Impact of fetal lead exposure on cord blood Insulin like growth factor-I levels and neonatal anthropometric parameters

Thesis

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List of Abbreviations

AAP ..... American Academy of Pediatrics

BHSD2..... 11beta-hydroxysteroid dehydrogenase type 2

BLLs ..... Blood lead levels

BMI..... Body mass index

BNF..... Brain-derived neurotropic factor

BWT ..... Birth weight

CDC ..... Center for Disease Control and Prevention

CS ……. Cesarean section

DHEA ..... Dehydroepiandrosteron

EGF ..... Epidermal growth factor

EPA..... Environmental Protection Agency

FGF..... Fibroblast growth factor

GA..... Gestational age

GH ..... Growth Hormone

HC..... Head circumference

HCG..... Human chorionic gonadotropin

HGF ..... Hematopoietic growth factor

IGFBP ..... Insulin growth factor binding proteins

IGF-I..... Insulin like Growth Factor I

IGF-II ..... Insulin like Growth Factor II

IGF-II ..... Insulin-like growth factor

IGF-IR..... IGF-I receptor

IGFs ..... Insulin like Growth Factors

IUGR ..... Intrauterine growth restriction

KDa..... Kilo Dalton

KXRF ..... In vivo X-ray fluorescence

LGA ..... Large for gestational age

MAC ..... Mid-arm circumference

MBLLs ..... Maternal blood lead levels

NGF ..... Nerve growth factor

NT3 ..... Neurotropin 3

NVD…… Normal vaginal delivery

Pb …….. Lead

PDGF ..... Platelet-derived growth factor

PTHrP ..... Parathyroid hormone–related protein

SGA ..... Small for gestational age

TGF-α ..... Transforming growth factor α

WHO ..... World Health Organization

Introduction

Lead has been documented to impact a variety of health outcomes including, neurodevelopment ***(Bellinger, 2008)***, cardiovascular disease ***(Navas-Acien et al., 2007)***, neurodegenerative diseases and cognitive decline ***(Weisskopf et al., 2004)***, immune system impairment ***(Dietert* and *Piepenbrink, 2006)***, renal system function, and adverse birth outcomes ***(Weaver et al., 2009)***. Many of these health impacts have been shown to occur at increasingly lower exposures suggesting that there is no 'safe' threshold to lead exposure ***(Cantonwine et al., 2009)***.

The principle routes of external exposure to and intake of lead usually occur through ingestion and inhalation ***(Hu et al., 2007).*** Lead exposure may affect the fetus in a number of detrimental ways. Because lead is readily transmitted from mother to fetus via the placenta, maternal exposure must be reduced to protect the fetus ***(Atabek et al., 2007).***

Insulin-like growth factor (IGF)-1 is a primary mediator of the effects of growth hormone (GH). IGF-1 stimulates systemic body growth, and has growth-promoting effects on almost every cell in the body, especially skeletal muscle, cartilage, bone, liver, kidney, nerves, skin, hematopoietic cell,

and lungs, IGF-1 also regulate cell growth and development ***(Delafontaine, 2005).***

High-level occupational lead exposures have been associated with adverse pregnancy outcomes, including intrauterine growth restriction and congenital anomalies ***(Gardella, 2001)***. A significant relationship was found between birth weight and lead burden in newborns **(*Atabek et al., 200*7*)***.

Aim of the Work

The present work aims at studying the impact of fetal lead exposure as reflected by maternal and cord blood lead levels, on cord blood IGF-1 concentration and anthropometric measures at birth in term neonates.

Sources and Exposure To Lead

Lead (pb) is one of the major metals that has gained considerable importance as a potent environmental pollutant ***(Flora et al., 2008).***

Although tremendous reductions in lead exposure to the general population have been achieved in most of North America and Europe, worldwide adults and children continue to be exposed to elevated levels through a variety of media and informal sector occupations ***(Meyer et al., 2008).***

The environment is still the most common source of exposure to lead, despite the removal or sharp reduction in recent years of some of lead's most pernicious reservoirs. When leaded fuel is burned, lead particles from the exhaust are released into the air, where they can be inhaled or settle into the soil ***(Lanphear et al., 2002).***

According to an American Academy of Pediatrics (AAP) policy statement on lead exposure in children, from 1976 to 1980 the median blood lead level in U.S. children between one and five years of age was 15 micrograms per deciliter; by 1999, this figure had been reduced to 1.9 micrograms per deciliter ***(AAP, 2005).***

Great progress has been made in this effort. According to the Centers for Disease Control and Prevention(CDC), the percentage of children between the ages of one and five with blood lead levels of 10 micrograms per deciliter or higher declined from nearly 78% in the mid-1970s to below 5% by the mid-1990s; by 1999-2000, this figure had decreased even further, to just over 2 % (***CDC, 2005).***

Adults showed similarly steep declines in blood lead levels during this period. Usually credited for this improvement were widespread prevention policies instituted by the federal government, especially those banning lead in gasoline and mandating aggressive lead screening in children (***CDC, 2006).***

Lead exposure can be especially detrimental during pregnancy, fetal development, and early childhood. Lead is widely understood to be transmitted from mother to fetus through the placenta, and an animal study done by ***Goyer***, found that maternal and fetal blood lead levels were "nearly identical ***(Gardella, 2001).***

Lead may also be stored in a person's bones for decades before being released into the blood stream or into soft tissues, there by doing further damage to that person's internal organs, or before being passed to the developing fetus during pregnancy ***(Hernandez. et al., 2002).***