Changes in circulating levels and cardiac expression of adiponectin system in children with heart failure after Ventricular Assist Device support

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Background: Ventricular Assist Device (VAD) is increasingly used as bridge to transplantation for the treatment adult and pediatric patients with end-stage Heart Failure (HF). Unloading of heart by VAD can lead to significant molecular, structural and functional changes of cardiac muscle in HF adult patients, including an improvement of the inflammatory process. Adiponectin (ADN), an anti-inflammatory adipokine, exerts anti-hypertrophic, anti-fibrotic and anti-apoptotic effects after binding to AdipoR1, AdipoR2 and T-CAD receptors. There is an apparently paradoxical increase of ADN levels in HF adult patients, probably due ADN resistance. VAD treatment leads to an increased cardiac expression of ADN receptors in HF adults. However, little is known about the role of ADN in HF children and the effects of VAD support on ADN system in these patients.

Purpose: The aims of this study were to evaluate: 1) the circulating ADN levels from HF children and a control group of healthy children; 2) the effects of VAD treatment both on circulating levels of ADN and on the cardiac expression of ADN system in pediatric patients with HF.

Methods: Circulating levels of ADN were measured in plasma samples collected from 8 HF children [age:57±33 (mean±SD) months; 2 males; 14.2±13.5 weight; 29±8 LVEF%] before and at 4 hrs, 1, 3, 7, 14 and 30 days after VAD implant. The ADN levels of paediatric patients at baseline were compared with a group of 107 [58±7 months; 67 males] healthy children. Expression levels of AdipoR1, AdipoR2, T-CAD were determined by real-time PCR in cardiac biopsies collected from HF children at the time of VAD implant (Pre-VAD) and at the time of heart transplantation (Post-VAD).

Results: Circulating levels of ADN were significantly higher in HF compared to healthy children (Figure 1A). In HF children, plasma ADN decreased significantly in early post-operative time-course (up to 3 days Post-VAD implant) and returned to pre-operative levels in 1 month (Figure 1B). In cardiac biopsies, mRNA expression of AdipoR1, AdipoR2, T-CAD increased significantly after VAD treatment compared to Pre-VAD (Figure 2A–C).

Conclusion: In pediatric patients, high circulating levels of ADN were associated with presence of HF and were modified by VAD implant, but remained significantly abnormal. On the other hand, an increased cardiac mRNA expression of ADN receptors was observed after VAD. These results could suggest the existence of a fine tuning of the ADN system at cardiac tissue level, able to mitigate plasma abnormality and favour the cardio-protective effect of ADN.

Figure 1

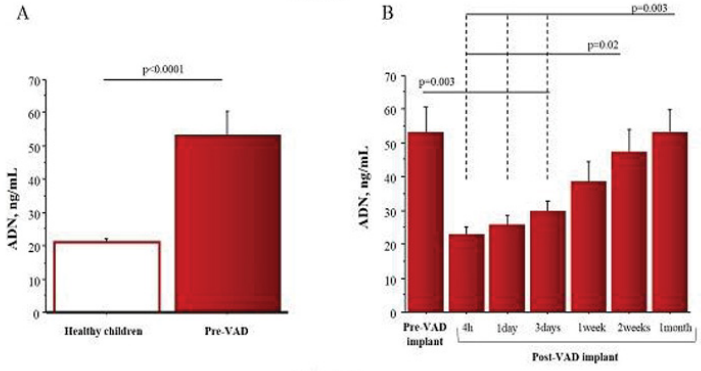

Figure 2