

Original article

Effect of oral clonidine and Tizanidine on hemodynamic responses after laryngoscopy in patients undergoing coronary artery bypass surgery

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Abstract

Objective: laryngoscopy and tracheal intubation are associated with hemodynamic and cardiovascular responses consisting of increased heart rate, blood pressure and tachycardia and dysrhythmias. 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. In this study we compared the effect of oral clonidine and tizanidine on hemodynamic responses after laryngoscopy in patients undergoing coronary artery bypass surgery.

Methods: Ninety patients age 30-70 years old underwent coronary artery bypass surgery with HR>50 b/min and EF>40% evaluated in this randomized double blinded study. Tizanidine 4 mg prescribed to group A, 0.2 mg clonidine to group B and placebo to group C, 90 minutes before laryngoscopy. systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and heart rate recorded before, During, 1 minute after laryngoscopy and then each 5 to 15 minutes after that.

Results: There was no significant differences in systolic blood pressure (p.value for repeated measure= 0.507), diastolic blood pressure (p.value for repeated measure=0.707) and mean arterial blood pressure (p.value for repeated measure=0.997) but there was a significant difference in heart rate (p.value for repeated measure= 0.036) between three groups. According to post_Hoc test there was a significant difference in heart rate between clonidine group and placebo group.(p.value=0.042) There was no significant differences in diabetes mellitus and hypertension, in side effects and in arrhythmia, ischemia and request for TNG, Esmolol and vasopressor between three groups.

Conclusion: According to the recent 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 three groups, tizanidine and clonidine (specially clonidine) could be recommended as useful drugs for premedication in general anesthesia in patients undergoing CABG surgery.

Keywords: clonidine and tizanidine, hemodynamic responses after laryngoscopy, coronary artery bypass surgery.

Introduction

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 dysrhythmias. Usually these changes are well tolerated by healthy individuals but In patients with coronary artery disease, hypertension or cerebrovascular disease, these changes may precipitate myocardial ischemia, myocardial infarction and cerebral hemorrhage so may be fatal.(1) 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, alfa2 agonists and opioids (5) 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 requirements and causing sedation, anxiolysis and analgesia. (6)

Clonidine is a α_2 -adrenoceptor agonist with sedative and analgesic effects, also has the beneficial effect of blunting hyperdynamic responses due to laryngoscopy and tracheal intubation.(1) 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.(7)

In this study we compared the effect of oral clonidine and tizanidine on hemodynamic responses after laryngoscopy in patients undergoing coronary artery bypass surgery.

Methods

After approval by the Ethical Committee and written informed consent, 90 patients were evaluated in this randomized double blinded study. All Patients age 30-70 years old underwent coronary artery bypass surgery with HR>50 b/min and EF>40% were included. Patients with intubation time more than 15 seconds or need for re intubation, left bundle branch block, AV node block and history of anticholinergic drug use were excluded from the study. Patients assigned into one of the three groups according to random – number table (30 patients in each group). Thizanidine 4 mg prescribed to group A, 0.2 mg

clonidine to group B and placebo to group C, 90 minutes before laryngoscopy. systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and heart rate recorded before, During , 1 minute after laryngoscopy and then each 5 to 15 minutes after that. Patients received TNG if SBP> 160mmHg , esmolol if HR>100 b/min and a vasopressor if SBP<80mmHg during the intubation. History of diabetes mellitus and hypertension , any arrhythmia and ischemia before, during and after laryngoscopy recorded in a questionnaire. headache, xerostomia and drowsiness recorded in a questionnaire before anesthesia too. All data analyzed using SPSS software version 15 and statistical tests (chi_square and repeated measure). P.values<0.05 was considered significant.

