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Original Article

Role of Lorazepam Premedication on Peroperative Hemodynamic Stability in Hypertensive Patients Undergoing Upper Abdominal Surgery

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Abstract:

Background: Hemodynamic stability during surgical anaesthesia in various surgeries have become a great concern. During operative procedure, patient with or without preexisting hypertension are at risk of development of peroperative hemodynamic instability. Surgical stress response induced by anxiety, surgical stimulation, pain can adversely affect the peroperative hemodynamic parameters, particularly in hypertensive patients.

Objectives: To assess the role of lorazepam premedication on hemodynamic stability during peroperative period in patients with hypertension undergoing upper abdominal surgery.

Materials & Methods: This was a prospective, observational study, carried among 46 hypertensive patients controlled by single anti-hypertensive drug who were scheduled for different upper abdominal surgeries at Bangabandhu Sheikh Mujib Medical University, Dhaka from January 2017 to June 2017. Patients were divided into two groups of twenty three patients each where Group I-received placebo tablet and Group II received lorazepam (1 mg). Hemodynamic parameters heart rate, systolic and diastolic blood pressure, ECG and peripheral capillary oxygen saturation (SpO2) were recorded just after intubation and 10 minutes interval during operative procedure.

Results: Among 23 patients of Group I, mean age was 41.78 ± 7.6 years and duration of surgery was 85.09 ± 19.91 minutes, while in Gropu II mean age was 42.02 ± 6.7 years and duration of surgery was 84.35 ± 17.04 minutes. Baseline values of heart rate, systolic blood pressure and diastolic blood pressure of two groups were not statistically significant. All these parameters were changed in both groups immediately after intubation and 10, 20, 30, 40, 50 and 60 minutes of peroperative period. And these difference of changes of hemodynamic parameters of two groups were found statistically significant. Regarding ECG tracing and peripheral capillary oxygen saturation (SpO2), no significant changes was found in either group.

Conclusion: Lorazepam significantly attenuetes hemodynamic changes in controlled hypertensive patients undegoing upper abdominal surgery.

Keywords: Lorazepam, hemodynamic stability, surgical strees response, preanesthetic medication, upper abdominal surgery

Introduction:

Hypertension is a common comorbidity in surgical patients. During induction of anesthesia patients with or without preexisting hypertension are likely to develop hemodynamic instability.[1] Studies show that hypertensive patients with a good control are still at risk of rise in blood pressure in preoperative period as they are tend to be more hemodynamically unstable during general anesthesia than normotensive subjects,[2,3,4] and that can lead to myocardial ischemia, ventricular arrhythmia, left ventricular failure, and cerebral hemorrhage.[5] Surgical stress response is associated with hemodynamic instability. Afferent noxious stimuli from surgical site stimulate sympathetic nervous system resulting in adrenergic response, then sudden increase in circulating catecholamines lead to hemodynamic instability.[6,7] Long duration of surgical procedure in certain abdominal surgeries as well as excessive blood loss can adversely affect the intraoperative hemodynamic parameters.[8]

To attenuate hemodynamic instability, a wide variety of agents are being used both during premedication and induction. Researchers have tried benzodiazepines, beta blockers, alpha 2 agonists, magnesium sulphate, opioids, and vasodilators during premedication to negotiate the hemodynamic variations.[9,10,11,12,13,14] Among the above premedication drugs, benzodiazepines has been proven to be satisfactory in alleviating the undesirable effects during the perioperative period.[15] Lorazepam, an intermediate acting benzodiazepine, rapid onset of action and relatively long half-life (10-20 hours), well absorbed orally, available in oral or parenteral routes, depress all levels of the CNS, including limbic and reticular formation.[16] Cost of lorazepam is quite feasible.[17] Some researchers considered lorazepam as a better option than diazepam or other benzodiazepines as premedication due to better efficacy as sedative-anxiolytic and unique property of antereograde amnesia with no adverse hemodynamic effects.[18,19] So current study was done to investigate the role lorazepam oral premedication for maintenance of hemodynamic stability in hypertensive patients undergoing upper abdominal surgery under general anesthesia.

Materials & Methods:

This was a Prospective Observational study, conducted in a tertiary level hospital of Dhaka city from January 20117 to June 2017.

Procedure:

This study was carried out with hypertensive patients controlled by single anti-hypertensive drug who undergo upper abdominal surgery under general anesthesia in Bangabandhu Sheikh Mujib Medical University, Dhaka according to inclusion and exclusion criteria. During pre-anesthetic assessment, every patient uderwent thorogh physical examination with ASA classifications. Total anaesthetic procedure was explained and informed consent was taken from the participants of the study.

