

Ophthalmology

KEYWORDS: Intubation, Haemodynamics, Melatonin, Dexmedetomidine, Jhansi

A COMPARATIVE EVALUATION OF ORAL MELATONIN, (I.V) DEXMEDETOMIDINE AND COMBINATION OF BOTH FOR ATTENUATION OF HAEMODYNAMIC RESPONSES TO LARYNGOSCOPY AND INTUBATION IN MIDDLE EAR SURGERY



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INTERNATIONAL JOURNAL
OF PURE MEDICAL RESEARCH**Abstract**

Introduction : Airway management is the evaluation, planning, and use of medical procedures and devices for the purpose of maintaining or restoring ventilation in a patient. Endotracheal intubation is required to provide a patent airway when patients are at risk for aspiration, when airway maintenance by mask is difficult, and for prolonged controlled ventilation. This research aimed to investigate the impact of Melatonin with Dexmedetomidine in mitigating cardiovascular responses to laryngoscopy and endotracheal intubation in candidate in cases supporting voluntary operation. **Aim and Objective:** To compare the role of Oral melatonin with (i.v) Dexmedetomidine alone and in combination of both for attenuation of haemodynamic responses during Laryngoscopy and intubation and compare the effect on haemodynamics. **Methods and methods:** This study was a randomized prospective double blinded study conducted in Department of Anaesthesiology and Critical Care, MLB medical College, Jhansi (UP) in patients posted for elective middle Ear surgeries during the period March 2018 to October 2019, minimum 150, patients were selected for the study. **Result and Conclusion:** Mean Heart Rate and Mean Systolic blood pressure was more stable and showed less variation from baseline heart rate value in group 3 patients (Melatonin and Dexmedetomidine combination) was more stable and showed less variation from baseline Systolic blood pressure value in group 3 patients. Mean Arterial saturation (SpO2) is >95 % in group 1, group 2 and group 3 patients, and in group 2, there were 6 cases reported where arterial saturation (SPO2) falls below 95% and 3 cases were reported where arterial saturation falls below 92% which is supplemented by oxygen, after iv infusion of study drug (Dexmedetomidine 1 µg/kg). It can be therefore be concluded that- Both Melatonin (6mg) and Dexmedetomidine (1g/kg) can attenuate the haemodynamic changes during laryngoscopy and intubation.

Introduction-

In 1940, Reid and Bracefirst described the hemodynamic response to laryngoscopy and intubation. The mechanisms of the responses to laryngoscopy and orotracheal intubation are proposed to be by somatovisceral reflexes¹. Laryngoscopy and endotracheal intubation cause stimulation of proprioceptors at the base of the tongue, that cause reflex sympathetic activation of vagal and glossopharyngeal afferents. This activation cause hypertension, tachycardia and increased intracranial tension². These effects can be well tolerated by ASA. Melatonin, (N_Acetyl_5_Methoxytryptamin) is an endogenous sleep-regulating hormone secreted by the pineal gland. Melatonin differs

from other premedial because it exerts the sleep-promoting effect by amplifying day/night differences in alertness & sleep quality and displaying a modest sleepinducing effect. The hypnotic, antinociceptive, anxiolytic properties of Melatonin makes this neurohormone a useful medicine in anaesthesia and critical care³. Melatonin 6 mg tablet if taken 120 minutes before operation then it can significantly decrease laryngoscopic surge. Dexmedetomidine is used as an adjuvant for premedication, especially in patients susceptible to preoperative and perioperative stress because of its sedative, anxiolytic, analgesic, sympatholytic, and stable hemodynamic profile. Dexmedetomidine decreases oxygen consumption in intraoperative period (up to 8%) and in postoperative period (up to 17%). Considering the above effects of melatonin and very limited study on the effect of melatonin on the attenuation of hemodynamic response to intubation as well as anesthetic requirements, we aimed to study whether preanesthetic oral melatonin attenuates hemodynamic responses to intubation and anesthetic⁴.

