



Research Brief

A comparative study of intravenous labetalol VS intravenous nitroglycerin in the treatment of hypertensive crises

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ABSTRACT

Hypertensive crises is still a major public health problem, causing end organ damage like myocardial infarction, stroke, and renal failure. Labetalol and nitroglycerine are among the two most commonly used medicine to control the blood pressure, but there is no head to head comparison between these two medicines. This was a prospective randomized non-blinded study which included 50 patients of hypertensive crises, out which 25 patients received intravenous labetalol and 25 patients received intravenous nitroglycerine. We found that labetalol controlled the blood pressure more rapidly in comparison to nitroglycerine, without causing any extra side effect.

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1. Introduction

Hypertension (HTN) is one of the most common chronic medical conditions. The Eighth Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC-8) classifies 4 stages of high BP: normal, Elevated, Hypertension stage 1, and Hypertension stage 2. A systolic BP > 180 mm Hg or a diastolic BP > 120 mm Hg in a patient is considered as “hypertensive crisis.”¹

Hypertensive emergencies are characterized by severe elevation in blood pressure (>180/120 mm Hg) complicated by evidence of acute target organ dysfunction.² Hypertensive urgencies on the other hand are characterized by severe elevation in BP without evidence of progressive target organ dysfunction. Hypertensive crises constitute both hypertensive emergencies and urgencies.^{2,3} Hypertensive emergencies without proper management carry one-year mortality rate of as high as 79%, with proper treatment this mortality rate decreases to 25%.⁴

Intravenous labetalol and nitroglycerine are amongst the most commonly prescribed agents to control acute severe hypertension.¹ Despite these being amongst the most commonly prescribed drugs

in patients with hypertensive crisis, no head to head comparative study data are available to compare the safety and efficacy of these two drugs. This study was conducted to fill this gap of knowledge.

2. Method

It was a hospital based Randomized control parallel assignment comparative study without any blinding, carried out during the period of November 2018 to November 2019, after getting clearance of local ethical committee and informed consent from patient. Total 50 patients were enrolled, of either sex, age ≥18 years, systolic blood pressure (SBP) ≥180 mm Hg and/or diastolic blood pressure (DBP) ≥120 mm Hg with evidence of acute end organ damage, SBP ≥220 mm Hg and/or DBP ≥130 mm Hg without evidence of any acute end organ damage. Those patients who have chronic obstructive pulmonary disease (COPD), acute or chronic liver failure, sinus bradycardia or atrio-ventricular block, acute pulmonary edema, known allergy to study drug, pregnant & lactating mother, known case of pheochromocytoma or left ventricular ejection fraction <35% were excluded. The study population was randomized using Random Allocation Software (<https://random-allocation-software.software.informer.com/download/?caa49a>). Laboratory tests like complete blood count (CBC), blood urea nitrogen (BUN), serum creatinine, Blood Sugar, ECG, Cardiac Troponin, chest X-ray, NCCT HEAD/CE-MRI was done as per the requirement. After the drug

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Table-1
Baseline characteristics of patients.

Parameters	Randomization Group		p-Value
	NTG (n = 25)	Labetalol (n = 25)	
Sex	Male	15	1
	Female	10	
Age	53.88 ± 12.959	54.00 ± 12.629	0.974
Haemoglobin (gm. %)	11.28 ± 1.926	11.08 ± 1.730	0.701
TLC (Per Cc mm)	11791.20 ± 5116.275	12184.00 ± 5135.390	0.788
Platelets (Per Cc mm)	275760.00 ± 119456.157	288160.00 ± 99045.309	0.691
Blood Sugar (mg %)	137.60 ± 30.303	137.00 ± 33.563	0.947
BUN (mg %)	19.52 ± 8.889	18.68 ± 9.254	0.745
Serum Creatinine (mg %)	1.61 ± 0.883	1.52 ± 0.663	0.668
Diabetes	3(12%)	4(16%)	1.00
Hypertension	9(36%)	12(48%)	0.567
CAD	2(8%)	1(4%)	1.00
CVA	0	0	1.00

(TLC-total leukocyte count, BUN-blood urea nitrogen, NTG-nitroglycerine, CAD-coronary artery disease, CVA-cerebrovascular accident).

administration sequential recordings of the blood pressure were taken at different time interval. The final time to achieve the target blood pressure was noted. Treatment goal was to reduce the MAP (mean arterial pressure) by 25% from baseline.

Injection Labetalol 20 mg was given as stat dose, followed by incremental doses of 20–80 mg every 10 minute until the desired BP goal was achieved. Maximum dose of labetalol was 300 mg. **Nitroglycerine** was started as intravenous infusion, starting at a dose of 5 µg/min and dose was up titrated every 2–5 minute, up to a maximum of 200 µg/min. In case of failure of control of blood pressure with the maximal dose of the study drug, open-label use of other study drug as well as other drugs was allowed.

