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Original Research Article

INCIDENCE OF HYPOTENSION DURING ANAESTHETIC INDUCTION IN HYPERTENSIVE PATIENTS TREATED WITH BETA BLOCKERS ALONE OR A COMBINATION OF BETA BLOCKERS AND CALCIUM CHANNEL BLOCKERS UNDERGOING ELECTIVE ORTHOPAEDIC AND GENERAL SURGERIES

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Abstract

Introduction: The response to anesthetic induction and airway manipulation in the presence of cardiovascular disease and antihypertensive therapy has not been adequately investigated.

Objectives: To study the incidence of hypotension during induction of anaesthesia in 60 hypertensive ASA II patients in the age group of 30-65 years on beta blockers (BB) alone or combination of beta blockers and calcium channel blockers (BB+CCB) until the morning of surgery, undergoing elective orthopaedic and general surgeries. To study and compare the hemodynamic effects of induction of anaesthesia in hypertensive patients on beta blockers alone or combination of beta blockers and calcium channel blockers.

Methods: This was a hospital-based prospective observational study for a duration of one year at the Department of Anesthesiology, Government Medical College, and Thiruvananthapuram. 60 hypertensive ASA II patients between 30 and 65 years of age receiving beta blockers or a combination of beta blockers and calcium channel blockers, of either sexes, who were willing to be a part of the study and met the inclusion criteria.

Results: There was a significant statistical difference between the two groups. 1 patient in the BB group and all 30 patients in the BB+CCB group developed hypotension, with an incidence of 6.67% and 100%, respectively (p value <0.001). There were 2 cases of bradycardia in both groups, which were not statistically significant.

Conclusion: Hypotension requiring treatment in patients receiving a combination of beta blockers alone group 1 (BB), or combination of beta blockers and calcium channel blockers alone group2 (BB+CCB).

Keywords: Anaesthetic Induction, Beta Blockers (BB) and Calcium Channel Blockers (CCB), Cardiovascular, Hypertension, Haemodynamic Changes, and Stress Responses Intubation

Introduction

Hypertension is defined as a persistent elevation of blood pressure of more than or equal to 140/90 mmHg. 1 Gupta et al. reported hypertension in Jaipur in 30% of men and 33% of women aged 20 years. The same group reported an incidence of hypertension in 44% of men and 45% of women in Mumbai. Joseph et al. reported it in 31% of men and 41% of women in Trivandrum. 4 Mohan et al. reported an age-adjusted prevalence of 14% in Chennai. And reported hypertension in 34.1% of middle-class executives in Mumbai, but after multiple

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BP measurements, it was confirmed in 26.8% of male and 27.6% of female officers. 7 Extrapolating the statistics from the general population, we can reasonably come to the conclusion that at least 20% of patients undergoing elective surgery are hypertensive. A sizable number of hypertensives are on beta-blockers or calcium channel blockers. There are a lot of studies that show the effects of beta blockers (BB) and calcium channel blockers (CCB) on various stages of general anesthesia. But studies regarding the effects of general anesthesia on patients taking beta blockers (BB) or calcium channel blockers (CCB) are sparse.

Methodology

Study Design: It was a prospective, observational study.

Study Setting: Department of Anesthesiology, Government Medical College, Thiruvananthapuram

Study Duration: One Year

Study population: 60 hypertensive ASA II patients between 30 and 65 years of age receiving beta blockers or a combination of beta blockers (BB) and calcium channel blockers (CCB) of either sexe.

