A Study of Oxidative DNA Damage, Lipid Oxidation and Antioxidant Activity in Neonates with Respiratory Distress Syndrome

Thesis

Submitted for partial fulfillment of Master degree in Pediatrics

By

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M.B. B.CH. (2010)

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2016

سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, I feel always indebted to **ALLAH**, *the Most Kind and Most Merciful.*

I wish to thank ***Professor Zeinab Anwar Elkabany,*** *Professor of Pediatrics, Faculty of Medicine, Ain Shams University, who offered me constructive ideas and guidance. Her help and support were the major factor for completion of the present work.*

I would like to express my deepest thanks and gratitude to ***Doctor Dina Mohamed M Shinkar,*** *Lecturer of Pediatrics, Faculty of Medicine- Ain Shams University, I am indebted to her for always being there to help, share and solve difficulties met in the present work. I really appreciate her being so generous with her effort, time and experience.*

My sincere appreciation to ***Professor Dr. Ahmed Shafik Nada,*** *Professor of Physiology, Radiation center for research and technology., for his valuable suggestions, good support and unlimited help during this work.*

Also, it is my great pleasure to express my deepest gratitude to ***Doctor Eman Abd El-Rahman Ismail,*** *Consultant of Clinical Pathology, Faculty of Medicine, Ain-Shams University and* ***Doctor Rania Ali Hassan El-Farrash,*** *Assistant Professor of Pediatrics, Faculty of Medicine, Ain Shams University, for the effort and time they spent.*

Lastly, I would like to thank my family for their support and great help to accomplish this work.

Saleh Arafa Gaballah

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List of Abbreviations

Abb.	Full term
AAP	*American Academy of Pediatrics*
AOPP	*Advanced Oxidation Protein Products*
ATP	*Adenosine triphosphate*
BPD	*Bronchopulmonary dysplasia*
CAT	*Catalase*
CBC	*Complete blood count*
CDH	*Congenital Diaphragmatic Hernia*
CH	*Cholesterol*
CO2	*Carbon dioxide*
CoQ10	*Coenzyme Q10*
CPAP	*Continuous positive airway pressure*
CRP	*C-Reactive Protein*
Cu	*Cupper*
DA	*Ductus arteriosus*
dL	*Deciliter*
DNA	*Deoxyribonucleic acid*
ELBW	*Extreme low birth weight*
ELISA	*Enzyme-linked immunosorbent assay*
FR	*Free radical*
FRC	*Functional Residual Capacity*
gm	*gram*
GPX	*Glutalthione peroxidase*
GPx	*Glutathione peroxidase*
GSH	*Reduced glutathvone*
GSSG	*Oxidized Glutathione*
GV	*Guaranteed volume*
H_2O_2	*Hydrogen peroxide*
Hb	*Haemoglobin*
HFOV	*High frequency oscillatory ventilation*

List of Abbreviations (Cont...)

Abb.	Full term
HMD	*Hyaline membrane disease*
HO•	*Hydroperoxyl*
HOCl	*Hypochlorous acid*
HPLC	*High-performance liquid chromatography*
IL-6	*Interleukin -6*
IL-8	*Interleukin-8*
IPPV	*Intermittent positive pressure ventilation*
IV	*Intravenous*
IVH	*Intraventricular hemorrhage*
Kg	*Kilogram*
LBW	*Low birth weight*
LDL	*Low-density lipoproteins*
MAS	*Meconium aspiration syndrome*
MDA	*Malondialdehyde*
ml	*Milliliter*
mmol/l	*Millimole/liter*
MV	*Mechanical ventilation*
NADH	*Nicotinamide adenine dinucleotide hydride*
NADPH	*nicotinamide adenine dinucleotide hydridephosphate*
NEC	*Necrotizing enterocolitis*
ng	*Nanogram*
NICU	*Neonatal intensive care unit*
NO	*Nitric oxide*
NO+	*Nitrosil*
NO_2•	*Free radical nitric dioxide*
O_2	*Singlet oxygen*
O_2•$^-$	*Superoxide anion*

List of Abbreviations (Cont...)

