Distinct immunologic effects of iron sucrose and iron isomaltoside 1000 on monocytes in vivo

Alexander B. Sellier, Lisa H. Fell, Sarah Seiler-Mueller, Adam M. Zawada, Danilo Fliser, Gunnar H. Heine

Department of Internal Medicine IV, Nephrology and Hypertension, Saarland University Medical Center, Homburg / Saar

Introduction
Iron deficiency substantially contributes to anaemia in patients with chronic kidney disease (CKD). Intravenous (i.v.) iron application represents the first-line-strategy of iron replacement in CKD G5 patients. Distinct iron preparations are available in clinical nephrology. Recent in vitro experiments from our group revealed that less stable i.v. iron preparations such as iron sucrose exert substantial immunomodulatory effects on monocytes, while more stable preparations such as ferric carboxymaltose and iron isomaltoside 1000 are virtually immunologically neutral. We now aimed to examine whether these in vitro findings are clinically relevant.

Methods
We analyzed the immunological effects of an i.v. iron supplementation with 500 mg iron sucrose or 500 mg iron isomaltoside 1000, respectively, on circulating monocytes in patients on peritoneal dialysis with iron deficiency anaemia. Therefore we determined the distribution of the three different monocyte subsets (classical, intermediate, nonclassical), monocytic surface expression of CD86, monocytc iron uptake and phagocytosis capacity via flow cytometry. Furthermore, we analyzed the monocytic surface expression of chemokine receptors (CCR5, CX3CR1) after administration of 500 mg iron sucrose.

Results
Iron isomaltoside 1000 had no significant impact on monocytic phenotype or function. However, administration of iron sucrose significantly lowered the phagocytosis capacity of classical monocytes within an hour. Additionally, we could show a reduced CD86 expression of all monocyte subsets within three hours after infusion with iron sucrose.

As a possible explanation for these compound-specific immunomodulatory findings, we could demonstrate that circulating monocytes more avidly take up iron sucrose than iron isomaltoside 1000.

Discussion
Expanding our earlier findings from in vitro studies, we now demonstrate a substance-specific immunomodulatory effect induced by less stable i.v. iron preparations.

Given the high burden of inflammatory and immune diseases among CKD patients, we are hopeful that our in vivo study may contribute to define more tailored anemia treatment strategies in clinical nephrology.

(Fell et al., Nephrol Dial Transplant. 2014 Apr;29(4):809-22)