Relationship Between Serum Hemojuvelin And Iron Requirement In Chronic Hepatitis C In Hemodialysis Patients

Thesis

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List of Abbreviations

AA	Amino acid
ACD	Anemia of chronic disease
ACEI	Angiotensin converting enzyme inhibitor
ACTR II A	Activin related protein
ALK	Activin like kinase
ALT	Alanine aminotransferase
ANg II	Angiotensin II
APKD	Adult polycystic kidney disease
APO TF	Apotransferrin
AST	Aspartate aminotransferase
BFU-E	Burst forming unit erythroblast
BMI	Body mass index
BMP	Bone morphogenetic protein
BMP RE	Bone morphogenetic protein responsive element
BP	Blood pressure
BUN	Blood urea nitrogen
CAMP	Cyclic adenosine monophosphate
CD	Cluster of differentiation
CERA	Continous erythropoietin receptor activator
CFU-E	Colony forming units erythroblast
CHC	Chronic hepatitis C
CHF	Congestive heart failure
CHILD C	Child-Pugh score system
CHr	Reticulocyte Hb content
Chronic GN	Chronic glomerulonephritis
CKD	Chronic kidney disease
CLD	Chronic liver disease
COMBI	Combined IDA and ACD
CRE B	Cyclic adenosine monophosphate responsive element binding protein
CREB H	Cyclic adenosine monophosphate responsive element binding protein hepatocyte specific
CRP	C reactive protein
CVS	Cardiovascular system
DCYTB	Duodenal cytochrome B
DM	Diabetes mellitus
DMT 1	Divalent metal transporter 1
Dry Wt	Dry weight

EASL	European Association for the Study of the Liver
E GFR	Estimated Glomerular filtration rate
EGF	Epidermal growth factor
EMA	European medicine agency
EPO	Erythropoietin
ER	Endoplasmic reticulum
ERK	Extracellular signal regulated kinase
ESA	Erythropoietin stimulating agents
ESRD	End stage renal disease
FDA	Food and drug adminstiration
FG	Fibrogen
FID	Functional iron deficiency
FLV CR1	Feline leukemia virus C receptor
FPN	Ferroportin
FV III	Fibronectin III
GDF 15	Growth differentiation factor 15
GPI	Glycosyl phosphatidyle inositol
HAMP	Hepatic anti microbial protein
Hb	Hemoglobin
Hb/HT	Hemoglobin/Hematocrit
HCT	Heamatocrit
HCV	Hepatitis c virus
HD	Hemodialysis
Hep3B	Human hepatoma cell line
HEPH	Hephaestin
HFE	Hemochromatosis iron protein
HFE 2	Hemochromatosis gene 2
HGF	Hepatocyte growth factor
HIF	Hypoxia inducible factor
HJV	Hemojuvelin
HO	Heme oxygenase
HO 1	Heme oxygenase 1
HRC	Hypochromic RBCs
Hs CRP	High sensitivity C reactive protein
HTN	Hypertension
HYPO %	Hypochromic RBCs
ID	Iron deficiency
Id 1	Inhibitor of DNA binding 1
IDA	Iron deficiency anemia
IL 6	Interlukine 6

IL-1	Interleukin 1
IL1β	Interleukin 1 beta
INF γ	Interferon gamma
IRE	Iron regulatory element
IRIDA	Iron refractory iron deficiency anemia
IRP	Iron regulatory protein
ISHD	Ischemic heart disease
IV	intravenous
JAK-2	Janus kinase -2
JH	Juvenile hemochromatosis
K& R	Kiss and run
KDIGO	Kidney disease improving global outcomes
KDOQI	Kidney disease outcomes quality initiative
L- RNA	Levoretatory ribo nucleo amine
LEAP-1	Liver expressed anti microbial peptide
LHD	Low hemoglobin density
LNMMA NG	L - N monomethyl arginin
LPS	Lipo polysaccharide
LRP 1	Low density lipoprotein receptor related protein 1
LV	Left ventricle
LVH	Left ventricular hypertrophy
M HJV	Membrane hemojuvelin
M RNA	Messenger ribonucleic acid
M TOR	Mammalian target of rapamycin
MAb	Monoclonal antibody
MAP	Mean arterial pressure
MAPK	Mitogen activated protein kinase
MCHC	Mean cell hemoglobin concentration
MFRN 1	Mitoferrin
MHC	Major histocompatibilty complex
MHD	Maintainance hemodialysis
MIA	Malnutrition inflammation anemia
MT2	Matriptase 2
NHANES	National health and nutrition examination
NTBI	Non transferrin bound iron
P SMAD	Phosphorylated SMAD
PAER 1	Prevalence of anemia in early renal insufficiency
PDGF BB	Platelate derived growth factor BB
PDGFRs	Platelate derived growth factor receptors

