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Research Article

ROLE OF MELATONIN IN ATTENUATION OF HAEMODYNAMIC RESPONSES TO LARYNGOSCOPY AND INTUBATION IN GENERAL ANESTHESIA

SOUPARNIKA SR, SANTHI KS, SUSAN T CHEERAN*

Department of Anaesthesiology, Government Medical College, Kottayam. Email: gesuryju@gmail.com

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ABSTRACT

Objective: The aim of the study was to study the effects of melatonin in attenuation of hemodynamic responses such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean blood pressure (MBP) to laryngoscopy and intubation (L&I) in general anesthesia.

Methods: This was a prospective and observational study conducted in a tertiary care teaching hospital on 120 patients aged 20–45 years belonging to American Society of Anaesthesiologists Grade I, undergoing elective surgery under general anesthesia. Selected patients were allotted into Group A (control group) and Group B (patients who took tablet melatonin 6 mg, 120 min before induction) of 60 patients each. Hemodynamic parameters such as HR, systolic, diastolic, and MBPs were recorded before the administration of drug (baseline), 120 min after administration of study drug (just before induction), immediately after induction, at L&I, just after L&I and at 1, 3, 5, and 10 min thereafter.

Results: The gender distribution and mean age of both groups were comparable. Both the groups were also comparable with respect to baseline values of HR, systolic, diastolic, and mean arterial pressure. The control group showed significant increases in HR, SBP, DBP, and mean arterial blood pressure after L&I and this increase persisted for the next 10 min. In the melatonin group, there was no significant increase in HR, systolic, diastolic, or MBP at any point of measurement after L&I.

Conclusion: Pre-treatment with 6 mg oral melatonin 120 min before induction of anesthesia is effective for attenuating hemodynamic responses to L&I without significant side effects.

Keywords: Melatonin, Stress response, Laryngoscopy, Intubation.

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INTRODUCTION

Laryngoscopy and endotracheal intubation are considered potent noxious stimuli which provoke hemodynamic responses leading to a marked increase in heart rate (HR) and blood pressure [1]. These events are especially detrimental to individuals who have limited myocardial reserve due to coronary artery disease, cardiac dysrhythmias, congestive heart failure, hypertension, cardiomyopathy, and geriatric age group [2]. Hence, it is mandatory to take measures to attenuate these pressor responses. During intubation of trachea, the laryngeal and tracheal sensory receptors are stimulated which result in the release of endogenous catecholamines resulting in tachycardia and hypertension [3].

Since the invention of laryngoscopy and endotracheal intubation, various drug regimens and techniques have been used from time to time to attenuate these stress responses. Some of such agents being opioids (fentanyl and alfentanil), calcium channel blockers (verapamil and diltiazem), sympatholytics (clonidine, dexmedetomidine, and methyldopa), beta-blockers (esmolol and propranolol), benzodiazepines (midazolam and alprazolam), barbiturates, propofol, pregabalin, and peripheral vasodilators (sodium nitroprusside and nitroglycerine) [4]. However, each agent has some limitations such as respiratory depression, hypotension, tachycardia, bradycardia, rebound hypertension, or allergic reactions. Hence, there has always been a need for a better agent.

Melatonin (N-acetyl-5-methoxytryptamine) is an endogenous sleep-regulating hormone secreted by pineal gland. It has sedative, analgesic, anti-inflammatory, anti-oxidative, and a chronobiotic. It has been used for sleep disorders, jet lag, perioperative anxiolysis and sedation, cognitive, and psychomotor functions. Exogenous administration of melatonin facilitates sleep onset and improves the quality of sleep. It is different from benzodiazepines and their derivatives in that it produces natural sleep pattern and does not lead to impairment of cognitive functions. It has been mainly studied in view of pre-operative anxiolysis, sedation in Intensive Care Unit, pre-operative cognitive, and psychomotor functions [5]. Hence this study was conceptualized to study the effect of melatonin in attenuation of hemodynamic responses such as HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean blood pressure (MBP) to laryngoscopy and intubation (L&I) in general anesthesia.

