

TITLE PAGE**Type of Article: Original Research Article****Title: Oral Melatonin Versus Pregabalin As Premedication For Attenuation Of Hemodynamic Response During Laryngoscopy And Intubation****Neeharika Arora¹, Tulika Mittal², Akash Gupta³, Sanjana Sinha^{4*}**¹Professor, ²Assistant Professor, ³Associate Professor, ⁴Junior Resident, Department of Anaesthesia, Rohilkhand Medical College and Hospital, Bareilly, UP, India***Corresponding Author and reprint request to:** Dr Sanjana Sinha, Junior Resident, Department of Anesthesiology, Rohilkhand Medical College and Hospital, Bareilly, UP India**Abstract****Background and Aim-**

Laryngoscopy and intubation are noxious stimuli invoking response like hypertension, tachycardia and arrhythmia. In high risk patient, response to laryngoscopy and intubation associated with morbidity and mortality thus study for better agent is going on.

Methods-

This is a randomised prospective double blind controlled study. 60 ASA status 1 and ASA 2 patients were divided into two equal group of 30 each patient. Group 1 received 6 mg oral Melatonin and Group 2 received 150 mg oral Pregabalin tablet 2 hours prior to induction of General anaesthesia. General anaesthesia techniques were standard for all patient. Primary outcome measured were heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure before and after induction, at intubation and 1, 3, 5 and 10 min after intubation. Secondary outcome measure were Ramsay sedation score, pain score by VAS.

Result-

All hemodynamic parameter increased immediately after intubation. Statistically significant difference between melatonin and pregabalin found in Heart rate immediately after intubation. Rise in heart rate immediately after intubation is less in melatonin as compared to pregabalin. In systolic blood pressure statistically significant difference were noted at 1 min and 3 mins after intubation. Systolic blood pressure increased immediately after intubation in both study group and attenuation was more in melatonin group at 1 min and 3 min after intubation. Statistically significant difference in Mean arterial blood pressure were at 3 mins after intubation. Attenuation of mean blood pressure was more in melatonin as compared to pregabalin and attenuation was statistically significant at 3 min after intubation.

Sedation score were significantly more in melatonin as compared to pregabalin group post extubation.

Pain scale via VAS scale was parallel in both study group.

Conclusion-

Melatonin and pregabalin both attenuate hemodynamic response to laryngoscopy & intubation but attenuation of hemodynamic response with melatonin is better .

Introduction-

Laryngoscopy and endotracheal intubation are essential procedure required in elective case as well as emergency resuscitative measure. It is required to secure patients airway as well as to provide oxygenation and ventilation. Despite of being critical part of anaesthesia still it is not free from hazard. These two are considered as noxious stimuli. Laryngoscopy alone generate same pressor response as done by laryngoscopy followed by intubation.

Hemodynamic stress response from airway instrumentation are due to sympathetic adrenergic response caused by epipharyngeal and parapharyngeal stimulation leading to significant rise in the catecholamine level that result in raised blood pressure and heart rate.[1]

It is detrimental in individual with limited cardiac reserve or cardiac disease.

Various method to attenuate sympathetic response to laryngoscopy and tracheal intubation are being used and research for better drug is going on.[1]

Melatonin (N-acetyl-5-methoxytryptamine) is an endogenous hormone secreted by pineal gland . It regulates circadian rhythm, improves sleep onset, duration and quality. It possesses sedative, hypnotic, analgesic, anti inflammatory, anti oxidant , mild hypotension and chronobiotic properties.[2]

Pregabalin is (S)-3 aminomethyl-5-methylhexanoic acid. It reduces synaptic release of several neurotransmitter like glutamate, nor adrenaline, serotonin, dopamine and substance by binding to alpha2 delta subunit resulting in reduced neuronal excitability and seizure. It has analgesic, anticonvulsant and anxiolytic effects and is useful in avoiding neuropathic component of acute nociceptive pain following surgery. [3]

Thus this study was designed to evaluate and compare the efficacy of Oral Melatonin and oral pregabalin for attenuation of hemodynamic response during laryngoscopy and intubation. Secondary aim was to compare post operative sedation level based on Ramsay sedation score and pain score based on visual analog scale.

Material and method-

Study was conducted after obtaining approval from institutional Ethics Committee, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh. This trial was registered on clinical trial registry , India .

Institutional Ethics Committee –IEC/RMCH/63/2022/AUG

CTRI registration number- CTRI/2022/12/048021

Inclusion Criteria-

This is a double blind randomized controlled trial. After taking well informed and written consent, 60 patients with ASA Grade 1 and 2, age between 18 -65yrs of age, either sex, BMI <30kg/m², patient undergoing surgeries requiring 2 hour long General anaesthesia requiring endotracheal intubation.

Exclusion Criteria-

Patients excluded in this study were patient with difficult airway, patient requiring more than 1 attempt at intubation, with uncontrolled diabetes or hypertension, obese, known allergy to drug, ASA grade 3 and 4, pregnant and lactating female and patient undergoing emergency surgeries.

