ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 09 | September - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COMPARATIVE ASSESSMENT OF ORAL GABAPENTIN AND MELATONIN FOR ATTENUATION OF HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION UNDER BIS CONTROLLED ANAESTHESIA: A PROSPECTIVE RANDOMIZED CONTROLLED STUDY

Anaesthesiology

Meeta Yadav SR, Department of Anaesthesia, SMS medical college, Jaipur, Rajasthan, India.
Meenal Jindal SR, Department of Anaesthesia, SMS medical college, Jaipur, Rajasthan, India.
R.K.Aseri Senior professor, Department of Anaesthesia, Barmer Medical College and Hospital, Barmer, Rajasthan, India

ABSTRACT

Introduction: Laryngoscopy and intubation cause sympathetic stimulation and arousal reactions. We evaluated the role of gabapentin and melatonin on hemodynamic responses to laryngoscopy and intubation as compared to placebo, when depth of anaesthesia was maintained at a constant bispectral index (BIS) range 40-50 (±5). **Methodology:** Ninety patients were randomised to receive either gabapentin (Group G), melatonin (Group M) or multivitamin tablet (Group P) orally 120 min before induction of anaesthesia in a double blind manner. After achieving BIS 40–50 (±5), laryngoscopy and intubation were performed. Heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded pre-drug, after premedication, after induction, and at 1,3,5 and 10 min following intubation. Statistical analysis was done using Chi-square test and t-test. **Results:** There was an increase in heart rate in all the groups after intubation which persisted till 10 minutes after intubation. But increase was less in melatonin group as compared to placebo group till 5 minutes post intubation ($P<0.05$). SBP, DBP, MAP decreased from baseline in melatonin group till 10 minute post intubation. SBP, DBP, MAP increased in gabapentin and placebo group 1 min after intubation and increase was maximum in group P ($P<0.05$) and then it decreased and became lower than baseline in both groups till 10 min. **Conclusion:** Both gabapentin and melatonin are safe and effective method in attenuating the pressor response to direct laryngoscopy and endotracheal intubation but melatonin is more effective than gabapentin. Gabapentin does not attenuate heart rate.

KEYWORDS

Gabapentin, melatonin, Bi-spectral index, hemodynamic response, laryngoscopy, tracheal intubation

INTRODUCTION

Laryngoscopy and intubation, being noxious stimuli, incite remarkable sympathetic activity. The pressor response, represented by an abrupt rise in the arterial blood pressure and heart rate (HR), arising 30s after laryngoscopy and intubation, returns to baseline values steadily within 5–10 min.[1] These transitory responses usually produce no consequences in healthy individuals but may be harmful to the patients having reactive airways, hypertension, coronary artery disease, myocardial insufficiency and cerebrovascular diseases.[2]

Common factors precipitating the pressor response to laryngoscopy and intubation are light planes of anaesthesia, prolonged time for the procedure, anatomically difficult view, greater force used to displace the tongue and more manipulations/attempts at laryngoscopy and intubation.[3] Several drugs and manoeuvres have been used for mitigating this stress response with variable benefits and side effects.[4]

Gabapentin (1-aminomethyl cyclohexane acetic acid), a structural analogue of gamma amino butyric acid and an anticonvulsant drug, is also used in the treatment of neuropathic pain. It inhibits the membrane voltage gated calcium channels[5], just like calcium channel blockers and may be due to its inhibitory action it is helpful in attenuating the cardiovascular responses to tracheal intubation[6],[7]. Other proposed mechanism is by decreasing the neurotransmitter glutamate.

Melatonin (N-acetyl-5-methoxytryptamine) is an endogenous hormone, secreted by pineal gland, helps in regulation of sleep. Exogenous administration of melatonin facilitates sleep onset and improves the quality of sleep in a natural pattern, making it's effect different from that of benzodiazepines[8]. Many authors have used this drug as premedication to evaluate the effect on preoperative anxiety, sedation, psychomotor and cognitive function[9],[10]. Recently melatonin has been used for attenuation of haemodynamic responses to laryngoscopy and intubation.