Material and Methods-

Present study was a randomized prospective double blinded study conducted in Department of Anaesthesiology and Critical Care, MLB medical College, Jhansi (UP) in patients posted for elective middle Ear surgeries during the period March 2018 to October 2019, minimum 150, patients was selected for the study. The study will be conducted after obtaining permission from the Institutional ethics committee and the identity of the patients would not be revealed. Following the approval from the Ethical committee, ASA I and II, patients between the age of 20 to 50 years of either gender and surgery requiring general anaesthesia for duration longer than 30 min, patients with normal airway with MPG I and MPG II, >90 degree neck movement, no buck teeth undergoing elective surgeries for middle EAR were included in this study. Exclusion criteria were diabetes, hypertension, psychiatric illness, intake of antipsychotics, sedatives and antiepileptic drugs, sleep disorders, obesity and drug allergy. Likewise, patients with anticipated difficult intubation and those requiring more than one attempt or more than 20 for laryngoscopy were excluded from the study.

All the selected 150 patients were randomly assigned to one of the following 3 groups and each group were containing 50 patients each.

- Group 1- Patients received oral Melatonin 6mg (2tablets) 2 hours before surgery with (i.v) N.S (0.9%) 50 ml, 10 min before start of surgery.
- Group 2- Patients received oral Vitamin D3(Placebo) 2 tablets 2 hours before surgery with (i.v) Dexmedetomidine 1 µ/kg in 50 ml, 10 min before start of surgery.
- Group 3- Patients received oral Melatonin (2 tablets) 2 hours

before surgery with (i.v) Dexmedetomidine 0.5 µ/kg in 50 ml, 10 min before start of surgery.

- The statistical analysis was done by using the SPSS software V-16. Values will be expressed as mean ± Standard deviation (SD) and as percentage for categorial parameters. Differences between groups was compared with Student's t-test for parametric continuous variables. ANOVA t-test for comparison between three or more than three groups. Chi-square test was applied for estimating the occurrence of categorical variables. A P value <0.05 was used as the threshold of statistical significance.

Results-

Table-1 Mean Heart Rate at different time intervals

HEART RATE	Group-1	Group-2	Group-3
Base Line	93.045.79	93.065.64	92.776.68
2 hrs after drug	87.576.15	93.045.65	86.007.14
After IV			
5 mint	86.616.96	85.876.24	84.296.59
10 mint	86.896.61	84.16.87	83.166.58
During laryngoscopy and intubation	97.276.38	95.875.83	93.706.24
Post-intubation			
1 mint	93.027.04	92.755.44	87.95.10
3 mint	90.87.08	89.875.25	87.925.49
5 mint	83.276.19	82.815.33	81.276.02
10 mint	79.286.07	77.795.81	76.834.76

Mean heart rate was lower (93.706.24) in group 3 patients, followed by (95.875.83) in group 2 patients and was more in group 1 patients (97.276.38) just after laryngoscopy and intubation. After intubation from (1 mint to 10 mint) the mean heart rate was more stable and shows less variation from the baseline in group 3 patients, followed by group 2 and then in group 1 patients.

Figure-1 Mean Heart Rate (H.R)at different time intervals

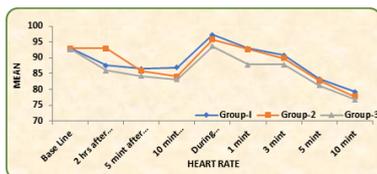


Table 2- Mean Systolic Blood Pressure (SBP) at different time intervals.

Systolic Blood Pressure	Group-1	Group-2	Group-3
Base Line	124.256.29	123.026.89	124.066.03
2 hrs. after drug	119.515.73	124.646.96	118.275.98
After IV			
5 mint	119.16.38	118.686.52	116.206.63
10 mint	118.136.52	114.546.66	111.735.98
During laryngoscopy and intubation	130.236.08	128.416.87	125.646.76
Post-intubation			
1 mint	126.006.31	124.936.83	121.196.21
3 mint	121.006.52	120.435.90	117.005.50
5 mint	118.006.62	115.335.47	110.305.33
10 mint	113.56.04	110.795.07	107.672.96

Mean duration of S.B.P was lower (125.646.76) in group 3, followed by (128.416.87) in group 2 and was (130.236.08) more in group 1 just after laryngoscopy and intubation. After intubation from (1 mint to 10 mint) the mean S.B.P was more stable and shows less variation from the baseline in group 3, followed by group 2 and then in group-1 patients.

Table 3- Mean Diastolic blood pressure(D.B.P) at different time intervals.

