.	After Induction	80.60	90.60	116.57	17.3	6.2347	<0.0001
4.	During Laryngoscopy and Intubation	135.03	138.03	153.93	27.2	2.5506	0.0134
5.	1 Minute after intubation	120.00	123.10	140.73	25.6	3.2359	0.0020
6.	2 Minutes after intubation	117.93	118.93	132.63	27.6	2.4061	0.0193
7.	3 Minutes after intubation	113.57	113.57	126.93	25.4	2.4784	0.0161
8.	5 Minutes after intubation	110.10	111.10	123.50	21.3	2.6491	0.0104
9.	10 Minutes after intubation	106.03	107.03	123.80	16.6	4.7637	< 0.0001
10.	30 mins intraoperative	109.20	110.90	121.27	14.4	3.2992	0.0017
11	60 mins intraoperative	108.03	111.03	121.63	12.2	3.7131	0.0005
12.	90 mins intraoperative	112.10	114.10	122.53	11.9	2.7219	0.0086
13.	120 mins intraoperative	117.23	115.23	119.93	8.74	1.5924	0.1167
14.	During extubation	139.77	138.77	153.67	12.2	3.9958	0.0002
15.	1 Minute after extubation	128.00	129.70	145.13	13.0	4.5166	< 0.0001
16.	3 Minutes after extubation	127.07	124.07	142.50	11.2	5.6215	<0.0001
17.	5 Minutes after extubation	122.30	121.50	135.97	6.77	6.1078	<0.0001

There was no statistically significant difference between the two groups' resting blood pressure levels (P value 0.1227). Following induction, the melatonin group's SBP rose by a considerably less amount than the control group's did during laryngoscopy (P= 0.0134). One minute after intubation (P 0.0020), two minutes (P 0.0193), and three minutes (P 0.0020) (P 0.0161). Both at 5 minutes (P=0.0104) and 10 minutes (P0.0001) post-intubation, there was a significant improvement. During the intra operation time, melatonin significantly reduced

ISSN 2515-8260 Volume 09, Issue 04, 2022

SBP compared to placebo at 30 minutes (P 0.0017), 60 minutes (P 0.0005), and 90 minutes (P 0.0086). During extubation, SBP rose in both groups. Nonetheless, this was significantly lower in the melatonin group before (P0.0002), after (P0.0001), and within 1 minute, 2 minutes, and 5 minutes of extubation (table 2).

Fig 1: Screenshot examples taken from Philips Sure Signs VM8 Monitors during the operation

There was no significant difference in MAP at baseline between the groups (P 0.5902). At all times, the non-melatonin group had a greater mean arterial pressure (MAP) than the melatonin group. After 1 minute (P=0.0241), 5 minutes (P=0.0193), and 10 minutes (P 0.0001) after intubation, the melatonin group had a significantly lower mean arterial pressure (MAP). At 60 minutes (P = 0.0047) and 90 minutes (P = 0.0227) during surgery, MAP was considerably lower in the melatonin group. Extubation (P=0.0177), 1 minute (P=0.0021), 3 minutes (P=0.0019), and 5 minutes (P 0.0001) following extubation all showed significantly smaller increases in MAP in the melatonin group. It is clear that the melatonin group has steady behaviour throughout the laryngoscopy, intraop period and extubation phases, whereas the placebo group displays erratic hemodynamic response.

Discussion

The current investigation is to determine whether or not melatonin can reduce the hemodynamic reactions to invasive procedures like laryngoscopy and intubation. Any number of physiological systems, including the endocrine and autonomic nervous systems, can be perturbed as a stress reaction to being under anaesthesia. Approximately 30–45 seconds after laryngoscopy, the anaesthetized patient's heart rate and arterial pressures (SBP, DBP, MAP) reach their maximum reflex cardiovascular effects. Reflex sympathetic discharge from stimulated epipharynx or larynx causes the hemodynamic shifts. The rise in heart rate and blood pressure is usually brief, sporadic, and unpredictable. In healthy people, occasional spikes in blood pressure or heart rate probably won't cause any lasting damage. However, people with hypertension, myocardial insufficiency, or cerebrovascular illness may be at risk from either. There are tense periods throughout general anaesthesia, but none more so than the time right before intubation. These alterations peak at around 1 minute after intubation and persist for another 5-10 minutes. When performing a laryngoscopy, the pharynx and larynx are stretched, which triggers a hemodynamic reaction. It was found that several pharmacological medications could be employed to dampen the hemodynamic response. The need for laryngoscopy, which stretches and presses on the laryngeal and pharyngeal tissues, rendered lidocaine spray surface anaesthesia ineffective. The stress response is not noticeably reduced by 1.5 mg/Kg lidocaine. Alterations in heart rate and arterial pressure can be managed with the help of volatile anaesthetic drugs administered at a deep anaesthetic level. However, it may cause hypotension and a slower recovery, and it is useless for rapid sequence intubation. Intra-operative hypotension brought on by vasodilators may necessitate invasive arterial pressure monitoring. Opioids such as fentanyl, buprenorphine, and alpha2 agonist dexmedetomidine, as well as medications including labetalol, diltiazem, verapamil, and nicardipine, have also been used. Finding the best treatment method(s), along with the optimal dosing and timing of those methods, is an ongoing process. Melatonin has recently been shown to have beneficial effects in dampening the haemodynamic response after intubation. There is a dearth of melatonin-related anaesthesia studies. The purpose of this research is to determine how melatonin affects the body's reaction to intubation, hemodynamic stability during surgery, and extubation. Extubation, recovery, and emergence issues are more common than intubation issues. There is a lack of consensus on many fronts, and no established norms or protocols.

