



Influence of Ventilation Modes on Cerebral Blood Flow Measurements of Intra- and Extracranial Arteries in Preterm Infants with Respiratory Distress Syndrome

**Thesis Submitted for partial fulfillment of MD degree
in Pediatrics**

By

Yasmin Aly Farid Mohamed Aly

M.B.B.Ch. (2006) M.Sc (2011)

Faculty of Medicine, Ain Shams University

Supervised by

Prof. Mohamed Sami El Shimi

Professor of Pediatrics

Faculty of medicine - Ain Shams University

Prof. Nehal Mohamed El Raggal

Professor of Pediatrics

Faculty of medicine - Ain Shams University

Prof. Hanan Mohamed Issa

Professor of Radiodiagnosis

Faculty of medicine - Ain Shams University

Dr. Ghada Ibrahim Gad

Assistant Professor of Pediatrics

Faculty of Medicine - Ain Shams University

Dr. Maha Mohamed Hassan

Assistant Professor of Pediatrics

Faculty of Medicine - Ain Shams University

**Faculty of Medicine
Ain Shams University**

2015



**تأثير طرق التنفس الصناعى على تدفق الدم فى الشرايين
المخية داخل وخارج الجمجمة فى حديثي الولادة المبتسرين
المصابين بمتلازمة صعوبة التنفس**

رسالة توطئة للحصول على درجة الدكتوراة فى طب الأطفال

مقدمة من

**الطبيبة / ياسمين على فريد محمد على
بكالوريوس الطب والجراحة - جامعة عين شمس (٢٠٠٦)
ماجستير طب الأطفال ٢٠١١**

تحت اشراف

الأستاذ الدكتور/ محمد سامى الشيمى

أستاذ طب الأطفال

كلية الطب - جامعة عين شمس

الأستاذة الدكتورة/ نهال محمد الرجال

أستاذ طب الأطفال

كلية الطب - جامعة عين شمس

الأستاذة الدكتورة / حنان محمد عيسى

أستاذ الأشعة التشخيصية

كلية الطب - جامعة عين شمس

الأستاذة الدكتورة / غادة إبراهيم جاد

أستاذ مساعد طب الأطفال

كلية الطب - جامعة عين شمس

الأستاذة الدكتورة / مها محمد حسن

أستاذ مساعد طب الأطفال

كلية الطب - جامعة عين شمس

كلية الطب

جامعة عين شمس

۲۰۱۵

Acknowledgment

First and foremost thanks to **ALLAH**, the Most Gracious and the Most Merciful for all the blessings He has given me.

I would like to acknowledge my senior supervisor, **Professor, Mohamed Sami El Shimi** Professor of Pediatrics, Ain Shams University, for giving me the honor to work under his supervision, with encouragement through this work.

Furthermore, I would also like to thank **Professor, Nehal Mohamed El Raggal** Professor of Pediatrics, Ain Shams University, for taking a lot of her time to precisely guide and review my work, trying to make it as complete and comprehensive as possible.

I would also like to thank **Professor, Hanan Mohamed Issa** Professor of Radiodiagnosis, Ain Shams University for her careful and kind supervision of this thesis.

In addition, I would like to express my gratitude to **Assistant Professor, Ghada Ibrahim Gad** Assistant Professor of Pediatrics, Ain Shams University and **Assistant Professor, Maha Mohamed Hassan** Assistant Professor of Pediatrics, Ain Shams University, for their efforts in producing this work.

I would like to thank **Dr, Amany Reda** Consultant of Neonatology Ain Shams University for her persistent support and encouragement that helped me to continue this work

Last but not least I would like to thank my family and colleagues for their indispensable help and support and all the patients in our unit for their cooperation. May Allah bless them all.

Yasmin Aly Farid

LIST OF CONTENTS

	Page
List of contents	i
List of abbreviations	ii
List of figures	ix
List of tables	xiii
Abstract	xv
Introduction	1
Aim of The Work	4
Review of literature	5
Respiratory distress syndrome	5
The mechanical ventilation	32
Cerebral hemodynamics in newborn	50
Patients and methods	85
Results	100
Discussion	139
Conclusion	157
Recommendations	159
Summary	160
References	165
Arabic summary	-