Age eligibility for study: 19-65 years old

Genders eligibility for study: Both male and female

Screening method: The preliminary screening panel for each patient was included the complete history, physical examination and the necessary laboratory tests.

Inclusion criteria:

1. Controlled hypertensive patients undergoing elective abdominal surgery
2. Hypertension is controlled by single drug (monotherapy)
3. Duration of surgery: 75 minutes to 90 minutes
4. ASA class II
5. Patients agree to participate in the study signing an informed written consent

Exclusion criteria:

1. Emergency abdominal surgery
2. Uncontrolled systemic hypertension
3. Controlled hypertension by combined therapy
4. Hypotension (SBP< 90 mm of Hg)
5. Patient getting any benzodiazepine group of drug
6. H/O cardiac disease e.g. ischemic, valvular heart disease or 2nd or 3rd degree heart block (evaluated by history, physical examination and ECG), DM, CKD, CLD, COPD, bronchial asthma (evaluated by history, physical examination and laboratory investigation)
7. Pregnant women
8. Difficult intubation
9. ASA class III and IV
10. H/O benzodiazepine allergy

Forty six (46) patients, scheduled for upper abdominal surgery were included in this study. They were divided into two groups (Group I-received placebo tablet and Group II received lorazepam 1 mg) of twenty three patients each.

For induction, patients from the both groups received fentanyl (1.5 mcg/ kg), propofol (1.5 mg/ kg) intravenously. Suxamethonium (2 mg/ kg) was given for muscle relaxation and intubation in both groups. Immediately after intubation, the patients were mechanically ventilated using circle system with an oxygen and nitrous oxide (33:66) to keep EtCO2 within 30-35 mm Hg. For muscle relaxation, vecuronium bolus 0.1 mg/ kg was given followed by intermittent dose of 0.03 mg/ kg 20 minutes intervals. Halothane 0.5 MAC, along with nitrous oxide and oxygen 66/ 33, were administered for maintenance of anesthesia. At the end of the surgery, neuromuscular blocking effects of vecuronium was reversed by administering neostigmine (0.04 mg/ kg) and atropine (0.02 mg/ kg), extubation was done and patient was transferred to post-operative care unit.

Heart rate, systolic blood pressure, diastolic blood pressure, ECG and peripheral capillary oxygen saturation (SpO2) were recorded just after intubation and 10 minutes interval during operative procedure. Any adverse effects like bradycardia, tachycardia, hypotension and hypertension (20% of preoperative level respectively on two consecutive recordings) was managed conventionally.

Statistical analysis:
Data was compiled, presented and appropriate statistical test was done in this study for drawing an appropriate conclusion. All results are expressed as mean±SD. Data were analyzed by students unpaired't' test and considered significant if $p<0.05$.

Observation and Results:
Comparison of mean age, gender and duration of surgery are presented in Table 1, and there were no significant difference between two groups.

Table-I: Demographic characteristics and duration of surgery in study group

Variable	Group I	Group II	P-value
Age (years)	41.78 ± 7.6	42.02 ± 6.7	0.91
Gender (M:F)	11:12	13:10	
Duration of surgery (min)	85.09 ± 19.94	84.35 ± 17.04	0.893

Baseline values of heart rate of two groups were not statistically significant. Heart rate was increased in Group I immediately after intubation and 10, 20, 30, 40, 50 and 60 minutes of peroperative period in comparison to Group II. And all these differences were statistically significant.

Table-II: Changes in heart rate (bpm)

Groups	Baseline	Heart rate at time after intubations						
		0 min	10 min	20 min	30 min	40 min	50 min	60 min
Group I	73±10	103±8	101±8	98±7	88±6	83±6	81±5	79±7
Group II	74±7	86±6	84±7	80±6	76±5	73±6	68±8	66±6
P value	0.697	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Values are expressed as mean ± SD. P value expressed as significant if p< 0.05 (CI-95%)

Baseline values of systolic and diastolic blood pressure of two groups were similar. Raise in blood pressure was observed in Group I immediately after intubation and 10, 20, 30, 40, 50 and 60 minutes of peroperative period when compared with Group II. And the differences were statistically significant (Table III & Table IV).

