Association between intravenous antihypertensive therapies and development of adverse events during hypertension management in the emergency department

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BACKGROUND

- The initial therapy for elevated blood pressure in the emergency department (ED) is aimed at lowering blood pressure gradually in order to avoid rapid changes in tissue perfusion and the development of ischemia[1,2].
- To date, there are no guidelines to recommend one antihypertensive agent over another and the choice of agent and dose is highly variable.

Minutes to 2 hours	2 to 6 hours	24 to 48 hours
Reduce MAP by < 25%	Target 160/100 mmHg	Gradually reduce to normal

- Purpose: To examine the impact of different intravenous (IV) antihypertensive agents on the development of adverse events during hypertension management in the ED.

OBJECTIVES

Primary Objective

- Determine the effect of individual IV antihypertensive agents on the development of adverse events in the treatment of hypertensive crisis'.
  - Rapid BP Reduction: Initiation of vasopressor therapy and/or fluid resuscitation within 2 hours of therapy
  - Hypotension: Decrease in SBP < 160 mmHg in the emergency department
  - Renal Failure: Development of AKI according to Acute Kidney Injury Network (AKIN) Criteria

Secondary Objective

- Identify the incidence and type of adverse events according to antihypertensive regimen.
- Characterize treatment of elevated blood pressure in the TUH ED.

METHODS

INCLUSION

- 18-89 years old
- Received any of the following:
  - *Sodium nitroprusside*
  - *Nitroglycerin*
  - *Hydralazine*
  - *Enalaprilat*
  - *Labetalol*
  - *Fenoldopam*
  - *Nicardipine*

EXCLUSION

- Length of stay < 48 hours
- Prisoners
- Pregnant/breastfeeding
- Positive pressure ventilation
- Diagnosis of the following:
  - *Aortic dissection*
  - *Intracranial hemorrhage (ICH)*
  - *ST segment elevation myocardial infarction (STEMI)*
  - *Ischemic stroke*

RESULTS

Screened N=584

Included N=129

Excluded N=455

< 48 hours	N=167	Positive Pressure Ventilation	N=36
ICH	N=139	STEMI	N=4
Ischemic Stroke	N=39	Age	N=4
Medication Not Given	N=36	Pregnant	N=1
Aortic Dissection	N=28	Incomplete Records	N=1

Figure 1. Incidence of Adverse Event

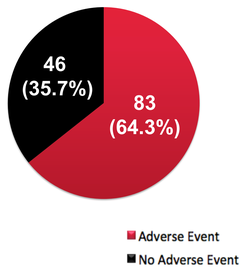


Figure 2. Type of Adverse Event

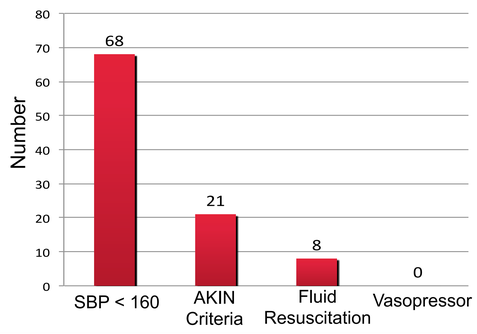


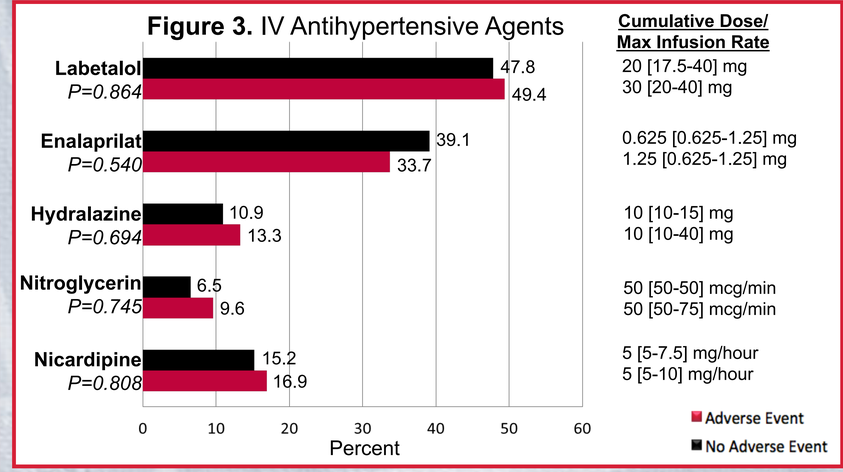
Table 1. Patient Demographics and Clinical Characteristics

