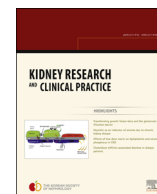




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Editorial

Niacin in patients with chronic kidney disease: Is it effective and safe?



Chronic kidney disease (CKD) is a world wide health problem. Cases of early-stage CKD are now reaching epidemic proportions. Only recently has CKD become a major priority of care for the health system. The decline in renal function in CKD is mediated by arterial hypertension, glomerular capillary hypertension and hyperfiltration, oxidative stress, inflammation, and lipid disorders. CKD itself results in profound alterations in lipid metabolism and plasma lipid profiles characterized by hypertriglyceridemia, diminished HDL cholesterol, impaired HDL maturation, and depressed HDL antioxidant and anti-inflammatory activities [1–3]. The associated dyslipidemia has been shown to contribute to aggravation of CKD and cardiovascular disease (CVD) in patients with CKD, and lipid-lowering therapies have proven effective in ameliorating progression of renal disease and CVD [4,5]. Cellular lipid accumulation in the kidney has been shown to promote or accelerate kidney disease in animal models of CKD (5/6 nephrectomized rats) [6].

CKD is known to be associated with accelerated arteriosclerosis and atherosclerosis. Importantly, CVD is the main cause of morbidity and mortality in patients with CKD. A recent study suggested the potential benefit of lipid-lowering mediation in preventing cardiovascular events in patients with CKD [7]. Abnormalities in calcium–phosphorus homeostasis, including significant elevations in serum phosphorus concentrations, are thought to contribute to arterial stiffening, hypertension, and CVD risk in patients with CKD [8–11]. Even serum phosphorus concentrations within the normative range are linearly associated with subclinical arteriosclerosis and the development of incident CVD [11]. Therefore, phosphorus-lowering drugs that simultaneously target other cardiovascular risk factors in CKD, for example, dyslipidemia, might have additive or synergic benefits.

In this issue of *Kidney Research and Clinical Practice*, Kang et al [11] evaluated whether low-dose niacin supplementation (500 mg/d for 6 months) can improve dyslipidemia and lower serum phosphorus. They also examined the frequencies of adverse effects in CKD patients (i.e., Stages 2–4) receiving low-dose niacin treatment. By retrospectively comparing the effects of dyslipidemia and serum phosphorus in 31 patients receiving niacin treatment to 30 CKD control patients who did not receive niacin treatment, they found that niacin treatment increased HDL cholesterol and decreased triglycerides and

serum phosphorus. In addition, niacin treatment improved the glomerular filtration rate compared to baseline values. There were few adverse effects, and only 8% of CKD patients discontinued niacin treatment. They concluded that low-dose niacin improves dyslipidemia, lowers serum phosphorus, and increases GFR in patients with CKD with a low frequency of adverse effects. The authors recommended that low-dose niacin is efficient and very well tolerated, which makes it ideal for the treatment of CKD patients with hyperlipidemia and hyperphosphatemia.

Niacin (nicotinic acid, vitamin B3) is a water-soluble vitamin that is critical for cellular metabolism [12]. As a broad-spectrum drug that can affect lipid levels, niacin inhibits adipocyte lipolysis via nicotinic acid receptors, lowering total cholesterol, triglyceride, LDL cholesterol, and VLDL cholesterol, and also increasing HDL cholesterol at a dose of 1–3 g/d [13–15]. Niacin also lowers serum phosphorus levels in patients with CKD, as it is also a direct inhibitor of phosphate absorption from the GI tract [15,16]. It is recently become well known that nicotinamide inhibits the Na Pi-2b and Na Pi-2a sodium-dependent phosphate cotransporters of the GI tract [17] and kidneys [18], respectively. Furthermore, niacin plays a key role in cardiovascular diseases and cardiovascular-related mortality by modifying both dyslipidemia and phosphorus levels [19]. Interestingly, Kang et al also demonstrated in their study that low-dose niacin treatment improved renal function in their study, which is only associated with niacin treatment. A recent study showed that niacin administration improves renal tissue lipid metabolism, renal function and structure, hypertension, proteinuria, and histological tubulointerstitial injury in an animal model of 5/6 nephrectomized rats [6]. The authors concluded that niacin supplementation mitigates the upregulation of oxidative stress and the inflammatory system in the kidney. However, in another study, niacin treatment (1 g/d for 4 weeks and advanced to 2 g/d for 20 weeks) in patients with CKD (i.e., Stages 2–3) did not show renoprotective effects [20]. Despite these positive roles of niacin, physicians hesitate to prescribe niacin because of its various adverse effects, such as prostaglandin-mediated hot flushing, liver function test disruption, exacerbation of peptic ulcer disease, nausea, vomiting, pruritus, hives, constipation, increased uric acid levels, and thrombocytopenia. Some of these adverse effects are slight and easily controlled by

symptomatic care, but some adverse effects such as hot flushing necessitate cessation of niacin administration [14,15]. The metabolism of niacin and nicotinamide in subjects with CKD has not yet been studied, so the appropriate dosing in such patients is unknown. Approximately 75 % of a dose of niacin is excreted in the urine as the parent drug and several metabolites (mainly the latter) in normal subjects, regardless of the type of the niacin preparation [19]. However, there is no published information available on the pharmacokinetics of niacin in patients with advanced CKD or end-stage renal disease. Therefore, before niacin can be used safely, niacin's side effects (chiefly facial flushing) must be minimized and the pharmacokinetics of niacin in patients with CKD or end-stage renal disease must be clarified.

In conclusion, recent experimental and clinical studies, including that of Kang et al [11], suggest that niacin and its metabolites nicotinamide could be used to treat hyperlipidemia and to lower phosphate levels in patients with CKD. However, further studies are needed to evaluate whether long-term treatment with low-dose niacin is effective, well tolerated, and safe and has a preventive effect on the progression of CKD.

Conflicts of interest

None.

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