Results

In this randomized double blinded study 90 patients age 30-70 years old underwent coronary artery bypass surgery with HR>50 b/min and EF>40% were included. There was no significant differences in systolic blood pressure (p.value for repeated measure= 0.507), diastolic blood pressure (p.value for repeated measure=0.707) and mean arterial blood pressure (p.value for repeated measure=0.997) but there was a significant difference in heart rate (p.value for repeated measure= 0.036) between three groups. (table. 1) According to post_Hoc test there was a significant difference in heart rate between clonidine group and placebo group. (p.value=0.042)

There was no significant differences in diabetes mellitus and hypertension between three groups. (p.value>0.05) (table.2). There was no significant differences in side effects between three groups (p.value>0.05) (table.3). There was no significant differences in arrhythmia, ischemia and request for TNG, Esmolol and vasopressor between three groups (p.value>0.05).

Discussion

Laryngoscopy and tracheal intubation are often associated with tachycardia, hypertension and arrhythmias, which may cause myocardial ischaemia, systemic hypertension, left ventricular failure and intracranial haemorrhage. These above mentioned effects may be serious in high risk patients like those with cardiovascular disease, increased intracranial pressure or anomalies of the cerebral vessels.(8)

Clonidine and Tizanidine are alpha2-adrenoreceptor agonists that 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 requirements and causing sedation, anxiolysis and analgesia. the antinociceptive effect of tizanidine is reportedly weaker than clonidine however tizanidine produces fewer side effects (such as hypotension

and bradycardia) than clonidine.⁽⁷⁾ In this study we compared the effect of oral clonidine and tizanidine on hemodynamic responses after laryngoscopy in patients undergoing coronary artery bypass surgery.

Table.1: mean hemodynamic changes between three groups.

p.value for repeated measure	groups			time	Variables
	C(placebo)	B(clonidine)	A(tizanidine)		
0.507	125.92± 19.59	120.36± 18.84	125.33±15.64	1 hour before	SBP
	145.17± 34.64	141.43± 30.76	146.83±28.47	Before induction	
	118.96± 25.98	112.46± 20.80	113.46±24.82	After induction	
	145.71± 38.93	128.16± 29.30	132.86±43.37	During	
	131.103±33.36	124.90± 33.23	126.13±33.40	1 min after	
	113.71±20.40	112.33± 16.97	112.66±22.41	5 min after	
	106.16±18.09	112.06± 18.88	112.76±19.28	10 min after	
	110.25±22.93	110.93± 15.35	120.13±14.48	15 min after	
0.707	77.77± 11.62	74.00± 09.50	76.66± 09.94	1 hour before	DBP
	77.81± 19.94	76.90± 13.78	75.80± 13.91	Before induction	
	69.66± 21.33	69.70± 14.64	66.86± 13.80	After induction	
	84.59± 24.21	78.83± 17.13	74.76± 24.01	During	
	73.51± 20.08	77.63± 27.21	72.76± 20.67	1 min after	
	66.18± 17.38	67.83± 11.43	65.53± 14.76	5 min after	
	60.55± 15.90	68.06± 13.80	64.60± 14.55	10 min after	
	62.29± 15.66	70.66± 10.95	67.30± 10.24	15 min after	
0.997	91.28±14.42	87.63± 11.01	93.28± 10.54	1 hour before	MAP
	97.92±22.92	100.80± 20.05	98.75± 20.37	Before induction	
	83.10±21.77	81.20± 15.98	81.75± 22.47	After induction	
	101.82±33.50	88.50± 18.81	90.10± 30.62	During	
	89.17± 26.84	89.30± 21.07	88.00± 24.34	1 min after	
	79.67± 18.26	84.50± 12.60	80.28± 17.74	5 min after	
	76.75±16.01	83.86± 13.57	83.50± 13.40	10 min after	
	75.78±17.57	80.80±16.60	79.07±15.46	15 min after	
0.036	75.51±9.77	73.82±6.59	78.89± 10.23	1 hour before	HR
	87.07±15.95	79.75±10.15	79.65±12.20	Before induction	
	86.96±15.21	81.10±81.96	83.96±13.39	After induction	
	93.70±19.16	86.75±08.97	86.58±11.44	During	
	89.22±12.92	81.20±09.83	84.86±10.79	1 min after	
	87.29±10.58	82.62±09.82	85.03±15.35	5 min after	
	86.85±15.49	81.72±09.26	79.62±13.22	10 min after	
	88.59±17.63	79.72±10.82	78.65±13.59	15 min after	

