Karolinska Institutet

Institutionen för klinisk forskning och utbildning, Södersjukhuset

Twin-twin transfusion syndrome (TTTS) - outcomes with special reference to cardiovascular function

AKADEMISK AVHANDLING
som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras på svenska språket i Södersjukhusets aula, plan 6, hiss C.

Fredagen den 31 maj 2013, kl 9.00

av
Cecilia Pegelow Halvorsen
Leg. läkare

Huvudhandledare:
Professor Mikael Norman
Karolinska Institutet
Institutionen för klinisk vetenskap, intervention och teknik (CLINTEC)

Bihandledare:
Docent Charlotta Grunewald
Karolinska Institutet
Institutionen för klinisk forskning och utbildning

Docent Sverker Ek
Karolinska Institutet
Institutionen för klinisk vetenskap, intervention och teknik (CLINTEC)

Fakultetsopponent:
Docent Daniel Holmgren
Göteborgs Universitet
Sahlgrenska Akademin

Betygsnämnd:
Professor Nina Nelson Follin
Linköpings Universitet
Institutionen för klinisk och experimentell medicin

Docent Bo Lundell
Karolinska Institutet
Institutionen för kvinnors och barns hälsa

Professor Torvid Kiserud
Universitetet i Bergen
Institutt for klinisk medisin

Stockholm 2013

ABSTRACT

Background

Fetal environment has become a subject for increasing interest when studying health and disease in adults. Monozygous (MZ) twins, especially gestations complicated with twin-twin transfusion syndrome (TTTS), offer a unique opportunity to study adverse developmental programming of the cardiovascular system. TTTS affects about 10% of pregnancies with a common placenta because of unbalanced blood flow across deep arteriovenous connecting vessels. The divergent hemodynamic loads of the donor and the recipient fetus often result in myocardial hypertrophy of the recipient heart.

The aims of this thesis were to evaluate intrauterine environmental contributions to vascular functions in twins with discordant birth weight (Paper I), to study long term effects of TTTS on cardiac structure and function (Paper II and IV) and to determine infant survival and neonatal outcome after fetoscopic laser coagulation therapy of TTTS in Sweden (Paper III).

Methods and Results

An observational study of 31 twin-pairs, mean age 8 years, with discordant weight at birth, showed that systolic blood pressure (SBP) was higher and endothelial function lower in the at birth smaller twin. In MZ twins with a history of TTTS (n= 9 pairs), there was no significant difference in SBP, but donor twins had narrower carotid arteries than recipient twins and carotid strain was higher (Paper I).

Echocardiography of 11 TTTS twin-pairs, mean age 9.6 years, prenatally treated with amnioreductions, showed no difference in cardiac structure but recipients had significantly lower diastolic ventricular filling compared with donors (Paper II). When examining a laser treated cohort of 19 TTTS twin-pairs, mean age 4.5 years, and 19 age-matched singleton controls, we found signs of a minor decrease in early diastolic ventricular filling in recipients compared with donors, but no differences in heart function or structure compared with controls (Paper IV).

From a hospital-based register of the first Swedish cohort of laser treated TTTS pregnancies (n = 71), we found that overall survival from treatment to one-year of age was 46%, and that in 61% of gestations, at least one twin survived infancy. Mean gestational age at birth was 30 weeks and mechanical ventilation was needed in 46% of liveborn twins (Paper III).

Conclusions

Exposure to fetal growth retardation may contribute to higher blood pressure, arterial narrowing and endothelial dysfunction in childhood (Paper I). Fetal and infant survival after fetoscopic laser coagulation of TTTS is still limited. If very preterm delivery is necessary, the neonatal team has to prepare for taking care of two high risk neonates mostly requiring respiratory support (Paper III). Despite different and severe fetal cardiac loading conditions, our long-term follow-up studies of twins surviving TTTS showed an overall cardiac structure and function within normal range. The signs of reduced diastolic function found in the group treated with amnioreductions (Paper II) were less pronounced in the laser treated cohort (Paper IV).

These observations indicate that the cardiac morbidity caused by TTTS resolves in childhood. This has important implications as clinical decision making in TTTS frequently involves choosing between accepting increased fetal cardiac morbidity in the recipient twin and delivery of two very preterm babies.

ISBN 978-91-7549-122-6