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

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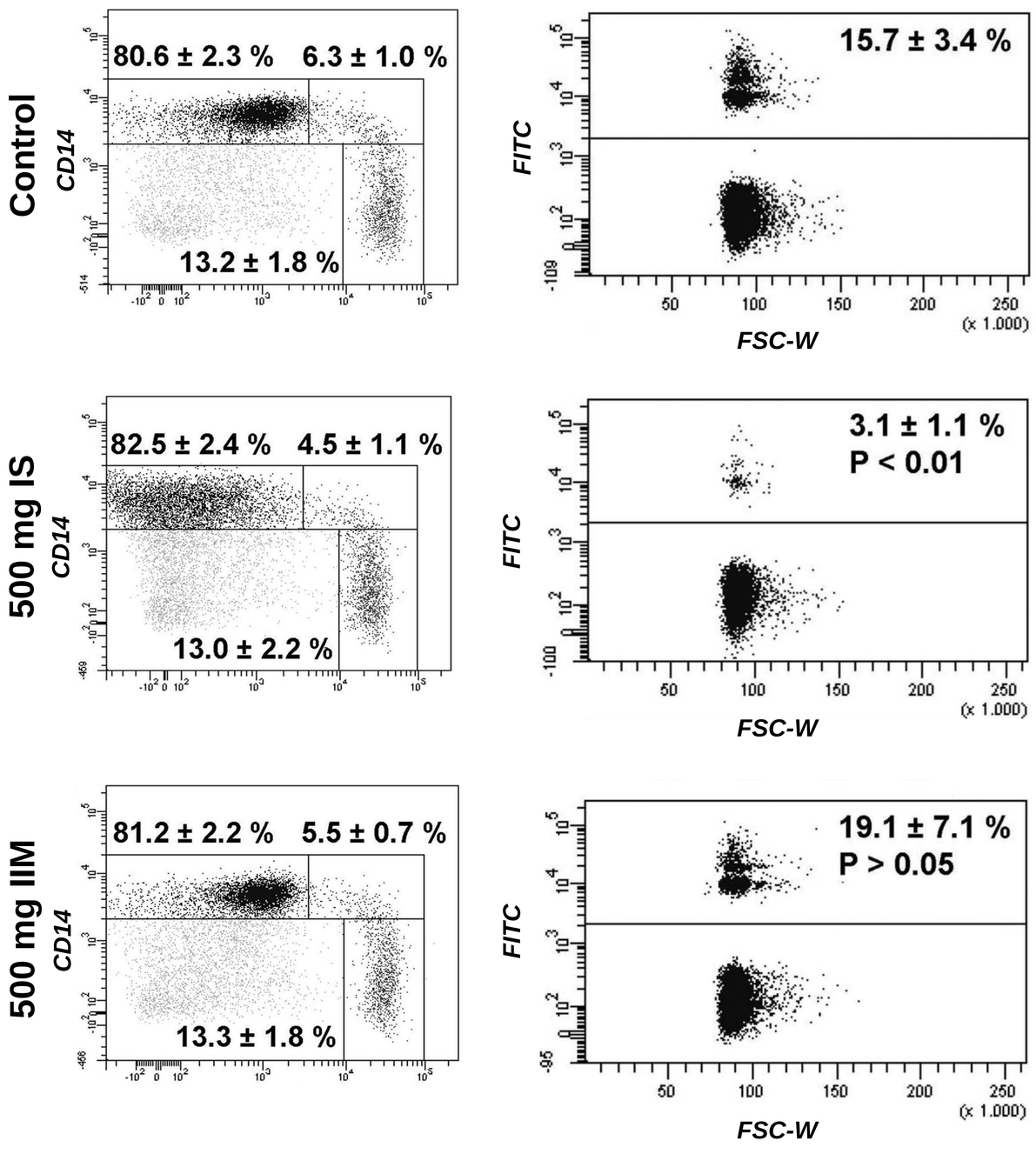
Introduction

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.

Monocytic subset distribution | **Phagocytosis capacity**

(after stimulation with 500 mg iron sucrose or iron isomaltoside 1000)



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

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, monocytic iron uptake and phagocytosis capacity *via* flow cytometry.

Furthermore, we analyzed the monocytic surface expression of chemokine receptors (CCR5, CX_3CR1) 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 immunological findings, we could demonstrate that circulating monocytes more avidly take up iron sucrose than iron isomaltoside 1000.