Method-

The patients were randomly divided into two group of 30 each. Group A receive oral tablet melatonin 6 mg and Group B receive oral pregabalin tablet 150 mg two hour prior to induction of anaesthesia.

Preanesthetic checkup was done one day prior to surgery and include detailed history, general physical as well as systemic examination and airway assessment of all patient. All routine investigation were done. **Basic demographic profile were noted.** All patient were kept fasted over night. Haemodynamic parameter such as heart rate, blood pressure, mean arterial blood pressure were recorded before administration of drug (baseline).

The intravenous administration of butorphanol 0.02 mg/kg and midazolam 0.02 mg/kg. Pre-oxygenation was done for 3 minutes, after which intravenous propofol 2 mg/kg was used to induce anaesthesia. Laryngoscopy and intubation was facilitated with Vecuronium 0.1 mg/kg.

Before induction, after administering i.v. medications, and before laryngoscopy, blood pressure (systolic, diastolic, and mean) and heart rate was monitored. A skilled anesthesiologist performed laryngoscopy and tracheal intubation within 20 seconds using the proper sized, cuffed endotracheal tube, 3 minutes after administering vecuronium. The patient were removed from the trial if an unexpectedly difficult intubation or a laryngoscopy takes more than 15 seconds.

Blood Pressure (Systolic blood pressure, Diastolic blood pressure and Mean arterial pressure) and heart rate were recorded immediately after intubation, then at 1 min, 3 min, 5 min, and 10 min after intubation.

At the end of surgery the residual neuromuscular paralysis was antagonised with injection Neostigmine 0.005mg/kg and injection Glycopyrolate 0.01mg/kg. Following

confirmation of recovery from anaesthesia and muscle relaxation, extubation was performed after thorough suctioning

Level of sedation and pain score were assessed immediately after extubation and patients were shifted to post anaesthesia care unit. Level of sedation and postoperative pain were assessed at 30mins 60mins and 120mins in post operative room.

Result-

TABLE-1. Demographic Table.

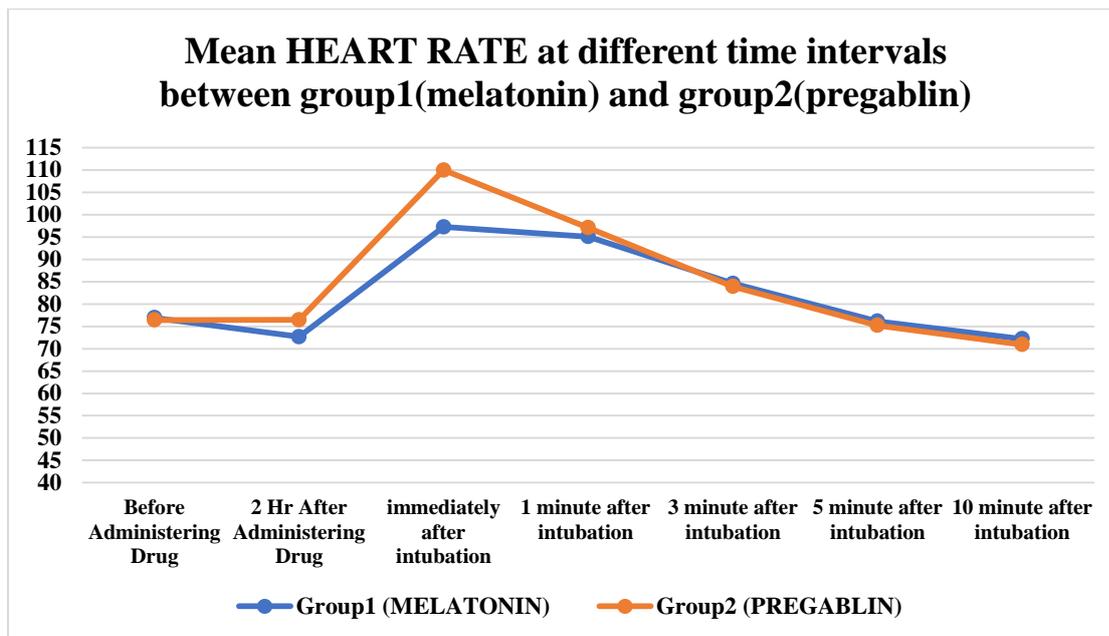
Demographic Variables	Group1(MELATONIN)	Group2(PREGABLIN)	
	Mean \pm SD	Mean \pm SD	P-Value
AGE(In Years)	41.77 \pm 8.65	42.3 \pm 8.8	0.810#
SEX(Male : Female)	10:20	13:17	0.426#
Body Weight(in KG)	56.63 \pm 10.55	61.0 \pm 10.3	0.110#
ASA Grade(I:II)	24:6	22:8	0.428#

statistically not significant.

TABLE-5 Comparison of mean Heart rate at different time Intervals in between Group1(MELATONIN) and Group2(PREGABLIN).

