Effect of Vitamin E Co-Aministration on Oxidative Stress Induced by Iron Sucrose IV Therapy on Anemic Hemodialysis Patients

Thesis Submitted for Fulfillment of M.Sc. Degree in Pharmaceutical Science (Clinical Pharmacy)

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AST	Aspartate aminotransferase
ALT	Alanine aminotransferase
ARI	Acute renal injury
AMI	Acute myocardial infarction
BUN	Blood urea nitrogen
Ca	Calcium
CBC	Complete blood count
CERA	Continuous erythropoietin receptor activator
CHF	Congestive heart failure
CKD	Chronic Kidney disease
CVD	Cardiovascular disease
ESRD	End stage renal disease
GFR	Glomerular filtration rate
GI tract	Gastrointestinal tract
HD	Hemodialysis
HDL	High density lipoprotein
HIF	Hypoxia inducible factor
Hgb	Hemoglobin
IM	Intramuscular
IREs	Iron response elements
IREGI	Ferroportin
IV	Intravenous
JAMA	The Journal of American Medical Association
LDH	Lactate dehydrogenase
LDL	Low density lipoprotein
MDRD	Modification of Diet in Renal Disease
NKF-	National Kidney Foundation- Kidney disease
K/DOQI	outcomes and quality initiative
NTBI	Non Transferrin Bound Iron
OxS	Oxidative stress
<i>p</i> -value	Probability value or significance level

PD	Peritoneal dialysis
PLTs	Platlets
PMP	Per million population
POD	Peroxidase
PPP	Polymerized Protein Puddles
rHuEPO	Recombinant Human Erythropoietin
RRT	Renal replacement therapy
Scr	Serum creatinine
SD	Standard deviation
SGOT	Serum glutamate oxaloacetate transaminase
SOD	Superoxide Dimutase
SGPT	Serum glutamate pyruvate transaminase
TBARS	Thiobarbituric acid reactive substances
TSAT	Transferrin saturation
Vit	Vitamin



Background:

Intravenous (IV) iron preparations are widely used in the management of anemia in end stage renal disease (ESRD) populations. These preparations are frequently administered with insufficient attention to the total body stores or presence of inflammation which is aggravated by excess iron. Iron infusion during the hemodialysis session increased the percentage of mononuclear cells with reactive oxygen species (ROS) production. The abnormalities in the antioxidant defense system and increased oxidative stress may lead to higher susceptibility to lipid peroxidation. Increased pro-oxidant activity (age, diabetes, hypertension, inflammation, incompatibility of dialysis membranes and solutions) in chronic kidney disease (CKD) patients goes together with reduced antioxidant defense (low levels of vitamin E, C, reduced glutathione system activity), which has been linked to several surrogate markers of atherosclerosis in patients with CKD. Antioxidant vitamins and dietary constituents (for example Vitamin E) may play an important role in protection against oxidative damage and, consequently, against atherosclerosis. Although there are studies evaluated biochemical alterations, endogenous antioxidants and vitamins in hemodialysis (HD) patients, there is lack of information about the relationships among oxidative stress biomarkers, vitamins and classical biochemical alterations. Among possible therapeutic approaches, the use of Vitamin E seems to be the most promising.

Objective:

Assess the effect of high dose Vitamin E administration on oxidative stress induced by IV Iron on anemic patients undergoing hemodialysis.

Design:

A prospective, randomized, interventional, open-labeled study.

Setting:

The study performed on 40 anemic chronic kidney disease patients undergoing hemodialysis at Ain Shams University Hospital, Cairo, Egypt, from August 2010 to December 2010.

Methods:

Patients were classified into two groups, Group 1 (control group) received IV iron sucrose during hemodialysis session and Group 2 (study group) received Vitamin E 1000 mg as a single high dose 6 hours before hemodialysis session plus IV Iron Sucrose during hemodialysis session. All patients gave their informed consent before starting the study.

Results:

As revealed from the results, malondialdehyde (MDA) levels in μmol/ml showed a value of 159.599±14.912 for Group A and 140.755±19.901 for Group B with statistical significance at p-value <0.05. Red blood cell count showed a highly significant difference at p-value< 0.01 for Group A 3.98±0.364 compared with 5.28±0.412 (RBCs 106/mm³) for Group B. A statistically significant p-value < 0.05 for Serum Ferritin level in μg/ml in Group A 938.860±87.653 compared with 899.886±126.563 in Group B, although this was not clinically significant. The clot retraction test showed a statistically significant value at p-value < 0.05 between both groups. Dry layer blood film showed less polymerized protein puddles and less deformed fibrin matrix than Group A. Liver function tests and kidney function tests remained stable in both arms. No gastrointestinal disturbances were observed.

Conclusion:

It could be concluded that Vitamin E single high dose administration before the hemodialysis session can effectively reduce oxidative stress induced by IV Iron Sucrose for hemodialysis patients. Once weekly single dose medication showed no potential side effects with high compliance to this specific group of patients

Key words: Anemia, Hemodialysis, IV Iron Sucrose, Vitamin E high dose