Primary Efficacy End-points was described as proportion of patients achieving treatment goals at 1 hour & reduction in mean systolic and diastolic pressure at 15 minute, 30 minute, 1, 6, 12 and 24 hour. Secondary Efficacy End-points was the timetaken to achieve target blood pressure & symptomatic improvement in patients with hypertensive emergencies. **Safety End-points** was Composite end-point of death and major adverse cardiovascular events (MACE), Hypersensitivity reactions, Headache, Bradycardia, and Methemoglobinemia.

All categorical variables were compared using chi-square test or fisher exact test whichever was applicable, continuous variables was expressed as mean ± standard deviation and they were compared using ANOVA test. Statistical analysis was performed using SPSS version 20.0 for windows. For safety evaluation, all categorical variables were compared using chi-square test or fisher exact tests whichever was applicable.

3. Results

Baseline characteristics of the patients is shown in **table-1**. This table compares all the baseline variables among the patients of the two groups. The *p* value for all the variables came out to be > 0.05. After initiation of medicine, blood pressure started declining, trend of which is shown in **table- 2**.

The SBP/DBP were compared using chi-square test. The significant differences were observed at 15 minute and the differences continued till 12 hour, where the *p* value was <0.05. Majority of patients (96%) in the Labetalol group achieved the target blood pressure at 1hour, while only 44% of the patient in the NTG group achieved the target blood pressure at 1 hour. Time to achieve the target blood pressure was more in NTG group (220.80 ± 196.510 min), in comparison to labetalol group (54.00 ± 65.383 min) which is statistically significant (*p*-value < 0.001). 52% of the patients among the NTG group required add on

Table-2

Trend of fall of blood pressure with the time in both group.

VARIABLE	Randomization Group		p-Value
	NTG (n = 25)	Labetalol (n = 25)	
Pulse Rate (per minute)	84.32 ± 6.750	84.20 ± 9.115	0.958
Baseline SBP	202.08 ± 11.895	203.44 ± 12.268	0.692
Baseline DBP	121.44 ± 3.441	121.68 ± 4.715	0.838
SBP (15 min)	193.20 ± 16.401	188.48 ± 13.270	0.269
DBP (15 min)	106.80 ± 7.895	104.80 ± 9.626	0.426
SBP (30 min)	179.76 ± 14.992	166.64 ± 19.033	0.009
DBP (30 min)	99.60 ± 6.831	91.20 ± 9.345	0.001
SBP (60 min)	165.68 ± 14.739	146.28 ± 14.536	<0.001
DBP (60 min)	89.84 ± 9.145	81.44 ± 8.297	0.001
SBP (360 min)	151.84 ± 14.375	142.32 ± 10.843	0.011
DBP (360 min)	83.12 ± 11.359	78.56 ± 5.903	0.081
SBP (12 h)	145.12 ± 9.951	139.28 ± 10.613	0.005
DBP (12 h)	78.80 ± 9.539	75.52 ± 5.075	0.136
SBP (24 h)	138.80 ± 8.963	134.16 ± 7.548	0.054
DBP (24 h)	74.16 ± 6.375	71.04 ± 3.470	0.037

(SBP- systolic blood pressure, DBP-diastolic blood pressure, MAP- mean arterial pressure).

drugs while only 4% (1 patient) from the labetalol group required add on drugs to quickly control the blood pressure.

There were two deaths reported in our study, both of the patients were from labetalol group. Both the patients who expired, had the diagnosis of CVA (cerebrovascular accident) with poor GCS of 3/15 and both expired after achieving the target BP. The difference was not significant as the *p* value was >0.05. No patients in the NTG group expired.

4. Discussion

This study was conducted on small cohort of acute hypertensive crisis patients, in which all qualified for the criteria of hypertensive emergency. There were no patients from hypertensive urgency group. The presenting complaints in our study were Nausea (44%), Chest pain (40%), Palpitation (36%), Vomiting (24%), Headache (24%), Neurological deficits (10%), Visual symptoms (2%), Oliguria (2%). Presenting complains in one study were chest pain > headache > dyspnea.⁵ Presenting complains in another study were headache > epistaxis > chest pain.⁶ Dyspnea was common presenting symptom in western studies but was not prevalent in this study as we excluded the patients with pulmonary edema, left ventricular failure, known airway disease i.e. COPD. The patients with above diagnosis were excluded because labetalol, one of our test drug was contraindicated in the above situation.

No significant difference was observed in time to achieve the target blood pressure in a study where sublingual NTG was compared against oral nifedipine.⁷ In another study oral nifedipine and intravenous labetalol regimens was found to be similarly effective in the acute control of severe hypertension in pregnancy.⁸ Our results vary from many western studies as our sample size was small (50 patients) and it was single centered.

5. Conclusion

This study has clearly revealed that labetalol is more efficacious than the NTG in controlling the BP among the patients of hypertensive crisis. Labetalol achieved target BP control in shorter time. Overall patient in NTG group also achieved target BP by 12h but significant number of patients (52%) needed add on drugs to control the blood pressure. Overall there were no significant differences in the adverse events.(Tables 1 and 2).

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Declaration of competing interest

Not declared.

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