

## Increasing Concerns About Tobacco and Nicotine Risks

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Received: 01 Sep. 2017; Accepted: 19 Dec. 2017

Smoking is among major preventable causes of death in the whole world, with the majority of deaths occurring in people from low- and middle-income areas (1-7). The recent study by Shekoohi *et al.*, compared the serum levels of active and inactive vitamin B12 among the Iranian male groups of 85 smokers and 85 nonsmokers (5). Although the serum levels of total vitamin B12 were similar in both groups, lower levels of the active form of the vitamin were detected among the smoker individuals (5). Among other mechanisms, cyanide cigarette smoke can combine with the active vitamin (hydroxocobalamin) and yield cyanocobalamin that is a non-active product (5). In conclusion, the serum total level of vitamin B12 is not a valid parameter to evaluate biological activity in smokers, and other forms of this vitamin should be measured (5).

Cardiovascular or pulmonary diseases and some malignancies have been directly associated with smoking; however, the effects on the renal system are less described (1). Recent systematic review and meta-analysis of prospective cohort study in general population indicated that smoking is independent risk factor for chronic renal disease (7). Worthy of note, compared with never-smokers the summary relative risks (SRRs) of incident chronic renal disease were 1.27 for ever-smokers, 1.34 for current smokers and 1.15 for former smokers; whereas the SRRs for end-stage renal disease development were 1.51 for ever-smokers, 1.44 for former smokers and 1.91 for current smokers (7).

Elevated levels of free radicals in tobacco smoking play a role in atherosclerosis, endothelial dysfunction and vascular disease progression, increasing the cardiovascular risks with decreased survival rate of the renal transplant recipients and of the grafts (1). Nicotine can cause microalbuminuria, increase renal vascular resistance and decrease glomerular filtration rate, effects related to the grade of drug exposure; thus, cotinine might be a useful biomarker to evaluate the status of smoking and the dose of nicotine (1). This procedure would be a very useful tool in the phase of pre-transplant evaluation because both donor and recipient smoking have a proven negative impact on survival (1).

Brazilian authors described nodular glomerulosclerosis in 62- and 64-year-old white males who were non-diabetic hypertensive smokers with dyslipidemia (2,3). Although smoking is a cause, the entity is called idiopathic nodular glomerulosclerosis; related conditions include chronic arterial hypertension and renal vascular disease (2,3). The features under light microscopy are similar to diabetic nephropathy; and electron microscopy shows thickened glomerular basal membrane, nodular expansion of mesangial matrix, and arterial hyalinosis, without immune complexes deposition (2,3).

Nicotine plays a major role in coronary events, aortic aneurysms, and peripheral artery disease associated with lipid disorder, insulin resistance, and renal atheromatous disease; in addition to the reduction of the effectiveness of most antihypertensive drugs (4). This parasympathomimetic alkaloid has been useful in smoking cessation therapy, but there is some concern about not well clear interactions with hydrogen sulfide (H<sub>2</sub>S). Experiments showed nicotine effects on kidney and heart concentration of H<sub>2</sub>S, which is involved in various systems of the physiology and pathophysiology in mammals (6).

Increasing evidence of renal involvement by nicotine adverse-effects strongly suggests that prospective studies should be done, including utilization of the alkaloid in smoking cessation programs, and quantification of smoking by cotinine levels (1,5).

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