Table.2: prevalence of diabetes mellitus and hypertension between three groups.

p.value	prevalence	groups	variables
0.495	36.7%	A	DM
	26.7%	B	
	23.3%	C	
0.557	46.7%	A	HTN
	36.7%	B	
	50%	C	

Table.3: side effects between three groups.

p.value	groups			Side effects
	C	B	A	
0.227	0%	6.7%	10%	headache
0.585	46.7%	53.3%	60%	drowsiness
0.349	73.3%	26.7%	36.7%	xerosthemia

SU CHOI et al compared the effect of thoracic epidurally injected 3 µg/kg clonidine with 2 µg/kg fentanyl and 1 mg/kg lidocaine on cardiovascular responses to intubation. they showed that hemodynamic responses to intubation in clonidine and fentanyl group was reduced and it was more significant in clonidine group, so clonidine injected via a thoracic epidural route may be an effective and specific means of reducing the cardiovascular response to laryngoscopy and intubation.(9) In our study only heart rate was reduced in clonidine and thizanidine group and similar to this study it was more significant in clonidine group.

Sameenakousar et al compared the effect of IV clonidine 2µg/kg with IV fentanyl 2 µg/kg and

placebo 5 mins before the laryngoscopy on cardiovascular responses to intubation. they showed that hemodynamic responses to intubation in clonidine and fentanyl group was attenuated more than placebo group and it was more significant about clonidine. Their study showed that clonidine was superior to fentanyl in the attenuation of the pressor response.(10)

Seyed Mojtaba Marashi et al compared the effect of clonidine and gabapentin premedication in modifying the hyperdynamic response following laryngoscopy and tracheal intubation. They showed that both clonidine and gabapentin have effective role in blunting hyperdynamic responses after laryngoscopy, more so with gabapentin.(1)

Nand Kishore Kalra et al compared the effect of clonidine 1 µg/kg and magnesium sulfate 50 mg/kg on hemodynamic responses during laparoscopic cholecystectomy. They showed that administration of magnesium sulfate or clonidine attenuates hemodynamic response (specially systolic blood pressure) after laparoscopic cholecystectomy. Although magnesium sulfate 50 mg/kg produces hemodynamic stability comparable to clonidine 1 µg/kg and blunts the hemodynamic response after laparoscopic cholecystectomy more effectively.(11)

In another study Kumkum Gupta et al compared the effect of clonidine 200 µg and pregabalin 150 mg on hemodynamic responses during laparoscopic cholecystectomy. They showed that both clonidine and pregabalin attenuate hemodynamic response after laparoscopic cholecystectomy.(12)

Timo J. et al compared the sedative and sympatholytic effects of 3 different doses of tizanidine (4,8, and 12 mg) and clonidine 150 µg. Their results indicate that the effects of a single 12-mg oral dose of thizanidine resemble those of 150 µg oral clonidine, but are of shorter duration. Thizanidine may thus be a useful alternative to clonidine as an orally active, short-acting alpha adrenoceptor agonist in the perioperative period.(13)

Masoomeh Tabari et al evaluates the effects of 4 mg oral Thizanidine on hemodynamic responses during operations. They showed that using oral Thizanidine as a premedication, yielded stability in blood pressure and heart rate during surgery and decreased required Propofol. Considering its short duration of action, Thizanidine use as a premedication is recommended for sedation and stabilization of hemodynamic responses during the operations. (14)

According to the recent study as in clonidine and thizanidine 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 three groups, thizanidine and clonidine (specially clonidine) could be recommended as useful drugs for premedication in general anesthesia in patients undergoing CABG surgery.

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