Laryngoscopy and intubation can cause sympathetic stimulation and arousal reactions. We therefore designed this study to evaluate the attenuation of this pressor response by gabapentin as compared to placebo, when the depth of anaesthesia was maintained at bi-spectral index (BIS) range 40–50 (±5) in all the patients.

METHODS

After approval from the Institutional Ethical Committee, the present study enrolled 90 patients of American Society of Anesthesiologists (ASA) physical status I and II, aged 18–60 years, of either sex, scheduled for elective surgery under general anaesthesia using induction with propofol and maintenance with atracurium and isoflurane. The exclusion criteria were refusal of consent; patients having history of treatment with gabapentin and melatonin; psychiatric patients; patients having chronic pain complaint; hepatic, renal or cardiovascular dysfunction; uncontrolled hypertension; epilepsy; pregnancy; anticipated difficult airway; anticipated major blood losses and fluid shift; patients on sedatives and drug allergies.

Ninety patients were divided into three groups of 30 patients in each group to receive either gabapentin 800mg (Group G) or melatonin 6mg (Group M) or multivitamin capsule (Group C). One person with randomization chart gave the drug to the patient on a particular day 120 min before induction. Laryngoscopy, intubation and monitoring of vitals were done by another person who was blinded to the drug used in each group.

In preoperative room, the study drug was administered with a sip of water 120 mins before surgery. In operation theatre, routine monitoring was done which included Heart Rate, Electrocardiogram (ECG), SpO_2, Non invasive Blood Pressure (NIBP), $EtCO_2$ and Bispectral Index monitoring (BIS). Inj. Glycopyrrolate 0.004mg/kg, inj. midazolam 0.05mg/kg, Inj. fentanyl 1 µg/kg were administered as **premedication.** 100% oxygen was administered to all patients for 3 mins before induction. **Induction** was done with Inj. propofol iv titrated to achieve **BIS value in range of 40-45 (±5).** Inj. succinylcholine 1mg/kg was given to facilitate endotracheal **intubation** with proper size cuffed endotracheal tube by same person each time. Anaesthesia was **maintained** with 60 % N_2O in oxygen and isoflurane 0.5-1 MAC. **Muscle relaxation** was achieved with atracurium 0.5mg/kg iv as loading dose and 0.1mg/kg as maintenance doses. Mechanical ventilation was adjusted to **normocapnia** (EtCO2 values of 35-38 mm of Hg). BIS was adjusted to maintain a value between 40-45 (±5). Surgical procedure was started after 10 minutes of intubation i.e. after recording of all readings. After completion of surgery, Inj. neostigmine 0.05 mg/kg and Inj. glycopyrrolate 0.01mg/kg were administered to **reverse** the residual neuromuscular blockade. Haemodynamic parameters like Heart Rate, Systolic, Diastolic and Mean Blood Pressures were recorded before administration of study drug (baseline), after premedication, immediately after induction, and at 1, 3, 5 and 10 min following intubation. After operation, the patients were monitored in recovery room for 1 hour, and then in post operative ward for next 24 hours. **Complications** like nausea, vomiting, bradycardia, hypotension, hypertension, respiratory depression, allergic reaction, sedation, restlessness if any, were also recorded.

RESULTS

Both the study groups were identical in terms of age, gender

distribution, weight and ASA status [Table 1].

