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Effect of oral clonidine and tizanidine on the induction dose of propofol and intubation response in general anesthesia

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Abstract---Background: Laryngoscopy and tracheal intubation are associated with hemodynamic and cardiovascular responses consisting of increased heart rate, blood pressure and tachycardia and dysarrhythmias. The alpha2-adrenoreceptor agonists such as clonidine and tizanidine have several beneficial actions during the perioperative period. They improve hemodynamic stability in response to endotracheal intubation and surgical stress. Objective: To study the effect of oral clonidine and tizanidine on induction dose of propofol and hemodynamic responses after laryngoscopy in patients undergoing surgery under general anesthesia Methods: Hundred patients in age group of 18-70 years old of ASA 1/2 undergoing elective surgeries under general anesthesia with tracheal intubation was included in the study. Tizanidine 4 mg prescribed to group A, 0.1 mg clonidine to group B 60 min before the time of induction or laryngoscopy. systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and heart rate recorded before induction, pre-intubation, after intubation at 0 min, and then at interval of 1,3,5 minute after laryngoscopy by an independent observer. Results: The study results show that there was a significant difference in mean

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dose of propofol with respect to the group (p=0.005). At 1 min, 3 min and 5 min post intubation all hemodynamic parameters heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure were significantly higher than the baseline values in tizanidine group (p<0.001) when compared to clonidine group. Conclusion: According to this study as in clonidine and tizanidine group (specially in clonidine group) heart rate reduced significantly after laryngoscopy, no significant side effects was reported and there was no significant differences in arrhythmia and ischemia and request for TNG, Esmolol and vasopressor between two groups, tizanidine and clonidine (specially clonidine) could be recommended as useful drugs for premedication in general anesthesia in patients undergoing surgery under general anesthesia.

Keywords---*Clonidine, Tizanidine, Hemodynamic responses after laryngoscopy.*

Introduction

Satisfactory preoperative preparation and pre-medication facilitate an uneventful perioperative course. The current practice of anesthetic premedication has evolved into generalized scheme that incorporates several aspects of patient care like decreasing preoperative anxiety, dampening intra operative noxious stimulus and its associated neuro endocrinal changes and minimizing postoperative adverse effects of anesthesia and surgery.[1]

Manipulation of the larynx such as laryngoscopy and tracheal intubation are associated with hemodynamic and cardiovascular responses consisting of increased circulating catecholamines, heart rate, blood pressure, myocardial oxygen demand, tachycardia and dysarrhythmias. Usually, these changes may precipitate myocardial ischemia, myocardial infarction and cerebral hemorrhage so may be fatal, by Numerous methods such as deepening of anaesthesia could blunt the stimulatory effects on the cardiovascular system induced by laryngoscopy and endotracheal intubation.[2] Also pretreatment with variety of drugs such as vasodilators,[3] beta-blockers,[4] calcium channel blockers, alpha 2 agonists and opioids,[5] regional nerve blocks, anesthetic and non-anesthetic adjuvants can decrease these responses.

The alpha2-adrenoreceptor agonists have several beneficial actions during the perioperative period. They exert a central sympatholytic action, improving hemodynamic stability in response to endotracheal intubation and surgical stress, reducing the opioid or inhalation agent requirements and causing sedation, anxiolysis and analgesia.[6,7,8]

Clonidine is a α2- adrenoceptor agonist with sedative and analgesic effects, also has the beneficial effect of blunting hyperdynamic responses due to laryngoscopy and tracheal intubation. Tizanidine, another alpha 2-adrenergic agonist that is used mainly as a centrally acting muscular relaxant for patients with painful muscular spasms. Both drugs reduce the need for opioids and benzodiazepines

during and after anesthesia. The antinociceptive effect of tizanidine is reportedly weaker than clonidine however tizanidine produces fewer side effects (such as hypotension and bradycardia) than clonidine.[9-15]

In this study we compared the effect of oral clonidine and tizanidine on the induction dose of propofol and hemodynamic responses in laryngoscopy in patients undergoing surgery under general anesthesia.

Methods

After approval by the Ethical and scientific Committee and written informed consent, 100 patients were evaluated in this randomized double blinded study. All Patients age 18-70 years old of ASA 1/2 underwent elective surgery under general anesthesia with tracheal intubation were included in the study.

