POTENTIAL ROLE OF THE ZINC–METALLOTHIONEIN AXIS IN EARLY MORPHOLOGICAL KIDNEY INJURY ASSOCIATED WITH EXPERIMENTAL DIABETES

Yuzboyev Oltinbek Abdullajon o'g'li
Central Asian Medical Institute, Assistant Lecturer
E-mail: oltinbek.yuzboyev.93@mail.ru

Annotation. *Early diabetic kidney injury results from interactions among hyperglycemia, oxidative stress, inflammation, cellular responses, and extracellular-matrix remodeling. Zinc has particular biological importance because it contributes to antioxidant defense and is linked to metallothionein synthesis. This thesis focuses on the potential zinc–metallothionein pathway rather than zinc concentration alone. The proposed integrated assessment combines renal zinc status, metallothionein expression, oxidative injury, glomerular morphology, and albuminuria to explore a possible protective mechanism in experimental diabetic kidney disease.*

Keywords: *diabetic kidney disease; zinc; zinc homeostasis; glomerulus; mesangial expansion; morphometry; metallothionein; oxidative stress*

Introduction. Early diabetic renal injury can develop before advanced functional impairment. Hyperglycemia may increase intracellular oxidative processes and promote inflammatory and fibrotic responses. At the glomerular level, these mechanisms can alter mesangial cell activity and increase extracellular-matrix accumulation. Zinc participates in antioxidant systems and cellular defense, while metallothionein is involved in metal binding and protection against cellular stress. The source article cites experimental findings in which zinc supplementation was associated with increased renal zinc and metallothionein and reduced oxidative injury.

Aim. To analyze the potential association between renal zinc status, metallothionein expression, oxidative stress, and early glomerular morphological changes in experimental diabetes.

Materials and Methods. Animals would be divided into control, experimental diabetes, and diabetes-with-zinc-correction groups. Blood, urine, and kidney tissue would be examined. Serum and urinary zinc would characterize systemic and renal zinc handling, while tissue zinc would indicate local renal status. Kidney sections would undergo histological and morphometric assessment of glomerular area and mesangial matrix fraction. Metallothionein expression could be evaluated by immunohistochemical or molecular methods. Albuminuria and selected biochemical indicators would provide complementary functional information. Statistical analysis

would examine associations among tissue zinc, metallothionein, oxidative injury, and morphology.

Results and Discussion. The expected pattern is a relationship between diabetes-associated oxidative stress and changes in renal zinc homeostasis. Reduced tissue zinc availability may accompany increased oxidative injury and altered glomerular morphology. If zinc correction enhances metallothionein expression and reduces oxidative damage, mesangial matrix expansion may be less pronounced than in untreated diabetic animals. A possible biological pathway is hyperglycemia → oxidative stress → altered zinc/metallothionein defense → extracellular-matrix accumulation and mesangial expansion. This pathway remains a hypothesis and requires experimental verification.

The scientific value of this approach is its integration of biochemical, molecular, functional, and morphological indicators. Morphometry demonstrates the structural component of injury, while zinc and metallothionein measurements may help explain the biological context. Such an integrated design may help investigate early structural changes before advanced renal dysfunction.

Conclusion. The zinc–metallothionein system may contribute to the renal response to experimental diabetes and may have a potential protective role against oxidative injury. Its relationship with mesangial matrix expansion deserves further investigation. Future studies should use real laboratory measurements, validated oxidative-stress markers, standardized morphometry, and appropriate statistical models to determine whether the observed associations are biologically meaningful and potentially causal.

References:

1. Gembillo G, Visconti L, Giuffrida AE, et al. Role of Zinc in Diabetic Kidney Disease. Nutrients. 2022;14(7):1353.
2. Özçelik D, Nazıroğlu M, Tunçdemir M, et al. Zinc supplementation attenuates metallothionein and oxidative stress changes in kidney of streptozotocin-induced diabetic rats. Biological Trace Element Research. 2012;150(1–3):342–349.
3. Tang Y, Yang Q, Lu J, et al. Zinc supplementation partially prevents renal pathological changes in diabetic rats. Journal of Nutritional Biochemistry. 2010;21(3):237–246.
4. Özçelik D, Tunçdemir M, Öztürk M, Uzun H. Evaluation of trace elements and oxidative stress levels in the liver and kidney of streptozotocin-induced experimental diabetic rat model. General Physiology and Biophysics. 2011;30(4):356–362.