Table 1: Demographics

Variable	Group G	Group M	Group P
Age(years),mean±SD	33.03±9.36	32.33±7.26	30.23±9.16
Weight (kg),mean±SD	59.13±9.05	58.10±9.32	59.13±11.92
Gender (male/female) (n=30)	17/13	16/14	16/14

n – Number of patients; SD – Standard deviation

Table 2 Comparison Of Changes In Mean HEART RATE ± SD Between

HEART RATE	G	M	P	P VALUE		
	MEAN ±SD	MEAN ±SD	MEAN ±SD	GM	MP	GP
BASELINE	78.70±10.06	80.16±10.34	82.63±11.39	0.58	0.38	0.16
AFTER PREMED	79.5 ±9.65	79.23±10.02	82.83±9.40	0.92	0.156	0.18
AFTER INDUCTION	81.37±10.52	81.17±9.81	83.6±8.86	0.94	0.32	0.38
1 MIN AFTER INTUBATION	99.17±9.51	97.33±10.00	103.63± 12.52	0.47	0.04	0.13
3 MIN AFTER INTUBATION	97.80±8.04	96.5±9.99	102.53± 12.29	0.75	0.04	0.08
5 MIN AFTER INTUBATION	94.33±9.63	93.43±10.95	100.43± 14.88	0.74	0.04	0.06
10 MIN AFTER INTUBATION	87.00±8.61	83.90±9.20	88.27±10.89	0.18	0.098	0.62

Increase in heart rate after intubation was maximum in placebo (P)group (103.63±12.52) and minimum in melatonin (M) group (97.33±10.00). In all groups maximum rise in heart rate was seen after 1 minute of intubation (group G – 99.17±9.51, group M -97.33±10.00, group P –103.63±12.52) and HR remained elevated above baseline value in all groups till 10 minutes after intubation. Between group M and group P, changes in heart rate were statistically significant after intubation till 5 minutes after intubation (P<0.05). [Table 2]

Table 3 Comparison Of Changes In Mean SBP ± SD Between Three Groups

SBP	G	M	P	P VALUE		
	MEAN ±SD	MEAN ±SD	MEAN ±SD	GM	MP	GP
BASELINE	123.83± 8.64	124.17 ±8.42	128.37 ±9.60	0.88	0.08	0.06
AFTER PREMED	121.80 ±8.71	120.93 ±9.36	125.4± 9.75	0.71	0.07	0.14
AFTER INDSUCTION	109.97± 8.76	108.97 ±9.61	109.03 ±8.50	0.68	0.98	0.68
1 MIN AFTER INTUBATION	125.90± 7.59	119.13 ±9.91	137.83 ±13.39	0.0043	<0.0001	0.0001
3 MIN AFTER INTUBATION	109.80± 7.71	108.57 ±7.54	118.63 ±14.09	0.53	0.001	0.004
5 MIN AFTER INTUBATION	104.10± 7.85	102.90 ±8.18	109.60 ±11.52	0.56	0.01	0.03
10 MIN AFTER INTUBATION	107.13± 8.67	103.93 ±9.07	108.2± 8.03	0.17	0.06	0.62

SBP increased in gabapentin and placebo group 1 min after intubation and increase was maximum in group P (137.83±13.39) and then it decreased and became lower than baseline in both groups till 10 min after intubation and SBP decreased in melatonin group as compared to baseline after intubation (119.13±9.91) and remained lower than baseline till 10 min after intubation.

Between group G and group M, changes in SBP were statistically significant at 1 minute after intubation (P<0.05). At 3,5,10 minute after intubation, changes in SBP were statistically not significant (P>0.05).

Between group M and group P, changes in SBP were statistically highly significant till 3 minutes after intubation (P<0.001) and statistically significant at 5 minutes after intubation (P<0.05)

Between group G and group P, changes in SBP were statistically highly significant at 1minute after intubation (P<0.001) and statistically significant at 3, 5 minutes after intubation (P<0.05). [Table3]