Patients ASA 3 or more, with need for re-intubation, pregnant and lactating mother, patients with uncontrolled chronic illness like DM, Asthma, renal or hepatic dysfunction, coronary artery disease, valvular heart disease, left bundle branch block, AV node block and history of anticholinergic drug use and any other hemodynamic instability were excluded from the study.

Patients were randomized into two groups by computerized analysis and routine preoperative medication with tab Ranitidine 150mg and tab Alprax 0,5 mg at 10 pm on the night before the surgery and the patient was kept fasting for 6hrs prior to surgery. An anesthesiologist administers Thizanidine 4 mg prescribed to group A, 0.1 mg clonidine to group B 60 minutes before laryngoscopy. Both the patient and the anesthesiologist administered the drug were blinded making the study double blinded.ECG, baseline systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and heart rate recorded. After preoxygenation for 3 minutes with 100% oxygen general anesthesia administered with midazolam 1mg I. V, Fentanyl 2mcg/kg I. V and titrated doses of I. V propofol was administered till loss to verbal command was observed. Dose of propofol given for loss of verbal command was recorded. After confirming successful ventilation 0.5mg/kg of I.V atracurium was administered and tracheal intubation was performed by trained anesthesiologist. Study parameters heart rate, noninvasive blood pressure and arterial saturation were recorded before induction, pre-intubation and after intubation at 00 min of intubation and interval of 1,3,5 min from time of intubation by an independent observer. Anaesthesia was maintained with nitrous oxide and oxygen mixture with 0.6% isoflurane and additional doses of atracurium as needed during the course of surgery. The residual neuromuscular blockade was reversed with inj. neostigmine 0.05mg/kg and inj. glycopyrrolate 0.01mg/kg I.V.

Data was analyzed using SPSS 22 version software. **Normality of the continuous data**, was tested by Kolmogorov–Smirnov test and the Shapiro–Wilk test. Continuous data was represented as mean and standard deviation. **Independent t test** was used as test of significance to identify the mean difference between two quantitative variables. **p value** (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.[16,17]

Results

In this randomized double blinded study 100 patients age 18-70 years old of ASA grade 1 and 2 undergoing elective surgeries under general anesthesia with tracheal intubation was included. There was significant high systolic blood pressure in tizanidine group at baseline and before intubation (p= 0.022* and p <0.001* respectively)when compared to clonidine group, diastolic blood pressure were higher in tizanidine group from baseline and follow ups except at 0 min of intubation(p<0.001*) and mean arterial blood pressure were higher at 0 and 1 min after intubation in tizanidine group (p = 0.461,p = 0.162) but there was a significant reduction in heart rate from baseline to after 5 min in the clonidine group (p <0.001*).The independent t-test results shows that there is a significant difference in mean of propofol with respect to the group (t=2.894, p = 0.005*).

Discussion

The hemodynamic stress response characterized by tachycardia, hypertension and arrhythmias to manipulation in the area of larynx by means of laryngoscopy and intubation is well recognized and has been a topic of discussion since 1940.
Sheen MJ et al[3] in 2014 stated the concept of anesthetic premedication was initially developed to counteract the side effects of general anesthesia.[3] Now we emphasize more about the efficacy of premedication in improving the general well being of patients and patient satisfaction after their surgery. the drugs Tizanidine and clonidine are also found to have beneficial effects on intubation and laryngoscopy related hemodynamic effects. propofol induction dose has also been noted to decrease in induction.

The current practice of anesthetic premedication has evolved into a generalized scheme that incorporates several aspects of patient care: decreasing preoperative anxiety, dampening intraoperative noxious stimulus and its associated neuroendocrinal changes and minimizing postoperative adverse effects of anesthesia and surgery.

Rational use of premedication in modern anesthesia practice should be justified by individual needs, the type of surgery and the anesthetic agents and techniques used.

In our study we choose Tab. clonidine and T. Tizanidine to observe the hemodynamic response to intubation and also see if there was a reduction in the dose of propofol required for induction after pre-medicating Patients 60 min before surgery.

Fifty patients were enrolled into each group and named as group C and group T depending on the drugs received. The chi-square test shows that there is no significant difference between the groups with respect to age, sex, ASA status and weight of the patients.

