Clinical Significance of Plasma Levels of Pentraxin-3 in Pre-eclampsia Patients

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SUMMARY AND CONCLUSION

Pre-eclampsia is a potentially serious condition that still accounts for significant morbidity and mortality for the mother and the neonate, complicating 5-7% of all pregnancies and exposing them to a 3- to 25-fold increased risk of severe obstetric complications. Although, the pathogenesis is not fully understood, it is now widely accepted that vascular endothelial dysfunction is the most astonishing and the principal event in the pathophysiology of the disease.

Researchers investigated the fact that endothelial dysfunction has been hypothesized to be part of an excessive maternal inflammatory response to pregnancy. Complement activation, activated circulating leukocytes, increased release of reactive oxygen species, and increased levels of various inflammatory cytokines in pre-eclampsia.

Pentraxin-3 (PTX-3) is a described inflammatory molecule that belongs to the well known CRP family. PTX-3 differs from CRP in terms of cellular origin, molecular inducers, and kinetics of production. It is expressed by different cells like endothelial cells, monocytes, macrophages, and fibroblasts exposed to inflammatory stimuli. PTX-3 plasma levels increase dramatically during endotoxic shock, sepsis, or other inflammatory conditions. Recent studies suggest that PTX-3 plays an important role in innate immunity, female fertility, and inflammatory processes, so this promoted us to investigate this molecule in pre-eclampsia.

In this regard, this study aimed to evaluate the clinical utility of pentraxin-3 in diagnosis of pre-eclampsia and assessment of severity of the disease in comparison to CRP. In addition, the role of PTX-3 and CRP in fetal growth was evaluated.

List of Abbreviations

ACE	Angiotensin-converting enzyme
ACOG	American College of Obstetrics and Gynecology
AM	Adrenomedullin
AMI	Acute myocardial infarction
AT1	Angiotensin II receptor-1
CBC	Complete blood picture
CKD	Chronic Kidney Disease
COC	Cumulus oophorus cells in ovary
CTBs	Cytotrophoblasts
DBP	Diastolic blood pressure
DCs	Dendritic cells
ELISA	Enzyme linked immunosorbent assay
eNOS	Endothelial nitric oxide synthase
ET-1	Endothelin-1
Flt-1	Fms-like tyrosine kinase-1
GA	Gestational age
HELLP	Hemolysis, elevated liver enzymes and low plateles
IFN-γ	Interferon-gamma
IGF	Insulin-like growth factor Pentraxin-3 (PTX3
IL-1	Interleukin-1
IL-10	Interleukin-10
IL-2	Interleukin-2
IUGR	Intrauterine growth restriction
KDa	Kilo Dalton
LPS	Lipopolysaccharide
MDL	Minimum detectable limit
MMPs	Matrix metalloproteinases

List of Abbreviations

NK	Natural killer cells
NO	Nitric oxide
NOS	Nitric oxide synthase
NPTXI	Neural pentraxin I
NPTXII	Neural pentraxin II
NSCLC	Non-small cell lung cancer
OMPs	Outer membrane proteins
PAI-1	Plasminogen activator inhibitor-1
PAPP-A	Pregnancy associated plasma protein A
PCR	Polymerase chain reaction
PDGF	Platelet derived growth factor
PTX-3	pentraxin-3
PlGF	Placental growth factor
PMNs	Polymorphonuclear
PP-13	Placental protein-13
RAS	Rennin angiotensin system
ROS	Reactive oxygen species
RT-PCR	Reverse transcriptase PCR
SAP	Serum amyloid P-component
SBP	Systolic blood pressure
SCLC	Small cell lung cancer
sEng	Soluble endoglin
sFlt1	Fms-like tyrosine kinase-1
SSC	Systemic sclerosis
TGF-β1	Transforming growth factor-β1
TLR	Toll-like receptor
TNF-α	Tumor necrosis factor -alpha
VEGF	Vascular endothelial growth factor

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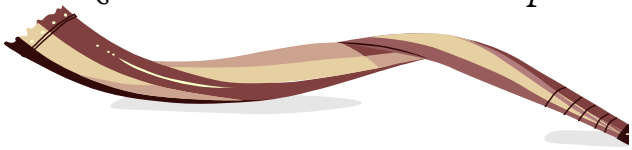

INTRODUCTION

Pre-eclampsia is a multisystem disorder specific to pregnant women. It remains one of the most important causes of maternal and fetal mortality and morbidity worldwide. It is the second largest cause of maternal mortality and affects 5% to 7% of pregnant women worldwide and approximately 3% of pregnant women in the western world ***(Aida et al., 2009).*** Pre-eclampsia is a major cause of preterm birth and intrauterine growth restriction accounting for 12-18% of pregnancy-related maternal deaths especially in developing countries **(*Sharon et al., 2008).***

In spite of its relevant epidemiologic impact, the complete pathogenesis of this disease still remains unclear, underlining a multifactorial etiology. Deficient remodeling of the spiral arteries during the interaction between maternal and fetal sides at the time of trophoblast invasion has been postulated as a cause of placental insufficiency. This would lead to the release of inflammatory factors in the systemic maternal circulation ***(Cetin et al., 2006).*** Endothelial dysfunction has been hypothesized to be part of an excessive maternal inflammatory response to pregnancy. Complement activation, activated circulating leukocytes, increased release of reactive oxygen species, and increased levels of various inflammatory cytokines in pre-eclampsia all agree with this hypothesis ***(Redman and Sargent, 2005)***.

Several laboratory markers were found for detecting haemostatic system alterations in pregnancies complicated by pre-eclampsia. Among these are fibronectin which is related to blood pressure in pregnancy, in addition to serum amyloid A (SAA) and C-reactive protein (CRP) which are markers of tissue damage and inflammation ***(Engin et al., 2007).***

Although these markers are altered in pre-eclampsia, they have a major disadvantage as they lack both specificity and sensitivity ***(Baumann et al., 2010).***

Pentraxin-3 (PTX-3) is a described inflammatory molecule that belongs to the well known CRP family. PTX-3 differs from CRP in terms of cellular origin, molecular inducers, and kinetics of production. It is expressed by different cells like endothelial cells, monocytes, macrophages, and fibroblasts exposed to inflammatory stimuli ***(Garlanda et al., 2007).*** PTX-3 plasma levels increase dramatically during endotoxic shock, sepsis, or other inflammatory conditions. Recent studies suggest that PTX-3 plays an important role in innate immunity, female fertility, and inflammatory processes, so this promoted us to investigate this molecule in pre-eclampsia ***(Souza et al., 2002).***

AIM OF THE WORK

The aim of the present study is to assess the clinical utility of PTX3 as an early predictor of pre-eclampsia and assessment of its severity in comparison to CRP. In addition, the relation of PTX3 to fetal growth will be evaluated.