Fig. 1: monocytic subset distribution

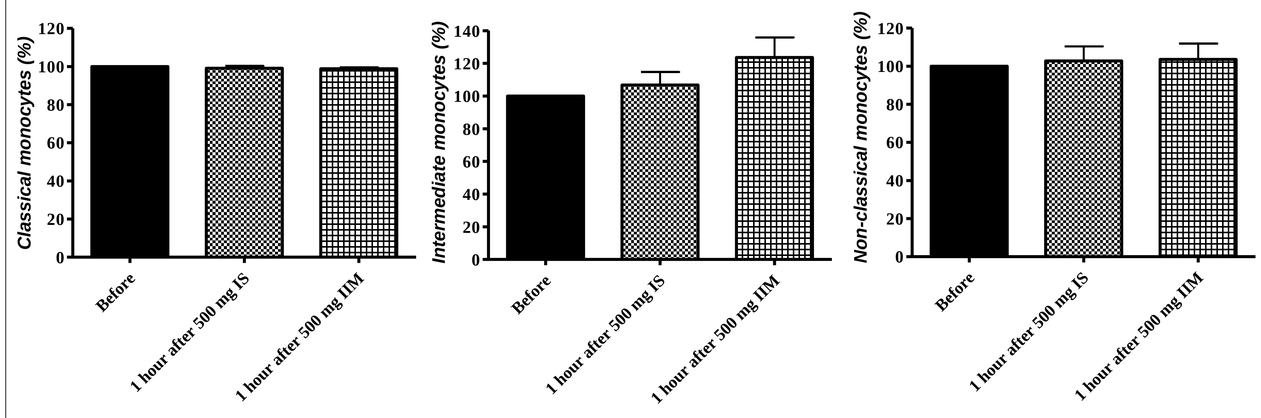


Fig. 2: Phagocytosis capacity

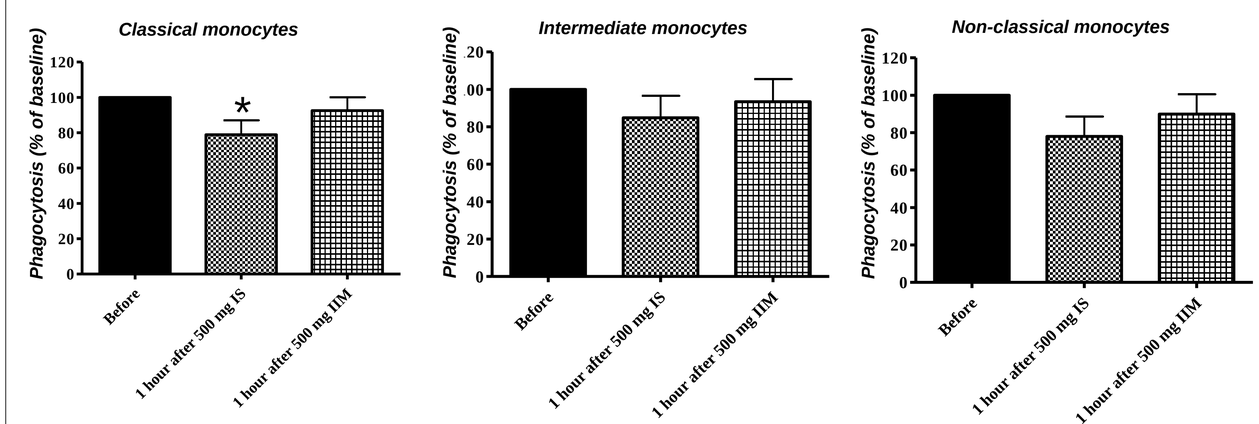


Fig. 3: Iron uptake (calcein assay)

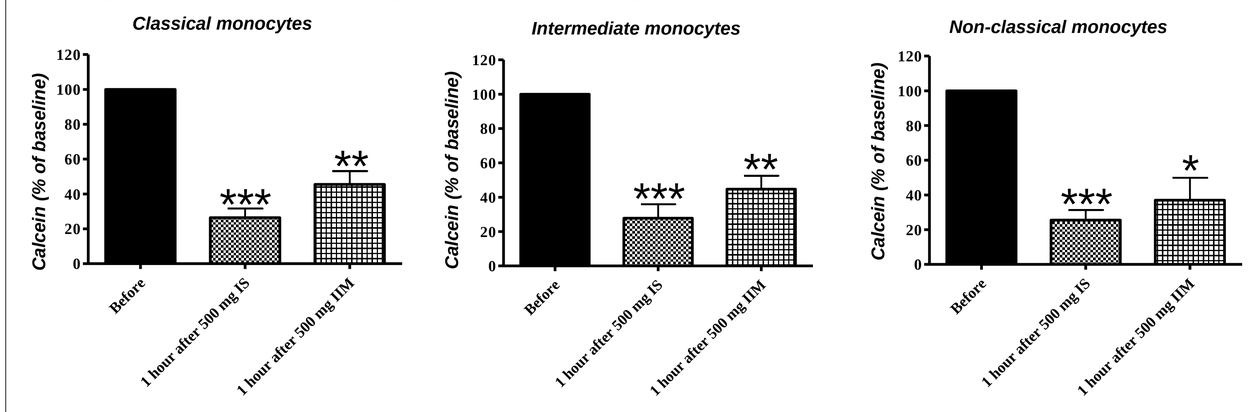
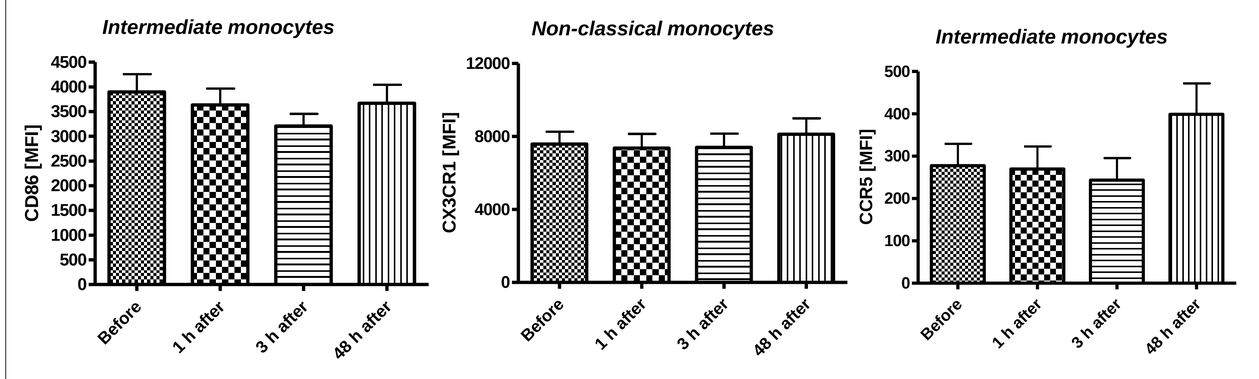


Fig. 4 - CD86 after IS | **Fig. 5 - CX3CR1 after IS** | **Fig. 4 - CCR5 after IS**



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.

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