Masoomeh Tabari et al[1] evaluates the effects of 4 mg oral Tizanidine on hemodynamic responses during operations. They showed that using oral Tizanidine as a premedication, yielded stability in blood pressure and heart rate

during surgery and decreased required Propofol. Considering its short duration of action, Tizanidine use as a premedication is recommended for sedation and stabilization of hemodynamic responses during the operations.

In our study it was observed that the clonidine group required significantly lower dosage of propofol than tizanidine. The independent t test results show that there is a significant difference in mean propofol with respect to the group (t value =2.894, p=0.005*). This is in concurrence with the findings of the above-mentioned study.

Moshtaghion H et al[7] study shows that the dose requirements of propofol for loss of eyelash reflex were significantly less in patients who received tizanidine 4mg and systolic diastolic blood pressures and heart rate were significantly reduced when compared to patients who received with 2mg of tizanidine.

Our study independent t test result shows that in tizanidine group had higher heart rate when comparing to clonidine group at baseline and all follow-up (p<0.001*) with the lowest rates after induction before intubation and the highest at the 00 min of intubation. In our study we find clonidine to be better than tizanidine with respect to heart rate variability from the baseline. There was no significant severe bradycardia noted in the study in either the groups.

In our study the independent t test result shows that cases in oral tizanidine group had significantly high SBP when comparing to clonidine group at baseline and before intubation (p-0.022*, p<0.001*) and significantly higher DBP when compared to clonidine group at baseline and follow-ups except 0 minute (p<0.001*)

In our study it was also noted that all the study parameters like SBP, DBP, MAP, HR at 1,3,5 min post intubation were significantly lower than baseline value in clonidine group (p<0.001*) when compared to tizanidine group.

Conclusion

From the study it can be concluded that in clonidine heart rate reduced significantly after laryngoscopy, no significant side effects were reported and there were no significant differences in arrhythmia and ischemia and request for TNG, Esmolol and vasopressor between two groups, tizanidine and clonidine (specially clonidine) could be recommended as useful drugs for premedication in general anesthesia in patients undergoing surgery under general anesthesia.

Table 1: Mean hemodynamic changes between two groups

Variable	Time	Group C	Group T	t value	P value
SBP	Baseline	128.48+12.228	134.56+13.811	-2.331	0.022*
	Before intubation	107.62+12.081	116.92+13.672	-3.604	<0.001*
	Intubation 0 min	126.30+13.661	126.26+12.906	0.015	0.988

	1 min	123.22+13.417	123.12+11.533	0.04	0.968
	3 min	119.12+12.802	120.92+10.511	-0.768	0.444
	5 min	115.18+12.972	119.76+10.636	-1.931	0.056
DBP	Baseline	77.66+8.019	86.08+11.508	-4.245	<0.001*
	Before intubation	62.10+9.740	74.34+10.259	-6.118	<0.001*
	Intubation 0 min	78.18+9.739	80.44+9.611	-1.168	0.246
	1 min	73.70+9.444	78.68+8.203	-2.815	0.006*
	3 min	70.38+8.678	76.64+7.602	-3.837	<0.001*
	5 min	67.10+8.593	75.92+7.208	-5.561	<0.001*
MAP	Baseline	94.48+8.700	100.78+11.184	-3.144	0.002*
	Before intubation	77.14+9.914	88.34+10.760	-5.413	<0.001*
	Intubation 0 min	93.94+10.568	95.46+9.945	-0.741	0.461
	1 min	89.84+9.645	92.44+8.767	-1.41	0.162
	3 min	86.36+9.066	91.12+7.881	-2.802	0.006*
	5 min	82.88+9.043	90.16+7.980	-4.268	<0.001*
HR	Baseline	74.00+8.704	87.70+13.877	-5.914	<0.001*
	Before intubation	60.72+9.201	80.90+11.864	-9.505	<0.001*
	Intubation 0 min	77.32+10.931	86.76+12.042	-4.104	<0.001*
	1 min	74.86+10.797	85.48+11.411	-4.78	<0.001*
	3 min	71.10+10.535	83.50+10.773	-5.866	<0.001*
	5 min	67.64+10.456	82.86+10.687	-7.198	<0.001*

Table 2: Mean Propofol requirement comparison between two Groups

Group	N	Mean	SD	t Value	p value
Clonidine	50	65.000	12.617	2.894	0.005*
tizanidine	50	57.660	12.742		

