DETECTION OF IRON DEFICIENCY ANAEMIA BY RETIC HAEMOGLOBIN (RET-He) IN HAEMODIALYSIS PATIENTS ON RECOMBINANT HUMAN ERYTHROPOIETIN (rHuEPO).

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ACD	Anaemia Of Chronic Disease
CRP	C reactive protein
DMTI	Divalent Metal Transporter1
DNA	Deoxyribonucleic Acid
ESRF	End Stage Renal Failure
Fe^{2+}	Ferrous
Fe^{3+}	Ferric
FID	Functional Iron Deficiency
Hb	Haemoglobin
HD	Haemodialysis
HRPZ	Hospital Raja Perempuan Zainab
IDA	Iron deficiency anaemia
MCH	Mean Cell Haemoglobin
MCV	Mean Cell Volume
rHuEpo	recombinant Human Erythropoietin

RET-He	Reticulocyte Hemoglobin content
ROC	Receiver operating characteristic curve
RDW	Red cell distribution width
sTfR	Soluble Transferrin Receptor
TIBC	Total iron binding capacity
TSat	Transferrin Saturation
ZPP	Zinc Protoporphyrin

DEFINITION

Classical iron deficiency anaemia	Depletion of storage and functional iron compounds. Decreased haemoglobinization of red cells.
Conventional method for iron	Method such as serum iron, transferrin/total iron binding capacity, transferrin saturation and ferritin.
Functional Iron Deficiency FID	Imbalance between the iron requirement of the erythroid marrow and the actual iron supply.
Iron restricted erythropoiesis	Condition whereby iron store depleted, low serum iron but normal or low hemoglobin.
Iron replete	Iron store present.
Iron deplete	Iron store reduced markedly or absent
Nutritional anaemia	Anaemia due to iron, B12 and Folate deficiency or due to alcoholism.

ABSTRAK

Kekurangan zat besi sering berlaku di kalangan pesakit buah pinggang peringkat akhir yang diberikan hormon erithropoitin (EPO) sebagai rawatan. Kekurangan zat besi adalah faktor utama yang menyebabkan pesakit tidak bertindak balas dengan baik dengan rawatan hormon tersebut.

Tujuan utama kajian ini adalah untuk menentukan ketepatan penggunaan RET-He (Retikulosit Hemoglobin) dalam mengenalpasti kekurangan zat besi di dalam pesakit hemodialisis yang diberikan hormon (EPO) berbanding parameter konvensional (ferritin dan penerima transferrin). Selain itu kajian ini juga diharap dapat mengenalpasti perubahan RET-He semasa pesakit diberikan rawatan hormone EPO serentak dengan pemberian zat besi, sama ada parameter ini berupaya menganalisa kadar zat besi yang mencukupi kepada pesakit.

Kajian ini telah dijalankan di HRPZ II bermula dari November 2008 hingga November 2009. Lima puluh lima sampel darah telah diambil dan dianalisa untuk RET-He, ferritin dan penerima transferrin. RET-He dianalisa oleh mesin XE-2100 (Sysmex) Ferritin pula oleh kaedah ELISA (AXSYM) dan penerima transferrin oleh kaedah ELISA (Biovender). Data akan dianalisa oleh program SPSS version 12.0.

Keputusan menunjukkan RET-He mempunyai signifikan dengan penerima transferrin, ferritin, MCV, MCH dan Indek ferritin ($p<0.01$) Min RET-He di dalam pesakit hemodialisis ialah 29.91±2.29 pg. Sensiviti dan specificity RET- He pula ialah 78.3% dan 92% bersama kawasan di bawah kecerunan 0.864. Peratusan pesakit kekurangan zat besi yang dapat dikesan oleh RET-He adalah 63.64%, oleh penerima transferrin 3.64% dan ferritin 0%. RET-He mempunyai hubungan yang signifikan terhadap penerima transferrin $r= 0.042$ dan indek ferritin $r=0.036$, walaubagaimanapun tiada hubungan yang signifikan terhadap ferritin. Kajian seterusnya menunjukkan pesakit yang dikesan mengidap kekurangan zat besi dan respon terhadap zat besi yang diberikan dapat dikesan dengan baik oleh RET-HE ($p<0.01$)

Sehingga kini pengesanan kadar kekurangan zat besi di kalangan pesakit hemodialisis yang diberikan hormon EPO oleh kaedah konvensional adalah rendah. Walaubagaimanapin kaedah yang terkini oleh RET-He menunjukkan bahawa ia adalah sensitif dan spesifik parameter untuk analisa status zat besi di dalam pesakit hemodialisis yang diberikan hormone EPO.

Oleh yang demikian kami mencadangkan penggunaan RET-He sebagai parameter utama untuk diagnosis kekurangan zat besi dan juga sebagai kaedah monitor tindak balas kepada rawatan intravenous zat besi kepada pesakit hemodialisis .

ABSTRACT

Iron deficiency anaemia (IDA) appears frequently in haemodialysis (HD) patients with rHuEPO (recombinant human erythropoietin) therapy. Iron deficiency is the most common factor associated with rHuEPO hyporesponsiveness. However current iron indices are inadequate to demonstrate the status or utility of iron in erythropoiesis. The aim of this study was to clarify the accuracy of RET-He in diagnosing IDA in haemodialysis patients with rHuEPO therapy compared with conventional iron parameters. Secondly to detect the changes in RET-He during iron supplementation for IDA patients, either this marker is a prospective and reliable indicator of iron sufficiency.

A cross sectional study was done at HRPZ II from November 2008 to November 2009. 55 samples was collected and analysed for RET-He, ferritin and sTfR. RET-He was measured with the XE-2100 (Sysmex). Ferritin values were determined using ELISA method by AXSYM and sTfR by ELISA Biovender. Data were analyzed using SPSS software version 12.0.

RET-He was significantly correlated with sTfR, MVC, MCH and TfR-F index ($p< 0.01$). Mean RET-He in haemodialysis patients was 29.91 ± 2.29 pg. Sensitivity and specificity of RET-He, 78.3% and 92 % respectively with AUC of 0.864. Percentage of IDA detected by RET-He was 63.64% but by sTfR and ferritin were 3.64% and 0% respectively. RET-He was significantly had aggrement with sTfR and TfR-F index, $r= 0.042$ and $r=0.036$ respectively, however no agreement with serum ferritin.

A follow up study showed those who were diagnosed had IDA respond to iron supplement can be detect very well by RET-He ($p< 0.01$).

To date detection rate of IDA in haemodialysis patients with rHuEPO by conventional method (sTfR & ferritin) was low. However our current method by RET-He shows that it is a sensitive and specific marker of iron status in haemodialysis patients with rHuEPO. Thus we strongly suggest using RET-He as a diagnostic tool for the detection of IDA as well as monitoring of responses to intravenous iron therapy in haemodialysis patients.