A Comparison of Vasopressor Utility for Drug Overdose Induced Shock

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Introduction

- Deaths in the US from drug overdose are steadily rising;[1] however, there remains no consensus on the ideal selection of adrenergic agent (vasopressor) in ED patients with circulatory shock after a drug overdose.
- Although high-dose insulin euglycemia (HIE) for beta-blocker (BB) and calcium-channel-blocker (CCB) overdose has become a first-line treatment based on excellent animal data, there remains little human evidence to support this practice.[2]

Objectives

- The primary objective of this study was to assess the impact of vasopressor choice and HIE use on mortality in drug overdose-related shock.

Methods

- Study Design: secondary data analysis of a prospective cohort of consecutive ED patients presenting with suspected drug overdose to two urban teaching centers between 2009-2014.
- Inclusion criteria: all adult patients also circulatory shock requiring vasopressors or HIE.
- Exclusion criteria: Pediatric patients (age <18 years), late-onset shock (5-half lives) and caustic ingestions.
- Independent variables were the choice of initial vasopressor (both drip and push-dose), as well as a subgroup analysis of BB and CCB overdose and HIE use. Subgroup analysis compared ICU length-of-stay and total pressor time in the BB/CCB subgroup.

Results

- Over a time period of 5 years (2009-2014) a total of 61 cases were identified of suspected drug overdose requiring vasopressors or HIE.
- 6 were excluded
  - 3 caustic ingestions, 1 insufficient information, 2 late-onset of shock
- A total of 55 overdoses qualified by inclusion/exclusion criteria, and 15 of these included a component of either BB/CCB overdose.

TABLE 1. Study Outcomes for All Patients

Study Outcomes	Mean or Percentage	Standard Deviation
Mortality 24 hours	20%	0.404
Mortality Hospital	43%	0.499
Pressor Time (m)	1,930	2,700
ICU Time (h)	117	158

- High Dose Insulin Euglycemia (HIE) Therapy:
  - Of the included cohort, 15 were suspected of involving a beta-blocker (10), a calcium-channel blocker (7), or both
  - Due to insufficient numbers of patients treated with HIE in either group, we were unable to assess for mortality benefit, ICU LOS, or total vasopressor time

Results

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TABLE 2

Initial Drip (or Push Dose)	Total	Mortality 24 Hour	Mortality In Hospital
Norepinephrine	23	2 (9%)	8 (35%)
Dopamine	11	2 (18%)	5 (45%)
Vasopressin	3	0 (0%)	1 (33%)
Phenylephrine	2	1 (50%)	1 (50%)
Dobutamine	1	0 (0%)	0 (0%)
Epinephrine	0	0	0
Epinephrine (Push Dose)	19	8 (42%)	16 (84%)
Phenylephrine (Push Dose)	12	1 (8%)	1 (8%)

- Mortality Benefit:
  - For all patients, approached mortality benefit when norepinephrine was the initial drip (p=0.097)
  - There was significant mortality benefit when phenylephrine was the initial push-dose medication given (p=0.008).
- Mortality Risk:
  - Significantly higher when epinephrine was the initial push dose medication given initially
    - p<0.05 24 hr mortality
    - p<0.05 in-hospital mortality

TABLE 3

Initial Drip (or Push Dose)	Fisher's Exact	Odds Ratio Mortality (24 or IH)
Norepinephrine	0.097	0.24 (24hr)
Epinephrine (Push Dose)	<0.001	21.33 (IH)
Phenylephrine (Push Dose)	0.008	.083 (IH)

Limitations

- Not a randomized, blinded study design
- Small sample size
- Most severe drug overdoses more likely to receive push-dose epinephrine
- More severe BB or CCB overdoses more likely to receive HIE

Conclusions

This data suggests that push-dose phenylephrine can be safe, effective, and may be superior to push-dose epinephrine as the initial medication in undifferentiated drug overdose patients with circulatory shock.

As any forthcoming randomized control trial on HIE is unlikely, more observational data is needed to show human benefit of this form of treatment.

Bibliography

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