Selection Criteria

Inclusion criteria:

- Hypertensive patients on beta blockers or a combination of beta blockers and calcium channel blockers, whose blood pressure is under control for at least 2 weeks
- ASA II
- 30-65 years
- Scheduled for elective surgery
- requiring tracheal intubation

Exclusion criteria:

- Hypertensive patients on antihypertensive other than beta blockers or calcium channel blockers
- Patients with uncontrolled hypertension
- Patients with pre-existing arrhythmias
- Patients with a left ventricular ejection fraction less than 30%
- Patients with a History of Congestive Cardiac Failure
- Patients with recent myocardial infarction (less than six months)
- Patients with symptomatic valvular heart disease
- Patients with a History of Asthma
- Obesity (body mass index (BMI) > 35)
- Patients with an anticipated difficult intubation
- Patients with chronic renal failure
- Patients with a History of Gastroesophageal Reflux
- Patients with the Presence of a Cardiac Pacemaker

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Sample size:

In the parent study analysis, 15% of patients on beta blockers and 55% of patients in the non-beta blocker group had one or more episodes of hypotension. So applying the formula

$$\text{Sample size } N = \frac{(Z_{\alpha/2}+Z_{1-\beta})^2\{P_1(100-P_1)+P_2(100-P_2)\}}{(P_1-P_2)^2}$$

P1 = 15% and P2= 55%

α = 0.05 and β=0.2

$$N = \frac{7.9\{(15X85)+(55X45)\}}{(40)^2}$$

N = 19 → 30

The calculated sample size required for the present study was obtained as 19 patients per group, which was approximately 30 per group.

Sampling technique: consecutive sampling was used for the study.

Study procedure: Patients are divided into two equal groups (30 each) on the basis of their treatment either with beta blockers alone group 1 (BB), or combination of beta blockers and calcium channel blockers alone group2 (BB+CCB). Antihypertensive drugs are to be continued up till the morning of surgery. Patients are pre medicated intravenous with Midazolam 1mg, Glycopyrrolate 0.2mg, Ondansetron 4mg & Morphine 3mg 15 minutes before induction. Baseline non-invasive blood pressure and heart rate are being monitored 3 minutes before induction of anaesthesia. Arterial oxygen saturation, non-invasive blood pressure and mean arterial pressure are to be recorded. Following pre-oxygenation, an initial dose of intravenous Thiopentone Sodium (4 mg/kg) is then administered over a period of 1 minute. Neuromuscular block is being provided with Succinyl choline at 2 mg/kg with precurarisation using a Vecuronium 0.5mg bolus intravenously before laryngoscopy and intubation. Laryngoscopy is accomplished within 15 seconds. Anaesthesia was maintained with an isoflurane concentration of 0.6% and an oxygen/nitrous oxide ratio of 50:50. Two anesthesiologists are involved in managing the cases. A third anesthesiologist who records the data and is unaware of the study groups to reduce bias. Non-invasive blood pressure and heart rate are recorded immediately before induction of anaesthesia and then every minute for three minutes following induction. Measurements are taken immediately after laryngoscopy and intubation and then every minute for 5 minutes. Hypotension is defined as systolic blood pressure less than 20% of baseline mean arterial blood pressure and bradycardia less than 50 beats per minute. Atropine (0.6 mg) is administered as an intravenous bolus if both hypotension and bradycardia are present. An intravenous mephentramine 6-mg bolus is administered if only hypotension is present. For heart rates less than 50 beats per minute, an atropine 0.6-mg intravenous bolus is used.

Ethical Considerations

Institutional ethical committee clearance was obtained (IEC No. 02/18/2017/MCT). Informed written consent was obtained from the participants.

Statistical Analysis

Data was entered in MS Excel and analysed using SPSS version 24. Descriptive statistics like mean and standard deviation were used for continuous variables and frequency and percentages for categorical variables. Inferential statistical tools like the Chi-square test,

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Fisher's exact test, and Repeated Measures Analysis of Variance (RM-ANOVA) were used, and a p value of less than 0.05 was considered significant.

Results

Both the BB and CCB+BB groups had 30 participants each. All of them belonged to the ASAII category. The minimum age in the beta blocker group is 35 years, whereas in the CCB+BB group it is 34 years. The maximum ages in the groups are 63 and 64 years, respectively. The mean age in the BB group is 49.53, whereas in the CCB+BB group it is 48.97, with a standard deviation of 8.32 and 8.97, respectively. The frequency and percentage of hypertensives on BB in the thirties are 6 and 20%; in the forties, 11 and 36.7%; in the fifties, 9 and 30%; and above 60, 4 and 13%, respectively. The frequency and percentage of hypertensives on CCB+BB in the thirties are 7 and 23%, in the forties, 9 and 30%, in the fifties, 11 and 36.7%, and above 60, 3 and 10%, respectively. 60% of the BB group were males (frequency = 18), whereas in the CCB+BB group, 36.7% (frequency = 11) were males (Table 1).

