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"Iron metabolism in patients on peritoneal dialysis"

Summary

Anemia is one of the most common complications of chronic kidney disease, affecting the vast majority of patients on dialysis. Anemia is one of the contributing factors responsible for more rapid progression to end-stage renal disease, decreased quality of life, decreased cardiovascular performance, cognitive impairment, increased rate of hospitalizations and increased mortality. Pathophysiology of CKD-related anemia is multifaceted and encompasses relative erythropoietin deficiency, iron deficiency (both absolute and functional), impaired hepcidin clearance, shorter erythrocyte lifespan, nutritional deficiencies. Furthermore, patients on dialysis are likely to develop chronic subclinical inflammation as a result of repeated exposure to dialyzer membrane and drains, as well as non-biocompatible dialysis fluid. Current knowledge of iron metabolism and its intricacies will hopefully help develop novel diagnostic and therapeutic measures to combat the burden of anemia in ESRD population.

The aim of this manuscript was to establish usefulness of novel markers of iron metabolism in diagnosing and monitoring anemia, iron deficiency and inflammation in a unique group of peritoneal dialysis patients. PD remains an underutilized method of renal replacement therapy and its prevalence in Poland amounts to meagre 4%. Consequently, studies conducted in PD population tend to be small and consistent data on numerous anemia-related subjects are lacking.

Since iron replenishment remains the first step in improving hemoglobin levels in dialysis patients, assessment of iron stores is pivotal in choosing the correct therapeutic approach. Standard diagnostic tests of iron deficiency include TSAT (which represents the pool of circulating iron available for erythropoiesis) and ferritin (which reflects iron stores but at the same time remains an acute phase reactant, whose concentration increases in the event of inflammation). We assessed several novel markers in a group of 58 PD patients – namely hsCRP , IL-6, sTfR, hepcidin-25, ERFE, GDF 15 and zonulin. The assays were performed both in serum and in dialysate. The results of our study reinforced the point that residual kidney

function is the most important parameter, that corresponds with higher serum hemoglobin, decreased circulating inflammatory markers, and overall better clinical outcomes.

Peritoneal membrane transport is one of the characteristics, that determine the rate in which small solutes cross the barrier between the blood flowing through the capillaries in the peritoneal wall and the fluid that dwells inside peritoneal cavity. We managed to prove that PMT strongly correlated with dialysate sTfR, dialysate hepcidin, dialysate GDF15 and dialysate zonulin, as well as serum IL6, serum and dialysate hs-CRP. It remains unclear whether the aforementioned findings are associated with the properties of the peritoneal membrane and effectiveness of removal of these molecules via convective transport, or they result from systemic and/or local intraperitoneal inflammation. This observation needs further studies. Fast peritoneal transport associated with intraperitoneal inflammation (e.g. in the event of dialysis-related peritonitis) results in high peritoneal membrane permeability not only for small solutes but also for middle-size molecules and proteins. Our study also determined, that concentration of zonulin in dialysate was significantly higher in fast-average transporters, which corresponded positively with the degree of inflammation as measured by serum hsCRP and IL-6.

STfR is less influenced by inflammation than other iron metabolism indices and may be a useful tool for assessing iron deficiency anemia in chronic disorders associated with increased level of systemic inflammation. However, in our study population, sTfR correlated positively with serum hepcidin and ferritin and dialysate hsCRP and IL6, which was in opposition to another study conducted in HD patients. The correlation of sTfR with dialysate hsCRP and IL6 may be an expression of unique iron status in peritoneum in PD patients. The role of ERFE in erythropoietic activity in PD patients requires further investigation.