Table 4 Comparison Of Changes In Mean DBP ± SD Between Three Groups

DBP	G	M	P	P VALUE		
	MEAN ±SD	MEAN±SD	MEAN±SD	GM	MP	GP
BASELINE	77.93±8.03	81.53±6.36	81.27±9.49	0.06	0.90	0.15
AFTER PREMED	76.53 ±5.18	77.50±7.55	78.23±11.48	0.57	0.77	0.46
AFTER INDUCTION	68.90±7.37	68.10±10.31	67.27±8.73	0.73	0.74	0.44
1 MIN AFTER INTUBATION	81.8±6.23	77.67±8.86	87.83±12.48	0.04	0.0006	0.02
3 MIN AFTER INTUBATION	69.83±8.81	68.10±7.84	75.47±10.95	0.42	0.004	0.03
5 MIN AFTER INTUBATION	65.13±7.46	63.93±7.89	69.33±8.62	0.55	0.01	0.048
10 MIN AFTER INTUBATION	65.70±7.41	65.50±6.83	65.93±7.70	0.91	0.82	0.91

Table 5 Comparison Of Changes In Mean MAP ± SD Between Three Groups

MAP	G	M	P	P VALUE		
	MEAN ±SD	MEAN±SD	MEAN± SD	GM	MP	GP
BASELINE	97.23±7.64	99.27±6.63	99.50±10.00	0.28	0.92	0.33
AFTER PREMED	95.07±6.32	95.20±6.83	98.17±10.01	0.94	0.19	0.16
AFTER INDUCTION	86.00±7.02	84.73±9.89	83.97±9.03	0.57	0.75	0.33
1 MIN AFTER INTUBATION	100.83±6.20	94.63±9.51	108.80±13.27	0.004	<0.0001	0.004
3 MIN AFTER INTUBATION	86.93±7.99	85.37±7.33	93.77±12.03	0.43	0.002	0.01
5 MIN AFTER INTUBATION	81.90±7.59	80.40±7.84	86.37±9.14	0.45	0.01	0.04
10 MIN AFTER INTUBATION	83.50±6.28	81.70±7.41	84.70±8.35	0.31	0.15	0.53

DBP and MAP increased in gabapentin and placebo group 1min after intubation and increase was maximum in group P (87.83±12.48), (108.80±13.27) and then they decreased and became lower than baseline in both groups till 10 min after intubation and DBP and MAP decreased in melatonin group as compared to baseline after intubation (77.67±8.86), (94.63±9.51) and remained lower than baseline till 10 min after intubation.

Between group G and group M, changes in DBP and MAP were statistically significant at 1 minute after intubation (P<0.05). At 3,5,10 minute after intubation changes in DBP were statistically not significant (P>0.05).

Between group M and group P, changes in DBP and MAP were

statistically highly significant till 1 minute after intubation (P<0.001) and statistically significant at 3, 5 minutes after intubation (P<0.05) Between group G and group P, changes in DBP and MAP were statistically significant till 5 minutes after intubation (P<0.05). [Table4,5]

Table 6 Comparison Of Changes In BIS Between Three Groups

BIS	G	M	P	P VALUE		
	MEAN ±SD	MEAN±SD	MEAN± SD	GM	MP	GP
BASELINE	97.47±0.97	97.40±0.89	97.57±0.86	0.78	0.46	0.67
AFTER PREMED	90.90±1.21	90.47±0.86	90.87±1.46	0.12	0.20	0.93
AFTER INDUCTION	40.4±1.92	39.67±1.42	40.4±1.57	0.09	0.06	1.00
1 MIN AFTER INTUBATION	50.63±1.13	49.77±1.41	51.47±1.53	0.01	<0.0001	0.018
3 MIN AFTER INTUBATION	43.9±1.27	43.03±3.63	44.47±1.2	0.22	0.04	0.08
5 MIN AFTER INTUBATION	40.3±1.37	39.97±1.47	40.8±1.03	0.37	0.01	0.11
10 MIN AFTER INTUBATION	42.33±4.30	41.63±4.43	43.37±3.37	0.54	0.09	0.30