Conclusions

Because of its versatility, melatonin could one day join the ranks of anaesthetics. As an anxiolytic and sedative, as a hypnotic, as an induction adjunct, perioperatively for analgesia, and to lessen the stress reaction to surgery, it can be an appealing choice for premedication. In addition to being an antioxidant, it also protects neurons. This research was conducted to learn how melatonin affects blood pressure and heart rate in reaction to a variety of invasive medical procedures, including laryngoscopy, intubation, and extubation. The haemodynamic responses to laryngoscopy and intubation can be mitigated by taking 6 milligrammes of melatonin orally 120 minutes before the procedure. It's also noted that melatonin helps to keep blood pressure and heart rate steady throughout surgery, and that it reduces the severity of the reactions after extubation.

Conflict of Interest: None

Funding Support: Nil

References

1. Ramlall V, Zucker J, Tatonetti N. Melatonin is significantly associated with survival of intubated COVID-19 patients. Med Rxiv, 2020.
2. Maqbool SF, Gupta KC, Mehta N. Comparative Clinical Evaluation of Preoperative Oral Pregabalin and Melatonin for Attenuation of Haemodynamic Responses to Laryngoscopy

and Intubation, 2020.

3. Ali ST, Asthana V, Gupta D, Singh SK. A Comparative Evaluation of Oral Clonidine, Dexmedetomidine, and Melatonin as Premedicants in Pediatric Patients Undergoing Subumbilical Surgeries. Romanian Journal of Anaesthesia and Intensive Care. 2020;27(1):35-42.
4. Gupta P, Jethava D, Choudhary R, Jethava DD. Role of melatonin in attenuation of haemodynamic responses to laryngoscopy and intubation. Indian journal of anaesthesia. 2016;60(10):712.
5. Chandra DK. Comparative study of Melatonin and Pregabalin for attenuation of hemodynamic stress response to laryngoscopy and endotracheal intubation in Laparoscopic Cholecystectomy. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), 2020, 19(10).
6. Choudhary S, Sharma S, Kumari I, Kalluraya S, Meena K, Dave T. Comparative evaluation of oral melatonin and oral clonidine for the attenuation of haemodynamic response to laryngoscopy and tracheal intubation a prospective randomised double blind study. Indian Journal of Anaesthesia. 2020;64(8):696.
7. Kumar R, Kumari K, Janweja S, Verma M, Sharma A, Paliwal B, *et al*. Role of melatonin in attenuation of hemodynamic response to intubation and anesthetic requirements: a randomized, controlled, double-blind study. Brazilian Journal of Anesthesiology (English Edition), 2021.
8. Ramlall V, Zucker J, Tatonetti N. Melatonin is significantly associated with survival of intubated COVID-19 patients. Med Rxiv, 2020.
9. Maqbool SF, Gupta KC, Mehta N. Comparative Clinical Evaluation of Preoperative Oral Pregabalin and Melatonin for Attenuation of Haemodynamic Responses to Laryngoscopy and Intubation, 2020.
10. Ali ST, Asthana V, Gupta D, Singh SK. A Comparative Evaluation of Oral Clonidine, Dexmedetomidine, and Melatonin as Premedicants in Pediatric Patients Undergoing Subumbilical Surgeries. Romanian Journal of Anaesthesia and Intensive Care. 2020;27(1):35-42.
11. Ravikiran H, Lakshman K, Ranganath N. Dose Effect Response of Melatonin Premedication in Oncosurgical Patients: A Randomised Controlled Trial. Journal of Clinical & Diagnostic Research, 2021,15(12).
12. Gooty S, Priyanka DSR, Pula R, Pakhare V, Ramachandran G. A Comparative Study of Effect of Oral Melatonin Versus Oral Midazolam as Premedicant in Children Undergoing Surgery Under General Anesthesia. Journal of Cellular and Molecular Anesthesia. 2021;7(3):160-167.
13. Ali M. A study on role of oral melatonin as premedicant in general anaesthesia at tertiary care hospital. IJMA. 2018;1(2):53-63.
14. Dhanachandra L, Singh LK. Haemodynamic responses to laryngoscopy and endotracheal intubation after intravenous dexmedetomidine: A comparison between two doses. Evid Based Med Healthc. 2019;6:520-6.
15. Bhashyam S, Prasad PK, Lakshmi BS. Comparative Evaluation of Oral Gabapentin versus Oral Pregabalin Premedication for Anxiolysis, Sedation, and Attenuation of Pressor Response to Endotracheal Intubation. International Journal of Scientific Study. 2015;2(12):32-36.
16. Quintard H, l'Her E, Pottecher J, Adnet F, Constantin JM, De Jong A, *et al*. Intubation and extubation of the ICU patient. Anaesth Crit Care Pain Med. 2017;36(5):327-341.

