Assessment of Interleukin-6 in Anemia with Chronic Renal Failure

Thesis

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Candidate

Khaled Mohammed Hamada

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List of Abbreviations

Abbr.	Full-term
ACE	: Angiotensin converting enzyme
ACEIs	: Angiotensin Converting Enzyme Inhibitors
ACR	: Albumin- to-creatinine ratio
ADH	: Antidiuretic hormone
ARBs	: Angiotensin Ii Receptor Antagonists
ARE	: Albumin excretion reate
CFU-E	: Colony-forming unit-erythroid cells
CKD	: Chronic kidney
CKD	: Chronic kidney disease
CTGF	: Connective tissue growth factor
DIC	: Dissociated intravascular coagulopathy
EGF	: Epidermal growth factor
EPO	: Erythropoietien
ESA	: Erythropoiesis-stimulating agent
ESRD	: End stage renal disease
ET-1	: Endothelin-1
FSGS	: Focal segmental glomerular sclerosis
GFR	: Glomerular filtration rate
HUS	: Hemolytic uraemic syndrome
KDIGO	: Kidney Disease Improving Global Outcomes
MCP-1	: Monocyte chemotactic protein-1

List of Abbreviations *(Cont.)*

Abbr.	Full-term
MCV	: Mean corpuscular volume
NHANES	: National Health and Nutrition Examination Survey
RAAS	: Rennin-angiotensin-aldosterone system
RBC	: Red Blood Cell
RHuEPO	: Recombinant human erythropoietin
SD	: Standard deviation
SPSS	: Statistical package for social science
TGF-B	: Platelet-derived growth factor-B
TNF	: Tumor necrosis factor
TSAT	: Transferrin saturation
TTP	: Thrombotic thrombocytopenic purpura

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Introduction

Chronic renal failure is a syndrome characterized by progressive and irreversible deterioration of renal function due to slow destruction of renal parenchyma, eventually terminating in death when sufficient numbers of nephrons have been damaged ***(Suresh et al., 2012)***.

Chronic kidney disease (CKD) affects approximately 26 million adults in the United Sates and millions of others are at risk. CKD is associated with significant morbidity and mortality, and these patients face many other medical problems related to CKD ***(Lankhorst and Wish, 2010)***.

Renal diseases are associated with a variety of hemopoietic changes. Anemia parallels the degree of renal impairment and its most important cause is failure of renal erythropoietin secretion. Other factors include chronic blood loss, hemolysis and bone marrow suppression by retained uremic factors ***(Suresh et al., 2012)***.

Anemia is a common problem in patients with CKD, and its incidence increases as glomerular filtration rate declines ***(Lankhorst and Wish, 2010)***.

There are other factors in chronic kidney disease which contribute to anemia. Acute and chronic inflammatory

conditions have a significant impact on anemia in the CKD population by proinflammatory cytokines decreasing EPO production and inducing apoptosis in colony-forming unit-erythroid cells (CFU-E). The early induction of apoptosis in CFU-E cells stops the process of development into RBC. Inflammatory cytokines have also been found to induce the production of hepcidin, a recently discovered peptide generated in the liver, which interferes with RBC production by decreasing iron availability for incorporation into erythroblasts. Red blood cells also have a decreased life span in patients with CKD ***(Besarab et al., 2009)***.

IL-6 appears to be the major cytokine responsible for the induction of hepcidin production in inflammation. Similarly, inflammatory cytokines such as IL-6 may also contribute to the increase in not only serum hepcidin but also serum ferritin in human diseases ***(Shah and Agarwal, 2013)***.

Inflammatory cytokines, such as interleukin-6 and TNF-α, have been shown to inhibit renal production of erythropoietin by activating GATA 2 binding protein and nuclear factor-kB. High levels of TNF-α and interleukin-6 have a tendency to inhibit proliferation of bone marrow erythroid progenitor cells ***(Shah and Aragwal, 2013)***.

Pekovic et al., study in the University Hospital Zemun-Belgrade reported that ESRD patients on dialysis with severe

heaver anemia had higher levels of IL-6 and TNF-α. Those patients were malnourished and their nutritional parameters were bad, and total correction of anemia leads to significant decreases in the plasma concentrations of the inflammatory cytokines, IL-6 and TNF-α ***(Pekovic et al., 2008)***.

Aim of the Work

The aim of this work is study the IL-6 as a marker of inflammatory process in anemia with chronic renal failure.

Chronic Renal Failure

CKD is a worldwide public health problem. The major outcomes of chronic kidney disease, regardless of cause, include progression to kidney failure, complications of decreased kidney function, and CVD. Increasing evidence indicates that some of these adverse outcomes can be prevented or delayed by early detection and treatment ***(Remuzzi, 2002).***

Definition:

According to Kidney Disease Improving Global Outcomes (KDIGO), CKD is defined as abnormalities of kidney structure or function, present for > 3 months, with implications for health ***(KDIGO, 2013).***

Kidney damage refers to a broad range of abnormalities observed during clinical assessment, which may be insensitive and non-specific for the cause of disease but may precede reduction in kidney function. Excretory, endocrine and metabolic functions decline together as the chronic kidnet diseases. GFR is generally accepted as the best overall index of kidney function.

A GFR < 60 ml/min/1.73m2 is referred to as decreased GFR and a GFR 15 ml/min/ 1.73m2 a kidney failure. AKL may occur in patients with CKD and hasten the progression to kidney failure ***(Hsu et al., 2008).***