	Group-1	Group-2	Group-3
Base Line	82.196.19	81.066.61	81.006.35
2 hrs after drug	78.005.34	82.336.85	77.105.98
After IV			
5 mint	79.574.90	78.796.58	76.176.08
10 mint	79.764.69	76.156.53	74.456.07
During laryngoscopy and intubation	87.655.38	85.255.86	82.276.52
Post-intubation			
1 mint	86.305.49	84.225.90	81.306.75
3 mint	82.506.20	81.684.87	78.694.69
5 mint	75.005.31	72.774.15	70.923.26
10 mint	71.643.82	69.973.52	70.023.58

Mean D.B.P was lower (82.276.52) in group 3, followed by (85.255.86) in group 2 and was more (87.655.38) in group 1 patients just after laryngoscopy and intubation. After intubation from (1 mint to 10 mint) the mean D.B.P was more stable and shows less variation from the baseline in group 3 patients , followed by group 2 and then in group 1 patients.

Table 4- Mean SPO2at different time intervals.

	Group-1	Group-2	Group-3
Base Line	96.590.71	96.970.79	97.040.77
2 hrs after drug	96.570.71	97.140.58	97.060.56
After IV			
5 mint	96.530.72	96.790.85	97.000.55
10 mint	96.510.72	96.291.80	96.770.63
During laryngoscopy and intubation	99.950.20	99.810.39	99.790.46

Mean arterial saturation (SPO2) was maintained above 99 % during laryngoscopy and intubation in all the three groups. Although fall in saturation are seen in group 2 patients before laryngoscopy and intubation due to sedation but it was not found significant. (p>0.05).

Discussion-

Laryngoscopy and Endotracheal intubation are potent stressful stimuli that provoke haemodynamic response like tachycardia and hypertension that can lead to myocardial ischemia, ventricular arrhythmia, left ventricular failure, and cerebral hemorrhage. For it an orally administered drug i.e.Melatonin(N-acetyl-5-methoxy-tryptamine) with several unique properties that make it ideal for attenuation of haemodynamic changes which occurs during laryngoscopy and intubation in comparison to the (i.v) infusion of Dexmedetomidine (alpha 2 agonist) which can also blunt the haemodynamic changes but with more complications such as hypotension and bradycardia in comparison of oral Melatonin. Premraj Nagarwal *et. al.*, (2019) conducted a study on Melatonin undergoing a Sternotomy (patients undergoing CABG) and concludes that Melatonin is an effective drug to attenuate cardiovascular responses of laryngoscopy, endotracheal intubation. Adithi Devi E, *et al.*,(2018) conducted a study on Melatonin (6 mg tablets) on 60 patients .The study concludes that exogenously administered Melatonin 6mg orally 120 min prior to intubation helps in attenuation of hemodynamic responses to laryngoscopy, intubation and extubation. It also helps in maintaining a stable hemodynamics intra-operatively. Second, melatonin which is used to allay preoperative anxiety in patients have also antinociceptive, antidepressant anxiolytic, blood pressure reducing activity and pain modulating effects and that when combined with low dose of Dexmedetomidine of 0.5 µg/kg can attenuate the haemodynamic changes with less sedation property in better way when compared with large dose of Dexmedetomidine 1 µg/kg respectively. Third,

Dexmedetomidine in(0.5g/kg) causes minimal haemodynamic changes alterations and complications like respiratory impairment, hypotension and bradycardia when given in low dose. As compared to larger dose of (1 µg/kg).

The primary outcome of our current study showed that orally administered Melatonin(6mg) with low dose (0.5µg/kg) of Dexmedetomidine can attenuate the haemodynamic changes occurs during laryngoscopy and intubation during middle Ear surgeries. The demographic data (age, sex, weight) was comparable in both the groups. Mean age was in groups 1;(35.88.45) in Group 2 (30.67.74) while in Group 3 (32.878.37). Male: Female was almost (1:1) in all the groups and hence comparable and also the difference in weight in all the groups was found insignificant. Priyamvada Gupta, *et. al.*, (2016) took normal airway sample population and excluded MPG grade III and IV and with comorbidity (diabetes, hypertension, psychiatric illness, intake of antipsychotics, sedatives and antiepileptic drugs, sleep disorders, obesity and drug allergy). In a study similar to ours, in this study also, we excluded the patients with difficult airway which need laryngoscopy more than 20 seconds and included the patients with MPG grade I and II with normal weight and BMI; >90 degree neck movement; no buck teeth and all the groups were comparable. In our study we found that non-invasive blood pressure in group 3 after immediate laryngoscopy and intubation was, mean Systolic BP (125.646.76) mmHg, mean Diastolic BP (82.276.52) mmHg and mean arterial BP was (96.334.92) mmHg and the mean heart rate just after laryngoscopy and intubation was (93.706.24) beats per minute. Ahmed A. Mohamed *et. al.*, (2014) concluded the study in 90 patients on melatonin drug and found that, dose of melatonin 6 mg can blunt the haemodynamic changes during laryngoscopy and endotracheal intubation, similarly as we found in group 1 patients. Similar result were also present in group 3 which are better than group 2 and 1, and with less cases of hypotension and bradycardia as observed in group 2 with large dose of Dexmedetomidine.

