Early Versus Late Renal Replacement Therapy in Preeclamptic Patient Complicated with Acute Kidney Injury

Thesis

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ABG	Arterial blood gases
ADQI	Acute dialysis quality initiative
AKI	Acute kidney injury
AKIN	Acute kidney injury network
APGAR	Appearance, pulse, grimace, activity, respiration.
aPTT	Activated partial thromboplastin time
ARF	Acute renal failure
ATN	Acute tubular necrosis
AVF	Arterio-venous fistula
BUN	Blood urea nitrogen
CBC	Complete blood count
CPB	Cardiopulmonary by pass
CKD	Chronic kidney disease
CNS	Central nervous system
Cr cl	Creatinine clearence
CRRT	Continous renal replacement therapy
CTG	cardiotocogram
CVP	Central venous pressure
CYRP 61	Cysteine-rich protein 61
DDS	Dialysis disequilibrum syndrome
E NOS	Endothelial nitric oxide synthetase
ESRD	End stage renal disease
FENa	Fractional excretion of sodium
FRF	Filter replacement fluid
FSGS	Focal segmental glomerulosclerosis
GBM	Glomerular capillary basement membrane
GFB	Glomerular filteration barrier
GFR	Glomerular filteration rate
HELLP	Hemolytic anemia ,elevated liver enzyme, low platelet
HUS	Hemolytic uremic syndrome

ICU	Intensive care unit
IHD	Intermittent hemodialysis
IL18	Interleukin 18
KIM 1	Kidney injury molecoule -1
L-FABP	Liver-type fatty acid binding protein
LMWH	Low molecoular weight heparin
MDRD	Modification of diet in renal disease formula
NGAL	Neutrophil gelatinase-associated lipocalin
NHE3	Sodium+hydrogen exchanger 3
NO	Nitric oxide
NSAID	Non steroidal anti-inflammatory drug
PD	Peritoneal dialysis
PE	preeclampsia
PIGF	Placental growth factor
PIRRT	Prolonged intermittent renal replacement
PT	Prothrombin time
RCT	Randomized control trial
RIFLE	Risk, injury, failure, loss and end stage
RRT	Renal replacement therapy
S.cr	Serum creatinine
SCUF	Slow continous ultra filteration
SEng	Soluble endogolin
SFlt	Soluble fms-like tyrosine kinase
TGFB 1	Transforming growth factor beta 1
TTP	Thromobotic thrombocytopenic purpra
UOP	Urine output
VEGA	Vascular endothelial growth factor A
VEGF	Vascular endothelial growth factor

Introduction

Preeclampsia and the HELLP syndrome account for about 40% of cases of acute kidney injury (AKI) in pregnancy. Up to 20% of women with severe preeclampsia develop HELLP syndrome, a constellation of hemolysis, liver injury, and thrombocytopenia **(*Kuklina et al., 2008).***

Acute renal failure (ARF) occurs in approximately 1% of women with severe preeclampsia and 3%-15% of women with HELLP syndrome and it can occur either in the ante partum or the early postpartum period **(*Gul et al., 2004)***.

AKI is a serious complication of critical illness that is associated with substantial morbidity and mortality **(*Hoste et al., 2006)***.

Extracorporeal renal replacement therapy (RRT) has long been used as supportive treatment of AKI, and has traditionally focused on averting the life threatening derangements associated with kidney failure (that is, metabolic acidosis, hyperkalemia, uremia, and/or fluid overload) while allowing time for organ recovery. Observations from a large multinational, multicenter survey found the prevalence of severe AKI supported with RRT in critically ill patients was approximately 6% **(*Uchino et al., 2005).***

Unfortunately, in the absence of refractory acidemia, toxic hyperkalemia and intravascular fluid overload contributing to respiratory failure; there is limited evidence to guide clinicians on when to initiate RRT in critically ill patients with AKI **(*Elahi et al., 2009).***

In 2002, during the second Acute Dialysis Quality Initiative (ADQI) Consensus Conference held in Vienzea, a classification of AKI called RIFLE (Risk, Injury, Failure, Loss, End-stage renal disease) was proposed based on the level of serum creatinine rise or urine output reduction .The RIFLE classification has been validated in many centers and it is the most current and accurate tool to define the level of AKI and the level of associated risk of mortality **(*Uchino et al., 2006).***

Aim of the work

The end point of this study was to clinically and biochemically evaluate early versus late renal replacement therapy (RRT) in preeclamptic patients as regard Intensive care unit (ICU) and duration of RRT and renal recovery.

I - Preeclampsia

Scientists and clinicians have studied preeclampsia (PE) and eclampsia for several decades. The conditions remain life-threatening; complications of pregnancy are the leading causes of maternal and fetal morbidity and mortality around the world, especially in developing countries. PE is defined as hypertension (≥ 140/90 mmHg) with substantial proteinuria (≥ 0.3 g/24 h) at or after 20 weeks' gestation **(*Han et al., 2014).***

The worldwide incidence of PE is 2-8%. It has been reported that nearly a half of maternal deaths and more than a half of fetal deaths can be attributed to PE worldwide. Eclampsia is defined as seizures occurring as a result of PE without any other explicit causes, and is also an important cause of both perinatal fetal and peripartum maternal death ***(Han et al., 2014).***

While edema is often noted in preeclampsia, it is not very specific for the disease. Moreover, there is evidence that even with patients who develop eclampsia before or after 32 weeks gestation; there are significant numbers of patients who do not develop edema **(*Naljayan and Karumanchi, 2013*).** Mortality increases with maternal age for both preeclampsia and eclampsia, and black women were 3:1 times more likely to die from

preeclampsia or eclampsia than white women **(*Naljayan and Karumanchi, 2013)***.

- **Risk factors**

Factors that increase the risk for preeclampsia development in a woman include prior history of preeclampsia, chronic hypertension, chronic kidney disease, pre gestational diabetes, multiple gestations, obesity, and age >40 years old **(*Powe et al., 2011).*** Other factors include a partner who fathered preeclamptic pregnancy with another woman, woman born as small for gestational age, and adverse outcomes in a previous pregnancy. Women with a history of preeclampsia also develop cardiovascular disease later in their life ***(Powe et al., 2011).***

- **Pathogenesis**

Preeclampsia and eclampsia remains unclear because it is a multifactor disease with no single causative factor. A multi-stage hypothesis can explain many of the multi systemic pathological alterations, including initial abnormal immune tolerance, followed by abnormal placentation and spiral artery remodeling, and subsequent placental hypoxia-ischemia, which induces the release of placenta-derived adverse factors into the maternal circulation ***(Valenzuela et al., 2012)***.

It is believed that abnormal placentation occurs early in pregnancy and that this leads to placental ischemia (Stage I). The ischemic placenta is thought to secrete soluble factors during the third trimester that in turn induces systemic endothelial dysfunction and the maternal syndrome of preeclampsia (Stage II) **(*Valenzuela et al., 2012*).** These factors can cause systemic inflammation and have extensive effects on the maternal body, and the kidney is usually the first and most severely affected organ thus, the kidney deserves particular attention because of its significant physiological and pathologic changes during pregnancy **(*Valenzuela et al., 2012)***.

Microvascular endothelial cell injury appears to play a central role in the pathogenesis of preeclampsia. Therefore, as expected, end organ damage is generally directed towards organ systems highly dependent on the microvasculature for normal function including the kidney, liver, and central nervous system (including the eyes), among others. In order to fully comprehend the pathogenesis and renal consequences of pre- eclampsia, an understanding of renal physiology is required **(*Powe et al., 2011).***