METHODS

This prospective and observational study done over a period of 12 months in our hospital included 120 patients who were posted for elective surgeries under general anesthesia. The study commenced after getting ethical clearance from the Institutional Review Board of our institute. Informed written consent was taken from all patients included in the study. Patients were allocated into two groups of 60 each.

- Group A – control group
- Group B – patients who were given tablet melatonin 6 mg pre-operative.

Inclusion criteria

Patients belonging to the American Society of Anaesthesiologists (ASA) physical status Grade I, age 20–45 years requiring general anesthesia for duration longer than 30 min were included in the study.

Exclusion criteria

Patients with comorbid illness such as diabetes, hypertension, psychiatric illness, intake of antipsychotics, sedatives, anxiolytics and antiepileptic drugs; sleep disorders, obesity, and drug allergy were excluded from the study. Likewise, patients with anticipated difficult intubation and those requiring more than three attempt or more than 20 s for laryngoscopy were excluded from the study. The pregnant and lactating females were also excluded from the study.

Methodology

All patients were evaluated and assessed in the pre-operative period. They were kept fasting for 6–8 h and received tablet alprazolam 0.25 mg at night and in the morning of surgery. In the pre-operative room, intravenous access was secured and fluid started. Group A was control group and did not get any tablets. Group B was given 6 mg melatonin tablet with a sip of water. Patients were watched for any episodes of nausea, vomiting, dizziness, headache, respiratory depression, arrhythmias, bradycardia, hypotension, and restlessness. 120 min after administration of drug patient was shifted to operation theatre. On receiving the patient in the operation theater, routine monitoring was commenced which included HR, electrocardiogram, SpO_2, non-invasive blood pressure (NIBP), and end-tidal carbon dioxide ($EtCO_2$). All the patients were administered 100% oxygen for 3 min before induction. Glycopyrrolate 0.004 mg/kg and fentanyl 2 µg/kg were administered intravenously. Induction was attained with intravenous Propofol 2 mg/kg intravenously. Succinylcholine was given intravenously 2 mg/kg to facilitate endotracheal intubation with proper sized cuffed endotracheal tube. Maintenance of anesthesia was attained with inhalation of Isoflurane 1 minimum alveolar concentration; nitrous oxide: Oxygen 60:40. Muscle relaxation was attained with Vecuronium bromide administered in the dose of 0.08 mg/kg intravenously as loading dose and one-fourth of the initial dose as maintenance doses. Mechanical ventilation was adjusted to maintain normocapnia ($EtCO_2$ values of 35–38 mmHg). Intravenous injection paracetamol 1 g was given slowly 15 min before completion of surgery for post-operative analgesia. At the end of surgical procedure, residual neuromuscular block was adequately reversed using IV neostigmine 2.5 mg and glycopyrrolate 0.4 mg. Patients were extubated and shifted to post-anesthesia care unit.

Hemodynamic parameters such as HR, systolic, diastolic, and MBPs were recorded before the administration of drug (baseline), 120 min after administration of study drug (just before induction), and immediately after induction, at L&I, just after L&I and at 1, 3, 5, and 10 min thereafter.

In the post-anesthesia care unit, the patients received the standard postoperative care including oxygen administration through face mask at 4–6 L/min and monitoring of HR, NIBP, respiratory rate, and SpO_2. Both groups were observed for any episodes of nausea, vomiting, dizziness, headache, respiratory depression, arrhythmias, bradycardia, hypotension, and restlessness till 24 h postoperatively.

Statistical analysis

Data were entered in MS EXCEL and analyzed using SPSS 23 software. The statistical test used for this study is descriptive statistics such as Mean Standard deviation and for significant level testing (p-value), independent sample test and Chi-square were used. For all tests, $p<0.05$ was considered as statistically significant.