Table 1: Age Group and Sex Distribution

Group	Age Group	Frequency	Percent	Sex	Frequency	Percent
BB	30-39	6	20.0	Male	18	60.0
	40-49	11	36.7			
	50-59	9	30.0	Female	12	40.0
	60-65	4	13.3			
	TOTAL	30	100.0	Total	30	100
CCB + BB	30-39	7	23.3	Male	11	36.7
	40-49	9	30.0			
	50-59	11	36.7	Female	19	63.3
	61-65	3	10.0			
	Total	30	100.0	Total	30	100.0

In the BB group 56.7% were hypertensive for less than 5 years, 33.3% between 6 and 10 years and 10% more than 10years. In case of CCB+BB group the percentages are 56.7% less than 5 years and the rest in between 5 and 10years. (Table 2)

Table 2: Duration of Hypertension

Group		Frequency	Percent
BB	< 5 years	17	56.7
	6 -10years	10	33.3
	> 10 years	3	10.0
	Total	30	100.0
CCB + BB	< 5 years	17	56.7
	6 -10years	13	43.3
	Total	30	100.0

In the BB group 10 patients were on 25mg (33.3%), 18 patients were on 50mg (60%) and 2 patients were on 100mg of atenolol (6.7%). Table 3 shows the frequency and percentage of drugs i.e. atenolol, metoprolol and amlodipine used in the CCB and BB group. (Table 3)

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Table 3: Antihypertensive Drugs used IN BB and CCB + BB Groups			
Group		**Frequency**	**Percent**
BB	Atenolol 25	10	33.3
	Atenolol 50	18	60.0
	Atenolol100	2	6.7
	Total	**30**	**100.0**
CCB + BB	Amlodipine 5 + Atenolol 25	15	50.0
	Amlodipine 5 + Atenolol 50	5	16.7
	Amlodipine 10 + Atenolol 50	6	20.0
	Amlodipine5 + Metoprolol 25	2	6.7
	Amlodipine5 + Metoprolol 50	2	6.7
	Total	**30**	**100.0**

Comparison of baseline parameters as shown in table 4 shows that all baseline parameters with an exception of MAP and SpO2 are not comparable as they show a p value less than 0.05 using student's t-test for independent means. (Table 4)

Table 4: Comparison of Baseline Parameters				
	Group	**Mean**	**Std. Deviation**	**P Value**
Baseline PR	BB	74.13	8.91	0.031*
	CCB + BB	70.33	2.43	
Baseline SBP	BB	133.70	7.07	0.001*
	CCB + BB	138.53	2.52	
Baseline DBP	BB	82.67	4.79	0.008*
	CCB + BB	79.97	2.33	
Baseline PP	BB	51.17	3.62	<0.001*
	CCB + BB	57.90	4.32	
Baseline MAP	BB	99.73	5.36	0.795
	CCB + BB	99.47	1.53	
Baseline SPO2	BB	99.43	0.50	0.820
	CCB + BB	99.40	0.62	

**indicates significant statistical difference at P<0.05*

Comparison of Pulse, SBP, DBP, PP, MAP and SpO2 at different points of time revealed that with an exception of SpO2 all other parameters showed a statistically significant difference between the 2 groups when compared at different time points (p<0.001, using Repeated Measures ANOVA with time as within factor and group as between factor. (Table 5, 6, 7)

Table 5: Comparison of Pulse and SPO2 at Different Time Points							
		Pulse Rate		**P Value**	**SPO2**		**P Value**
	Group	**Mean**	**Std. Deviation**		**Mean**	**Std. Deviation**	
Baseline	BB	74.13	8.91	0.028	99.43	0.50	0.837
	CCB+BB	70.33	2.43		99.40	0.62	

