Pathophysiology of fetal intrauterine central shunts in high-risk pregnancies: a prospective observational Doppler study

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PATHOPHYSIOLOGY OF FETAL INTRAUTERINE CENTRAL SHUNTS IN HIGH RISK PREGNANCIES: A PROSPECTIVE OBSERVATIONAL DOPPLER STUDY

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This thesis is dedicated to all the families

affected by adverse pregnancy outcomes

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ABSTRACT

The primary objective of antenatal assessment and monitoring is to ensure wellbeing of the fetus and the mother. There are different methods of assessment during pregnancy and in labour. Doppler ultrasound is one of the tests widely used in clinical practice in the evaluation of pregnancies that are at a greater risk of developing maternal or fetal complications due to uteroplacental insufficiency.

Doppler ultrasound enables evaluation of sequential changes in circulatory haemodynamics in the fetus by evaluation of the fetus for signs of brain sparing and severity of redistribution of circulation. Recognition of abnormal Doppler flow patterns helps the clinician to optimise the appropriate timing of delivery.

Identification of the 'high risk' fetus, before any changes of fetal compromise become evident, still remains one of the major dilemmas in contemporary clinical practice.

This thesis seeks to explore the role of Doppler monitoring fetal intrauterine central shunts as a method of identifying the 'high-risk' fetus before any other established parameters, such as, fetal biometry, fetal weight or flow waveforms in umbilical artery become abnormal. This thesis also evaluates the role of serial Doppler monitoring of fetal central shunts in those fetuses where IUGR has been established.

This is based on the premise that the intrauterine shunts are present in fetal circulation to work closely with the placenta to ensure appropriate nutrition and oxygenation of the fetus, bypassing the lungs.

Four prospective longitudinal studies were designed to evaluate the role of fetal intrauterine shunts in adaptive response mechanisms in cardiovascular stress. Two models were taken into consideration: an 'acute cardiovascular stress' model and a 'chronic cardiovascular stress' model.

To study the 'response to acute cardiovascular stress' in high-risk fetuses, a cohort of mothers undergoing fetal intrauterine transfusion for fetal anaemia were selected. These fetuses were scanned immediately before and after transfusion, and Doppler flows through all the intrauterine shunts were documented and compared with fetoplacental and cerebral circulation.

To study the 'response to chronic cardiovascular stress', a prospective longitudinal observational study was designed and the sequence of changes in Doppler ultrasound of the fetal central shunts studied and compared with the Doppler flow waveforms of

normal pregnancies with a group of pregnancies complicated by uteroplacental insufficiency.

Normograms were designed for all the Doppler parameters and flows from adverse pregnancy outcomes were compared to the normogram.

The pregnancy outcomes in the longitudinal study were correlated with placental pathology.

Our study showed that although changes were demonstrated in the flow patterns within central shunts, these changes were not statistically significant in the ‘acute cardiovascular stress model’, suggesting that there may be other haemodynamic alterations in acute cardiovascular stress.

However, in the ‘chronic cardiovascular stress model’, the results suggest that the intrauterine cardiac shunts may play an important role in redistribution of fetal flows in early stages of growth restriction, suggesting that Doppler ultrasound monitoring of foramen ovale can be potentially used as a screening tool to identify high-risk fetuses as early as 16 weeks.

DECLARATION

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

I give consent to this copy of my thesis, when deposited in the University Library, being made available for loan and photocopying, subject to the provisions of the Copyright Act 1968.

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Nayana Anupam Parange

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At times our own light goes out and is rekindled by a spark from another person. Each of us has cause to think with deep gratitude of those who have lighted the flame within us.
Albert Schweitzer 1875-1965

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ABBREVIATIONS

UPI	Uteroplacental insufficiency
GRIT	Growth Restriction Intervention Trial
TRUFFLE	Trial of Umbilical and Fetal Flow in Europe
SGA	Small for gestational age
AGA	Appropriate for gestational age
CSA	Constitutionally small for age
IUGR	Intrauterine growth restriction
ASSHP	Australasian Society for the study of Hypertension in Pregnancy
RANZCOG	Royal Australian and New Zealand College of Obstetricians and Gynaecologists
ASUM	Australasian Society of Ultrasound in Medicine
RCOG	Royal College of Obstetricians and Gynaecologists
NICE	National Institute for Clinical Excellence
ACOG	American college of Obstetricians and Gynaecologists
ISUOG	International society of ultrasound in obstetrics and gynaecology
CTG	Cardiotocography
SFH	Symphysio Fundal Height
DFMR	Daily fetal movement record
VAST	Vibroacoustic stimulation test
ECG	Electrocardiography
USG	Ultrasonography
BPP	biophysical profile
APGAR	Criteria used to evaluate the newborn baby based on the baby's Appearance, Pulse, Grimace, Activity, Respiration
FBS	fetal blood sampling
NIRS	Near infrared spectroscopy
HbO2	oxyhaemoglobin
dHb	deoxyhaemoglobin
Hb	haemoglobin
PO2	partial pressure of oxygen in the plasma phase of arterial blood
AEDV	absent end diastolic velocity
REDV	reverse end diastolic velocity
NICU	neonatal intensive care unit
IVH	intraventricular haemorrhage

HIE	hypoxic ischaemic encephalopathy
BPD	Biparietal diameter
HC	Head circumference
AC	Abdominal circumference
FL	Femur length
EFW	estimated fetal weight
UA	Umbilical artery
UAD	Uterine artery Doppler
MCA	Middle cerebral artery
DV	Ductus venosus
IVC	Inferior vena cava
Dao	Descending aorta
PA	Pulmonary artery
DA	Ductus arteriosus
FO	Foramen ovale
SVC	Superior vena cava
IVC	Inferior vena cava
RA	Right atrium
LA	Left atrium
RV	Right ventricle
LV	Left ventricle
RI	resistance index
PI	pulsatility index
S/D Ratio	Systolic/ Diastolic ratio
S/a ratio	ratio to systolic to 'a' wave
PIV	pulsatility index of veins
PVIV	peak velocity index for veins
E/A	ratio of early to late diastolic filling
VTI	velocity time integrals
TAMx	time averaged maximum velocity
TI	thermal index
MI	mechanical index
ALARA	as low as reasonably acceptable
CPR	Cerebroplacental ratio
RI	resistance index
PI	pulsatility index
S/D Ratio	systolic/diastolic ratio

S/a ratio	ratio of systolic to 'a' wave
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E/A	ratio of early to late diastolic filling
VTI	velocity time integrals
TAMx	time averaged maximum velocity
TI	thermal index
MI	mechanical index
ALARA	As Low As Reasonably Acceptable or achievable
SV	stroke volume
CO	cardiac output
CCO	combined cardiac output
RCO	right cardiac output
LCO	left cardiac output
TR	tricuspid regurgitation
CW	continuous wave
PD	Pulsed Doppler
BMI	body mass index
PCOS	polycystic ovarian syndrome
RMC	recurrent miscarriage
IUT	intrauterine transfusion
WCH	Women’s and Children’s hospital, Adelaide
SA	South Australia

ORIGINAL CONTRIBUTIONS AND SCIENTIFIC PRESENTATIONS RELATED TO THIS THESIS

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TABLES AND FIGURES

APPENDIX: Supplementary files enclosed in the CD-ROM