List of Abbreviations

List of Abbreviations

AC	Assist control
ACA	Anterior cerebral artery
ACOM	Anterior communicating
ANOVA	One-way analysis of variance
ASL-MRI	Arterial spin labeled perfusion magnetic resonance imaging
ATP	Adenosine tri-phosphate
BPD	Bronchopulmonary dysplasia
BUN	Blood urea nitrogen
BW	Birth weight
CBC	Complete blood picture
CBF	Cerebral blood flow
CBFV	Cerebral blood flow velocity
CBG	Capillary blood gases
CBV	Cerebral blood volume
CCHD	Cyanotic congenital heart disease
CDFI	Color Doppler flow imaging
CDI	Color Doppler imaging
CLD	Chronic lung disease
CMV	Conventional Mechanical Ventilation
CO ₂	Carbon-Dioxide
COE	Cerebral oxygen extraction
CPAP	Continuous positive airway pressure
Cr	Creatinine
CRP	C- reactive protein
CS	Caesarean section
CTA	Carotid abnormalities
CTS	Closed Tracheal suctioning
CUS	Cranial ultrasound
CXR	Chest X-ray

List of Abbreviations

DM	Diabetes Mellitus
DSA	Digital subtraction angiography
Edi	Electrical activity of the diaphragm
EDV	End diastolic velocity
ELBW	Extremely low birth weight
FiO ₂	Fraction of inspired oxygen
FLM	Fetal lung maturity
GA	Gestational age
GLH	Germinal layer hemorrhage
GM	Germinal matrix
GSH	Gray-scale histogram
HCO ₃	Bicarbonate
HF	High Frequency
HFFI	High frequency flow interrupter
HFJV	High-frequency jet ventilation
HFOV	High Frequency Oscillator Ventilator
HFV	High frequency ventilation
HHFNC	Heated, humidified and high-flow nasal cannula
HIE	Hyoxic-ischemic encephalopathy
HMD	Hyaline membrane disease
HPI	Hemorrhagic parenchymal infarction
ICA	Internal carotid artery
ICH	Intracranial hemorrhage
IMV	Intermittent mandatory ventilation
IVH	Intraventricular hemorrhage
L/S	Lecithin/Sphingomyelin
LBC	lamellar body count
LVO	Left ventricular output
MABP	Mean arterial blood pressure
MAP	Mean airway pressure

List of Abbreviations

MCA	Middle cerebral artery
MRI	Magnetic resonance imaging
MV	Mean velocity
NAVA	Neurally adjusted ventilator assist
NCPAP	Nasal continuous positive airway pressure
NEC	Necrotizing enterocolitis
NGT	Nasogastric tube
NICU	Neonatal intensive care units
NIH	National Institute of Health
NIPPV	Noninvasive nasal intermittent positive pressure ventilation
NIR	Near infrared
NIRS	Near infrared spectroscopy
NPO	Nil per os
NVD	Normal vaginal delivery
OFC	Occipito frontal circumference
OTS	Open tracheal suctioning
PaCO ₂	Arterial carbon dioxide tension
PaO ₂	Arterial oxygen tension
PAV	Proportional assist ventilation
PCA	Posterior cerebral artery
PCOM	Posterior communicating
PCV	Packed cell volume
PDA	Patent ductus arteriosus
PE	Pre-eclampsia
PEEP	Positive end expiratory pressure
PET	Positron emission-tomography
PFO	Patent foramen ovale
PGE ₂	Prostaglandin E2
PI	Pulsatility index
PIP	Peak inspiratory pressure

List of Abbreviations

PLV	Pressure - Limited Ventilation
PMA	Postmenstrual age
PPHN	Persistent pulmonary hypertension
PROM	Premature rupture of membrane
PRVC	Pressure- regulated volume control
PSV	Pressure support ventilation
PSV	Peak systolic velocity
PVE	Periventricular echodensities
PVHI	Periventricular venous hemorrhagic infarction
PVL	Periventricular leukomalacia
RBS	Random blood sugar
RCT	Randomized control trial
RDS	Respiratory distress syndrome
RI	Resistive Index
ROP	Retinopathy of prematurity
RR	Respiratory rate
SctO ₂	Mixed venous saturation
SIMV	Synchronized intermittent mandatory ventilation
SP	Surfactant-specific proteins
SpO ₂	O ₂ saturation by pulse oximetry
SVC	Superior vena cava
TAm _{ax}	Time average maximum velocities
TCPL	Time-cycled pressure limited
Ti	Inspiratory time
TTN	Transient tachypnea of the newborn
UOP	Urinary output
US	Ultrasound
UTI	Urinary tract infection
V/Q	Ventilation perfusion
VEGF	vascular endothelial growth factor