	Group1 (MELATONIN)	Group2 (PREGABLIN)		
Heart Rate	Mean \pm SD	Mean \pm SD	t-Value	P-Value
Before Administering Drug	76.93 \pm 5.58	76.43 \pm 8.78	-0.263	0.793 #
2 Hr After Administering Drug	72.67 \pm 6.31	76.47 \pm 9.32	1.850	0.069 #
immediately after intubation	97.27 \pm 10.12	109.97 \pm 15.47	3.762	<0.001 *
1 minute after intubation	95.07 \pm 8.42	97.07 \pm 13.52	0.688	0.494 #
3 minute after intubation	84.6 \pm 6.56	83.93 \pm 8.91	-0.330	0.743 #
5 minute after intubation	76.13 \pm 4.9	75.2 \pm 8.08	-0.541	0.590 #
10 minute after intubation	72.2 \pm 5.24	70.93 \pm 8.23	-0.711	0.480 #

*statistically significant ,# statistically not significant.



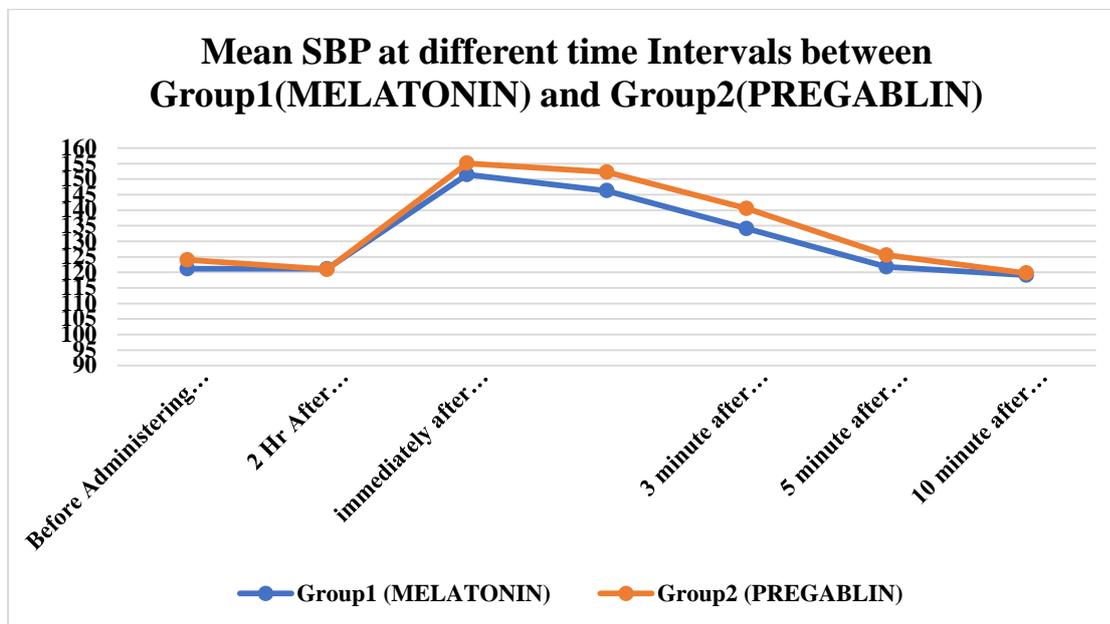
Baseline mean heart rate seen in table 1 and fig in both groups was comparable to baseline. In both groups the baseline heart rate was 76.93+5.58 in group 1 and 76.43+ 8.78 in group 2. (p=0.793, >0.05). 2 hours after administration of drug the heart rate was 72.67+ 6.31 in group 1 and 76.47+ 9.32 in group 2 (P>0.05 p= 0.069). Both groups showed a rise in heart rate after intubation as shown in fig 1 and table 2. Immediately after intubation the mean heart rate in group 1 was 97.27+ 10.12 and in group 2 it was 109.97+15.47 which was statistically significant (p=0.001). In both groups the mean heart rate came to baseline 5 minutes after intubation. At other time intervals the heart rate was not statistically significant.

TABLE-6 Comparison of mean SBP at different time Intervals in between Group1(MELATONIN) and Group2(PREGABLIN).

	Group1 (MELATONIN)	Group2 (PREGABLIN)		
SBP	Mean ± SD	Mean ± SD	t-Value	P-Value
Before Administering Drug	121.13 ± 10.84	124.0 ± 11.72	-0.984	0.329 #
2 Hr After Administering Drug	121.13 ± 10.84	120.93 ± 11.41	0.070	0.945 #
immediately after intubation	151.47 ± 12.06	155.07 ± 9.75	-1.272	0.209 #
1 minute after intubation	146.27 ± 10.14	152.27 ± 8.85	-2.442	0.018*
3 minute after intubation	134.07 ± 12.11	140.55 ± 9.71	-4.453	<0.001 *
5 minute after	121.73 ± 11.19	125.57 ± 10.14	-1.390	0.170 #

intubation				
10 minute after intubation	119.07 ± 9.42	119.73 ± 9.91	-0.267	0.790 #

*statistically significant ,# statistically not significant.