17. Asai T, Koga K, Vaughan RS. Respiratory complications associated with tracheal intubation and extubation. British journal of anaesthesia. 1998;80(6):767-775.
18. Langeron O, Bourgain JL, Francon D, Amour J, Baillard C, Bouroche G, *et al*. Difficult intubation and extubation in adult anaesthesia. Anaesthesia Critical Care & Pain Medicine. 2018;37(6):639-651.
19. Smith MM, Kuhl G, Carvalho PRA, Marostica PJC. Flexible fiber-optic laryngoscopy in the first hours after extubation for the evaluation of laryngeal lesions due to intubation in the pediatric intensive care unit. International journal of pediatric otorhinolaryngology. 2007;71(9):1423-1428.
20. Yildiz M, Tavlan A, Tuncer S, Reisli R, Yosunkaya A, Otelcioglu S. Effect of dexmedetomidine on haemodynamic responses to laryngoscopy and intubation. Drugs in R & D. 2006;7(1):43-52.
21. Brown J, Gregson FKA, Shrimpton A, Cook TM, Bzdek BR, Reid JP, *et al*. A quantitative evaluation of aerosol generation during tracheal intubation and extubation. Anaesthesia. 2021;76(2):174-181.
22. Miller KA, Harkin CP, Bailey PL. Postoperative tracheal extubation. Anesthesia & Analgesia. 1995;80(1):149-172.
23. Kewalramani A, Partani S, Sharma NP, Sharma V. Comparison of labetalol versus dexmedetomidine to assess the haemodynamic responses to laryngoscopy and intubation during induction of general anaesthesia–A prospective, randomized, controlled study. Indian J Clin Anaesth. 2016;3(4):512-517.
24. Hill RS, Koltai PJ, Parnes SM. Airway complications from laryngoscopy and panendoscopy. Annals of Otology, Rhinology & Laryngology. 1987;96(6):691-694.
25. Quintard H, l’Her E, Pottecher J, Adnet F, Constantin JM, Dejong A, *et al*. Intubation et extubation du patient de réanimation. Anesthésie & Réanimation. 2018;4(6):523-547.
26. Newmark JL, Ahn YK, Adams MC, Bittner EA, Wilcox SR. Use of video laryngoscopy and camera phones to communicate progression of laryngeal edema in assessing for extubation: a case series. Journal of Intensive Care Medicine. 2013;28(1):67-71.
27. Lu C, Zhang LM, Zhang Y, Ying Y, Li L, Xu L, *et al*. Intranasal dexmedetomidine as a sedative premedication for patients undergoing suspension laryngoscopy: a randomized double-blind study. PloS one. 2016;11(5):e0154192.
28. Bhatnagar V, Jinjil K, Dwivedi D. Time to include video laryngoscope as a tool for extubation in difficult airway cases!. Indian Journal of Anesthesia. 2019;63(8):677-678.
29. Warner MA, Fox JF. Direct laryngoscopy and endotracheal intubation complicated by anterior tracheal laceration secondary to protrusion of preloaded endotracheal tube stylet. A&A Practice. 2016;6(4):77-79.
30. Khatami SF, Parvaresh P, Behjati S. Common complications of endotracheal intubation in newborns, 2011.
31. Efe EM, Bilgin BA, Alanoglu Z, Akbaba M, Denker C. Comparison of bolus and continuous infusion of esmolol on hemodynamic response to laryngoscopy, endotracheal intubation and sternotomy in coronary artery bypass graft. Revista Brasileira de Anestesiologia. 2014;64:247-252.
32. Gupta P, Jethava D, Choudhary R, Jethava DD. Role of melatonin in attenuation of haemodynamic responses to laryngoscopy and intubation. Indian journal of anaesthesia. 2016;60(10):712.