IS-038

## OXIDATIVE STRESS RELATED DISEASES IN THE FETUS AND THE NEWBORN

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10.1136/archdischild-2014-307384.38

Many evidences have correlated neonatal diseases with oxidative stress (OS) caused by the harmful effect of free radicals (FRs). FRs are reactive oxygen and nitrogen species formed as a result of normal cellular metabolism and have many roles in cell signalling pathways. FRs can be also produced in the course of hypoxia, ischemia, ischemia-reperfusion, hyperoxia, inflammation and as consequence of exposition to many endogenous and exogenous oxidising agents. OS injury occurs when tissues, cells and biomolecules undergo an excessive exposition to oxidising agents, both endogenous (substances produced by inflammatory cells) and exogenous (environmental toxins). The FRs production exceeds antioxidant defences and OS occurs. OS is on the basis of several human pathologies such as stroke, hypertension, diabetes, rheumatic diseases, multiple sclerosis, neurodegenerative diseases and cancer. In Neonatology, OS is involved in the development of several FR-related diseases (FRRD) such as oxidative hemolysis, intraventricular haemorrhage, necrotizing enterocolitis, retinopathy of prematurity, chronic lung disease, renal failure. The damaging effect of FRs in perinatal period may be demonstrated by measuring OS biochemical markers in amniotic fluid and in cord blood. Intrauterine hypoxia induces OS in pregnancies with fetal growth restriction (FGR). Prostanoids concentration, actually considered as the best biomarker of OS, are particularly elevated in amniotic fluid of pregnancies with Down syndrome affected fetuses and in cord blood of newborns from maternal chorioamnionitis. They also have a significant predictive value to early detect pregnancies at high risk of premature rupture of membranes, fetuses suffering FGR and newborns who will develop the FRRD.

IS-039

## ANTIOXIDANT STRATEGIES: WHERE ARE WE NOW?

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10.1136/archdischild-2014-307384.39

Part of asphyxia-related brain damage occurs upon reoxygenation. Renewed availability of oxygen activate biochemical pathways and neuronal cell death. Important pathways are: 1) Calcium-induced formation of neurotransmitters; 2) formation of (pro-) radicals; 3) activation of inflammation; 4) induction of apoptosis; 5) depletion of growth factors. Four important sources of free radicals are: 1) Nitric oxide (NO)related formation of peroxynitrite. It is reported that selective iNOS/eNOS inhibitor 2-iminobiotin induced neuroprotection after asfyxia in animal models. 2) Pro-radicals, such as non proteinbound-iron (NPBI), lead to formation of hydroxyl free radicals. NPBI chelation with deferoxamine, which has also a stabilising effect on HIF1-alpha and stimulates trophic factors, showed encouraging results in experimental models. 3) Formation of superoxide radical by metabolisation by xanthine-oxidase (XO) can be blocked by XO-inhibitors such as allopurinol. 4) Metabolisation of arachidonic acid to prostaglandin leading to superoxide can be blocked by cyclo-oxygenase inhibitors. Since XO-derived superoxide occurs upon reoxygenation after asphyxia, a trial with allopurinol to the mother with signs of perinatal fetal hypoxia has been started. Activation of inflammatory factors after asphyxia is recognised to be related to post-aphyxial brain damage.

Rather than monotherapy directed to one pathway, a combination of drugs intervening in various pathways in relation with the time-profile of these pathways, might achieve optimal reduction of reperfusion injury.

## Long-term Outcome After Critical Illness: The Need for Appropriate Care Continues After Discharge from the ICU

IS-040

CRITICAL ILLNESS: EARLY RECOGNITION OF STRESS AND ITS LONG-TERM IMPACT ON THE CHILD AND FAMILY IS IMPORTANT TO OFFER THE RIGHT INTERVENTIONS

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10.1136/archdischild-2014-307384.40

Children and their parents who are exposed to medical lifethreat due to illness or injury are at risk for developing symptoms of posttraumatic stress of psychosocial problems which should be monitored during follow up and treated. Several initiatives which can be used during follow-up using the internet are presented.

A set of material that could be used is the Paediatric Traumatic Stress Toolkit (http://www.nctsnet.org/). This toolkit is created by the National Child Traumatic Stress Network (NCTSN) and comprises both practical tools and training materials to health care professionals to enhance trauma-informed practice. After considering the A-B-C's (airway-breathing-circulation), professionals should consider the D-E-F's (distress-emotional support-family) we modified the material for Dutch families and health care professionals www.nahetziekenhuis.nl and evaluated this material.

Health Related Quality of Life (HRQOL) questionnaires are increasingly used in clinical practice. These Patient Reported Outcomes (PROs) are provided to the paediatrician to facilitate communication with patients during a consultation. Currently, the use of PROs in daily clinical practice is very time consuming and often has logistical problems. The use of a web-based programme can overcome these problems and contributes to an improved use of PROs in clinical practice. We therefore developed an easily accessible website (www.hetklikt.nu) for outpatient treatment and a training programme for paediatricians to maximise the effectiveness and the practical use of PROs (for demonstration: username PRO and password: KLIK).

## Neonatal Extracorporeal Membrane Oxygenation, Risk Factors for the Brain and Long Term Neurological Outcome

IS-041

NEONATAL ECMO AND RISK FACTORS FOR THE BRAIN

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10.1136/archdischild-2014-307384.41

Background Neonatal extracorporeal membrane oxygenation (ECMO) is a lifesaving therapeutic approach in newborns suffering from severe, but potentially reversible, severe respiratory