Baseline mean SBP in group 1 and 2 were 121.13 + 10.84 and 124.0 +11.72, 2 hours before administering the drug(p= 0.329 not significant) and SBP was 121.13+ 10.84 in group 1 and 120.93+ 11.41 in group 2 after administering drug(p=0.945). Maximum rise in mean SBP in group 1 and 2 were seen in fig 2 and table 3 was 151.47+12.06 and 155.07+ 9.75 . 1 minute after intubation the mean SBP was 146.27 + 10.14 in group 1 and 152.27+8.85 in group 2 which was statistically significant (p= 0.018) . 3 minutes after intubation the mean SBP was 134.07 + 12.11 in group 1 and 140.55+ 9.71 in group 2 which was statistically significant (p= 0.001). After 5 minutes of

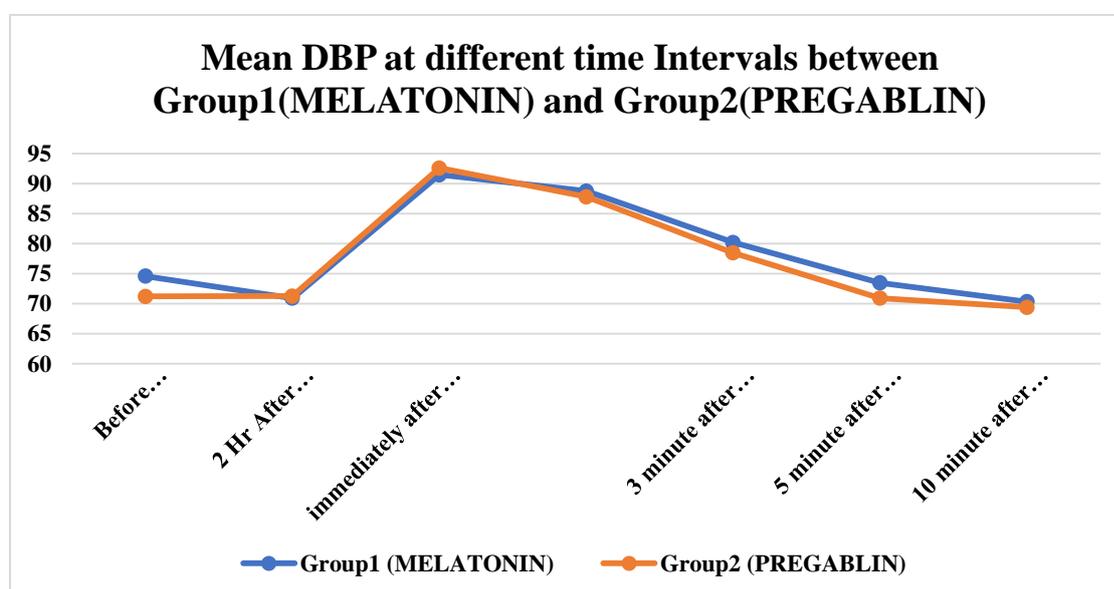
intubation the mean SBP cameback to baseline in group 1 but returned to

baseline after 10 minutes to baseline in group 2.

TABLE-7 Comparison of mean DBP at different time Intervals in between Group1(MELATONIN) and Group2(PREGABLIN).

	Group1 (MELATONIN)	Group2 (PREGABLIN)		
DBP	Mean ± SD	Mean ± SD	t-Value	P-Value
Before Administering Drug	74.6 ± 8.27	71.2 ± 6.59	-1.760	0.084 #
2 Hr After Administering Drug	70.93 ± 8.66	71.27 ± 6.46	0.169	0.866 #
immediately	91.47 ± 7.77	92.6 ± 6.85	0.599	0.551 #

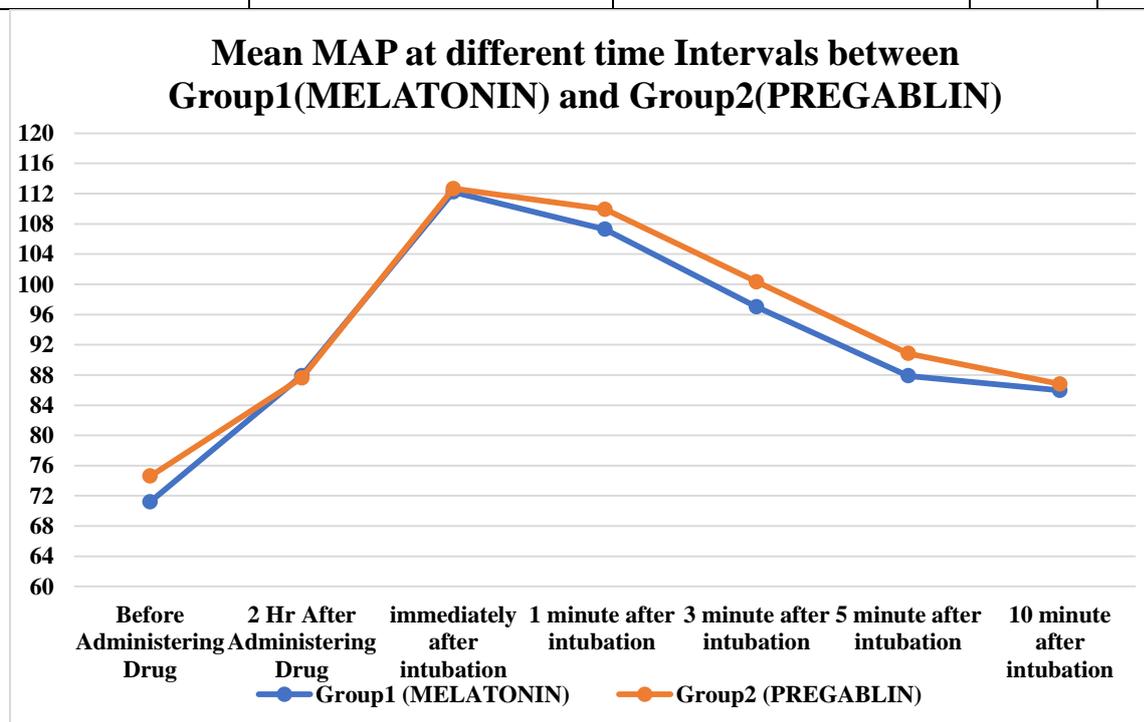
after intubation				
1 minute after intubation	88.77 ± 6.36	87.8 ± 5.88	-0.611	0.543 #
3 minute after intubation	80.2 ± 7.03	78.47 ± 6.76	-0.973	0.335 #
5 minute after intubation	73.47 ± 6.75	70.93 ± 5.7	-1.571	0.122 #
10 minute after intubation	70.33 ± 6.85	69.4 ± 6.2	-0.553	0.582 #



