PERFUSION INDEX AS A PREDICTOR OF THE INCIDENCE OF HYPOTENSION IN PRE-ECLAMPTIC PREGNANT PATIENTS AFTER SPINAL ANAESTHESIA FOR CAESAREAN SECTION

Thesis Submitted for the Partial Fulfillment of the Master Degree in Anesthesiology

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2015

Abstract

This study was conducted at Kasr Al Aini hospitals in the duration of six. This study was conducted in a group of full term pregnant patients with pre-eclampsia aged 18-40 years not documented to have peripheral vascular disease (DVT, limb ischemia). The comparison was done between prespinal perfusion index using a special pulse oximeter probe (masimo device, radical 7) and post spinal perfusion index (PI) to determine the relation between them.We found that Perfusion index was not able to predict which patients will develop hypotension following spinal anesthesia (AUC= 0***.583***, P value = ***0.402***). Baseline PI ranged from 0***.65*** to ***2.10***, with a mean value of ***1.40***.

Keywords:-

DAMP- IUGR- AV- HYPOTENSION- PRE-ECLAMPTIC

ACKNOWLEDGMENT

First and foremost, thanks to **Allah**, *the beneficial and the merciful.*

I would like to express my deepest gratitude and sincere thanks to ***Prof. Dr. Tarek Abdel Barr,*** *Professor of anesthesiology, Faculty of medicine, Cairo University, who kindly helped me a lot in this thesis. It is a great honor for me to work under his supervision with his honesty and modesty.*

I would like also to thank ***Assistant Prof. Dr. Amira Refaie Hassan,*** *assistant Professor of Anesthesiology, Faculty of Medicine, Cairo University and* ***Dr. Ahmed Ibrahim El-Sakka,*** *lecturer of Anesthesiology, Faculty of medicine, Cairo University, for their sincere guidance and remarkable thoughts throughout the whole work.*

Finally, thanks for the patients who participated in the present work, hoping that this thesis would be helpful in minimizing their suffer and pain.

LIST OF ABBREVIATIONS

ATN	Acute tubular necrosis
AUC	Area under curve
AV	Anchoring villi
BL	Baseline
BMI	Body mass index
CS	Cesarean section
CSE	Combined spinal epidural
DAMP	Damage-associated molecular pattern molecules
DAP	Diastolic arterial pressure
DIC	Disseminated intravascular coagulopathy
DVT	Deep vein thrombosis
ECTB	Extravillous cytotrophoblast
FV	Floating villi
GA	General anesthesia
GFR	Glomerular filtration rate
HELLP	Hemolysis, elevated liver enzymes, low platelet count
HIF	Hypoxia inducible factors
HLA	Human leukocytic antigen
HR	Heart rate
IL	Interleukin
INR	International normalized ratio
IUGR	Intrauterine growth retardation
LA	Local anesthetic
LDH	Lactate dehydrogenase
MAP	Mean arterial pressure
NIAP	Non-invasive arterial pressure
NO	Nitric oxide
PBL	Peripheral blood leukocyte
PE	Preeclampsia
PG	Prostaglandin
PI	Perfusion index
PLGF	Placenta growth factor
ROC	Receiver operating characteristic
ROS	Reactive oxygen species
SaO_2	Arterial oxygen saturation
SAP	Systolic arterial pressure
SET	Signal extraction technology
TNF	Tumor necrosis factor
TX	Thromboxane

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Introduction

Pre-eclampsia is a disorder that starts in pregnancy after twenty weeks of gestation manifesting as hypertension and proteinuria with at least one maternal organ dysfunction involvement with an incidence of 5-10% of all pregnancies. [1,2] Pre-eclampsia is considered a leading cause of fetal and maternal morbidity and mortality in developing countries with estimated 50,000 maternal deaths per year. [3] The use of spinal anesthesia in pre-eclamptic pregnant woman is of considerable benefit, as these patients present particular hazards with general anaesthesia. However the incidence of hypotension is high during spinal anaesthesia for CS. Hypotension incidence is about 95 %. [4,5] Hypotension during spinal anaesthesia for caesarean delivery is a result of decreased vascular resistance due to sympathetic blockade and decreased cardiac output due to blood pooling in blocked areas of the body. [6-8]

Avoiding such hypotension is extremely important in preeclamptic patients as they are relatively hypovolaemic and the fetus may be already compromised by placental insufficiency. Peripheral vascular tone has been shown to be decreased in parturients at term, especially in those who are multiparous and it may have an influence on the degree of hypotension. [9-11]

Masimo device is a noninvasive monitoring platform enabling the assessment of multiple blood constituents and physiologic parameters that previously required invasive or complicated procedures. [12] One of this physiologic parameter is perfusion index (PI). PI is the ratio of nonpulsatile to pulsatile blood flow through the peripheral capillary bed.