BIS value was kept between 40-50(±5) during intubation and till 10 minutes after intubation. BIS value was on higher side of selected range at 1 min after intubation. Increase was less in melatonin group and difference was statistically significant as compared to gabapentin and placebo group. At 3 and 5 minute after intubation, BIS value was less in melatonin group as compared to gabapentin and placebo group. (P value<0.05) [Table 6]

Table 7 Side Effects And Complications

	G	M	P
INTRAOPERATIVE			
Bradycardia	--	--	--
Hypotension	--	1	--
Arrhythmia	--	--	--
Bronchospasm	--	--	--
POSTOPERATIVE			
Bradycardia	--	--	--
Arrhythmia	--	--	--
Respiratory depression	--	--	--
Restlessness	--	--	--
Bronchospasm	--	--	--
Nausea / vomiting	--	1	1

No significant side effects, such as intraoperative bradycardia, arrhythmias, bronchospasm, or postoperative respiratory depression, bronchospasm, bradycardia / tachycardia, hypotension / hypertension, arrhythmias or any other side effects were noted in any of the groups. [Table 7]

DISCUSSION

Laryngoscopy and intubation are known to cause an increase in HR and blood pressure.[1,3] In the present study, the effect of oral gabapentin and oral melatonin on the hemodynamic responses was compared to oral multivitamin group (placebo) after achieving an adequate depth of anaesthesia, that is BIS value 40–50 (±5). In our pilot study, we observed that BIS levels of 40–50 provided better conditions for laryngoscopy than BIS 40–60. Laryngoscopy and endotracheal intubation, similar to any other peripheral noxious stimulus, might produce a reflex response in the reticular activating system of brainstem, it can lead to wakefulness, making the planes of anaesthesia lighter.[11] Hence, maintaining the BIS values at 40–50 during the induction of anaesthesia may decrease such responses.

Gabapentin has been used to attenuate the pressor response to laryngoscopy and intubation, mechanism of which is not fully known. *A.Fassoulaki* & *colleague*(2006)[6] found that oral gabapentin used as premedication attenuate the hemodynamic response to laryngoscopy & intubation. *Memiş* and *colleagues* (2006)[7] showed that oral administration of gabapentin 800 mg but not 400 mg given 1 h before operation blunted the arterial pressure and HR increase in the first 10 min after endotracheal intubation.

Melatonin (*N*-acetyl-5-methoxytryptamine) is a pineal gland hormone which controls the circadian rhythm. It has been used for sleep disorders, jet lag, perioperative anxiolysis and sedation, cognitive and psychomotor functions.[10] We assumed that its inhibitory actions on central nervous system responsible for sedation and anxiolysis may have a role in attenuating haemodynamic responses to laryngoscopy and intubation. **Rosenberg et al (2010)**[12] studied the role of perioperative melatonin in the modification of surgical stress response indicating that melatonin has sympatholytic activity. This is in support of our assumption. The peak effect of exogenous melatonin ranges from 60 to 150 min.[13] Based on this, we made a hypothesis that melatonin can provide haemodynamic stability during laryngoscopy and intubation when given 120 min before the procedure. We performed a pilot study in which we did not observe the desired effects with 3 mg but with 6 mg oral melatonin and not at 90 min but after a period of 120 min.

Increase in heart rate after intubation was maximum in placebo(P) group and minimum in melatonin (M) group. In all groups, maximum rise in heart rate was seen after 1 minute of intubation and HR remained elevated above baseline value in all groups till 10 minutes after intubation.

Our study suggested that gabapentin does not attenuate heart rate as compared to placebo. This is supported by **A.Fassoulaki & colleague (2006)**[6] and **Montazeri K et al (2011)**[14] in their study. While **Serhat Koc and colleague (2007)**[15] observed that oral gabapentin 1000 mg given 1 h prior to operation resulted in significant decreases in MAP and HR during study period (p<0.05). This effect was considered to be dose dependent.