Baseline mean DBP (seen in group 4 and fig 4) was comparable in both groups, 74.6+ 8.27 in group 1 before administering the drug and 2 hours after administration it was 70.93+ 8.66 and was 71.2+ 6.59 before drug administration in group 2 and 71.27+ 6.46 after drug administration. Both groups showed rise in mean diastolic blood pressure after intubation. Maximum rise in mean DBP was 91.47+ 7.77 in group 1 and 92.6 + 6.85 in group 2 which was just after intubation. In both groups mean DBP came to baseline 5 minutes after intubation. Throughout study mean DBP was clinically insignificant ($p>0.05$).

TABLE-8 Comparison of mean MAP at different time Intervals between Group1(MELATONIN) and Group2(PREGABLIN).

	Group1 (MELATONIN)	Group2 (PREGABLIN)		
MAP	Mean \pm SD	Mean \pm SD	t-Value	P-Value
Before Administering Drug	71.2 \pm 6.59	74.6 \pm 8.27	-1.760	0.084 #
2 Hr After Administering Drug	87.89 \pm 6.65	87.6 \pm 8.76	0.144	0.886 #
immediately after intubation	112.22 \pm 7.86	112.67 \pm 7.91	-0.218	0.828 #
1 minute after intubation	107.29 \pm 6.71	109.93 \pm 6.39	-1.564	0.123 #
3 minute after intubation	97.0 \pm 5.98	100.32 \pm 7.49	-3.933	<0.001 *
5 minute after intubation	87.87 \pm 6.65	90.83 \pm 7.23	-1.654	0.103 #
10 minute after intubation	85.96 \pm 5.98	86.8 \pm 7.35	-0.488	0.627 #

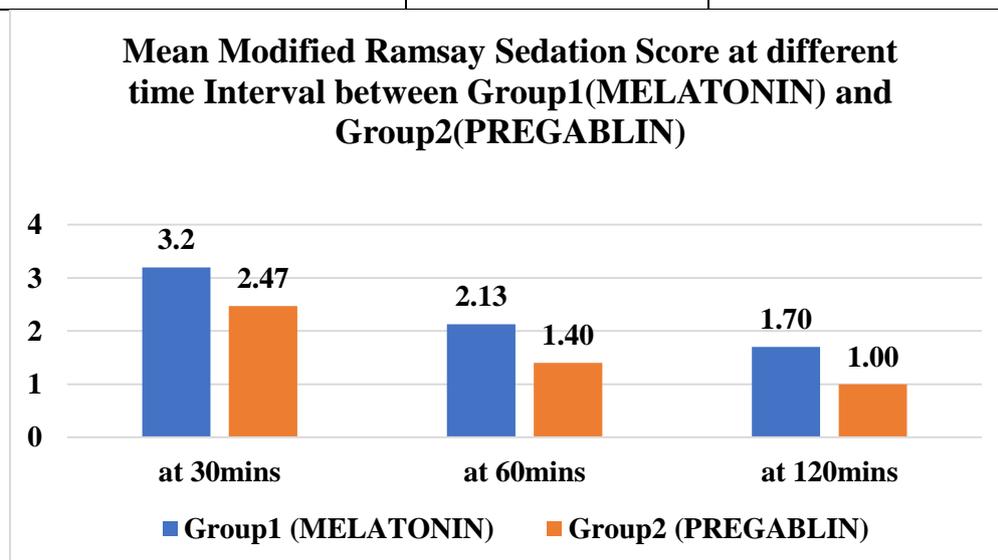


Baseline mean MAP in group 1 and group 2 was 71.2+ 6.59 and 74.6+ 8.27 , 2 hours before drug administration. 2 hours after drug administration mean DBP was 87.89+ 6.65 in group 1 and 87.6+ 8.76 in group 2 (p= 0.886). Both groups showed a rise in mean MAP after intubation. Maximum rise in mean MAP was 112.22+ 7.86 in group 1 and 112.67+ 7.91 in group 2. The difference in mean arterial pressure was statistically significant between both

groups at 3 minutes after intubation with mean in group 1 is 97.0 ± 5.98 and in group 2 is 100.32 ± 7.49 ($p < 0.001$). The result at other time intervals was not statistically significant.

