Preoperative Curcumin for Prevention of the Inflammatory Response in Patients Undergoing Cardiopulmonary Bypass: A Swine Model

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Background

- Curcumin is derived from turmeric, which is used extensively as a flavoring and coloring agent in curries and mustards, and has been safely consumed by humans for centuries. Its use has included that of an anti-inflammatory agent in Ayurveda, an ancient Indian system of medicine. (King, 2011).
- A recent study evaluated the role of curcumin in murine cardiac hypertrophy with different doses of curcumin (50, 75, and 100 mg/kg/d) and determined that curcumin blocked cardiac hypertrophy in vitro in a dose-dependent manner. It was also found to prevent as well as reverse cardiac hypertrophy induced by aortic banding (AB). This study concluded that curcumin has the potential to protect against cardiac hypertrophy, inflammation, and fibrosis. (Li, 2008).
- Given the potential role of curcumin in reducing inflammation, we completed a double blinded, prospective pilot study evaluating inflammatory markers in a swine model, including TNF-α, IL-6, IL-1β, and ICAM-1.

Anesthetic Management

- Common crossbred swine, between 12-20 kilograms were fed approximately 130 mg/kg of curcumin for 3 days prior to surgery.
- The animals were anesthetized with a combination of Telazol or ketamine, xylazine, and an anticholinergic if needed. After ensuring a surgical level of anesthesia, the animals were given rocuronium as needed to maintain muscle relaxation throughout the procedure.
- The animals were intubated and central femoral venous and arterial access was obtained to facilitate drug delivery, ABGs, interleukin labs, electrolyte and hemodynamic monitoring.
- Continuous infusions of fentanyl (10-200 µg/kg/hr) and midazolam (50-1500 µg/kg/hr) were used to minimize hemodynamic changes related to fluctuations in sedation.

Simulation of Cardio-Pulmonary Bypass

- The chest was entered via left thoracotomy or sternotomy, and the pericardium dissected and opened. 200 units/kg of heparin given as anticoagulation for ECMO.
- Venous ECMO cannulas were placed in either the external jugular vein or the right atrial appendage and arterial cannulas in the carotid artery, femoral artery and aorta.
- VA ECMO was initiated and flows were increased to 100 ml/kg/min simulating full VA-ECMO support.
- ECMO flow was maintained via the internal jugular vein or right atrial appendage as the site for venous access, but the arterial blood flow alternated between the common carotid artery, the femoral artery, and the aortic cannulas.
- A series of recordings were taken in sequential fashion during manipulation of the VA-ECMO flow ("runs") including:
  - baseline on VA-ECMO
  - dobutamine of 2.5 µg/kg/min; 5 µg/kg/min; 7.5 µg/kg/min; 10 µg/kg/min
  - esmolol 300 µg/kg/min with phenylephrine titrated to maintain afterload
- Each of these "runs" were repeated utilizing one, two or three of the arterial cannulas.
- Blood samples were collected at 3 time points in each of the swine and levels of IL6, IL8, IL1-β and ICAM-1:
  - following anesthetic induction but pre-ECMO
  - 30 minutes on ECMO
  - pre-termination of ECMO

Discussion

Our results demonstrated significantly decreased average levels of TNF-alpha, IL-6 and ICAM-1 in those animals who received curcumin preoperatively compared to those who did not. Despite our small sample size, the p values for ICAM-1 did reach statistical significance, however, for TNF-alpha and IL-6 they did not. These results deserve additional study and we anticipate using this project as a starting point for further clinical trials with human subjects.