Parameter	No Adverse Event (N=46)	Adverse Event (N=83)	P-value
Age (years)	55.0 ± 11.9	53.5 ± 12.4	0.494
Weight (kg)	79 [68.5-100]	82 [70-105]	0.273
Male	23 (50.0)	41 (49.4)	0.948
African American	40 (87.0)	65 (78.3)	0.227
Comorbidities			
Hypertension	*40 (87.0)*	*75 (90.4)*	*0.566*
Diabetes	*17 (37.0)*	*33 (39.8)*	*0.754*
Chronic Kidney Disease	*16 (34.8)*	*21 (25.3)*	*0.254*
Congestive Heart Failure	*9 (19.6)*	*20 (24.1)*	*0.555*
Coronary Artery Disease	*12 (26.1)*	*17 (20.5)*	*0.465*
Home Hypertensive Therapy	33 (71.7)	68 (81.9)	0.179
Emergency	30 (65.2)	62 (74.7)	0.254
Altered Mental Status	*8 (17.4)*	*12 (14.5)*	*0.659*
Shortness of Breath	*6 (13.0)*	*14 (16.9)*	*0.565*
Pulmonary Edema	*10 (21.7)*	*17 (20.5)*	*0.866*
Troponin Elevation	*14 (30.4)*	*27 (32.5)*	*0.807*
Acute Chest Pain	*11 (23.9)*	*23 (27.7)*	*0.639*
Acute Renal Disorder	*9 (19.6)*	*14 (16.9)*	*0.701*
Systolic Blood Pressure (mmHg)	204.8 ± 27.9	185.9 ± 29.9	0.001
Mean Arterial Pressure (mmHg)	147.0 ± 22.0	138.0 ± 22.6	0.032
Serum Creatinine (mg/dL)	1.50 [1.21-5.20]	1.44 [1.00-2.32]	0.111
ICU Admission	11 (23.9)	23 (27.7)	0.639
Oral Antihypertensive	13 (28.3)	21 (25.3)	0.715
Topical/Sublingual Nitroglycerin	14 (30.4)	39 (47.0)	0.067
Nephrotoxic Agents	38 (82.6)	67 (80.7)	0.792

Categorical data are expressed as total patients (percent)
Continuous data are mean ± standard deviation or median [interquartile range]

RESULTS (cont.)

Figure 3. IV Antihypertensive Agents



Cumulative Dose/ Max Infusion Rate

Labetalol	20 [17.5-40] mg 30 [20-40] mg
Enalaprilat	0.625 [0.625-1.25] mg 1.25 [0.625-1.25] mg
Hydralazine	10 [10-15] mg 10 [10-40] mg
Nitroglycerin	50 [50-50] mcg/min 50 [50-75] mcg/min
Nicardipine	5 [5-7.5] mg/hour 5 [5-10] mg/hour

Table 2. Logistic Regression Model for Independent Predictors of Adverse Events

Variable	Odds Ratio	95% Confidence Interval	P-Value
Baseline Systolic Blood Pressure	0.97	0.96 – 0.99	0.001
Topical/Sublingual Nitroglycerin	3.38	1.32 – 8.64	0.011
Baseline Serum Creatinine	0.87	0.77 – 0.98	0.026
Enalaprilat Use	0.43	0.17 – 1.08	0.073
Nicardipine Use	3.03	0.87 – 10.62	0.083

The use of intravenous nitroglycerin, hydralazine, labetalol, admission to the ICU, ED triage score, home HTN therapy, concomitant nephrotoxic medication use, and organ damage on admission were not associated with the development of an adverse event during hypertension management. Area under the receiver operating curve: 0.756; Hosmer Lemeshow Test: 0.896.

CONCLUSION

- There is no association between intravenous antihypertensive agents and the development of adverse events.
- Concomitant use of topical or sublingual nitroglycerin is associated with a three fold increased risk of adverse events.

REFERENCES

1. National High Blood Pressure Education Program. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Arch Intern Med. 1997;157:2413-46.
2. Jones AE, Yiannibas V, Johnson C, et al. Emergency department hypotension predicts sudden unexpected in-hospital mortality: a prospective cohort study. Chest. 2006 Oct;130(4):941-6.

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