Efficacy of Hydroxocobalamin as Treatment for Nifedipine-Induced Shock

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BACKGROUND

- Hydroxocobalamin is currently approved for use in treating cyanide toxicity.
- Adverse effects include increased blood pressure.
- Increased blood pressure has also been noted in healthy humans, humans treated for cyanide toxicity and porcine models of cyanide toxicity.
- Recent studies:
  - Demonstrate successful use of hydroxocobalamin in treating vasopressor shock during cardiac bypass.
  - Provide data supporting improvement of blood pressure in swine models of hemorrhagic shock.

Mechanism of Action:

- Hydroxocobalamin inhibits nitric oxide synthase and scavenges nitric oxide (NO), and it is this activity which has been linked to increases in mean arterial pressure (MAP).
- Several studies have demonstrated that NO is an important chemi- nal mediator of vasopressor shock.
- Hydroxocobalamin is theorized to act via vasodilation through the NO pathway.

HYPOTHESES

Primary Hypothesis:

- Hydroxocobalamin will improve survival in swine with nifedipine-induced shock.

Secondary Hypotheses:

- Hydroxocobalamin will improve hemodynamics in swine with nifedipine-induced shock.
- Hydroxocobalamin will improve laboratory markers of perfusion (creatinine, lactate, etc.) in swine with nifedipine-induced shock.

METHODS

- IAUCP approved study of Yorkshire swine (36-50 kg).
- Sedated with alpha-chloralose, mechanically ventilated, and instrumented for drug delivery and hemodynamic monitoring.
- Ozone response curves of nifedipine (NP) and hydroxocobalamin (HX) performed.

RESULTS

Mortality

- Animals were divided into 3 groups:
  - Group 1: Control (n=9)
  - Group 2: Nifedipine + saline (n=9)
  - Group 3: Nifedipine + hydroxocobalamin (n=9)
- Nifedipine (0.256 mg/kg/min) infused
- Toxicity reached when MAP decreased by 20%.

Change in Hemodynamics:

- Raw data was analyzed at specific time points using the Bonferroni correction.
- Significant differences in MAP and diastolic blood pressure (DBP) were noted (p<0.05).

Primary Hypothesis:

- Experimental Protocol
- Baseline Characteristics
- Secondary Hypotheses:

CONCLUSION

- Hydroxocobalamin did not improve mortality in this model of nifedipine toxicity.
- Significant changes in hemodynamics were noted with and compared to raw and predicted hemodynamic data.
- May suggest benefit as a bridge to other therapy (inhibition of HCO3, ECMO, transfer).
- Further investigation of hydroxocobalamin as a treatment for nifedipine and other calcium channel blocker toxicity is warranted.
- Alternative dosing strategies.

ACKNOWLEDGEMENTS

Funding for the project made possible by:
- Department of Emergency Medicine Research Division of Carolinas Medical Center.
- Special thanks to Kristin Engebretsen, Vik Bebarta, and Dave Tanen for their assistance.
- Thanks to Edwards LifeSciences for in-kind donation of EVO-1000 monitor.

REFERENCES
