

Hemodynamic Effects Of Neonatal Patent Ductus Arteriosus Shunting On Cerebral, Renal And Mesenteric Blood Flow

Thesis

*Submitted for partial fulfillment of masters degree in
pediatrics*

By

Reham Helmy Amin Helmy

M.B.B.Ch, Ain Shams University (2004)

Supervised by

Professor Doctor Safaa Shafik Imam

Professor of Pediatrics

Faculty of Medicine - Ain Shams University

Professor Doctor Hanan Eisa Mohamed

Professor of Radiodiagnosis

Faculty of Medicine - Ain Shams University

Doctor Rania Ali Hassan El-Farrash

Lecturer of Pediatrics

Faculty of Medicine - Ain Shams University

Faculty of Medicine

Ain Shams University

2010

تأثير التغيرات فى دورة المخ والكلى والأمعاء الدموية فى الأطفال المصابين بالقناة الشريانية القلبية المفتوحة

رساله

توطئة للحصول على درجه الماجستير فى الاطفال

مقدمة من

ريهام حلمي أمين حلمي سعد

بكالوريوس الطب و جراحة

كلية الطب – جامعة عين شمس (2004)

تحت إشراف

أ.د/ صفاء شفيق امام

أستاذ طب الأطفال

كلية الطب – جامعة عين شمس

أ.د/ حنان عيسى محمد

أستاذ الأشعة التشخيصية

كلية الطب – جامعة عين شمس

د/ رانيا على حسن الفراش

مدرس طب الأطفال

كلية الطب – جامعة عين شمس

كلية الطب

جامعة عين شمس

2010

To my dear Professor

Dr. Safaa Shafik Imam

There are no words that I can express how I fell about what you have done for me....

I was stuck for a long time. I knew it was time to change but didn't know how. Working with you has changed my life. Through one to one discussion sessions, and written exercises, I have made changes on the inside. I have reclaimed the pieces that I lost along the way. I am now moving forward. You have the ability to see where and how people are stuck. You provide the tools and information for the work to be done in order for change to take place.

I am very grateful for all the support, advice and wonderful guidance you have given. You have had a profound, motivating effect in every area of my life, leading me to re-evaluate many problem issues and inspiring me to realize ambitions and dreams. Your spiritual guidance has changed my whole outlook.

Thank you Dr. Safaa, for all your love and kindness. You have guided me, with such a depth of wisdom, and helped me in such a fundamental way

So I shall risk... and trust ... and believe ... and hope ... and have faith ... Thank you "Isn't enough!"

***Your's Student,
Reham***

Acknowledgment

First and foremost, thanks to GOD, to whom I related any success in achieving any work in my life.

This thesis would not have been made without the help and support of many. I would like to extend my sincere gratitude to all those who made it possible.

*My heartfelt thanks and sincere appreciation to **my dearest mother & sister** for their continuous support and loving encouragement throughout my life. Without them...I'm nothing.*

*Words can never express my deepest gratitude & sincere appreciation to **Prof. Dr Safaa Shafik**, my first promoter. Without her this project would never have been realized. Her great effort and meticulous follow every word and information throughout this text, made this work palatable. Thank you for your valuable expert scientific guidance.*

*My deep sincere & gratitude to **Prof. Dr. Hanan Eisa** my second promoter, for her faithfully motherly advices and support. Thank you for your great advices.*

*My deepest gratitude & sincere appreciation to **Dr. Rania Ali**, my third promoter, for her generous assistance with the steps and the revision of this research. Thank you for your endless patience.*

My deep thanks to all my professors and co-workers of the neonatal intensive care unit (NICU), Ain-Shams University.... My fourth promoters...

❖ ***Dr. Amany Rēda** for her kind encouragement and constructive guidance*

❖ ***Dr. Hala Gabr, Dr. Manal, Dr. Samia** for their effort and moral support.*

My deep thanks to all the Staff of Pediatrics for providing me all the facilities and hospitality in the practical performance of this research.

*Thank to all my friends and co-partners, **Ihab Foll**, **Israk Hassan** (Demerdash hospital), **Dr Waleed Salah** (Assistant lecturer community Ain Shams)....For their company and support during hard times, no matter what.*

My sincere thanks to all the individuals and parents who have participated in this research.

I extend my gratitude to the people that have contributed to the funding of this research.

Thanks

CONTENTS

	Page
List of Abbreviations	I
List of Figures	IV
List of Tables	VII
Introduction and Aim of the work.	1
Review of literature	5
Patent Ductus Arteriosus.....	5
I) Definition	5
II) Anatomy	6
II) Physiology	7
▪ The Fetal to Neonatal Circulatory Transition...	7
▪ Cerebral circulation	13
▪ Intestinal circulation	17
▪ Renal circulation	19
IV) Pathophysiology	23
▪ Changes in myocardial performance	23
▪ Changes in pulmonary circulation and lungs ..	27
▪ Changes in systemic organ perfusion	28
V) Epidemiology	28
▪ Incidence	28
▪ Risk Factors.....	29
VI) Clinical Presentation	31
▪ PDA in premature infants	31
o PDA in preterm with little or no Lung Disease	31
o PDA in Preterm Recovering from Lung Disease	37
o PDA in Preterm with Lung Disease	40

CONTENTS (Cont.)