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Preinduction1 min	BB	70.07	8.53	0.833	99.43	0.50	0.837
	BB+CCB	69.73	2.23		99.40	0.62	
Preinduction2 min	BB	70.43	8.22	0.29	99.43	0.50	0.837
	BB+CCB	68.80	1.52		99.40	0.62	
Preinduction3 min	BB	71.37	8.61	0.317	99.43	0.50	0.837
	BB+CCB	69.73	2.23		99.40	0.62	
Induction	BB	76.93	10.23	0.001	99.43	0.50	0.837
	BB+CCB	70.20	2.62		99.40	0.62	
Induction 1 min	BB	74.40	7.44	<0.001	99.43	0.50	0.837
	BB+CCB	64.37	4.35		99.40	0.62	
Induction 2 min	BB	70.50	9.84	0.006	99.43	0.50	0.837
	BB+CCB	64.87	4.60		99.40	0.62	
Induction 3 Min	BB	74.23	8.33	<0.001	99.43	0.50	0.837
	BB+CCB	65.13	1.63		99.40	0.62	
Intubation	BB	79.27	9.20	<0.001	99.43	0.50	0.837
	BB+CCB	65.13	1.63		99.40	0.62	
Intubation 1min	BB	75.27	9.20	0.015	99.43	0.50	0.837
	BB+CCB	70.93	2.33		99.40	0.62	
Intubation 2 min	BB	72.53	8.42	<0.001	99.43	0.50	0.837
	BB+CCB	65.63	2.19		99.40	0.62	
Intubation 3 min	BB	69.40	5.44	<0.001	99.43	0.50	0.837
	BB+CCB	62.43	2.03		99.40	0.62	
Intubation 4 min	BB	68.13	4.88	<0.001	99.43	0.50	0.837
	BB+CCB	60.30	1.99		99.40	0.62	
Intubation 5 min	BB	67.17	6.40	<0.001	99.43	0.50	0.837
	BB+CCB	60.30	1.99		99.40	0.62	

Table 6: Comparison of SBP and DBP at Different Time Points

		SBP		P Value	DBP		P value
	Group	**Mean**	**Std. Deviation**		**Mean**	**Std. Deviation**	
Baseline	BB	133.70	7.07	0.001	82.67	4.79	0.008
	CCB+BB	138.53	2.52		79.97	2.33	
Preinduction 1 min	BB	137.77	7.86	<0.001	82.67	4.79	0.041
	BB+CCB	149.10	2.83		80.60	2.46	
Preinduction 2 min	BB	138.00	7.53	<0.001	82.67	4.79	0.284
	BB+CCB	148.90	3.21		81.60	2.49	
Preinduction 3 min	BB	138.00	7.53	<0.001	82.67	4.79	0.284
	BB+CCB	148.77	2.49		81.60	2.49	
Induction	BB	138.00	7.53	<0.001	82.67	4.79	0.484
	BB+CCB	148.70	2.34		81.97	2.57	
Induction 1 min	BB	126.40	11.92	<0.001	68.93	6.79	0.555
	BB+CCB	106.90	10.58		70.07	8.04	
Induction 2 min	BB	126.43	9.74	<0.001	67.67	6.93	0.328
	BB+CCB	103.17	7.12		66.07	5.55	
Induction 3 min	BB	128.23	7.00	<0.001	68.27	6.47	<0.001
	BB+CCB	101.27	2.61		61.30	3.51	

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Intubation	BB	128.23	7.00	<0.001	68.27	6.47	<0.001
	BB+CCB	101.27	2.61		61.30	3.51	
Intubation 1min	BB	142.87	6.76	<0.001	88.30	6.24	<0.001
	BB+CCB	132.37	3.66		80.97	4.07	
Intubation 2 min	BB	138.63	6.42	<0.001	82.23	6.72	<0.001
	BB+CCB	126.87	4.12		76.13	4.09	
Intubation 3 min	BB	135.03	6.63	<0.001	73.83	7.34	0.038
	BB+CCB	121.73	4.70		70.57	3.95	
Intubation 4 min	BB	133.03	6.63	<0.001	69.10	7.60	0.003
	BB+CCB	117.53	5.15		64.23	3.29	
Intubation 5 min	BB	130.70	6.80	<0.001	66.73	7.47	0.101
	BB+CCB	117.53	5.15		64.23	3.29	

