

Changes of PON1 paraoxonase and lactonase activities in hemodialysis and renal transplant patients

By Ferenc Sztanek, M.D.

Supervisor: György Paragh, M.D., D.Sc.

UNIVERSITY OF DEBRECEN, INSTITUTE OF INTERNAL MEDICINE

DOCTORAL SCHOOL OF HEALTH SCIENCES

Summary

Our current study is the first account of the alteration of lactonase activity in ESRD patients. Moreover, we showed in hemodialyzed and renal transplant patients that PON1 lactonase activity correlates with paraoxonase activity, homocysteine levels and serum ADMA levels. We conclude that hyperhomocysteinemia, elevated ADMA levels, reduced PON1 activity and decreased ability to hydrolyze homocysteine-thiolactone may lead to an increase in N-homocysteinylated and oxidatively modified protein levels, which might contribute to the accelerated atherosclerosis in uremic and renal transplanted patients.

Our results show significantly lower activities of the antiatherogenic PON1 in obese HD patients compared to malnourished subjects. Despite our findings regarding the reverse epidemiology for the mortality of HD patients, further studies are needed to reveal the real effects of nutritional state on atherosclerosis in obese and malnourished CKD patients. There is growing evidence in the literature to support our initial hypothesis that the antioxidant properties of PON-1 enzyme are closely associated with PON1 paraoxonase activity and not with lactonase activity. Therefore, in the present study we have primarily investigated the relationship between PON1 paraoxonase activity and the antioxidant status in chronic kidney disease depending on nutritional status. Our goal was to evaluate the alteration of PON1

paraoxonase and lactonase activities and their correlations with nutrition levels in malnourished, normal-weight and obese hemodialyzed patients. Our result suggests that PON1 paraoxonase activity may be a reliable marker regarding the progression of renal failure in malnourished subjects compared with the obese hemodialyzed patients. To our best knowledge, there is no specific substance or enzyme, which can determine the lactonase activity of PON1 enzyme. Otherwise, we have shown in our previous study that the PON1 lactonase activity was not independent of PON1 paraoxonase activity in patients with chronic kidney disease.

Tárgyszavak:

krónikus vesebetegség, PON1 laktonáz, PON1 paraoxonáz, tápláltsági állapot

Keywords:

chronic kidney disease, nutritional state, PON1 lactonase, PON1 paraoxonase