	Page
▪ PDA in term infants	41
▪ PDA in older infants and children	43
o Infants with Small Ductus Arteriosus	43
o Infants with Moderate Ductus Arteriosus...	45
o Infants with Large Ductus Arteriosus	48
VII) Other diagnostic techniques	52
▪ Cardiac Catheterization	52
▪ Angiography	54
▪ Magnetic Resonance Imaging Or Computed Tomography Scan	55
VIII) Differential diagnosis	56
IX) Complications	59
X) Management	60
XI) Prevention	74
Patients and methods	75
Results	87
Discussion	113
Summary	134
Conclusion	139
Recommendations	140
References	141
Appendix	--
Arabic Summary	--

LIST OF ABBREVIATIONS

A	: Artery
ACA RI	: Anterior cerebral artery resistive index
AGA	: Small for gestational age
AMBU	: Ambu-bag
Ant Hge	: Antepartum Hemorrhage
Ao	: Aorta
BFVs	: Blood flow velocity
BP	: Blood pressure
BPM	: Beat per minute
BUN	: Blood urea nitrogen
BW	: Body weight,
CA	: Chorio-amnioitis
Cox-1	: Cyclo-oxygenase-1 enzyme
Cox-2	: Cyclo-oxygenase-2 enzyme
CPAP	: Continuous positive air way pressure
CS	: Cesarean section
DA	: Ductus arteriosus
Dao	: Descending aorta
DM	: Diabetes mellitus
ECG	: Electrocardiogram
Echo	: Echocardiography
EDV	: End-diastolic volume
EF	: Ejection fraction
ESV	: End-systolic volume
ETT	: Endotracheal tube
F	: Female
G	: Grams
GA	: Gestational age
GEB	: Gastrointestinal bleeding
GIT	: Gastrointestinal tract
HC	: Head circumference
Hct	: Hematocrit
HS	: Highly significant

LIST OF ABBREVIATIONS (Cont.)

hsPDA	: Hemodynamically significant PDA
Ht	: Height
HTN	: Hypertension
i.v.	: Intravenous
ICH	: Intracranial hemorrhage
IMV	: Intermittent Mandatory Ventilation
IPPV	: Intermittent positive pressure ventilation
IVC	: Inferior vena cava
IVH	: Intraventricular hemorrhage
LA	: Left atrium
LA-AO	: Left atrium to aortic root ratio
LCA	: Left carotid artery
LSCA	: Left subclavian artery.
LV	: Left ventricle
M	: Male
MAP	: Mean arterial pressure
MG	: Multi-gravidarum
MPA	: Main pulmonary artery
n	: Number
NCPAP	: Nasal Continuous positive air way pressure
NEC	: Necrotizing enterocolitis
NICU	: Neonatal intensive care unit
NS	: Non significant
NVD	: Normal vaginal delivery
OFC	: Occipito-frontal circumference
Oliguria	: Urine output <1 cc/kg/hr
PA	: Pulmonary artery
PDA	: Patent ductus arteriosus
PE	: Preeclampsia
PEEP	: Positive end expiratory pressure
PG	: Primigravida
PG	: Prostaglandins
Plat	: Platelets count ($\times 10^3/\text{mm}^3$)
PROM	: Premature rupture of membrane

LIST OF ABBREVIATIONS (Cont.)

PT	: Prothrombin time
PTN	: Pulmonary hypertension
PTT	: Partial thromboplastin time
PV	: Pulmonary vein
R	: Right
RA RI	: Renal artery resistive index
RA	: Right atrium
RCA	: Right carotid artery
RDS	: Respiratory distress syndrome
RI	: Resistive index
RPA	: Right pulmonary artery
RSCA	: Right subclavian artery
RV	: Right ventricle
RVR	: Relative vascular resistance
S	: Significant
S. Creat	: Serum Creatinine level (mg/dl)
SGA	: Small for gestational age
Sig.	: Significance
SMA RI	: Superior mesenteric artery resistive index
SVC	: Superior vena cava
TFI	: Total fluid intake.
TLC	: Total leucocytic count
TxA2	: Thromboxane A2
UTI	: Urinary tract infection
V	: Vein.
VD	: Vaginal delivery
VSD	: Ventricular septal defect
Wt	: weight