Cardiovascular responses to Dexmedetomidine bolus has been described as a transient rise in blood pressure and a decrease in heart rate followed by a fall in blood pressure. A slow loading dose ranging from (0.2-0.6)ug/kg/hr are recommended for less haemodynamic alterations. Jorden *et. al.*, (2001) observed that high bolus doses of Dexmedetomidine do not always result in hypotension and Venn *et. al.*, (1999) reported that high doses of Dexmedetomidine may be used safely without changes in hemodynamics when they are infused over 10 minutes. But in our study Dexmedetomidine (1g/kg) shows 5 cases of hypotension and 4 cases of bradycardia in Group 2 patients. There was 1 case of hypotension and 1 case of bradycardia with Dexmedetomidine low dose (0.5 g/kg) combined with Oral Melatonin and also with better sedation scoring on RSS scaling as compared to Group 1 and 2 patients. When Dexmedetomidine was used in low doses with melatonin, it showed less variation in Heart rate, systolic and diastolic blood pressure, mean arterial pressure and SpO₂ as compared to group 1 and 2. Bon Sebastian, *et. al.* (2017) have used Dexmedetomidine in a dose of 0.5 and 1 µg/kg and found them to be effective in attenuation of stress response to laryngoscopy and endotracheal intubation but with more cases of decreased arterial saturation (SPO₂) below 92% in some cases, similarly as we noted in group 2 where 3 patient need oxygen supplementation when there SPO₂ falls below 92%. Menda *et al.*, (2010) conducted a study on ischaemic heart disease patients undergoing fast-track coronary artery bypass graft comparing Dexmedetomidine 1 µg/kg and placebo. In our study the mean Heart rate (bpm) during laryngoscopy and intubation was (93.706.24) in group 3, in comparison to (95.875.83) of group 2 and (97.276.38) of group 1. This shows less variation in mean Heart rate in Group 3 patients from baseline value of mean heart rate in comparison to group 1 and 2 patients. Heart rate was more stable after 1min, 3min, 5min and 10 min of intubation in group 3 patients than in group 1 and 2 patients. Following after laryngoscopy and intubation Diastolic B.P(mmHg) was (82.276.52) in group 3, in comparison to (85.255.86) of group 2

and (87.655.38) of group 1. This shows less variation of mean Diastolic B.P in group 3 patients from baseline value of Diastolic BP in comparison to group 1 and 2 patients. Diastolic B.P was more stable after 1 min, 3min, 5min and 10 min of intubation in group 3 patients. Following after laryngoscopy and intubation Mean arterial pressure (MAP) mmHg was (96.334.92) in group 3, in comparison to (99.335.86) of group 2 and (101.334.30) of group 1. This shows less variation in MAP in group 3 patients from baseline value of MAP, in comparison to group 1 and 2 patients. MAP was more stable after 1min, 3min, 5min and 10 min of intubation in group 3 patients. Manne *et al.*, (2014) noting the effects of low-dose Dexmedetomidine infusion on hemodynamic stress response, sedation and post-operative analgesia requirement in patients undergoing laparoscopic cholecystectomy also observed increasing sedation levels with Dexmedetomidine. Dexmedetomidine in a dose of 1 µg/kg has been shown to cause increased sedation levels and need for oxygen supplementation by few authors. In our study we found that sedation scoring by RSS scale is (2.39±0.49) in group 3 and (1.85±0.36) group 1 while it is more in (3.37±0.49) group 2 patients which needed oxygen supplementation in 3 cases when oxygen saturation (SPO₂) <92%. So desired and suitable sedation (RSS= 2) was achieved by group 3 patients as compared to groups of 1 and 2 patients.

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