Abb.	Full term
O_3	Ozone
OD	Optical density
OFC	Occipitofrontal Circumference
OH•	Hydroxyl radical
P-A view	Posteroanterior view
PDA	Patent ductus arteriosus
PEEP	Positive end expiratory pressure
Pg	Picogram
PH	Power of hydrogen
PLs	Phospholipids
PROM	Premature rupture of membrane
PUFAs	Polyunsaturated fatty acids
PVL	Periventricular leukomalacia
RDS	Respiratory distress syndrome
RNS	Reactive nitrogen species
RO•	Alkoxyl
ROO•	Peroxyl
ROOH	Hydroperoxide
ROP	Retinopathy of prematurity
ROS	Reactive oxygen species
SOD	Superoxide dismutase
STORCH	Syphilis, Toxoplasmosis, Other agents, Rubella, Cytomegalovirus, Herpes simplex.
TAC	Total antioxidant capacity
TBA	Thiobarbituric acid
TBARS	Thiobarbituric Acid Reactive Substances
TNF-a	Tumor necrosis factor alpha

List of Abbreviations (Cont...)

Abb.	Full term
TPN	*Total parenteral nutrition*
TTN	*Transient tachypnea of newborn*
UK	*United Kingdom*
umol	*Micromole*
USA	*United States of America*
VLBW	*Very low birth weight*
Wk	*Weak*
Zn	*Zinc*
μg	*Microgram*
μl	*Microliter*
°C	*Celsius*
$1O_2$	*Singlet oxygen*
8-OHdG	*8-Hydroxy-desoxyguanosine*

ABSTRACT

Background: Preterm neonates with respiratory distress syndrome are at high risk of oxidative stress and they are very susceptible to free radical oxidative damage. In nuclear and mitochondrial DNA, 8-hydroxy-2' -deoxyguanosine (8-OHdG) is one of the predominant forms of free radical-induced oxidative lesions, and has therefore been widely used as a biomarker for oxidative stress. **Aim:** To assess oxidant-antioxidant balance in preterm neonates with RDS as well as the role of lipid peroxidation and oxidative DNA damage in the development of neonatal RDS. **Methods:** the study included 80 preterm neonates less than 34 weeks of gestational age; 40 had RDS and 40 without RDS enrolled as controls. All newborns were subjected to detailed medical history, thorough clinical examination. The degree of respiratory distress was assessed according to Down score. Respiratory distress grade was determined according to chest X ray. Laboratory investigations included complete blood count, random blood sugar, arterial blood gases, total antioxidant capacity (TAC), malondialdehyde (MDA) as an index of lipid peroxiadation, 8-OHdG levels by ELISA and trace elements (copper, zinc, calcium, magnesium and iron). **Results:** Neonates with RDS had lower birth weight and gestational age in comparison to control group. There was no significant difference in maternal age, parity, mode of delivery, PROM, maternal disease and steroid intake between mothers of neonates with RDS and control group. TAC, MDA and 8-OHdG were significantly high compared with control group. No significant difference was found as regard trace elements (zinc, calcium, magnesium, iron) except for copper which was significantly lower in neonates with RDS. TAC was significantly lower among neonates with RDS at day 3 compared with day 1 while MDA and AOPPs, 8-OHdG were significantly higher at day 3. 8-OHdG levels at day 1 and day 3 were significantly higher in neonates in RD grade 4 compared with those in grades 2 or 3 and among patients on mechanical ventilation as well as those with positive CRP values. 8-OHdG levels at day 3 were also significant in relation to mortality. 8-OHdG levels at days 1 and 3 are negatively correlated to gestational age, birth weight, OFC and PH. There was significant positive correlation with each of maternal age, duration of ventilation and duration of

hospitalization as well as MDA and CO2. Multivariable regression model showed that maternal age, gestational age, birth weight, OFC, duration of ventilation, duration of hospitalization and MDA were the significant independent variables related to elevated 8-OHdG levels at day 1 and 3. **Conclusions:** Oxidative stress is induced in neonates with RDS which is manifested as increased lipid peroxidation and oxidative DNA damage. This is accompanied by alterations in the antioxidant defense status which may also play a role in the pathogenesis of RDS. AOPPs could be considered a reliable novel marker for oxidative stress among neonates with RDS. It is necessary to limiting exposure of the preterm infants to oxygen at high percentage and to high positive pressure during resuscitation and subsequent ventilation.

Keywords: Oxidative DNA Damage, Lipid Oxidation, Antioxidant Activity and Respiratory Distress Syndrome