PFe	Plasma iron
PRCA	Pure red cell aplasia
PTH	Parathyroid hormone
RBCs	Red blood cells
RCT	Randomized controlled trial
RES	Reticuloendothelial store
RGM	Repulsive guidance molecule
Rhu EPO	Recombinant human erythropoietin
ROS	Reactive oxygen species
R-SMAD	Receptor activated SMAD
SC	Subcutaneous
SHJV	Soluble hemojuvelin
sHJV.Fc	Soluble hemojuvelin-Fc fusion protein
Si RNA	Small interfering ribonucleic acid
SMADS	Human homolog of Drosophila mad - mother against decapentaplegic
STAT 3	Signal transducer and activator of transcription 3
STFR	Soluble transferrin receptor
STFR\ Log Ferritin	Soluble Transferring Receptor\ Logarithm Ferritin
T.Bilirubin	Total.bilirubin
TF	Transferrin
TFR	Transferrin receptor
TGFβ	Transforming growth factor beta
TGN	Transgolgi network
TIBC	Total iron binding capacity
TID	True iron deficiency
TMPRSS6	Trans membrane serine protease 6
TNF	Tumor necrosis factor
TNFα	Tumer necrosis factor alfa
TRNA	Transfer ribonucleic acid
TSAT	Transferrin saturation
TWSG 1	Twisted gastrulation 1
URR	Urea reduction ratio
VEGF	Vascular endothelial growth factor
VHL	Von hipple lindau
WHO	world health organization
α2 M α 2	Alfa 2Macroglobulin-methyle amine activated

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Introduction

Anemia is a common problem in patients with end stage renal disease (ESRD) and increases mortality and morbidity in these patients, especially related to cardiovascular events ***(Lankhorst and Wish, 2010).***

Anemia associated with chronic kidney disease (CKD) is multifactorial: inadequate production of endogenous erythropoietin (EPO) for the degree of anemia, iron deficiency, blood loss, shortening of life span of erythrocytes, presence of inhibitors of erythropoiesis in plasma and vitamin deficiency ***(Mercadel et al., 2012).***

Our understanding of iron metabolism has advanced dramatically in the past few years, mainly as a result of the discovery of hepcidin ***(Papanikolaou et al., 2005).***

Hepcidin is a peptide produced by the liver, it suppresses intestinal iron uptake and release from internal stores by facilitating the degradation and internalization of the only known iron exporter, ferroportin (FPN), which is expressed on the surface of enterocytes, hepatocytes and macrophages ***(Babitt and Lin, 2010).***

Hemojuvelin (HJV) is aprotein that is responsible for the iron overload condition known as juvenile hemochromatosis (JH). HJV highly expressed in the liver, skeletal muscle and heart, seems to play a role in iron absorption and release from cells and has anti-

inflammatory properties, it regulate hepcidin expression specifically in the iron sensing pathway ***(Huang et al., 2005).***

Thus, disruption of HJV results in inappropriate regulation of hepcidin expression and consequently causes either iron overload or iron deficiency ***(Lee et al., 2010).***

Hepatitis C virus (HCV) infection is the most common cause of chronic liver disease in the world and also common among chronic hemodialysis (HD) patients ***(Fujita et al., 2007).***

Nearly present between 4% to 70% in patients on HD ***(Li et al., 2011).***Patients with chronic HCV infection often have increased liver iron ***(Miura et al., 2008).***

HCV positive HD patients have been found to have low levels of serum prohepcidin which might account for iron accumulation together with lower iron and erythropoietin (EPO) requirements in those patients ***(Caliskan et al., 2012).***

HJV was found to be elevated in HD patients and correlated to kidney function and iron status. It appears that HJV could be a new player in the iron metabolism in HD patients ***(Malyszko (A) et al., 2012).***

Aim of the Work

1. To measure the level of hemojuvelin in hemodialysis patients.
2. To identify the association of hemojuvelin level with iron parameters in hemodialysis patients.
3. To compare hemojuvelin level in hepatitis C virus positive hemodialysis patients to those who are hepatitis C virus negative.