LIST OF FIGURES

Fig.	TITLE	Page
1	Schematic representation of embryonic development of PDA.	5
2	Variations in PDA configuration illustrated with the classification of Krichenko et al.	6
3	Diagram of the fetal circulation	8
4	Diagram of Cerebral circulation: showing Circle of Willis and Arteries of Brain	13
5	The splanchnic circulation	17
6	The renal circulation	19
7	Echocardiograms from two premature infants	34
8	Echocardiograms showing PDA	34
9	Doppler Echocardiograms representing PDA flow.	35
10	Ductus arteriosus demonstrated by chest roentgenogram and Angiogram.	42
11	Posterior-anterior chest roentgenograms in two children each with a patent ductus arteriosus	45
12	Angiograms of PDA.	54
13	Central circulation and closure options in Patent ductus arteriosus	68
14	Example of Gianturco coil occlusion of PDA.	71
15	Example of PDA closure with a Nit-Occlud PDA occlusion device	72
16	Example of PDA occlusion with an Amplatzer duct occluder device.	73
17	Group classification.	87
18	Mean PDA size of the patients and the control groups.	90
19	Closure of PDA after 2nd course of treatment in the 2 studied groups under treatment compares to the control group received no treatment.	91
20	The mean resistive indices of anterior cerebral, mesenteric and renal artery of patients and	94

Fig.	TITLE	Page
	controls group before treatment (day 1).	
21	The mean resistive indices of anterior cerebral, mesenteric and renal artery of patients and controls group after treatment (day 3).	94
22	Mean resistive indices of anterior cerebral, mesenteric and renal artery before and after indomethacin treatment.	95
23	Mean resistive indices of anterior cerebral, mesenteric and renal artery before and after ibuprofen treatment.	96
24	Renal function tests of patients and control groups before treatment on day 1).	105
25	M Renal function tests of patient and control groups after treatment on day (3).	105
26	M-mode echocardiogram of the aorta at the level of the valve leaflets demonstrating the measurement of the aortic and the left atrial dimension (LA/Ao:1.19; case no. 49).	108
27	Suprasternal view of an infant with PDA showing the aortic arch and its major branches. The innominate artery arises from ascending aorta, the left carotid and subclavian arteries arises from the left arch as it becomes the descending thoracic aorta. The right pulmonary artery seen in cross section beneath the aortic arch (case no. 4).	108
28	Parasternal short axis view of an infant with PDA (case no. 37)	109
29	Parasternal view showing PDA measuring 0.2 at pulmonary end and 0.6 at ampulla (case no. 60)	109
30	Doppler color flow examination from the parasternal short axis view of an infant with PDA (case no. 51)	110
31	Continous flow doppler on PDA	110

Fig.	TITLE	Page
32	Pulsed flow Doppler showing spectral analysis of anterior cerebral artery of normal RI of 0.758 (case no. 55)	111
33	Pulsed flow Doppler showing spectral analysis of right renal artery of RI 0.7 (case no. 16).	111
34	Pulsed flow Doppler showing spectral analysis of superior mesentric artery in two different patients, both showing normal spectral flow inspite of the difference in the RI range and spectral form (case no. 20 and 43)	112

LIST OF TABLES

Table	Title	Page
1	The demographic data and the anthropometric measurements of each of the 2 studied groups of patients under treatment compares with the control group	88
2	PDA size and LA/AO ratio of the 2 studied groups of patients under treatment compares to the control group	89
3	PDA size and LA/AO ratio of the 2 studied groups of patients under treatment	89
4	Patent ductus arteriosus closure after 1 st course of treatment whether indomethacin (group I) or ibuprofen (group II)	90
5	Closure of PDA after the 1 st and 2 nd course of indomethacin and ibuprofen treatment	91
6	The hemodynamic effects of PDA (Cardiac function and Sonographic data) of the 2 studied groups of patients and the control group on day 1 and day 3	92
7	The hemodynamic effects of PDA (Cardiac function and Sonographic data) of the 2 studied groups of patients after treatment; on day 3	93
8	The hemodynamic effects of PDA (Cardiac function and Sonographic data) before and after indomethacin treatment	95
9	The hemodynamic effects of PDA (cardiac function and Sonographic data) before and after ibuprofen treatment	96
10	Complications occurred in the 2 studied neonates of PDA under treatment when compared to the control group	97
11	Complications in the 2 studied groups of patients under treatment	98

Table	Title	Page
12	Correlation studies between PDA size, LA-AO ratio and MAP with the RI of ACA, SMA and RA of all the studied neonates	99
13	Association between ductal steal (LA-AO ratio and MAP) and the resistive indices among neonates who developed complications	100
14	Regression model to study effect of ACA RI as a risk of Intracranial Hemorrhage	101
15	Regression model to study effect of SMA RI as a risk of NEC, GIT bleeding and GIT Perforation.	101
16	Regression model to study effect of RA RI as a risk of Oliguria	102
17	Laboratory data and urine output of the control group and the 2 studied groups of patient before and after treatment	103
18	Laboratory data and urine output of the neonates of both groups under treatment	104
19	Laboratory data and urine output of the neonates before and after indomethacin treatment	106
20	Laboratory data and urine output of the neonates before and after ibuprofen treatment	107