RESULTS

It is observed from Table 1 that there was no statistically significant difference in age distribution among the two groups.

Table 2 shows that the two groups were comparable with respect to gender distribution.

Fig. 1 shows that in Group A (Control group), there was a rise in HR from baseline values at laryngoscopy (93.76±13.06) and persisted thereafter till 10 min. In the melatonin group (Group B), there was no rise in HR from baseline values at the time of laryngoscopy (64.76±9.18). Thereafter, it was maintained at lower values at all points of time till 10 min after laryngoscopy and intubation ($p<0.0001$).

Baseline Mean SBP was comparable between the two groups ($p>0.05$).

Fig. 2 shows that SBP was higher from baseline values in control group during L&I (139.98±16.35). Thereafter, this increase persisted at all points of time until 10 min ($p<0.0001$). In the melatonin group, there was no rise following L&I (112.52±8.96) and the patients were stable at all points of time after the administration of the drug ($p<0.0001$).

Baseline Mean DBP was comparable between the two groups ($p>0.05$). Fig. 3 shows that in Group A DBP was higher from baseline values during L&I (85.15±12.66) and persisted until 10 minutes thereafter ($p<0.0001$). In the melatonin group, there was no rise during

Table 1: Age distribution among both the groups

	Group	n	Mean	Std. deviation	t	p-value
Age	Group A	60	35.26	6.52	1.7	0.61
	Group B	60	33.23	6.1349		P>0.05

Table 2: Gender distribution among Group A and Group B

Group	Sex		Total
	Male	Female	
Group A			
Count	28	32	60
% within Group	46.7	53.3	100.0
Group B			
Count	32	28	60
% within Group	53.3	46.7	100.0
Total			
Count	60	60	120
% within Group	50.0	50.0	100.0

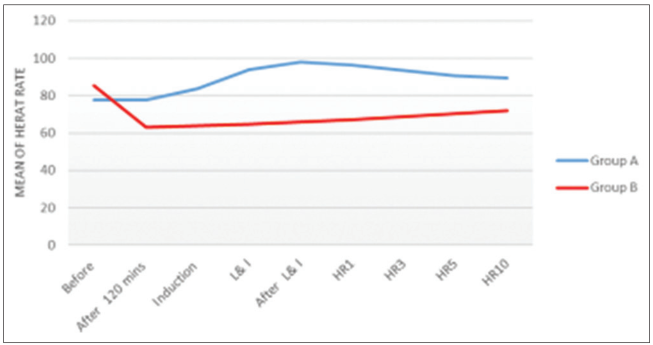

Fig. 1: Heart rate at various points of time (beats/min)

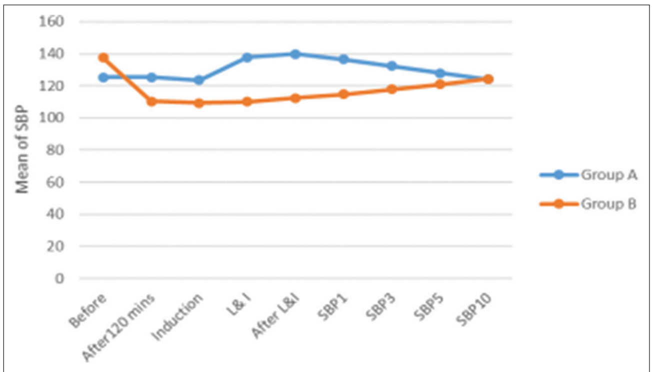

Fig. 2: Systolic blood pressure at various points of time (mmHg)