TABLE-9 Comparison of mean Modified Ramsay Sedation Score at different time Interval between Group1(MELATONIN) and Group2(PREGABLIN).

	Group1(MELATONIN)	Group2(PREGABLIN)		
Modified Ramsay Sedation Score	Mean \pm SD	Mean \pm SD	t-Value	P-Value
at 30mins	2.47 ± 0.57	3.2 ± 0.61	-4.805	<0.001 *
at 60mins	1.4 ± 0.56	2.13 ± 0.63	-4.758	<0.001 *
at 120mins	1.0 ± 0	1.7 ± 0.47	-8.085	<0.001 *



The mean of Ramsay sedation score at different time Interval were statistically significant. The mean sedation score at 30 min was 2.47 ± 0.57 in group 1 and 3.2 ± 0.61 in group 2 and was statistically significant with $p = < 0.001$. At 60 min Sedation score in group 1 is 1.4 ± 0.56 and in group 2 is 2.13 ± 0.63 and result was statistically significant with $p = < 0.001$. At 120 min the mean of sedation score in group 1 is 1.0 ± 0 and Group 2 1.7 ± 0.47 and result was statistically significant with $p = < 0.001$.

TABLE-10 Comparison of mean VAS at different time Interval between Group1(MELATONIN) and Group2(PREGABLIN).

	Group1(MELATONIN)	Group2(PREGABLIN)		
VAS	Mean \pm SD	Mean \pm SD	t-Value	P-Value
at 30mins	0.82 \pm 0.01	0.96 \pm 0.04	1.819	0.074#
at 60mins	1.26 \pm 0.12	1.38 \pm 0.23	1.798	0.077#
at 120mins	2.92 \pm 0.42	3.12 \pm 0.46	1.758	0.083#

The mean of visual analog scale for post operative pain at 30 min , 60 min and 120 min was statistically not significant.

Discussion-

In this prospective randomised double blind study we found significant attenuation of hemodynamic response to laryngoscopy and intubation in group A as compared to group B.

Intubation and laryngoscopy can produce tachycardia, hypertension, increased intracranial and intraocular pressure thus need for attenuation of hemodynamic response during laryngoscopy is required.

Devvara et al when comparing role of oral melatonin 6mg and 9 mg with placebo for attenuation of pressor response to laryngoscopy found no statistical difference in blood pressure and heart rate in both groups receiving medication. Thus 6mg melatonin was preferred in this study. Bhawana et al when comparing oral pregabalin 75 mg and 150mg with placebo in depletion of haemodynamic response to intubation found considerable rise in heart rate and mean arterial blood pressure with 75mg group and significant reduction of blood pressure with 150 mg group thus 150 mg of pregabalin was preferred. [4-5]

Peak effect of melatonin range from 60 to 150 mins and for pregabalin is 1 hour. Thus drug was administered 2 hours prior to induction.[4]

Very few studies were done where melatonin compared with pregabalin in attenuation of hemodynamic response to laryngoscopy and postoperative sedation score and pain scale via VAS.

The mechanism of Melatonin in circulation is complex. Heart rate lowering effect is due to its anxiolytic action. It is due to synergy between melatonergic and GABAergic system. Decrease in blood pressure by binding to specific melatonin receptor in blood vessel and interfering with vascular response to catecholamine and by smooth muscle relaxation of arterial wall by increasing nitric oxide availability. It also has free radical scavenging effect leading to dilatation of blood vessel . Sedative effect is due to binding at GABA-A receptor [1]

Pregabalin is structurally similar to inhibitory neurotransmitter GABA binds to alpha 2 delta subunit of voltage gated calcium channel thus inhibiting neuronal signaling. It has analgesic, anticonvulsant and anxiolytic property . It reduces hyper excitability of dorsal horn neuron induced by tissue damage thus pregabalin have role in treatment of post operative pain. It increases duration of non rapid eye movement and decreases rapid eye movement.[3]

In our study there is significant difference in hemodynamic parameter in both drug noted.

All hemodynamic parameter increased immediately after intubation.

Rise in **heart rate** was less as compared to pregabalin immediately after intubation and statistically significant. In our study we found that there was minimal difference in heart rate prior to administration of drug and 2 hours later. Heart rate was greater in pregabalin group after intubation as compared to melatonin and difference was significant. Immediately after intubation the mean heart rate in group 1 was 97.27 ± 10.12 and in group 2 it was 109.97 ± 15.47 which was statistically significant ($p=0.001$). Heart rate at all other times showed minimal difference and it returned to baseline 5 minutes after intubation.