PI can be used to assess peripheral perfusion dynamics due to changes in peripheral vascular tone. [13]

By searching the literature, we found only one study that tested PI in pregnant non-preeclamptic women and it concluded that higher baseline PI was associated with profound hypotension and that baseline PI could predict the incidence of spinal anaesthesia induced hypotension during Caesarean delivery. [14] This study will be the first to be done on pregnant preeclamptic patients.

Pathophysiology and diagnosis of preeclampsia

Preeclampsia is an idiopathic multisystem disorder specific to human pregnancy and puerperium. The syndrome is characterized by hypertension and proteinuria, and a common fetal feature is intrauterine growth restriction after 20 weeks of gestation. (15)

The global incidence of preeclampsia has been estimated at 5-14% of all pregnancies. Preeclampsia is the third leading pregnancy-related cause of death, after hemorrhage and embolism. Preeclampsia is also associated with adverse fetal outcomes, including intrauterine growth retardation (IUGR), placental abruption and oligohydramnios. 10-15% of maternal deaths are directly associated with preeclampsia and eclampsia.

Hypertensive disorders are the second most common obstetrical cause of stillbirths and early neonatal deaths, accounting for 23.6%. (16)

The etiology of preeclampsia remains unknown. Numerous theories have attempted to explain the disease. As Preeclampsia is a disease unique to the human pregnancy. Advances in research have been limited by the lack of an adequate animal model. (17)

There are several lines of evidence supporting a role for maternal immune response in the development of preeclampsia. (18)

First, several immune-associated risk factors increase the probability that a woman will develop preeclampsia, including preexisting autoimmune disease.

Second, primiparity, suggesting that the response to paternal antigens plays a role.

Finally, concentrations of inflammatory cytokines are significantly increased, and placental production of the anti-inflammatory cytokine IL-10 is decreased, in women with preeclampsia. [19]

The human leukocyte antigen (HLA) system also appears to play a role in the defective invasion of the spiral arteries. women with pre-eclampsia show reduced levels of 2 subtypes of human leukocyte antigen known as human leukocyte antigen G and of human leukocyte antigen E. [20]

The Danger Model suggests that stress or abnormal cell death in pregnancy-related tissues causes expression of specific danger signals and potential activation of antifetal immunity. The initiating factor is recognition of Damage-associated molecular pattern molecules (DAMPs) generated as a result of poor placentation, oxidative stress, endothelial cell dysfunction , altered glucose metabolism or many other incompatibilities at the gene or protein level .[21]

The precise role of genetic factors in the development of pre-eclampsia is unclear. There is no specific contributory gene has been identified, but several susceptibility genes may exist . Studies have indicated an association between pre-eclampsia and polymorphisms of genes that control blood pressure, coagulation or oxygen-free-radical metabolism such as renin, angiotensinogen, endothelial nitric oxide synthase (eNOS), methyltetrahydrofolate or lipoprotein lipase. None of the genetic variants tested were found to confer a high risk of disease development. [22][23]

The Endothelial Model suggests that abnormal invasion of trophoblastic tissue may increase endothelial damage, causing an imbalance between thromboxane (TXA2) and prostacyclin (PGI2), resulting in compromised uteroplacental circulation. [18]

The Platelet Factor Model proposes that platelet dysfunction causes surface-mediated platelet activation, decreased sensitivity to PGI2, increased release of TXA2 and serotonin leading to further platelet aggregation, and up regulation of the uteroplacental renin angiotensin aldosterone system (RAAS). Up regulation of the uteroplacental RAAS causes increased in blood flow but may also contribute to maternal hypertension.[18]

The multiple factors that have been proposed to contribute to preeclampsia can be divided into four main categories as shown in figure 1. Biological models have been used to show that factors in each category contribute to the main symptoms of preeclampsia (hypertension and proteinuria). In addition, these factors influence each other. [24]

