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Being born with congenital heart block - Risk factors, growth and development

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ABSTRACT

Congenital heart block (CHB) is a rare but life-threatening disease associated with the presence of Ro and La autoantibodies in the mother of the child affected. CHB is one of the manifestations of neonatal lupus erythematosus (NLE) that may also include several other manifestations such as a skin rash and cytopenias. Although the link between Ro and La autoantibodies and the risk for CHB has been recognized for decades, a recurrence rate of 12-17% in subsequent pregnancies suggests that other risk factors also contribute to disease pathogenesis. Furthermore, as CHB is rare disease, little is known about outcome and health in these children. The aim of this thesis was therefore to investigate outcome, health and antibody levels in children with CHB as well as risk factors for CHB development.

In our results we reveal that increased maternal age and seasonal timing of birth are novel risk factors for CHB in autoantibody positive pregnancies. Furthermore, when analyzing antibody levels in children born to mothers with Ro/SSA autoantibodies, we have demonstrated that maternal autoantibodies decrease rapidly in the infant circulation during the first few weeks of life among both breast-fed and non-breast-fed infants and are not correlated to NLE skin manifestations. We have also demonstrated that an autoantibody-associated complete CHB diagnosis after the neonatal period is possible, advocating testing of maternal serology at the time of diagnosis.

Our results demonstrate that newborns with fetal signs of atrioventricular block (AVB) II-III have a significantly lower weight at birth than those with AVB I or normal conduction and do not show signs of catch-up during the first 12 months of life. Fetuses with AVB I or normal atrioventricular conduction have significant but smaller weight retardation at birth, but showed a rapid catch-up during the first two postnatal months, indicating that they have a good prognosis. Looking at long-term growth, we demonstrate that children with complete CHB are weight restricted both in comparison to their siblings without CHB and the Swedish reference standards from birth to 2-3 years of age, when a catch-up is initiated. From the age of 9-11 they have normal body measurements as a group and do not significantly deviate from the reference standards. When investigating neurodevelopment, our data indicate that in addition to well established factors such as male sex and being born preterm, both maternal SLE and CHB may influence neurodevelopment as learning impairment was significantly influenced by maternal SLE ($p < 0.005$), while attention deficits was influenced by both maternal SLE ($p < 0.05$) and CHB in the child ($p < 0.05$).

In conclusion, our results indicate that maternal age and seasonal timing of birth are risk factors for CHB development, information that may be useful to consider when pregnancy is planned. As antibody levels decreased in the infants and were not correlated to NLE skin manifestations, we conclude that there is no reason not to recommend breast-feeding in children born to anti-Ro and or La positive women. Although children with CHB are weight retarded during their first years of life, they appeared to spontaneously initiate a catch-up in weight around the age of 2-3 years. However, as the group of children with CHB did not reach the reference standards until the age of 9-11, careful follow-up of individuals with CHB regarding nutrition and growth is recommended. In addition, follow-up of neurodevelopment should be considered for children with CHB, especially if the mother is diagnosed with SLE. An early diagnosis is one way to help these children overcome their difficulties during childhood and school years and make sure that they obtain the support needed.

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