List of Abbreviations

VG	Volume guarantee
VILI	Ventilator-induced lung injury
VLBW	Very low birth weight
VT	Volume-targeted
VTV	Volume-targeted ventilation
WBC	white blood cells
WM	White matter
Δ CBV	Change in cerebral blood volume

LIST OF FIGURES

Fig. No.	Title	Page
1	Schematic outlines of the pathology of respiratory distress syndrome (RDS)	15
2	Microscopic appearance of lungs of an infant with respiratory distress syndrome. Hematoxylin and eosin stain shows hyaline membranes (pink areas)	16
3	Radiological grading of RDS	21
4	Pressure waveform for both volume- and pressure-limited breaths	43
5	Heated, Humidified, High-Flow Nasal Cannula. Optiflow TM Junior Nasal Cannula	49
6	Circle of Willis	55
7	Transcranial US showing grade 1 intracranial hemorraghe	71
8	Transcranial US showing grade 2 intracranial hemorraghe	72
9	Transcranial US showing grade 3 intracranial hemorraghe	72
10	Transcranial US showing grade 4 intracranial hemorraghe	73
11	Transcranial US showing PVL grade 1	75
12	Transcranial US showing PVL grade 2	75
13	Transcranial US showing PVL grade 3	76
14	Transcranial US showing PVL grade 4	76
15	Positions of the near-infrared spectroscopy (NIRS) sensors	84
16	New Ballard scoring	90
17	Mean hemoglobin level in the four study groups. Group 1, SIMV; Group 2; HFV; Group 3, CPAP;	110

List of figures

Fig. No.	Title	Page
	Group 4, Control	
18	Mean hematocrit in the four study groups. Group 1, SIMV; Group 2; HFV; Group 3, CPAP; Group 4, Control	110
19	Mean pH in the four study groups. Group 1, SIMV; Group 2; HFV; Group 3, CPAP; Group 4, Control	112
20	Mean PaCO ₂ in the four study groups. Group 1, SIMV; Group 2; HFV; Group 3, CPAP; Group 4, Control	112
21	Mean HCO ₃ ⁻ concentration in the four study groups. Group 1, SIMV; Group 2; HFV; Group 3, CPAP; Group 4, Control	113
22	Mean SpO ₂ in the four study groups. Group 1, SIMV; Group 2; HFV; Group 3, CPAP; Group 4, Control	113
23	Average PI as measured from the ACA, MCA, or ICA in the four study groups. Group 1, SIMV; Group 2; HFV; Group 3, CPAP; Group 4, Control	125
24	Average RI as measured from the ACA, MCA, or ICA in the four study groups. Group 1, SIMV; Group 2; HFV; Group 3, CPAP; Group 4, Control	126
25	Average T _{Amax} as measured from the ACA, MCA, or ICA in the four study groups. Group 1, SIMV; Group 2; HFV; Group 3, CPAP; Group 4,	127
26	: Neck US Cross section view in preterm neonate neck	134
27	Transcranial US view in preterm neonate sagittal and temporal view	134
28	Neck US: Cross section view in preterm neonate on HFV showing ICA Doppler indices	135

List of Figures

Fig. No.	Title	Page
29	Transcranial US in preterm neonate on HFV sagittal and temporal views showing ACAand MCA Doppler indices	135
30	Neck US: Cross section view in preterm neonate on SIMV showing ICA Doppler indices	136
31	Transcranial US in preterm neonate on SIMV sagittal and temporal views showing ACAand MCA Doppler indices	136
32	Neck US: Cross section view in preterm neonate on CPAP showing ICA Doppler indices	137
33	Transcranial US in preterm neonate on CPAP sagittal and temporal views showing ACAand MCA Doppler indices	137
34	Transcranial US in preterm neonate not ventilated (control) sagittal and temporal views showing ACAand MCA Doppler indices	136

LIST OF TABLES

Table. No.	Title	Page
1	The advantages and disadvantages of the pressure-limited TCPL ventilators	40
2	Showing differences between VTV and PLV	42
3	Down's score	86
4	Patients' characteristics in the four study groups	101
5	Neonatal biometric measures in the four study groups	102
6	Obstetric history of the mothers in the four study groups	103
7	Average temperature, mean arterial blood pressure, and urine output in the four study groups	105
8	Relevant clinical findings in the four study groups	106
9	Results of laboratory work-up in the four study groups	108
10	Average values of Capillary blood gases analysis in the four study groups	111
11	RDS grade by chest roentgenography and relevant echocardiographic and transcranial ultrasound findings in the four study groups	114
12	Feeding route and type of milk in the four study groups	116
13	Need for inotropes, vasopressors and	118