Role of Soluble Transferrin Receptor in diagnosing Iron Deficiency Anemia in maintenance hemodialysis patients

Thesis

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قالوا
سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
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Marwa Eid Abdulhady Naker

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List of Abbreviation

ACD	Anemia of chronic disease
ACEI	Angiotensin Converting Enzyme Inhibitor
ARBs	Angiotensin receptor blockers
AVF	Arterio-venous fistula
CHR	Content of Hb in reticulocytes
CKD	Chronic kidney disease
CLL	Chronic lymphocytic leukemia
CRP	C-reactive protein
ELISA	Enzyme linked immunosorbent assay
EMPs	Erythropiotein mimetic peptides
EPO	Erythropiotein
ESA	Erythropioesis stimulating agents
ESRD	End stage renal disease
Hb	Hemoglobin
HIF1	Hypoxia inducible factor 1
HIF-PHIs	Hypoxia-inducible factor prolyl hydroxylase inhibitors
HIF-PHD	Hypoxia-inducible factor Prolyl hydroxylase
ID	Iron deficiency
IDA	Iron deficiency anemia
IL1	Interleukin 1
IL6	Interleukin 6
IRMA	Immuno-radiometric assay
IV	Intravenous
KDIGO	Kidney disease improving global outcome
KDOQI	Kidney disease outcome quality initiative
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration

MCV	Mean corpuscular volume
MDS	Myelodysplastic diseases
NO	Nitric oxide
NPP	Negative predictive value
PPV	Positive predictive value
PTH	Parathyroid hormone
RBCs	Red blood cells
ROS	Reactive oxygen species
STFRs	Soluble transferrin receptors
TFR	Transferrin receptor
TFR-F	Transferrin receptor - ferritin index
TGF B	Transforming growth factor B
TIBC	Total iron binding capacity
TNF	Tumor necrosis factor
TSAT	Transferrin saturation
WBCs	White blood cells
ZnPP\H	Zinc protoporphyrin/heme
ZPP	Zinc protoporphyrin

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Abstract

Background: Diagnosis of iron deficiency is traditionally based on ferritin and other iron parameters becomes difficult in end stage renal disease patients due to the inflammatory condition which affects these markers and masks the iron deficiency. Serum soluble transferrin receptor (sTfR) is able to be a reliable indicator for assessing iron status, as it is not affected by inflammatory procedures.

Aim: To evaluate the usefulness of serum soluble transferrin receptors in iron deficiency anemia detection in comparison to the classic markers of iron status in prevalent hemodialysis patients.

Methods: This case-control study assessed sTfR in 80 prevalent ESRD patients on regular hemodialysis in 2 groups. Group A (N=40): CRP >10 and group B (N=40):CRP <10 and apparently healthy 8 control subjects.

Results: The cut of value of STFRs in hemodialysis patients was 12.5 mg\l. The prevalence of STFRs in patients with CRP<10 was 85%, while in patients with CRP>10 was 92.5% (P-value 0.288). STFRs have high sensitivity 88.75, specificity 100, PPV100% and NPV 47.1%. The hemodialysis patients who have elevated STFRs have risk 1.22 times to have iron deficiency anemia if CRP <10 (odds ratio: 1.22) and 3.14 times if CRP>10 (odds ratio: 3.14). There was significant difference on comparing patients with CRP<10, CRP>10 and control as regard Hb and STFR with P-value 0.0001 and 0.0001 respectively.

Conclusion: Serum soluble transferrin receptor is highly sensitive and specific marker for iron deficiency in hemodialysis patients especially in patients with high CRP level.

Key-words: soluble transferrin receptors, iron deficiency anemia, hemodialysis.

Introduction

Anemia is a common finding in hemodialysis patients. There are numerous factors that relate renal dysfunction to anemia such as:

1- Accumulation of uremic toxins that act as apoptosis inducers in erythroid precursors in bone marrow.
2- Raised quantities of free radicals and reactive oxygen species (ROS) – for instance nitric oxide (NO) and superoxide anions – synthesized by activated macrophages, affecting erythroid precursors
3- Blood loss related to hemodialysis procedure and gastrointestinal hemorrhage
4- Dilutional anemia due to disturbance of kidney filtration and excessive retention of fluids **(Banerjee, 2009).**

Reduced production of erythropoietin synthesized by endothelial cells of the capillaries surrounding kidney tubules during the course of renal complication, is another contributing factor to anemia **(Lodish H.; et al., 2010).**

Erythropoietin therapy – nowadays administered as recombinant human erythropoietin – is one of the main approaches to correct anemia in hemodialysis patients. One of the most important reasons of unresponsiveness to this treatment is shortage of body iron supply. Therefore, a precise assessment of iron storage in hemodialysis patients is of vital

value to identify patients with actual iron deficiency and adjust treatment accordingly ***(*Tomczak-Watras *et al., 2009)***

The gold standard for identification of iron deficiency induced anemia is iron stain on liver or bone marrow biopsy samples **(Wulfhekel et al., 1999).**

This is a precise approach, yet an invasive one, and in case of existence of any replacement it is better avoided. One alternative approach is evaluation of two red blood cell indices – mean corpuscular volume (MCV) and mean corpuscular hemoglobin concentration (MCHC) and detection of microcytic and hypochromic red blood cells as confirmation of existence of iron deficiency. Nevertheless, these two parameters are affected by the existing inflammation **(Koulaouzidis et al., 2009)**

Serum ferritin and transferrin saturation (TSAT) are two most commonly done tests used for evaluating iron deficiency anemia. However, these tests do not consistently reflect the iron status of patients with CKD on hemodialysis (**Saboor et al., 2011)**

Serum ferritin and transferrin are considerably influenced by acute phase responses in inflammation. Total iron binding capacity (TIBC) is a negative acute phase reactant. Moreover, TSAT fluctuates because of diurnal variation in serum iron

levels. In recent years, soluble transferrin receptor (sTfR) has been introduced as a sensitive, early and valuable new marker of iron depletion (**Majeed et al., 2016)**

STfR is a truncated form of the transferrin receptor present on erythroblasts in bone marrow and many other cells. As sTfR concentration is not usually affected by inflammation or infection but in conditions where iron deficiency co-exists with anemia of chronic disease, sTfR raises secondary to underlying iron deficiency (**Latif et al., 2017).**

Aim of the work

The aim of this study is to evaluate the usefulness of serum soluble transferrin receptors in iron deficiency anemia detection in comparison to the classic markers of iron status in prevalent hemodialysis patients.