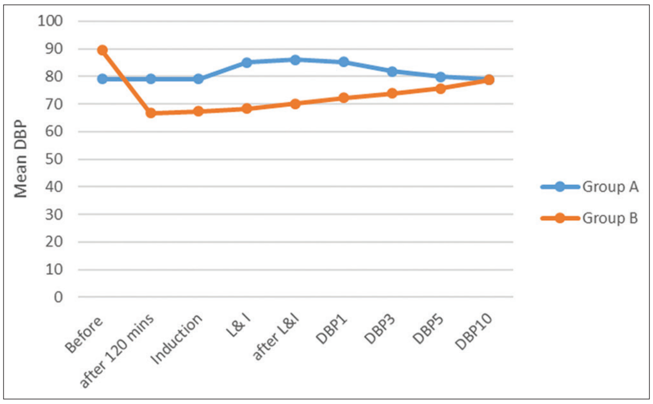

Fig. 3: Diastolic Blood Pressure at various points of time (mm hg)

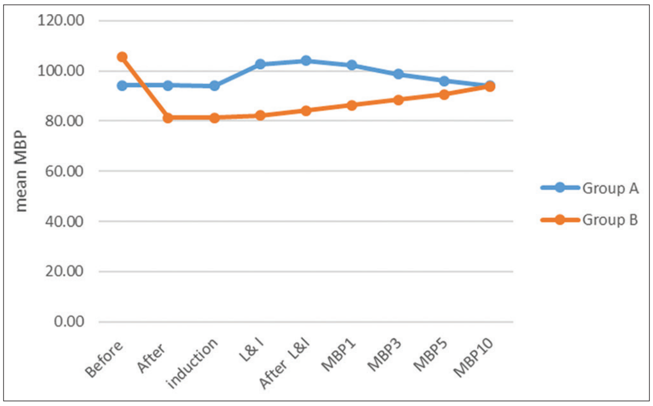

Fig. 4: MBP at various points of time (mmHg)

laryngoscopy (68.28±7.41) and patients were stable at all points of time after the administration of the drug (p<0.0001) Fig 3.

In Group A, MBP initially was 94.32±7.84, and it rose to 104.02±13.27 and sustained between 102 and 93. But in Group B (Melatonin Group) initial value was 105.52±7.94 and it reduced to 82.25±6.27 and maintained between 82 and 79. MBP was higher from baseline values in control group during L&I. Thereafter, this increase persisted at all points of time until 10 min (p<0.0001). In the melatonin group, there was no rise and patients were stable at all points of time after the administration of the drug (p<0.0001) Fig 4.

DISCUSSION

The present study was aimed at assessing the role of melatonin in attenuating hemodynamic responses to L&I. The study was carried out in 120 ASA 1 patients who were divided into 60 in each group. Group A was taken as control group and Group B got 6 mg Melatonin orally. Hemodynamic parameters such as HR, systolic, diastolic, and MBPs were recorded before the administration of drug (baseline), 120 min after administration of drug (just before induction), immediately after induction, at L&I, just after L&I and at 1, 3, 5, and 10 min thereafter.

In Group A (Control group), there was a rise in HR from baseline values at laryngoscopy which attained statistical significance at 1 min and persisted thereafter till 10 min. In the melatonin Group B, there was no rise in HR from baseline values at the time of laryngoscopy. Thereafter, it was maintained at lower values at all points of time till 10 min after L&I (p<0.0001). Similar findings were obtained by Rosenberg *et al.* who studied the role of perioperative melatonin in the modification of surgical stress response indicating that melatonin has sympatholytic activity [6].

SBP, DBP and MBP were higher than baseline values in control group during L&I and increase further during all points of time where as in Melatonin group, there was fall in values and trend maintained during all points of measurement after laryngoscopy and intubation. Mohamed *et al.* compared the role of oral melatonin 6 mg and 9 mg with placebo administered 1 h before surgery in attenuating pressor response to laryngoscopy and intubation. They observed that there was a reduction of blood pressure with regard to systolic, diastolic and MBP; and perfusion index in both melatonin groups as compared to the placebo group [7].