Table 7:Comparison of Pulse Pressure and MAP at Different Time Points

		Pulse Pressure		P Value	MAP		P Value
	Group	**MEAN**	**Std. Deviation**		**Mean**	**Std. Deviation**	
Baseline	BB	51.17	3.62	<0.001	99.73	5.36	0.8
	CCB+BB	57.90	4.32		99.47	1.53	
Preinduction 1 min	BB	55.33	4.07	<0.001	101.10	5.70	0.037
	BB+CCB	68.50	3.94		103.47	1.83	
Preinduction 2 min	BB	55.33	4.07	<0.001	101.13	5.50	0.011
	BB+CCB	66.97	4.80		103.97	1.77	
Preinduction 3 min	BB	55.33	4.07	<0.001	101.13	5.50	0.01
	BB+CCB	66.57	4.17		104.03	1.83	
Induction	BB	55.47	3.74	<0.001	101.13	5.50	0.006
	BB+CCB	66.90	3.29		104.23	1.89	
Induction 1 min	BB	57.47	7.83	<0.001	88.13	8.08	0.01
	BB+CCB	36.23	4.72		82.37	8.73	
Induction 2 min	BB	58.77	5.71	<0.001	87.27	7.43	<0.001
	BB+CCB	37.10	4.39		78.43	5.77	
Induction 3 min	BB	59.97	4.38	<0.001	88.27	6.27	<0.001
	BB+CCB	40.07	5.09		74.67	2.17	
Intubation	BB	59.97	4.38	<0.001	88.27	6.27	<0.001
	BB+CCB	40.07	5.09		74.67	2.17	
Intubation 1min	BB	54.63	4.57	0.031	106.60	6.07	<0.001
	BB+CCB	51.40	6.55		98.10	2.52	
Intubation 2 min	BB	56.73	5.09	<0.001	101.07	6.13	<0.001
	BB+CCB	50.73	6.70		93.07	2.66	
Intubation 3 min	BB	61.20	4.95	<0.001	94.27	6.73	<0.001
	BB+CCB	51.17	7.08		87.63	2.57	
Intubation 4 min	BB	63.93	5.33	<0.001	90.43	6.68	<0.001
	BB+CCB	52.97	7.08		82.00	2.38	
Intubation 5 min	BB	63.90	5.05	<0.001	88.07	6.90	<0.001
	BB+CCB	52.97	7.08		82.00	2.38	

Discussion

A decrease in systemic arterial pressure follows the induction of anesthesia with either propofol or thiopentone when used in combination with fentanyl and muscle relaxants. [8] There are not many studies conducted on the response to induction of anesthesia, and the majority of studies on the topic have concentrated on the effects of different induction agents

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in ASA-1 patients.[9,10]. Intraoperative hypotension occurring in patients with ischemic heart disease can be deleterious because myocardial blood flow to regions supplied by narrowed coronary arteries is pressure dependent. [11] Whether intra-operative hypotension is a risk factor for postoperative myocardial infarction is still controversial. [12] Some studies have demonstrated that intra-operative hypotension increases the risk of post-operative cardiac and renal complications in high-risk populations. [13]. Blood pressure (BP) and heart rate (HR) increase after tracheal intubation, which has been extensively studied. [14,15] These hemodynamic changes are of little concern in relatively healthy patients but can be detrimental in the high-risk population. [16,17]