References

1. Tabari M, Alipour M, Esalati H. Evaluation of Oral Tizanidine Effects on intraoperative Hemodynamic Responses During Direct Laryngoscopy Under General Anesthesia. Iranian Red Crescent Medical Journal. 2013;15(7):541-6
2. Giovannitti Jr JA, Thomas SM, Crawford JJ. Alpha-2 adrenergic receptor agonists: a review of current clinical applications. Anesthesia progree.2015;62(1):31-8.
3. Sheen MJ, Chang FL, Ho ST. Anesthetic premedication: new horizons of an old practice. Acta Anaesthesiologica Taiwanica 2014;52(3):134-42.
4. Rathore P, Saini V, Ahmed F, Chatterjee R, Rathore M. A Comparative study of oral clonidine versus oral pregabalin on hemodynamic responses to laryngoscopy and endotracheal intubation under General Anesthesia. International Journal of Medical and Biomedical studies,2019;1;3(4). https://doi.org/10.32553/ijmbs.v3i4.224

5. Kaur H, Gupta M, Sethi D. Effect of intravenous clonidine on pressor response to laryngoscopy and intubation and induction dose of propofol. Journal of Evolution of Medical and Dental Sciences-JEMDS,2017;6(15):1167-70.
6. Agrawal M, Asthana V, Sharma JP. Efficacy of intravenous midazolam versus clonidine as premedicants on bispectral index guided propofol induction of anesthesia in laproscopic cholecystectomy: A randomized control trial. Anesthesia essays and researches. 2014;8(3):302.
7. Moshtaghion H, Mirjalili M, Abdollahi HM, Vaziribozorg S. Effect of oral clonidine and Tizanidine on hemodynamic responses after laryngoscopy in patients undergoing coronary artery bypass surgery. International Journal of Medical Investigation. 2016;50(4):136.
8. Sane S, Khoshkbary M, Abbasyvash R, Mahoori AR. Evaluation of the effect of preoperative oral tizanidine in on the rate of anesthetic consumption and hemodynamic changes in Tiva (total intravenous anesthesia). Journal of Global Pharma Technology.2016;8(12):441-6.
9. Kotwni DM, Kotwani MB, Kamdar B. Comparative clinical study of the effect of oral clonidine premedication on intraoperative hemodynamics in the patients undergoing laparoscopic cholecystectomy. International Surgery Journal.2017;4(30:950-60.
10. Talakoub R, Abbasi S, Maghami E, Zavareh SM. The effect of oral tizanidine on postoperative pain relief after elective laparoscopic cholecystectomy. Adv Biomed Res. 2016; 5:19.
11. Fazio G, Vernuccio F, Grutta G, Re GL. Drugs to be avoided in patients with long QT syndrome: Focus on the anesthesiological management. World journal of cardiology.2013;5(4):87.
12. Shoeibi G, Mohammadi SS, Ahangari A, Marashi S, Borji A,Yaghooti AA. Effects of oral Tizanidine premedication on pain and hemodynamic responses after spinal needle skin puncture. Archives of Anesthesiology and critical care.2015;1(1):18-20.
13. Yazicioglu D, Caparlar C, Akkaya T, Mercan U. Tizanidine for the management of acute postoperative pain after inguinal hernia repair: a placebo-controlled double-blind trial. European Journal of Anesthesiology (EJA).2016;33(3):215-22.
14. Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2022). Post-pandemic health and its sustainability: Educational situation. *International Journal of Health Sciences*, *6*(1), i-v. https://doi.org/10.53730/ijhs.v6n1.5949
15. Ahiskalioglu A, Yayik AM, Ahiskaligolu EO, Dostbil A, Doymus O, Karadeniz E. Ultrasound guided bilateral superficial cervical block and preemptive single dose oral tizanidine for post thyroidectomy pain: a randomized controlled double blinded study. Journal of Anesthesia.2018;32(2):219-26.
16. Aronson JK, editor. Meylers side effects of drugs: the international encyclopedia of adverse drug reactions and interactions. Elsevier; 2015.
17. Yan F, Robert M, Li Y. Statistical methods and common problems in medical or biomedical science research. Int J Physiol Pathophysiol Pharmacol. 2017;9(5):157-163.
18. Krousel-Wood MA, Chambers RB, Muntner P. Clinicians' guide to statistics for medical practice and research: part I. Ochsner J. 2006;6(2):68-83.