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THE IMPACT OF OXIDATIVE STRESS ON RENAL FUNCTION

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Abstract
Oxidative stress is a key pathogenic mechanism contributing to acute and chronic kidney injury. Excessive production of reactive oxygen species (ROS) overwhelms renal antioxidant defenses, resulting in cellular damage, inflammation, vascular dysfunction, and fibrosis. This article reviews molecular mechanisms of oxidative stress–induced renal injury, summarizes recent experimental and clinical findings, and discusses therapeutic strategies aimed at attenuating oxidative damage to improve renal outcomes.

Keywords: Oxidative stress, renal dysfunction, ROS, nephropathy, antioxidants.

Introduction

The kidneys play a fundamental role in maintaining internal homeostasis through filtration, electrolyte regulation, blood pressure control, and endocrine functions. Various pathological conditions—including diabetes mellitus, hypertension, ischemia–reperfusion injury, and exposure to nephrotoxic agents—impair renal physiology. A unifying mechanism underlying these diverse disorders is **oxidative stress**, defined as excessive formation of reactive oxygen species relative to antioxidant capacity.

Oxidative stress contributes to both acute kidney injury (AKI) and chronic kidney disease (CKD). The resulting cellular injury, inflammation, and progressive fibrosis lead to nephron loss and deterioration of renal function. Understanding these mechanisms is crucial for identifying therapeutic targets to prevent kidney damage.

2. Mechanisms of Oxidative Stress in Kidney Injury

2.1. ROS Production and Mitochondrial Dysfunction

The mitochondria are the primary source of ROS in renal tubular cells. Under pathological conditions such as hyperglycemia or ischemia, electron leakage from the mitochondrial respiratory chain leads to excessive superoxide formation. This disrupts ATP synthesis, damages mitochondrial DNA, and initiates apoptotic pathways.

2.2. Lipid, Protein, and DNA Damage

ROS induce lipid peroxidation of cell membranes, leading to altered permeability and cell death. Proteins undergo oxidation, resulting in enzyme inactivation, impaired transport function, and structural instability. DNA oxidation triggers mutations and apoptosis, contributing to nephron loss.

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2.3. Inflammatory Pathways

Oxidative stress activates redox-sensitive transcription factors, particularly NF-κB and AP-1. This stimulates the production of pro-inflammatory cytokines (IL-6, TNF-α, IL-1β), chemokines, and adhesion molecules. Chronic inflammation accelerates renal fibrosis.

2.4. Endothelial Dysfunction

ROS reduce nitric oxide (NO) bioavailability, impairing vasodilation and renal microcirculation. This leads to glomerular hypertension, albuminuria, and progressive sclerosis.

2.5. Fibrosis and Extracellular Matrix Accumulation

Oxidative stress stimulates transforming growth factor-β1 (TGF-β1), a key profibrotic mediator. TGF-β1 promotes extracellular matrix deposition and tubular atrophy—hallmark features of CKD progression.

3. Clinical Evidence

Clinical studies consistently demonstrate elevated oxidative biomarkers in kidney diseases. For example:

- Patients with diabetic nephropathy show increased malondialdehyde (MDA) and decreased superoxide dismutase (SOD) activity.
- CKD patients exhibit higher levels of 8-hydroxy-2'-deoxyguanosine (8-OHdG), a marker of oxidative DNA damage.
- Ischemia–reperfusion injury in kidney transplantation is strongly correlated with ROS generation and impaired graft function.

Antioxidant therapies have shown varying degrees of improvement in creatinine clearance, albuminuria, and inflammatory markers.

4. Therapeutic Approaches

4.1. Pharmacological Antioxidants

- **N-acetylcysteine (NAC):** replenishes glutathione stores and reduces ROS.
- **Vitamin E and C:** scavenge free radicals and reduce lipid peroxidation.
- **Coenzyme Q10:** improves mitochondrial stability.
- **Mitochondria-targeted antioxidants (e.g., MitoQ):** currently under active investigation.

4.2. Lifestyle Interventions

- Diet rich in fruits, vegetables, and polyphenols.
- Improved glycemic control in diabetes.
- Regular physical exercise enhances antioxidant enzyme activity.

4.3. Novel Experimental Therapies

- NADPH oxidase inhibitors
- TGF-β1 pathway blockers
- Stem cell–derived exosomes with antioxidant properties

Although promising, these treatments require extensive clinical trials.

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5. Conclusion

Oxidative stress plays a central role in the pathogenesis of kidney injury. By damaging cellular structures, promoting inflammation, and inducing fibrosis, ROS contribute significantly to the development and progression of AKI and CKD. Therapeutic strategies targeting oxidative stress—both pharmacological and lifestyle-based—offer potential to preserve renal function. Further research is required to refine antioxidant therapies and translate experimental findings into clinical practice.

References

1. Halliwell, B., & Gutteridge, J. M. (2015). Free Radicals in Biology and Medicine. Oxford University Press.
2. Forbes, J. M., & Cooper, M. E. (2013). Mechanisms of diabetic complications. Physiological Reviews, 93(1), 137–188.
3. Zorov, D. B., Juhaszova, M., & Sollott, S. J. (2014). Mitochondrial ROS-induced ROS release. Physiological Reviews, 94(3), 909–950.
4. Vaziri, N. D. (2004). Oxidative stress in uremia. Nature Clinical Practice Nephrology, 1(2), 82–93.
5. Ortiz, A., et al. (2020). Chronic kidney disease and oxidative stress. Kidney International Supplements, 10(1), e1–e20.
6. Tbahriti, H. F., et al. (2013). Oxidative stress in chronic kidney disease. International Journal of Nephrology, 1–7.
7. Balogun, R. A., et al. (2017). Oxidative stress in ischemia–reperfusion injury. American Journal of Nephrology, 46(4), 260–270.
8. Li, S., et al. (2019). Antioxidant therapies in CKD. Journal of Cellular and Molecular Medicine, 23(4), 2385–2402.
9. Tran, M., et al. (2011). Role of mitochondrial dysfunction in AKI. Nature Medicine, 17(1), 17–23.
10. Daenen, K., et al. (2019). Oxidative stress biomarkers in kidney disease. Nephrology Dialysis Transplantation, 34(2), 1–15.

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