Kumar et al when comparing melatonin and placebo in reducing haemodynamic response found minimal rise in heart rate in melatonin group which stabilised after 5 minutes similar to our study[6] . Gupta et al also studied the effects of melatonin in attenuation of haemodynamic responses also found minimal rise in heart rate in melatonin group and returned to baseline in 1 minute [1] . Mukherjee et al also compared melatonin and pregabalin and concluded substantial reduction in heart rate in 1 , 2 , 4 and 6 minutes in melatonin and pregabalin group [8]. Maqbool et al also compared oral pregabalin and melatonin and found that in melatonin group there was rise in heart rate post intubation and was statistically significant 1 minute after intubation. It returned to baseline 5min after intubation in melatonin group and 10 minutes in pregabalin group [7] . Similar to previous studies, melatonin as premedication attenuated heart rate, in melatonin group and there was less significant rise in heart rate immediately after intubation and heart rate returned to baseline like previous studies

Systolic blood pressure showed a lower value to baseline in pregabalin group in comparison to melatonin two hours after administration but was statistically insignificant. During intubation, systolic blood pressure was raised in both the study groups but increase was more in pregabalin group which was not significant statistically. Systolic blood pressure was lowered in melatonin group at 1 min and 3 min post intubation and significant statistically. 1 minute after intubation the mean SBP was 146.27 ± 10.14 in group 1 and 152.27 ± 8.85 in group 2 which was statistically significant ($p=0.018$) . 3 minutes after intubation the mean SBP was 134.07 ± 12.11 in group 1 and 140.55 ± 9.71 in group 2 which was statistically significant ($p=0.001$). Systolic blood pressure in both groups reached baseline at 5 minutes.

Kumar et al when comparing melatonin and placebo found there was a lower blood pressure in melatonin group than baseline when compared to placebo but not significant. Post intubation there was rise in SBP in both groups, but more in placebo group and is statistically significant. It reached baseline in 5 minutes in melatonin group and 10 min in placebo group [6]. Singh et al who studied pregabalin found that maximum rise in systolic blood pressure at

4 minutes post intubation whereas in placebo group, SBP at baseline was higher and statistically significant. SBP was higher at 4 min, 6 min and statistically significant when compared to pregabalin[9].

Mukherjee et al on comparing melatonin and pregabalin for reduction of haemodynamic response to intubation found that SBP was below baseline in both and not significant but when compared to placebo it was statistically significant. During intubation SBP rose in all 3 groups but was more in placebo group. SBP went below baseline at 4 minutes in melatonin and 6 minutes in pregabalin group. [8]

Maqbool et al. , on comparing oral melatonin to oral pregabalin also concluded that no rise in SBP during induction in melatonin and below baseline at 3minutes , in pregabalin group SBP started decreasing post intubation and by 10 min it attained attenuation.[7]

All above studies showed that melatonin and pregabalin both attenuate SBP but melatonin does it better. Our study concurs with previous studies.

DBP decreased from baseline in melatonin group in 2 hours after administration of drug when compared to pregabalin at baseline. DBP increased immediately post intubation in both groups and reached baseline by 5 minutes post intubation. Result was statistically not significant. Mukherjee et al who compared melatonin and pregabalin found a similar result. DBP was lower in melatonin group at baseline and rose immediately post intubation in both groups . In both groups DBP started decreasing at 2 minutes post intubation and attained baseline at 6 min and 8 min and stability by 10 minutes. But there was a substantial difference in diastolic blood pressure at all time intervals when melatonin and pregabalin were compared to placebo group [8]. Thus Melatonin and pregabalin were found to attenuate DBP but was statistically not significant.

MAP at baseline increased after administering drug in both groups but was not significant. It increased post intubation in both groups. Lowering of MAP was significant at 3 minutes post intubation and achieved baseline 5 minutes in melatonin group and 10 minutes in pregabalin group. Maximum rise in mean MAP was 112.22 ± 7.86 in group 1 and 112.67 ± 7.91 in group 2. The difference in mean arterial pressure was statistically significant between both groups at 3 minutes after intubation with mean in group 1 is 97.0 ± 5.98 and in group 2 is 100.32 ± 7.49 ($p < 0.001$)

Kumar et al and Gupta et al who compared melatonin to placebo found MAP below baseline in melatonin group when compared to placebo 120 min after administration of drug [6,1]. There was a rise in MAP in both groups post intubation but rise was more in placebo group compared to melatonin. In melatonin group decreased below baseline at 1 min and sustained attenuation at 3 minutes. Difference in MAP when compared to placebo when compared to melatonin was significant 120 minutes after administration of drug, just after induction, at 1minutes , 2minutes , 3 minutes and 10 minutes post intubation[6,1].

Maqbool et al who compared oral pregabalin and melatonin found at induction rise in MAP in pregabalin and placebo group in comparison to melatonin. Rise was more in pregabalin compared to placebo whereas no rise in melatonin group. At 1 minute after induction MAP of melatonin group reached below baseline and reached 10 min baseline in pregabalin group. In melatonin group there was no rise and patient was stable at all times[8]. This result parallels our result and reflects both drugs diminish haemodynamic response to laryngoscopy but melatonin does it better.