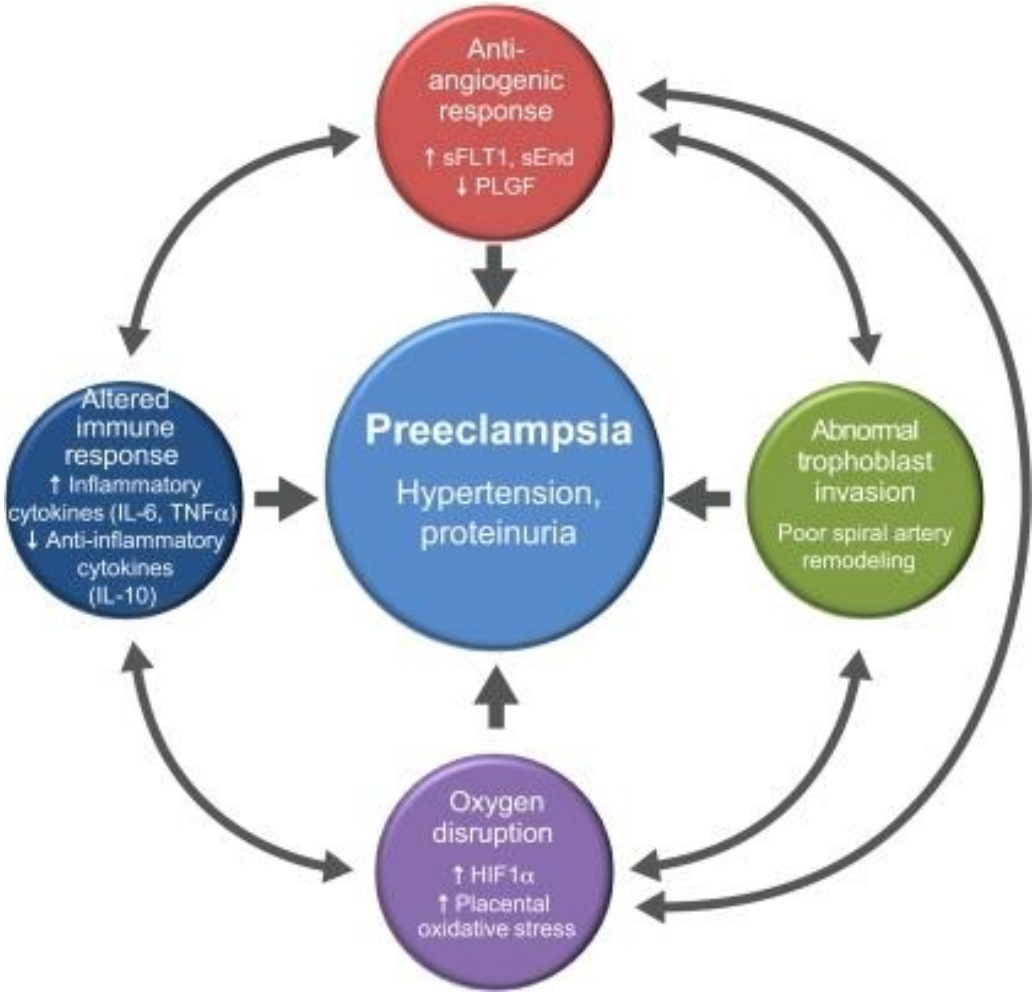

Figure 1: factors contributing to the pathophysiology of preeclampsia [25]**. sFLT : soluble form of Fms-like tyrosine kinase-1, PLGF: Placental growth factor , HIF: Hypoxia inducible factor .**

Risk factors

Major Risk factors for preeclampsia are stated in table 1. The connection between the risk factors of preeclampsia is poorly understood.[26]

Table 1: major risk factors for preeclampsia [27]

Risk factor	OR or RR (95% CI)
Antiphospholipid antibody syndrome	9.7 (4.3–21.7)
Renal disease	7.8 (2.2–28.2)
Prior pre-eclampsia	7.2 (5.8–8.8)
Systemic lupus erythematosus	5.7 (2.0–16.2)
Nulliparity	5.4 (2.8–10.3)
Chronic hypertension	3.8 (3.4–4.3)
Diabetes mellitus	3.6 (2.5–5.0)
Multiple gestations	3.5 (3.0–4.2)
Strong family history of cardiovascular disease	3.2 (1.4–7.7)
(heart disease or stroke in first-degree relatives)	2.5(1.7–3.7)
Obesity	2.3–2.6 (1.8–3.6)
Family history of pre-eclampsia in first-degree relative	1.68 (1.23–2.29) for nulliparas 1.96 (1.34–2.87) for multíparas
Advanced maternal age (40 years)	

CI, confidence interval; OR, odds ratio; RR, relative risk

Pathophysiology

Regardless of the mechanism, the prime pathogenesis of preeclampsia is abnormal placentation. It occurs with the presence of placenta and resolution begins with its removal. The pathophysiology of preeclampsia develops in two stages: early and late.

The early stage involves abnormal placentation. Early in normal placental development, extravillous cytotrophoblasts invade the uterine spiral arteries of the decidua and myometrium. These invasive fetal cells replace the endothelial layer of the uterine vessels, transforming them from small resistance vessels to flaccid, high-caliber capacitance vessels. This vascular transformation allows the increase in uterine blood flow needed to sustain the fetus through the pregnancy. [20]

In preeclampsia, this transformation is incomplete. Cytotrophoblast invasion of the arteries is limited to the superficial decidua, and the myometrial segments remain narrow and undilated. Cytotrophoblasts fail to adequately invade the myometrial spiral arteries. This is shown in figure 2. The spiral arteries fail to become dilated and may even show signs of atherosis. Placental perfusion is reduced and this leads to release of vasoactive substances. [28]