# Study on L-Arginine/Nitric Oxide Pathway and Endothelin-1 in Neonates with Respiratory Distress Syndrome: Correlation with Oxygenation Index and Development of Broncopulmonary Dysplasia

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# دراسة على مسار اللام أرجينين- أوكسيد النيتريك و الإندوثيلين-١ في حديثىالولادة المصابين بمتلازمة صعوبة التنفس : و علاقتهما بمؤشر الأكسجة و حدوث عسر التقويم الشعبى التنفسى


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# Abstract

Respiratory distress syndrome and its sequel Broncopulmonary dysplesia remain an important cause of morbidity and mortality in neonates, in spite the great progress and advanced management modalities.

In our study, the levels of L-arginine and endothelin-1 were measured in the serum of preterm neonates with respiratory distress syndrome in the 1st day of life and were compared with preterm neonates without RDS as a control group.

Serum L-arginine in the 1st day of life was significantly lower in the neonates with RDS than the control group. Serum endothelin-1 was significantly higher in the neonates with RDS compared with the control group.

Both L-arginine and endothelin-1 levels showed no statistical difference as regard gender, mode of delivery nor the administration of antenatal steroids.

A significant negative correlation was found between L-arginine and birth weight in the neonates with RDS while a non significant positive correlation was reported between L-arginine and the severity of the disease measured by oxygenation index.

On the other hand, Endothelin-1 has a non significant positive correlation with both gestational age and Oxygenation Index and a significant positive correlation with the birth weight.

Endothelin-1 was found to be significantly higher in the BPD group than the survivor group in the studied cases from day one of life.

In conclusion; further studies are recommended to use L-arginine as a supplementation therapy for RDS patients instead of using Inhaled Nitric Oxide therapy with its limitation.

Moreover, serum endothelin-1 level can be used as an early indicator for BPD.



Key words: L-arginine, Endothelin-1, Preterm, Oxygenation index.

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# List of Abbreviations

| | |
|---|---|
| ABG | Arterial blood gases |
| AOE | Antioxidant enzyme |
| ARDS | Adult respiratory distress syndrome |
| BPD | Bronchopulmonary dysplasia |
| cGMP | Cyclic guanisine monophosphate |
| CBC | Complete blood count |
| CLD | Chronic lung disease |
| CMV | Control mode ventilation |
| CPAP | Continuous positive air way pressure |
| ED | Endothelium dysfunction |
| EDRF | Endothelium relaxing factor |
| ET-1 | Endotheline-1 |
| GA | Gestational age |
| Hb | Hemoglobin |
| HFV | High frequency ventilation |
| HMD | Hyaline membrane disease |
| HR | Heart rate |
| INO | Inhaled nitric oxide |
| IL | Interleukin |
| IUGR | Intra uterine growth retardation |
| IVH | Intraventricullar haemorrhage |
| L/S | Lecithinlsphingomyelin |

| | |
|---|---|
| LBC | Lamellar body count |
| LT | leukotrienes |
| MAP | Mean airway pressure |
| MAS | Meconium aspiration syndrome |
| MRNA | Messenger ribonucleic acid |
| NEC | Necrotizing enterocolitis |
| NICU | Neonatal intensive care unit |
| NO | Nitric oxide |
| NOS | Nitric oxide synthesae |
| O2 | Oxygen |
| OI | Oxygenation index |
| PC | Phosphotidylcholine |
| PCo2 | Arterial partial pressure of carbon dioxide |
| PCR | polymerase chain reaction |
| PDA | patent ductus arteriosius |
| PECAM | Platelets endothelium adhesion Molecule |
| PG | Phosphatidylglycerol |
| PI | Phosphatididylinositol |
| PIE | pulmonary interstitial emphysema |
| PLTs | Platelets |
| PMA | Post menstrual age |
| Po2 | Arterial partial pressure of oxygen |
| PPHTN | Persistent pulmonary hypertension of the Newborn |
| PPV | Positive pressure ventilation |
| PT | Preterm |
| PVH | Per ventricular haemorrhage |
| RBCs | Red blood cells |
| RDS | Respiratory distress syndrome |
| SNIPP | Synchronized nasal intermittent positive pressure ventilation |
| SOD | Super oxide dismutase |
| TA | Tracheal aspirate |
| TGFα | Transforming growth factor α |
| TLC | Thin layer chromatography |

| | |
|---|---|
| TPN | Total parental nutrition |
| TTN | Transient tachypnea of newborn |
| TV | Tidal volume |
| VLBW | Very low birth Weight |
| VR | Vascular resistance |
| WBCs | White blood cells |
| WT | weight |

# Introduction

Preterm birth is the largest single cause of perinatal morbidity and mortality in infants without major anomalies. Complications of prematurity account for greater than 70% of fetal and neonatal deaths annually and more than one third of health care expenditures during the first year of life ***(Martin et al., 2003).***

Respiratory distress syndrome (RDS) and its sequel broncopulmonary dysplasia continue to be major contributor of morbidity and mortality in preterm infants, as it is the most common cause of respiratory failure in neonates ***(Jobe and Bancalari, 2001) .***

Progress in neonatal intensive care unit (NICU) is closely related to improvement in the management of respiratory failure in preterm infants ***(Ammari et al., 2006).***

L-arginine is the substrate for the synthesis of Nitric oxide (NO), a potent vasodilator in systemic, gastrointestinal and pulmonary circulation ***(Meng-Cheng et al., 2006).***

***Colagrande et al., (2006)*** have proved that NO plays a critical role in the regulation of normal blood pressure,

vascular resistance, preservation of endothelial function and protection against ischemic reperfusion damage**.**

***Canpolat et al., (2005)*** have demonstrated an early decrease in blood L- arginine level in neonates with RDS. Moreover, this study showed that the level of L-arginine is inversely related to the severity of RDS, as measured by oxygenation index**.**

***Niu et al., (2005)*** reported that ET-1 can be used as a marker for pulmonary endothelial injury. They documented an increase of plasma ET-1 concentrations in infants with RDS. Moreover, a significant increase in ET-1 concentration in the tracheal aspiration of infants who developed late broncopulmonary dysplasia was documented from day one of life**.**

# Aim of Work

The present study was conducted to:

- Investigate the relationship between the level of serum L-arginine in preterm neonates and the severity of respiratory distress syndrome as measured by oxygenation index.
- Investigate the relationship between serum L-arginine level and the outcome of RDS in preterm neonates.
- Investigate the relationship between the level of serum Endothelin-1 in preterm neonates and the severity of respiratory distress syndrome as measured by oxygenation index.
- Verify the use of serum Endothelin-1as a marker for early prediction of BPD.