Melatonin also does not decrease heart rate below baseline till 10 mins of intubation and it was more than baseline till 10 minutes post intubation but increase was less as compared to gabapentin and placebo. Above all, changes were statistically significant with placebo till 5 min after intubation. In contrast **Gupta et al (2010)**[8] observed that in melatonin group there was insignificant increase in heart rate at time of laryngoscopy and intubation which settled within 1 min post intubation.

SBP, DBP and MBP followed same trends in our study. BP increased in gabapentin and placebo group 1min after intubation and increase was maximum in group P and then it decreased and became lower than baseline in both groups till 10 min after intubation. SBP, DBP & MBP was less in melatonin group as compared to baseline after intubation and remained lower than baseline till 10 min after intubation.

Our study suggests that both gabapentin and melatonin attenuate SBP, DBP, MBP as compared to placebo till 5 min after intubation. This is more with melatonin (In fact, lower than baseline at all points after intubation till 10 minutes) as compared to gabapentin group which is statistically significant at 1 min after intubation.

In another study, **Kaya et al (2008)**[16]reported that gabapentin 800 mg given 2 hours prior to surgery prevented the increase in MAP after tracheal intubation but not the HR. In a recent study comparing 600 mg and 1000 mg doses of gabapentin, **Bafna et al (2011)**[17] found that gabapentin 1000 mg given before operation significantly attenuated the hemodynamic response to laryngoscopy and intubation, whereas gabapentin 600 mg had no effect. **Bala I et al (2015)**[18] showed that the pretreatment with gabapentin 800 mg in single or double doses is equally effective in attenuating the hypertensive response associated with laryngoscopy and tracheal intubation in treated hypertensive patients.

Gupta et al (2010)[8] observed that in melatonin group, Blood pressure was lower than baseline values at all points of time till 10 min after

intubation as compared to the control group in which there was a significant rise.

Keeping BIS at lower range, there was a significant decrease in haemodynamic variables throughout, which may actually be desirable in certain surgeries where induced hypotension may be beneficial. BIS monitoring serves the goal of maintaining adequate depth of anaesthesia well and reducing the requirement of IV induction agents, volatile agents and analgesics.[19] Since, the BIS values increase with unpleasant stimuli, it can be utilised as an objective marker for quantifying hypnosis that proved advantageous to assess the blunting of the pressor response.[20]

Mahajan L et al (2018)[21] studied the role of iv dexmedetomidine and magnesium sulphate on pressor responses to laryngoscopy and intubation as compared to placebo, when depth of anaesthesia was maintained at a constant bispectral index (BIS) range 40-50 (±5). They concluded that at BIS levels 40-50 (±5) there was no pressor response to intubation in the placebo Group. Dexmedetomidine and magnesium sulphate significantly reduced the heart rate and blood pressure from baseline.

In future, research can be planned on evaluating the pressor responses with or without BIS monitoring. Further, the impact of BIS on haemodynamic variability during laryngoscopy and intubation can be compared between different BIS ranges of 40–50 and 50–60.

CONCLUSION

Both gabapentin 800mg and melatonin 6mg, given 120 minutes prior to laryngoscopy and intubation are safe and effective method in attenuating the pressor response to direct laryngoscopy and endotracheal intubation but melatonin is more effective than gabapentin. Gabapentin does not attenuate heart rate. Melatonin decreases heart rate as compared to placebo but heart rate remained elevated than baseline till 10 minutes post intubation.

