Research Article

A Study on Efficacy of Intravenous Labetalol in Hypertensive Urgency in Emergency Room

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ABSTRACT

Hypertensive urgency poses a serious risk if not treated effectively. This study was conducted to assess the efficacy on intravenous labetalol among patients with hypertensive urgency presenting to the Emergency room. A prospective observational study was conducted from October 2015 to March 2016, in the Emergency room of a tertiary care teaching hospital, among patients with hypertensive urgency i.e. BP greater than 180/120 mm Hg without target end-organ damage. Intravenous Labetalol 10mg, which is standard treatment protocol was administered. The BP and heart rate were recorded after 30 and 60 minutes. Efficacy was measured in percentage reduction of systolic BP in one hour. Frequency, percentage, mean, standard deviation and inter-quartile range were used to summarize descriptive statistics. Paired t test and Student's t test were applied to test significance of differences. Total 81 patients with mean age 58.14±15.22 years were included, of them more than two-third (67.9%) were males. The mean reduction in systolic blood pressure one hour after administration of labetalol was 41.04±19.83 mm Hg, which gives a mean percent reduction of 20.29±9%. There was significant reduction in BP and heart rate ($p<0.001$). No adverse reactions were noted in the patients. There was no significant difference in efficacy of labetalol between those aged above and below 60years. The study reports that intravenous labetalol is a safe and effective treatment for hypertensive urgency patients in an emergency room setting.

Keywords: Hypertensive urgency, Blood Pressure, Labetalol.

INTRODUCTION

Hypertensive crisis is defined as a rapid, inappropriate, symptomatic elevation in blood pressure, which is a common clinical occurrence that accounts for as many as 3% of all emergency department visits.[1,2]The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) divides hypertensive crisis into two categories: hypertensive emergency and hypertensive urgency.[3] Hypertensive emergency is characterized by a severe elevation in BP in conjunction with end- organ damage.[4]On the other hand, hypertensive urgencies are situations where the patient's elevated blood pressure ultimately poses a serious risk if it is not treated aggressively.[5,6] Hypertensive emergencies such as hypertension with acute heart failure and pulmonary edema also require initial blood pressure control with appropriate therapy and intensive care monitoring.

Labetalol is an adrenoreceptor blocking drug with combined α- and β-blocking properties. These result in a more favorable hemodynamic profile for labetalol compared with 'pure' β-blockers or 'pure' α-blockers in both hypertensive urgency and emergency. In this study the efficacy of intravenous labetalol was assessed among patients with hypertensive urgency presenting to the emergency room. Also, the effect of labetalol was compared between those aged above and below 60 years.

MATERIALS AND METHODS

Study design and setting

A prospective observational study was done in the Emergency department of Amrita Institute of Medical Science (AIMS), a tertiary care teaching hospital located in Kochi city in Southern India.

Study population

All patients presenting to the ER and diagnosed with 'hypertensive urgency' between the study period of October 2015 and March 2016 were included in the study. 'Hypertensive urgency' as per JNC 7 is defined as blood pressure greater than 180/120 mm Hg without target organ damage.[7] Pregnant women and patients who were less than 18 years of age were excluded from the study. Patients included in the study were given an intravenous bolus of Labetalol 10mg after ensuring that there was no contraindication for the same, which includes asthma, severe Chronic Obstructive Pulmonary Disease, decompensated Congestive Heart Failure, bradycardia and 2nd or 3rd degree heart block. Intravenous labetalol is the standard treatment protocol adopted in the Institute. Ethical committee of Amrita Institute of medical science granted permission for conducting the study.

Study variables

Initial recordings of Blood pressure (BP), heart rate and oxygen saturation were noted. A baseline ECG was also

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taken. Therapeutic target was to reduce the systolic blood pressure to utmost 25% of the initial recording. Repeat measurements of BP and heart rate were recorded 30minutes and 60minutes after the administration of the drug. Efficacy was measured as percent reduction in systolic blood pressure. Adverse effects of labetalol such as dizziness, light headedness, nausea, tingling sensation of scalp and fatigue were noted.

Statistical analysis

Data was entered in MS Excel and analyzed using IBM Statistical Package for Social Sciences version 20. Descriptive statistics were summarized as frequency, percentages, mean and standard deviation. Paired-t test was used to test the significance of difference and Student's t test was applied to test significance of differences between those aged above and below 60 years. P value of less than 0.05 was considered to be statistically significant.