In our study, the heart rate showed a rise of 2 beats/min in the BB group versus no change in the BB + CCB group during induction when compared to baseline. Post tracheal intubation, the heart rate increased by 5 beats/min in the BB group and dropped by 5 beats/min in the BB + CCB group. There was no change in post-incision HR in the BB group and an increase of 3 beats per minute in the BB + CCB group. The SBP fell 2 minutes after induction in both groups (8 9.7 mm in BB vs. 36 7.1 mm of Hg in BB + CCB groups). The SBP increased by 9mm in the BB group, whereas in the BB+CCB group it actually dropped by 7 mmHg after laryngoscopy and intubation. Thereafter, SBP fell by 4 mm in the BB group and by 21mm in the BB+CCB group when compared to baseline at 5 minutes post intubation. The DBP in the BB group dropped from 82.5 mmHg to 69 mmHg at 2 min post induction, whereas in the BB+CCB group it dropped from 80 to 70 mmHg. The DBP then rose to 88 mmHg in the BB group, whereas in the BB+CCB group it rose to 81 mmHg. At 5 min post intubation, the DBP settled at 67 and 64 mmHg, respectively, in the BB and BB+CCB groups. During induction, the PP rose in the BB group from a mean of 51 mmHg to 57 mmHg, whereas in the BB+CCB group it fell from 58 to 36 mmHg. During intubation, the PPs in the BB and BB+CCB groups were 54 and 50 mmHg, respectively. At the time of incision, the PP in the BB group rose to 64 mmHg, but in the BB+CCB group it remained more or less at 53 mmHg. In the BB group, the MAP dropped from a baseline of 100 mmHg to 87 mmHg at 2 minutes post induction, then rose above the baseline to 106.6 mmHg 1 minute after intubation, only to settle at 88 mmHg at the time of incision. In the BB+CCB group, the baseline was similar to the BB group. The fall during induction was more profound, from 100 mmHg to 74.6 mmHg at 3 min post induction. After intubation, the MAP rose to 106.6 mmHg in the BB group, whereas in the BB+CCB group it rose to 98 mmHg. At the time of incision, the MAPs in the two groups were 88 and 82 mmHg, respectively. When hypotension was defined as a 20% drop in MAP from baseline, it was observed that 1 patient in the BB group and all 30 patients in the BB+CCB group developed hypotension, with an incidence of 6.67% and 100%, respectively. Using the Chi-Square test, this difference was significant (p value <0.001). When hypotension was defined as a 40% drop in MAP from baseline, it was observed that 1 patient in the BB group and all 3 patients in the BB+CCB group developed hypotension, with an incidence of 6.67% and 10%, respectively. Using Fischer's exact test, this difference was not significant (p value of 0.612). It was observed that 2 patients in the BB group and all 3 patients in the BB+CCB group developed hypotension, which required pressor support, with an incidence of 6.67% and 10%, respectively. No significant difference was noted (p = 0.999, using Fisher's exact test). It is important to note that although all patients in the BB+CCB group developed hypotension during induction, the hypotension didn't last long or the blood pressure didn't drop to dangerously low levels so as to warrant pharmacological intervention except in 3 cases. On the contrary, in the BB group, even though there were no episodes of hypotension statistically, there were two cases of hypotension serious enough to warrant intervention.

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A comparison of pulse, SBP, DBP, PP, MAP, and SpO2 at different points in time revealed that, with the exception of SpO2, all other parameters showed a statistically significant difference between the 2 groups when compared at different time points ($p<0.001$, using Repeated Measures ANOVA with time as a within factor and group as a between factor).

Conclusion

Antihypertensive therapy with a combination of beta blockers and calcium channel blockers can affect the hemodynamic responses at induction of anesthesia and expose patients to hypotension. The mean fall in SAP after induction exceeded 20% of baseline in all patients in the BB+CCB group during the post-induction period. The hemodynamic response to laryngoscopy, intubation, and incision was obtunded, but at the expense of pre-intubation low pressures, and the SAP again fell to less than 20% of the baseline 5 minutes post-laryngoscopy. There is a further need to quantify these changes associated with different antihypertensive drugs, both alone and in different combinations and induction techniques, and identify patients at risk of exaggerated responses so that timely, appropriate measures are taken.

Conflict of Interest: Nil

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