Coxdiac Autonomic Neuropathy is Highly Predictive for Survival in Children with Mauriac Syndrome

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Introduction. Diabetic autonomic neuropathy (DAN) is highly predictive for subsequent mortality of the patients. The main reason for death is terminal renal insufficiency. Asymptomatic DAN can be established by testing heart rate (HR) and HR variability (HRV) at rest and during sympathetic and vagal stimuli. Worsened HRV is related to the cardiac autonomic neuropathy (CAN).

Objective. To assess asymptomatic CAN and its predictive value for survival in children with diabetes and Mauriac syndrome.

Material and methods. Twelve children (7 boys, 5 girls) with Mauriac syndrome (growth retardation, hepatomegaly and delayed puberty) were included in a cross-sectional study for CAN. Ten of them were born between 1980-1987 and two children in 2001 and 2005.

Time-domain (HR and coefficient of variation of HR) and Frequency-domain analysis with total power (TP) of HRV and low/high frequency ratios (LF/HF) were performed. They were based on R-R intervals of electrocardiograms in children under 18 years of age. The results were compared to 346 age/sex matched controls and 204 diabetic children with normal growth. The diabetes were divided in to a groups based on their metabolic control. First five groups had no late complications, but differed with their mean values of long lasting HbA1c: 7.8, 8.9, and >10% respectively. Sixth group consisted of 30 children with poor control (HbA1c>10%) and microangiopathy. The children with Mauriac syndrome presented the last 7th subgroup in the study. Deviations out of referent 25-75 percentiles or ±2 SDs were accepted as abnormal for HR and HRV at rest and during respiratory and orthostatic stimuli.

Results. Mean age of children with Mauriac syndrome at diagnosis of diabetes was 3.4±2.5 years (8 months to 8.5 years); mean age at the investigation 15.3±2.7 years (9.7 to 17.9); diabetes duration 12.1±3 years (7.6 to 15.9); mean growth retardation was ±3.27±0.92 SDs (Table 1). These children had significantly younger age at diagnosis and longer duration of diabetes than others, p<0.05.

Most children with Mauriac syndrome had one or more late chronic complications, but initial nephropathy dominated in all of them at the time of the study for CAN.

The most sensitive frequency domain analysis outlined significantly not only 7th, but 6th group from the other diabetic children (Fig.3 and Fig.4). Suppressed respiratory arrhythmia was expressed by low TP and high LF/HF ratio.

Discussion. In our cross-sectional study asymptomatic CAN, expressed with significant tachycardia at rest and lowered respiratory arrhythmia was available in children with poor metabolic control that have one or more late complications. They were diagnosed with most sensitive frequency domain analysis. Less sensitive time domain analysis outlined only significantly children with Mauriac syndrome from the others. Irrespective of methods of investigation HR and HRV in children with Mauriac syndrome showed the most severe impairment of HR and HRV.

Conclusions. Children with Mauriac syndrome developed asymptomatic cardiac autonomic neuropathy before age of 18 years together with initial nephropathy and other late complications. Early age of diabetes and chronic insulin deficiency with persisting hyperglycemia were the most important risk factors for poor prognosis. CAN predicted poor survival and early death among patients who developed Mauriac syndrome in their childhood.