RESULTS AND DISCUSSION

A total of 81 patients were included in the study. Mean age was 58.14±15.22 years and 67.9% were males. Baseline characteristics of the patients are given in table 1.

Table 1: Baseline Characteristics of the study population

Characteristic	Frequency (n)	Percentage (%)
Age (in years)		
21-40	11	13.6
41-60	32	39.5
61-80	35	43.2
>80	3	3.7
Gender		
Male	55	67.9
Female	26	32.1
Systolic BP (mm Hg)		
180 - 200	45	55.6
200 - 220	24	29.6
>220	12	14.8
Diastolic BP(mm Hg)		
120 - 130	53	65.4
130 - 140	21	25.9
>140	7	8.6
MAP(mm Hg)		
140 - 150	37	45.7
150 - 160	34	42.0
>160	10	12.3
Heart Rate (beats/minute)		
60 - 100	49	60.5
>100	32	39.5

Mean initial Systolic BP was 199.93±16.83 mm Hg, diastolic BP was 127.46±7.41 mm Hg, mean arterial pressure (MAP) was 151.61±8.32 mm Hg and heart rate was 96.11±14.20 beats per minute. The oxygen saturation and baseline ECG were normal for all patients. The effect of Labetalol on BP and heart rate is given in table 2. The mean reduction in Systolic BP one hour after administration of Labetalol was 41.04±19.83 mm Hg which gives a mean percent reduction of 20.29±9% (IQR 14.80-24.88). Labetalol showed a significant reduction in both systolic and diastolic BP. MAP reduced from 151.61±8.32 mm Hg to 121.39±11.38 mm Hg in one hour and this was statistically significant ($p<0.001$). Heart rate reduced from 96.11±14.20 to 85.78±14.61 and this drop in heart rate was also statistically significant ($p<0.001$). Distribution of patients by percentage reduction in systolic blood pressure is furnished in table 3. Time dependent mean systolic blood pressure response to labetalol is represented in figure 1. None of the patients reported any adverse effect from Labetalol.

For subgroup analysis, patients were divided into two groups as elderly i.e. aged above 60 years and those below 60 years. There were 38 elderly patients and 43 patients below 60 years. No statistically significant differences were found between the two groups in terms of BP and heart rate. This is given in table 4.

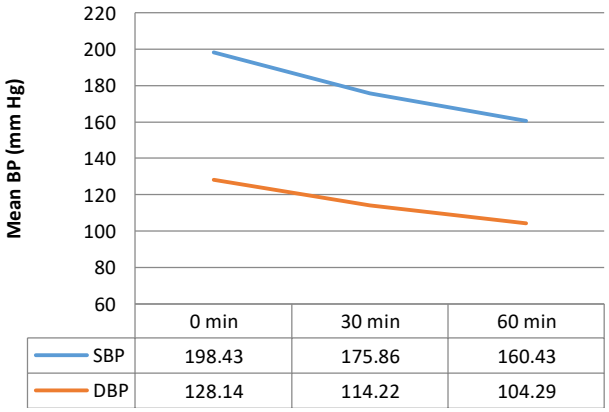

Figure 1: Time dependent response to Labetalol

The present study showed that the mean percent reduction in systolic BP one hour after administration of intravenous Labetalol was 20.29±9%. Goal is to reduce the blood pressure by no more than 25%(within minutes to 1 or 2 hours) as excessive reduction in blood pressure can precipitate coronary, cerebral, or renal ischemia and possibly infarction.[8] Also there was no statistically significant difference in the effect of labetalol among the elderly compared to others. A study conducted at Haukeland hospital in Norway, revealed that intravenous bolus injection of labetalol induced an immediate fall in blood pressure by around 22.4% in patients with severe hypertension.[9] Another study conducted by Goa et al showed that labetalol administered intravenously, as repeated bolus injections or slow intravenous infusion, rapidly lowered blood pressure within 5 to 30 minutes in 70% to 95% of patients.

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Table 2: Effect of Labetalol on BP and heart rate.