REFERENCES

1. Reid LC, Brace DE. Irritation of respiratory tract and its reflex effect on heart. Surg Gynecol Obstet 1940;70:157.
2. Kovac AL. Controlling the hemodynamic response to laryngoscopy and endotracheal intubation. J Clin Anesth 1996;8:63-79.
3. Joffe AM, Deem SA. Physiologic and pathophysiologic responses to intubation. In: Benumof J, Hagberg CA, editors. Benumof and Hagberg's Airway Management. 3rd ed. Philadelphia: Elsevier Saunders; 2012. p. 184-95.
4. Charuluxananan S, Kyokong O, Somboonviboon W, Balmongkon B, Chaisomboonpan S. Nicardipine versus lidocaine for attenuating the cardiovascular response to endotracheal intubation. J Anesth 2000;14:77-81.
5. Gee NS, Brown JP, Dissanayake VU. The novel anticonvulsant drug, gabapentin, binds to alpha2 delta subunit of calcium channel. J Biol chem. 1996;271:5768-76.
6. Fassoulaki A, Melemeni A, Paraskeva A, Petropoulos G. Gabapentin attenuates the pressure response to direct laryngoscopy and tracheal intubation. Br J Anaesth. 2006;96(6):769-773.
7. Memis D, Turan A, karamanlioglu B, Seker S, Ture M. Gabapentin reduces cardiovascular responses to laryngoscopy and tracheal intubation. Eur J Anaesthesiol.2006;23(8):686-90.
8. 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.
9. Maittra S, Baidya DK, KhannaP. "Melatonin in perioperative medicine: Current perspective." Saudi J Anaesth 2013;7:315-21.
10. Patel T, Kurdi MS. "A Comparative study between oral melatonin and oral midazolam on preoperative anxiety, cognitive, and psychomotor functions." J Anaesthesiology Clinical Pharmacology 2015;31:37-43.
11. Kanaya N, Nakayama M, Fujita S, Namiki A. Haemodynamic and EEG changes during rapid-sequence induction ofanaesthesia. Can J Anaesth 1994;41:699-702.
12. Rosenberg J, Gögenur I, Lykkesfeldt J. Modification of surgical stress response by perioperative melatonin administration. Dan Med Bull 2010;57:4144.
13. Melatonin. Monograph. Altern Med Rev 2005;10:326-36. Available from: http://www.altmedrev.com/ publications/10/4/326.pdf.
14. Montazeri K, Kashefi P, Honarmand A, Safavi M, Hirmanpour A. "Attenuation of the pressor response to direct laryngoscopy and tracheal Intubation: oral clonidine vs. oral gabapentin premedication." J Res Med Sci 2011 Mar; 16(Suppl1): S377-S386.
15. Serhat KOC, Dilek Memis, Necdet Sut. "The preoperative use of gabapentin, dexamethasone and their combination in vericocele surgery: A randomised controlled trial." Anesth Analg 2007; 105: 1137-1142.
16. Kaya FN, Yavascaoglu B, Baykara M, Altun GT, Gülhan N, Ata F. "Effect of oral gabapentin on the intraocular pressure and haemodynamic responses induced by tracheal intubation." Acta Anaesthesiol Scand 2008;52:1076-80.
17. Bafna U, Goyal VK, Garg A. "A comparison of different doses of gabapentin to attenuate the haemodynamic response to laryngoscopy and tracheal intubation in normotensive patients." J Anaesthesiol Clin Pharmacol 2011;27:43-6.
18. Bala I, Bharti N, Ramesh NP. Ramesh. "Effect of gabapentin pretreatment on the hemodynamic response to laryngoscopy and tracheal intubation in treated hypertensive patients." Acta Anaesthesiologica Taiwanica 53 (2015) 95-98.
19. Song D, Joshi GP, White PF. "Titration of volatile anaesthetics using bispectral index facilitates recovery after ambulatory anaesthesia." Anaesthesiology 1997;87:842-8.
20. Ekman A, Lindholm ML, Lennmarken C, Sandin R. "Reduction in the incidence of awareness using BIS monitoring." Acta Anaesthesiol Scand 2004;48:20-6.
21. Mahajan L, Kaur M, Gupta R, Aujla KS, Singh A, Kaur A. **"**Attenuation of the pressor responses to laryngoscopy and endotracheal intubation with intravenous dexmedetomidine versus magnesium sulphate under bispectral index-controlled anaesthesia: A placebo-controlled prospective randomised trial." Indian J Anaesth 2018;62:337-43.