ADMINISTRATION OF INTRAVENOUS IRON PREPARATIONS INDUCES COMPLEMENT ACTIVATION IN PATIENTS

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INTRODUCTION AND AIMS: Intravenous (IV) iron drugs are still a cornerstone in the management of anemia, either in patients with chronic kidney disease (CKD), or with other conditions leading to anemia, such as gastrointestinal (GI) bleeding. However, hypersensitivity reactions can occur after treatment with these IV iron preparations. The exact mechanism behind these reactions has not been fully elucidated yet. Recently, it has been demonstrated that iron preparations have the ability to activate complement in vitro. We investigated whether IV iron also activates complement in vivo.

METHODS: Plasma samples were collected from 80 patients that were treated for anemia with iron preparations, including 52 non-CKD (mostly anemic due to GI losses) and non-dialysis CKD, and 28 undergoing maintenance hemodialysis (HD). In the non-dialysis patients, samples were collected prior to, and 60 minutes after finishing IV iron treatment. In the HD patients, samples were collected during two consecutive sessions - one session without IV iron and one session where IV iron was administered. Iron sucrose was given to the HD patients and non-dialysis (CKD) or non-CKD patients, while ferric carboxymaltose was given only to the latter ones. Finally, MBL, C1q, Properdin, Factor D, C3d/C3-ratios and CSb-9 were measured.

RESULTS: In the anemic patients, IV iron induced complement activation since mean values of plasma sCSb-9 levels significantly increased 60 minutes after the iron infusion. In addition, Factor D levels were reduced after iron treatment in these patients, suggesting consumption due to alternative pathway activation. Similarly, in patients undergoing HD, increased sCSb-9 levels were found at the end of the HD session with iron treatment compared to the session without iron.

CONCLUSIONS: In summary, these findings show that IV iron preparations induce complement activation in vivo, both in non-CKD and HD patients. Furthermore, complement activation by IV iron seems to occur via the alternative pathway. However, the exact mechanism through which iron nanoparticles activate complement and how this translates into inflammation or allergy remains to be elucidated.