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Effects of Particulate Matter on Inflammation, Oxidative Stress, and Fibrosis in Animal Model of Chronic Kidney Disease

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Objectives : Epidemiologic analysis have demonstrated an association between exposure to particulate matter (PM) with respiratory, cardiovascular, and kidney diseases. However, no studies have investigated the causal role of PM in the development or pregression of kidney disease. The activation of endoplasmic reticulum (ER) stress, NLRP3 inflammasome, and oxidative stress are the key mechanisms underlying renal injury. This study aims to explore the effects of artificially manufactured PM (APM) on the kidneys in an animal model of CKD using unilateral ureteral obstruction (UUO).
Methods : Male Sprague-Dawley rats were divided into four groups: Normal control, APM (5 mg/kg, administration for 3 or 5 times via intratracheal instillation), UUO, and UUO+APM. BUN, proteinuria, and renal histology including macrophage marker ED-1 expression were assessed. Markers of ER stress (GRP78, ATF4, CHOP, and cleaved caspase-1), NLRP3 inflammasome (NLRP3 and ASC), oxidative stress (nitrotyrosine, SOD2, catalase, and GPx1) and renal fibrosis (F4/80, α-SMA, and osteopontin) were analyzed in kidney tissue at 9 or 14 days following APM exposure.
Results : Rat in the UUO group exhibited increased BUN, tubulointerstitial fibrosis, and upregulated expression of GRP78, ATF4, CHOP, NLRP3, ASC, and cleaved caspase-1. Markers of renal fibrosis are upregulated in the UUO group, with increased nitrotyrosine level and reduced SOD2, catalase, and GPx1. In the APM+UUO group, ED-1, GRP78, and CHOP increased at 9 and 14 days, while NLRP3, cleaved caspase-1, F4/80, and osteopontin upregulated at 14 days. In normal rats, APM exposure also increased ATF4, cleaved caspase-1, NLRP3, oxidative stress imbalance, and upregulated F4/80 and osteopontin.
Conclusions : Exposure to APM resulted in enhanced expression of markers of renal inflammation, ER stress, oxidative stress, NLRP3 inflammasome, and fibrosis in both normal and UUO rat models. These findings suggest a potential causal role of PM in kidney disease in individuals with both normal renal function and CKD.