Our study results of mean arterial pressure showed similar trends to the study by Ismail and Mowafi, in which mean arterial pressure decreased after melatonin pre-medication and extended to the early post-operative period. This mild hypotensive effect of melatonin may be beneficial in elderly patients, particularly those at cardiovascular risk [8].

Gupta *et al.* studied role of melatonin in attenuation of hemodynamic responses to laryngoscopy and intubation and found that pre-treatment with 6 mg melatonin administered orally 120 min before induction of anesthesia is effective for attenuating hemodynamic responses to laryngoscopy and intubation. These results were similar to the present study [9].

In a study by Naguib and Samarkandi patients who received pre-medication with 5 mg melatonin 100 min preoperatively had a significant decrease in anxiety levels and increase in levels of sedation before operation with no amnesia for pre-operative events. Our study also observe increased sedation in the melatonin group with the administered dose [10, 11].

In our series of patients, there were no significant side effects such as bradycardia, arrhythmias, respiratory depression, restlessness, nausea, and drug interactions.

Limitations

The limitations of our study were that we did not compare different doses of melatonin and effects at different time intervals of administration of melatonin. We also did not assess anxiety scores and did not perform psychoanalytic tests in the post-operative period. Assessment of extubation responses and evaluation of plasma norepinephrine levels during various time intervals also were not done.

CONCLUSION

Pre-treatment with 6 mg melatonin administered orally 120 min before induction of anesthesia is effective for attenuating hemodynamic responses to laryngoscopy and intubation. There were no significant side effects such as bradycardia, arrhythmias, respiratory depression, restlessness, or nausea during perioperative period.

AUTHOR'S CONTRIBUTION

All the authors contributed to the preparation of the final manuscript.

REFERENCES

1. Henderson J. Airway management in the adult. In: Miller RD, editor. Miller's Anaesthesia. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010. p. 1573-610.
2. Gill NP, Wright B, Reilly CS. Relationship between hypoxaemic and cardiac ischaemic events in the perioperative period. Br J Anaesth 1992;68:471-3.
3. Brian JP, Norton ML. Principles of airway management. In: Healy TE, Knight PR, editors. Wylie and Churchill-Davidson's. 7th ed. London: Arnold Press; 2003. p. 443.
4. Ugur B, Ogurlu M, Gezer E, Aydin ON, Gürsoy F. Effects of esmolol, lidocaine and fentanyl on haemodynamic responses to endotracheal intubation: A comparative study. Clin Drug Investig 2007;27:269-77.
5. Maitra S, Baidya DK, Khanna P. Melatonin in perioperative medicine: Current perspective. Saudi J Anaesth 2013;7:315-21.
6. Rosenberg J, Gögenur I, Lykkesfeldt J. Modification of surgical stress response by perioperative melatonin administration. Dan Med Bull 2010;57:4144.
7. Mohamed AA, Atef HM, El Kassaby AM, Ismail SA, Helmy AM.

Effects of melatonin premedication on the hemodynamic responses and perfusion index during laryngoscopy and endotracheal intubation. Med J Cairo Univ 2013;81:859-67.
8. Ismail SA, Mowafi HA. Melatonin provides anxiolysis, enhances analgesia, decreases intraocular pressure, and promotes better operating conditions during cataract surgery under topical anaesthesia. Anesth Analg 2009;108:1146-51.
9. Gupta P, Jethava D, Choudhary R, Jethava DD. Role of melatonin in attenuation of haemodynamic responses to laryngoscopy and intubation. Indian J Anaesth 2016;60:712-8.
10. Naguib M, Samarkandi AH. Premedication with melatonin: A double blind, placebo controlled comparison with midazolam. Br J Anaesth 1999;82:875-80.
11. Naguib M, Samarkandi AH, Riad W, Thalaj A, Alotibi W, Aldammas F, *et al*. Melatonin vs. midazolam premedication in children: A double-blind, placebo controlled study. Eur J Anaesthesiol 2005;22:189-96.