Sedation score post extubation at 30 min, 60 mins and 120 min in post operative room were more in melatonin as compared to pregabalin. Our study was supported by Nasr et al and Khanna et al.[10, 11]

Similar result was seen in study conducted by Khanna et al based on evaluation of melatonin, pregabalin and alprazolam as premedication for post operative pain and sedation posted for laproscopic surgery. They concluded that sedation in melatonin is more than pregabalin and alprazolam at 30 mins, 2 hours, 4 hours, 6 hours, 8 hours and 12 hours[11].

Nasr et al who conducted study comparing efficacy of melatonin and pregabalin on postoperative pain and perioperative anxiety in gynecological surgery. They also came to conclusion that sedation is more in melatonin group as compared to pregabalin at 30 mins, 2 hour, 4 hour, 6 hour, 8 hour and 12 hour post extubation[10].

No significant difference in Postoperative VAS for pain between two study group. The time for first analgesic demand, number of patients requiring diclofenac at 30 min, 60min and 120 min postoperatively were similar.

Result regarding postoperative pain is backed up by result from Nasr et al and Khanna et al.[10-11]

Nasr et al study reflects that post operative pain scale in melatonin and pregabalin based on VAS at 30 min, 2 hour, 4,6,8, 12 hour depending on demand and number of patient requiring analgesic were similar[10].

Khanna et al study on postoperative pain score in melatonin, pregabalin and alprazolam were comparable at all time interval and intragroup comparison at all interval not statistically significant. [11]

Melatonin is considered as wonder drug in anaesthesia and critical care with wide spectrum of uses including antioxidant and neuroprotective property beside hypnosis, anxiolysis, analgesia. [1]

Limitation of this study are we did not measure plasma melatonin level after melatonin premedication. We didn't assess plasma catecholamine level which is more objective for evaluating hemodynamic response. Intraoperative bispectral index monitoring for deciding depth of anesthesia and requirement of induction dose of propofol was not used in our study.

Conclusion-

Our result concluded that oral Melatonin 6mg as well as oral pregabalin 150mg is effective in blunting hemodynamic stress response to laryngoscopy and tracheal intubation. Melatonin is found to be more effective than pregabalin in lowering of systolic and diastolic blood pressure and heart rate changes associated with laryngoscopy. Post operative Sedation is more in melatonin group as compared to pregabalin and Visual analog scale were parallel in both study group. To summarize both melatonin and pregabalin attenuates hemodynamic stress response but attenuation of hemodynamic response is better with melatonin.

References-

1. Gupta P. Role of Melatonin in attenuation of hemodynamic responses to laryngoscopy and intubation. *Indian Journal of Anesthesia*. 2016 Oct;60(10):712–18.
2. Maitra S, Baidya DK, Khanna P. Melatonin in perioperative medicine: Current perspective. *Saudi journal of anesthesia*. 2013 Jul;7(3):315-21.
3. Taylor, C.P., Angelotti, T. And Fauman, E., pharmacology, and mechanism of action of pregabalin: calcium channel alpha 2 delta subunit as a target for antiepileptic drug discovery. *Epilepsy research*. 2007 feb 1;73 (2) : 137-50.
4. Devtara A, Gandhi A, Damor M, Jain S, Sharma A, Verma A. Attenuation of hemodynamic pressor response during laryngoscopy and intubation : A clinical study of premedication with different doses of oral Melatonin. *Acad.Anesthesiol.Int*. 2020Feb; 5(2) :75-79.
5. Rastogi Bhawana. oral pregabalin premedication for attenuation of hemodynamic pressor response of airway instrumentation during general anesthesia. *Indian journal of anesthesia*. 2012 Feb;56(1):49–54.
6. Kumar R, Kumari K, Janweja S, Verma M, Sharma A, Paliwal B, Kishan R. 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 Aug 21:1-7.
7. Maqbool SF, Gupta KC, Mehta N. Comparative Clinical Evaluation of Preoperative Oral Pregabalin and Melatonin for Attenuation of Hemodynamic Responses to Laryngoscopy and Intubation. *IOSR Journal of Dental and Medical Sciences*; April 2019; 18(4): 35-40.
8. 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 (IOSRJDMS)*. 2020;19(10) : 04-12.

9. Singh D, Yadav JS, Jamuda BK, Singh P. Oral pregabalin as premedication on anxiolysis and stress response to laryngoscopy and endotracheal intubation in patients undergoing laparoscopic cholecystectomy: A randomized double-blind study. *Anesthesia, essays, and researches*. 2019 Jan;13(1):97-104.
10. Nasr DA. Efficacy of preoperative melatonin versus pregabalin in perioperative anxiety and postoperative pain in gynecological surgeries. *Egyptian Journal of Anesthesia*. 2013 Nov;30(1):89–93.
11. Khanna J, Katoch M, Rajpur S. Comparative evaluation of melatonin, pregabalin and alprazolam as premedicant for perioperative anxiety and post operative pain for laparoscopic surgeries. *JK Science*. 2019 Jun ;21(2):64-71.