UMBILICAL CORD SERUM AND MATERNAL SERUM INSULIN LIKE GROWTH FACTOR I IN UNCOMPLICATED PREGNANCY AND IN PREGNANCY COMPLICATED BY PREECLAMPSIA

Thesis
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Contents

Continued

Continued

List of Tables

Continued

List of Figures

Continued

List of Abbreviations

AC	Abdominal Circumference
AGA	Appropriate for Gestational Age
ALS	Acid Labile Subunit
APGAR 1 min	APGAR Scoring After 1 Minute (Appearance, Pulse, Grimace, Activity, and Respiration)
APGAR 5 min	APGAR Scoring After 5 Minutes
BPD	Bi-Parietal Diameter
cFn	Cellular Fibronectin
CSF	Cerebrospinal Fluid
CVD	Cardiovascular Disease
DBP	Diastolic Blood Pressure
EPH-gestosis	Edema, Proteinuria and Hypertension
FL	Femur Length
Fn	Fibronectin
HC	Head Circumference
hCG	Human Chorionic Gonadotrophin
hGH	Human Growth Hormone
IGFs	Insulin-Like Growth Factors
IGF-I	Insulin-Like Growth Factor-I
IGF-II	Insulin-Like Growth Factor-II
IGFBPs	Insulin-Like Growth Factors Binding Proteins
IL-6	Interleukin-6
IUGR	Intrauterine Growth Retardation
KD	Kilo Dalton
MSA	Multiplication Stimulating Activity
MSAFP	Maternal Serum A-Fetoprotein
M W	Molecular Weight
NKB	Neurokinin B
NSILA	Non-Suppressible Insulin Like Activities
ng /ml	Nanogram/Ml
OGTT	Oral Glucose Tolerance Test
PDE5	Phosphodiesterase 5
PE	Pre-Eclampsia
PGI_2	Prostacyclin
PIH	Pregnancy Induced Hypertension
PlGF	Placental Growth Factor
Roc curve	Receiver Operator Characteristic Curve

Continued

sFlt1	Soluble fms-Like Tyrosine Kinase
SGA	Small for Gestational Age
SBP	Systolic Blood Pressure
SHBG	Sex Hormone Binding Globulin
Sms	Somatomedins
SmA	Somatomedin A
SmB	Somatomedin B
SmC	Somatomedin C
TNF-α	Tumor Necrosis Factor-Alpha
TxA_2	Thromboxane
VEGF	Vascular Endothelial Growth Factor

Introduction

INTRODUCTION

Preeclampsia is a disorder that is believed to affect to some degree 1 in 10 of all pregnancies. It is the commonest single cause of maternal and fetal mortality, and currently there is no cure other than termination of the pregnancy ***(Roberts and Redman, 1993).*** The causes of preeclampsia are complex and not fully understood, but the condition may be associated with poor placentation ***(Brosens et al., 1972).***

It is assumed that poor placentation and the associated obstructive lesion of the spiral arteries called acute atherosis, lead to placental ischemia ***(Redman and Sargent, 2000).*** It is possible that preeclampsia causes placental ischemia, although it is more likely that placental ischemia causes preeclampsia especially because poor placentation is an early preclinical development ***(Combs et al., 1993).***

It is presumed that blood born agents arising from the ischemic placenta are the cause of the generalized endothelial cell damage that gives rise to the preeclampsia syndrome ***(Roberts et al., 1989).***

Preeclampsia is characterized by hypertension, proteinuria and edema which remits after delivery ***(Dekker and Sibai, 1991).*** Many lines of evidence point to an important role for the insulin-like growth factors (IGFs) in embryonic and fetal growth in human pregnancy ***(Jones and Clemmons, 1995)*** and during preeclampsia maternal serum IGF-I concentrations are lower than those in normal pregnant women ***(Halhali et al., 1995 & Giudice et al., 1997).*** The actions of IGFs are modulated by a series of at least six high affinity-

binding proteins, named as IGF binding proteins that are ubiquitously expressed. The role of these IGFBPs in IGF action is not clear, but it has been demonstrated that these proteins may enhance or inhibit IGF-cellular effects ***(Rosenfeld et al., 1999).*** In the circulation, IGFBP-3 is the major carrier protein for IGF-I and IGF-II; approximately 95% of IGF-I is bound to IGFBP-3 ***(Binoux and Hossenlopp, 1988).*** In a study done by ***Wang et al. (1996)*** decreased serum IGFBP-3 levels were observed in preeclamptic women, but in another study, this protein was not significantly decreased in preeclamptic patients ***(Giudice et al., 1997; Varma et al., 1993).***

In normal pregnancy, maternal serum levels of IGF-I decrease early but increase again from gestational week 22 onward. Maternal IGF-I is believed to originate mainly from the maternal liver, and human growth hormone has been suggested to be a main stimulator of its synthesis ***(Wang et al., 1996).*** Preeclampsia is also associated with reduced utero--placental blood flow and fetal intrauterine growth retardation ***(National High Blood Pressure Education program working group, 1990; Redman, 1991).*** Insulin-like growth factor-I (IGF-I) may be involved in both normal and abnormal fetal growth ***(Chard, 1994).***

Under physiological conditions, approximately 75% of IGF-I circulate as a high molecular mass (150-kDa) ternay complex formed by IGF-I, IGFBP-3 and an acid-labile subunit; 24% is bound to other IGFBPs, and the remaining 1% circulates as free IGF-I ***(Rajaram et al., 1997).***