Table-III: Changes in systolic blood pressure (mmHg)

Groups	Baseline	Systolic blood pressure at time after intubations						
		0 min	10 min	20 min	30 min	40 min	50 min	60 min
Group I	117±6	134±8	125±7	122±7	122±5	120±3	120±3	126±7
Group II	116±6	118±6	113±7	113±8	114±9	112±7	113±7	110±5
P value	0.75	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Values are expressed as mean ± SD. P value expressed as significant if p< 0.05 (CI-95%)

Table-IV: Changes in diastolic blood pressure (mmHg)

Groups	Baseline	Diastolic blood pressure at time after intubations						
		0 min	10 min	20 min	30 min	40 min	50 min	60 min
Group I	79±7	109±6	104±5	103±7	98±5	95±4	95±7	91±6
Group II	81±8	87±7	85±3	84±8	83±6	83±7	82±7	82±8
P value	0.37	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Values are expressed as mean ± SD. P value expressed as significant if p< 0.05 (CI-95%)

There was no significant change in ST segment and no arrhythmia was found from ECG tracing in any patient of both group. And there was no change of peripheral capillary oxygen saturation (SpO2) in any patient of both group.

Discussion:
Hemodynamic instability of hypertensive patients during surgical anaesthesia is a complex issue to address. Several pharmacological techniques were introduced and evaluated to counteract this problem but result is still controversial. Current study was conducted to evaluate the effect of single dose lorazepam as preanesthetic medication to prevent or counteract hemodynamic instability in hypertensive patients undergoing upper abdominal surgery.

Variation in different hemodynamic parameters occurs during induction of anesthesia and intubation of patient.[20] Laryngoscopy and endotracheal intubation both are potent stressful stimuli that provoke hemodynamic response.[21] Surgical stress response has been linked with adverse perioperative cardiac outcomes. The magnitude of response is related to intensity of surgical stimulus, can be amplified by other factors, including psychological stress, hypothermia, circulatory depression. Surgical procedures elicit sympathetic nervous system response, which can increase myocardial oxygen demand by increasing heart rate and arterial blood pressure. Activation of sympathetic nervous system may also cause coronary artery vasoconstriction, which in turn predispose to myocardial ischemia. So, from the beginning of surgery, there is a casecade of stress hormones that leads to hemodynamic instability. In patients with pre-existing cardiac disease, a decreased stress response might be helpful to attenuate the incidence of peroperative ischemia, and reduced mortality and morbidity.[22,23]

Lorazepam is a benzodiazepine with anxiolytic have little or no sedative and hypnotic properties, no hangover effect, with early onset of effects and relatively long half-life; by increasing the action of gamma-aminobutyric acid (GABA). It is completely absorbed from GIT and peak plasma concentration is achieved within 2 hours. 85-93% of drug is bound to plama protein with a free unbound fraction of 8-12%. The plasma half life of lorazepam is about 15 hours. It is conjugated in liver to the pharmacologically inactive glucoronide, which is then excreted in urine. No dosage adjustment is needed in patient with mild to moderate hepatic and renal impairment.[24, 25]

The present study, evaluated the effect of single dose oral lorazepam premedication for attenuation of

hemodynamic stress response in upper abdominal surgery. As the mean difference of all baseline haemodynamic parameters were statistically insignificant ($p>0.05$) in unpaired t-test, the significant attenuation of hemodynamic pressor response was observed in Group II. And, there was no significant change in ST segment and no arrhythmia was found from ECG tracing in any patient of both groups. In this study, 1 mg orally administered lorazepam had sedated the patients preoperatively and attenuated the hemodynamic pressor response effectively in peroperative period. Several mechanisms may contribute to attenuate hemodynamic changes. Preoperative anxiety deleteriously affect hemodynamic stability.[26] That's why sedative drugs are used as preanesthetic medication to reduce the apprehension experienced. Lorazepam posses several properties like anxiolysis, sedation and appeared to be a better option than diazepam as anxiolytic sedative night before operation.[19] Benzodiazepines attenuate the cortisol response, helps the patient to be less anxious and provides sedation and amnesia for surgery. The increase in hemodynamic values in the Group I may be due to inadequate sedation and surgical stress response.[27,28] Our findings correspond with result of several previous studies where role of lorazepam in maintainance of hemodynamic stability was investigated.[29,30,31]

Conclusions:

Patients with preexisting hypertension are at risk of development of peroperative hemodynamic instability when undergo general anesthesia which has a deleterious effect on patients health during postoperative period. Current research found effectiveness of lorazepam premedication to attenuate hemodynamic stability in hypertensive patients controlled by monotherapy when they were scheduled for elective upper abdominal surgery. Large scale studies are needed to compare the efficacy and safety of lorazepam with other benzodiazepines in terms of peroperative hemodynamic stability.

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