STUDIES ON TREATMENT OF RENAL ANEMIA IN PATIENTS ON CHRONIC HEMODIALYSIS

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Abstract:
In patients with chronic kidney disease, treatment with erythropoiesis-stimulating agents (ESA) effectively corrects anemia. Most of these patients also need supplementation with regular iron injections to secure iron availability for proper erythropoiesis. Following intravenous iron injection, non-transferrin bound iron (NTBI) can appear in the circulation, capable of inducing harmful oxidative reactions. Direct measurement of free iron with the robust technique electron spin resonance (ESR) has not been used to investigate this issue in humans.
The main purposes of this thesis were to use ESR to study the levels of NTBI and oxidative stress after intravenous (IV) iron injection and to compare two commercially available IV iron formulations, low-molecular weight iron-dextran (ID) and iron-sucrose (IS), regarding this topic. In addition, the impact of two different hemodialysis modalities on iron homeostasis and the effect of modifying the ESA administration praxis on ESA requirement, were studied.
Sixty-four patients on chronic hemodialysis treatment participated in these studies. To investigate the appearance of NTBI and induction of oxidative stress, blood samples were collected before and after IV iron injections. To compare two different hemodialysis modalities, a prospective, randomized, patient-blinded study, with conventional hemodialysis (HD) and on-line hemodiafiltration (HDF), in a 2x2 months design, was conducted. Finally, a retrospective register study was performed on 18 patients, comparing periods with two different erythropoietin administration routines. After injection of IS, a parallel increase in oxidative stress and NTBI was noted, while no induction of oxidative stress was seen following injection of ID. After treatment with HDF, the levels of the iron-regulating peptide, 25-hepcidin, were in all cases within the reference interval. A change in ESA administration regimen, to less frequent dose-adjustments and no withheld doses, could be an explanation for the observed approximately 20 % reduction in ESA requirement.
In conclusion, IS injection, but not ID injection, “leaks” catalytically active iron into the blood stream, which then initiates a burst of intravascular oxidative reactions. The increased clearance of 25-hepcidin by HDF could be of benefit for the dialysis patient, bringing the pathological iron homeostasis found in this population toward a more normal state. An erythropoietin regimen with optimal frequency of dose adjustments can reduce ESA demand and thereby decrease health care cost.

Keywords: Hemodialysis, erythropoietin, iron, oxidative stress, hepcidin.

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AVHANDLINGEN BASERAS PÅ FÖLJANDE DELARBETEN:

I. BERGUR V. STEFÁNSSON, BÖRJE HARALDSSON, ULF NILSSON
Ascorbyl free radical reflects catalytically active iron after intravenous iron saccharate injection.
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II. BERGUR V. STEFÁNSSON, BÖRJE HARALDSSON, ULF NILSSON
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III. BERGUR V. STEFÁNSSON, MATS ABRAMSON, ULF NILSSON, BÖRJE HARALDSSON
Hemodiafiltration improves plasma 25-hepcidin levels. A prospective, randomized, participant-blinded, cross-over study, comparing hemodialysis and hemodiafiltration.
Submitted for publication.

IV. BERGUR V. STEFÁNSSON, BÖRJE HARALDSSON, ULF NILSSON
The consumption of erythropoiesis stimulating agents can be reduced by a new administration regimen.
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