	0 min	60 min	Mean difference	95% CI	p value
Systolic BP	199.93±16.83	158.89±19.06	41.04±19.83	36.65 - 45.42	<0.001
Diastolic BP	127.46±7.41	102.64±12.01	24.82±10.95	22.39 - 27.24	<0.001
MAP	151.61±8.32	121.39±11.38	30.22±11.40	27.70 - 32.74	<0.001
Heart Rate	96.11±14.20	85.78±14.61	10.33±8.60	8.43 - 12.24	<0.001

Table 3: Distribution of patients by percent reduction in Systolic BP

Percentage reduction in SBP	Frequency (n)	Percent (%)
<15	20	24.7
16-25	37	45.7
>25	24	29.6

Table 4: Comparing the effect of Labetalol among those aged above and below 60 years

	Time	Mean ± Standard deviation (SD)		p value
		Below 60 (n=43)	Above 60 (n=38)	
Systolic BP (mm Hg)	0 min	198.43±15.86	201.54±17.87	0.547
	60 min	160.43±21.19	157.23±16.58	0.454
	Difference	38.00±19.60	44.31±19.80	0.154
Diastolic BP (mm Hg)	0 min	128.14±8.07	126.72±6.66	0.456
	60 min	104.29±12.47	100.87±11.38	0.197
	Difference	23.86±11.04	25.85±10.90	0.417
MAP (mm Hg)	0 min	151.57±8.78	151.66±7.90	0.963
	60 min	123.00±12.56	119.66±9.81	0.184
	Difference	28.57±11.67	32.00±10.97	0.177
Heart Rate	0 min	96.98±14.32	95.18±14.21	0.501
	60 min	86.45±14.23	85.05±15.18	0.669
	Difference	10.52±8.83	10.13±8.46	0.837

In the same study labetalol was also shown to be more effective than propranolol in Black patients, and lowered heart rate to a lesser extent than β-blocker. Elderly patients also responded well to labetalol.[10] In our study labetalol caused significant reduction in both systolic and diastolic BP. Similar finding was reported in a study by Huey et al but the same study reported an insignificant change in heart rate which was in contrast to our study finding of significant change in heart rate following administration of Labetalol. [11]

There are multiple options for the treatment of hypertensive urgency in emergency setting. Oral drugs that can be used in hypertensive urgency includes Nifedipine, Captopril, Clonidine, Furosemide, Prazosin, Nicardipine, and Lacidipine; Parenetral drugs include Labetalol, Hydralazine, Enalaprilat, Urapidil, Fenoldopam, Diazoxide and Nitroprusside.[12] Most of these drugs used in hypertensive urgency are hampered with serious side effects. Nitroprusside is a powerful vasodilator that requires constant surveillance as it can lead to a sudden drop in blood pressure.[12] Diazoxide, another parenteral anti-pressor agent also induces very rapid fall in blood pressure, but in addition can cause reflex tachycardia, cerebral vascular accidents and myocardial infarction owing to unwanted hypotension.[13-15] Reflex tachycardia is a frequent problem encountered during the use of hydralazine.[16]

Labetalol is an antihypertensive agent with a unique mode of action involving both alpha and beta-adrenoceptor blockade. The drug lowers BP partly by blocking the alpha-adrenoceptors in the peripheral arterioles and thereby lowering the peripheral vascular resistance. The resulting reflex increase in sympathetic drive to the heart is controlled by concurrent blockade of beta-adrenoceptors in the heart.[17] The hemodynamic effects of labetalol are therefore quite different from those of the pure beta-adrenoceptor- blocking drugs and the mechanism for lowering the BP could be generally considered more desirable. Labetalol is a fast-acting antihypertensive agent with an onset of action within 2–5 minutes when administered intravenously, and 15 to 30 minutes when given orally.[18,19] Labetalol can cause a moderate fall in heart rate in most patients.[18,19] In fact the hemodynamic changes induced by labetalol can be

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mimicked by the combination of Prazosin and Tomalol or by combining other vasodilator or alpha-adrenoceptor blockers with beta-receptor blocking drugs.[20, 21] The fall in cardiac output is less with labetalol compared to pure beta-receptor blockers and this makes labetalol less hazardous in cardiac failure.[22, 23]

CONCLUSION

The study shows that labetalol is a safe and effective antihypertensive agent in hypertensive urgency in an emergency room setting due to the reasons such as: 1) Prompt BP reduction to prevent hypertensive emergency, 2) No adverse consequences to acute therapy, 3) Acute medication loading results in improved short-term BP control and 4) It is pertinent to note that efficacy remains the same in different age group.

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