



Niacin: Does it Affect 8-hydroxy-2-deoxyguanosine Levels in Patient with Low HDL Cholesterol?

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Abstract

We aimed to determine whether niacin improve plasma HDL-cholesterol levels by decreasing 8-Hydroxydeoxyguanosine (8-OHdG) as a biomarker of oxidative DNA damage or not. Patients (n=32) with low HDL-cholesterol levels (≤ 40 mg/dl) were included in the study. Lipoprotein profiles (total cholesterol, HDL-C, and total triglycerides) were measured in all patients. LDL-C was calculated as described by Friedewald et al. Before and after 16 week of niacin therapy serum 8-OHdG was measured. There were significant difference between pre and post treatment plasma HDL-C and 8-OHdG levels. We concluded that niacin may raise HDL-C levels. The improvement of plasma HDL-C levels may have a protective effect on endothelial dysfunction. By reducing the level of 8-OHdG, niacin may decrease DNA damage. Thus, niacin therapy may be consider as an alternative to statins or fibrates in patients in whom fail to sufficiently correct low HDL-C levels.

Key Words: Niacin, 8-OHdG, HDL cholesterol

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Introduction

Niacin (nicotinic acid) has been used for more than 30 years to treat plasma lipid disorders and to prevent atherosclerotic cardiovascular disease [1]. Niaspan prolonged release tablets contain the active ingredient nicotinic acid (also known as niacin), which is a member of the group of B vitamins. Niacin blocks fatty acid flux from adipose tissue. It also suppresses hepatic assembly and release of very low-density lipoprotein; this latter effect reduces TG levels and decreases the number of small dense LDL particles. Niacin may also block a putative HDL holoparticle catabolic receptor responsible for intrahepatic degradation of HDL, thereby increasing the effective half-life of HDL and raising HDL-C concentrations [2].

Low levels of HDL, also known as hypoalphalipoproteinemia (HA), includes a variety of conditions, ranging from mild to severe, in which plasma concentrations of alpha lipoproteins or HDL [3]. The US National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) redefined the HDL level that constitutes a formal cardiovascular disease (CHD) risk factor. Treatment of isolated low HDL has gained increasing importance in the literature in the recent years. According to the ATP III, if a patient's TG levels are below 200 mg/dl and HDL is low (isolated low HDL), the administration of drugs that increase HDL (fibrates or nicotinic acid) can be considered. Statins exert only a modest effect [3].

8-OHdG is a biomarker of cellular oxidative stress but might also be a risk factor for atherosclerosis and diabetes. The oxidative hydroxylation of guanine in the 8-position is the most frequent and most mutagenic lesion in nuclear DNA. Many authors have examined the relationship between oxidative stress and several diseases such as cancer, obesity, diabetes, and hypercholesterolemia.

Recent data have indicated that niacin also decreases C-reactive protein levels, improves endothelial dysfunction, increases the endothelial and leukocyte oxidation-reduction (redox) state *in vitro*, inhibits cytokine-induced monocyte adhesion to human endothelial cells, improves plaque stability, and reduces thrombosis [4,5,6]. Thus, we aimed to evaluate HDL-C and 8-OHdG levels after niacin treatment.

Subject and Methods

Patients (32 male) having low HDL cholesterol levels (≤ 40 mg/dl) and control subjects (20 male) were included in the study. Written informed consent was obtained from all participants prior to enrollment into study. The study protocol was conducted according to the guidelines of the Declaration of Helsinki and had been approved by the local Ethic Committee. Subjects were excluded from the study for diabetes, renal disease, liver disease, gout, hyperuricemia, peptic ulcer disease, history of myositis, untreated hypothyroidism, and cancer. All patients underwent niacin prolonged release tablets (niaspan, Abbott). Niacin tablets were dispensed at 4-week intervals in increasing doses of 50, 250, and 500 mg twice daily. Normal maintenance dose was 1500 mg every night at bedtime. Blood samples were collected in the first visit (pretreatment) and second visit (16-weeks after initiation of therapy). Serum 8-OHdG was measured using an ELISA Kit, Cayman Chemical, USA. The test utilizes an anti-mouse IgG-coated plate and a tracer consisting of an 8-OHdG conjugate. This format has the advantage of providing low variability and increased sensitivity compared with assays that utilize an antigen-coated plate. Procedure was as described in the protocol provided by the manufacturer. Absorbance was measured at 450 nm using a Microplate Reader Multiscan FC (Thermo-Scientific).

Lipoprotein profiles (total cholesterol, HDL-C, and total triglycerides) were measured on plasma samples, obtained after an overnight fast. LDL-C was calculated. Statistical analysis of data was performed with 95% confidence at windows package program. Mann Whitney U test was used for comparison of data between groups. $p < 0.05$ value was considered to be statistically significant.

Results

The distribution of the groups in terms of age and gender were similar. The data of the subjects are shown in table 1. The mean duration of treatment was 16 weeks for the patients.

Table 1. Demographic data and laboratory parameters of subjects

	Control Group	Patient Group (pre-treatment)	p value
Age (year)	50,4±3,53	50,7±5,27	0.85
Gender (Male)	20	32	-
HDL (mg/dl)	41±1,3	39±1,2	<0,01
TG (mg/dl)	268±17,4	278±22,5	>0,05
LDL (mg/dl)	97±3,8	105±3,9	>0,05
8-OHdG (ng/ml)			
(mean±SD)	0,27±0,03	0,26±0,03	>0,05

8-OHdG levels was 0,26±0,03 in period of pretreatment. But, it was measured 0,25±0,02 after treatment. Ultimately, we detected that there was statistically significant decrease at 8-OHdG levels after treatment (p=0,036). Similarly, It was found statistically significant increase at serum HDL-C levels (p=0,01) (Table 2).

Table 2. Serum HDL-C levels

	Patient Group (pre-treatment)	Patient Group (post-treatment)	p value
HDL (mg/dl)	39±1,2	41±1,3	<0,01
8-OHdG (ng/ml)			
(mean±SD)	0,26±0.03	0,25±0,02	<0,05

Discussion

The use and effects of niacin on plasma lipoproteins were first described over fifty years ago. Niacin was the first drug to show efficiency in reduction of both major cardiovascular events and mortality in patients with prior myocardial infarction [7]. The routine use of early preparations of niacin was limited by side effect profile. Niacin has been superseded in recent years with the advent of newer lipid-modulating interventions [3,4,8]. However, whether niacin itself is used routinely in the future will depend on the outcomes of two large outcome trial (AIM-HIGH and HPS2-THRIVE) [9,10]. There are conflictive effects besides positive effects of niacin on lipid profile. However, it should be considered priority at treatment. Because, niacin may reduces the DNA damage and inflammation. This “pleiotropic” role may well play a significant role in the beneficial effect of niacin on cardiovascular outcomes both systemically and at a local/cellular level. Ultimately, we wanted to emphasize that the niasin treatment should be kept in mind priority in routine practice.

Conclusion

Our results suggest that beside the HDL-C decreasing effect, niacin may decrease DNA damage by reducing the level of 8-OHdG.

Abbreviations: HDL-C (High density lipoprotein cholesterol), LDL-C (Low density lipoprotein cholesterol), TG (Triglyceride), 8 OHdG (8 hydroxy-2-deoxyguanosine)

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