Abstract

TITLE: ALTERATIONS OF THE KYNURENINE/TRYPTOPHAN PATHWAY IN SINGLE VENTRICLE INFANTS UNDERGOING STAGE 3 PALLIATION

Purpose of Study: Infants undergoing staged palliation for single ventricle heart defects represent a uniquely vulnerable patient population. There are currently no validated biomarkers to guide risk evaluation and clinical decision making prior to Stage 3 palliation (S3P). Analysis of the Kynurenine/Tryptophan pathway (KP) presents a possible method of risk stratification, as the KP has been implicated previously in disease states involving pulmonary vasculature.

Methods: 74 infants undergoing S3P at the Children's Hospital of Colorado were enrolled during pre-operative evaluation with blood sample collected at pre-operation, 2h, 24h, and 48h post-operation. A blood sample was also obtained from 47 age-matched healthy controls undergoing non-cardiac surgery requiring IV access. Clinical data were collected from the electronic medical record. Metabolite concentrations were quantified using tandem mass spectroscopy.

Summary of Results: KP mapping showed a statistically significant difference in metabolite concentrations between patients undergoing S3P (cases) and control patients for the following metabolites (case v control, p): Kynurenine (282.14 v 370.56 ng/mL, p = 6.14e-10*)*, Tryptophan (8491.37 v 10654.09 ng/mL, p = 2.04e-7*)*, Picolinic acid (43.45 v 71.17 ng/mL, p = 2.16e-5), Serotonin (113.06, 153.89 ng/mL, p = 3.33e-4), 3-hydroxykynurenine (13.56 v 8.75 ng/mL, p = 3.33e-4), and Quinolinic acid (58.95 v 41.4 ng/mL, p = 9.41e-3). A one-way ANOVA demonstrated statistically significant differences in metabolite concentrations across four time points for all metabolites except serotonin. Picolinic acid and kynurenic acid concentrations were elevated at 2 hours post-op before trending downwards. Kynurenine was elevated at 2 and 24 hours post-op and remained above baseline at 48 hours. Increased concentrations of kynurenic acid at 24 hours and 48 hours were correlated with an increased length of stay (p = 8.16e-4).

Conclusions: Children with SVHD undergoing S3P experience a significant disturbance in tryptophan metabolism at baseline compared to healthy controls, with further changes during the post-operative period. The association of increased post-operative kynurenic acid with increased length of stay implicates alterations in the KP in post-surgical outcomes. Further analysis will investigate the correlation between KP metabolites and additional clinical outcomes after S3P.