1548287

Increased RNA Editing in Children with Cyanotic Congenital Heart Disease-a New Epigenetic Mechanism Affecting Postoperative Course

Borik, S[1]; Simon, A[2]; Nevo-Caspi, Y[1]; Mishali, D[1]; Amariglio, N[2]; Rechavi, G[2]; Paret, G[1]
[1]Safra Children's Hospital, Chaim Sheba Medical Center, Tel Hashomer, Israel; [2]Chaim Sheba Medical Center, Tel Hashomer, Israel

Objectives: Cyanotic infants undergoing cardiac surgery often demonstrate a complex post-operative course, partly dictated by the expression of inflammatory and cardiac genes. Some of these genes undergo epigenetic regulation, such as A-to-I RNA editing, which may emerge as a global post-transcriptional modification. We hypothesized that A-to-I RNA editing is altered in cyanotic children with congenital heart disease (CHD) and thus may affect their postoperative recovery.
Methods: RNA was extracted from blood samples collected from 37 CHD patients, pre-operatively and eight hours after cardiac surgery. Patients were divided into a cyanotic group and an acyanotic group. Each patient sample was analyzed for A-to-I RNA editing in an intronic segment of the MED13 gene, shown to play a role in cardiac disease. RNA expression levels of the enzymes responsible for RNA editing, ADAR1 and ADAR2, were examined using quantitative real time (RQ) PCR.
Results: A-to-I RNA editing was significantly higher among the cyanotic CHD patients (n=19) than among the acyanotic ones (n=18) both before and after surgery. This was manifested by the average editing at the seven most highly edited sites (27.4% ±8.5% vs. 20.8%±10.2%; p=0.038) and editing at specific sites, e.g. position 14 (20.2% ± 5.1% vs. 14.5% ± 5.2%; P = 0.002). Cyanotic patients exhibited a more complicated postoperative course than acyanotic patients (longer pediatric intensive care unit stay, more mechanical ventilation days, and elevated inotropic scores). ADAR2 RNA levels were significantly lower among cyanotic patients, suggesting a possible adaptation to hypoxia.
Conclusions: Children with Cyanotic CHD manifest significantly higher rates of RNA editing both before and after surgery. Post-transcriptional RNA changes may influence the cyanotic pathophysiology and influence surviving hypoxia and difficult peri-operative conditions.