Inflammatory and hematological disturbances associated with resistance to recombinant human erythropoietin therapy in CKD anemia in a rat model

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Anemia of chronic kidney disease (CKD) is treated with recombinant human erythropoietin (rHuEPO); however, some patients become hyporesponsive. Our aim was to study the hematological and inflammatory disturbances associated to resistance to rHuEPO therapy using the remnant kidney rat model of CKD anemia.

Wistar rats were divided in 4 groups: Sham, CRF and rHuEPO treated groups (200IU/kg b w/wk) - responders (CRF200) and non-responders (CRF200NR). Blood was collected for hematological and biochemical analysis; kidney tissue was collected for gene and protein analysis.

The CRF200 group corrected anemia, while the CRF200NR group developed anemia after an initial response to rHuEPO therapy. CRF and CRF200NR groups showed a trend to higher CRP levels; CRF200NR showed also high levels of renal inflammatory markers.

Our data suggest that the development of anemia/rHuEPO resistance is associated with a higher systemic and renal inflammation, favoring hypoxia and triggering an increase in renal expression of fibrosis markers, which will enhance the inflammatory response, creating a cycle that promotes disease progression.