SUBCLINICAL NEPHROTOXICITY CAUSED BY SMOKING AND OCCUPATIONAL SILICA EXPOSURE AMONG MALE KENYAN INDUSTRIAL WORKERS

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Abstract

Occupational exposure to silica and cigarette smoking could lead to slow and progressive renal injury. Assessment of renal injury based on the concentrations of blood urea nitrogen (BUN), serum creatinine (S.Cr) or total urinary protein (U.TP) is insensitive since these parameters could be within normal ranges despite considerable impairment of the renal function because of the great reserve capacity of the kidney. Urinary biomarkers which could be used to detect nephrotoxicity at early stages and defects on various parts of the nephron include: the high molecular weight protein albumin for evaluating glomerular integrity; the low molecular weight proteins α_1-microglobulin (U.α_1M) and retinol binding protein (U.RBP) for assessing tubular reabsorption function; the brush border enzyme leucine aminopeptidase (U.LAP), lysosomal enzyme N-acetyl-β-D-glucosaminidase (U.NAG) and cytoplasmic enzyme glutathione-S-transferase (U.GST) for indicating proximal tubular injury. Animal studies have identified brush border enzymes alkaline phosphatase (U.ALP) and γ-glutamyltransferase (U.γ-GT) and cytoplasmic enzyme lactate dehydrogenase (U.LDH) as potential urinary biomarkers of renal injury. The nephrotoxic effects caused by silica exposure have been studied elsewhere but the effect of silica exposure on the urinary excretion of microalbumin (U.Malb), total protein (U.TP), alkaline phosphatase (U.ALP), γ-glutamyltransferase (U. γ-GT), and lactate dehydrogenase (U.LDH), aspartate aminotransferase (U.AST) and alanine aminotransferase (U.ALT) has not been studied with human subjects from Kenya. The present study investigated early signs of renal injury due to silica exposure and smoking by measuring urinary indicators of nephrotoxicity and the association of this excretion to work duration. The study subjects comprised 37 silica exposed (33 non smokers, median age 43.50 years; 4 smokers, median age 26.00years), and 46 male reference workers (38 non smokers, median age 37.50 years; 8 smokers, median age 40.50 years). Reference (less than 10 years, median age 32.40 years, n = 20; more than 10 years, median age 43.67 years, n = 26) and silica exposed male workers (less than 10 years, median age 29.00 years, n = 17; more than 10 years, median age 47.33 years, n = 20) were further grouped into those with work duration of less than ten years and those with work duration of more than ten years. Glomerular function was studied by determining the urinary

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levels of microalbumin (U.Malb), while proximal tubular structural integrity was studied by determining the activities of the enzymes alkaline phosphatase (U.ALP), γ-glutamyltransferase (U.γ-GT), lactate dehydrogenase (U.LDH), aspartate aminotransferase (U.ALT) and alanine aminotransferase (U.AST). In addition, the levels of urinary silicon (U.Si) and creatinine (U.Cr) were also measured. Compared with the: reference nonsmoking male workers, nonsmoking silica exposed male workers excreted significantly increased levels of U.TP, U.Malb, U.ALP, U.γ-GT and U.LDH; reference smoking male workers, smoking silica exposed male workers excreted significantly increased levels of U.TP, U.Malb, and U.LDH. Silica exposed male workers with work duration of less than ten years had significantly reduced U.γ-GT compared to silica exposed male workers with work duration of more than ten years. Among the silica exposed male workers with work duration of less than ten years, U.TP was negatively correlated with work duration. In conclusion, the present study confirms: that silica exposure may lead to nephrotoxicity; that smoking has also a nephrotoxic effect on the kidney and is synergistic to nephrotoxicity of silica exposure; that the elevation of some of the measured urinary parameters in silica exposed male workers is not associated with work duration; that urinary excretion of U.TP, U.Malb, U.ALP, U. γ-GT and U.LDH could be useful biomarkers for glomerular function and proximal tubular injury; and that U.AST and U.ALT may not be relevant in the diagnosis of renal injury.

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