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Ezetimibe, Oxidized Low Density Lipoprotein, Lp (a), and Dyslipidemia

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In the recent paper published by Nozue *et al.* (J Atheroscler Thromb, 2010; 17(1): 37-44)¹⁾, the authors investigated the effects of the intestinal cholesterol absorption inhibitor, ezetimibe, on lipids and other risk markers for atherosclerosis in subjects with hyperlipidemia.

The effects of ezetimibe in different clinical scenarios of cardiovascular disease are not well known, and its effects beyond cholesterol reduction are yet less explored, when compared with those attributed to the inhibition of cholesterol synthesis by statins. In the paper published by Nozue *et al.*, the authors indicated that the administration of ezetimibe for 12 weeks resulted in beneficial effects on biomarkers for atherosclerosis.

Nozue *et al.* postulated that the two groups, ezetimibe 10 mg monotherapy, and ezetimibe 10 mg plus a statin, apparently produced the same results after 12-week follow-up; however, there was no study regarding the effects of statins alone, since these agents are capable of reducing low-density lipoprotein cholesterol (LDL-C), C-reactive protein (hs-CRP), triglycerides, and oxidized LDL (oxLDL)^{2, 3)}; in addition, the particular potency of each drug as a hypolipidemic agent could have been taken into account, as demonstrated in the Discovery study⁴⁾.

These observations on lipid alterations and oxidative parameters could have been evaluated with the addition of another group of patients receiving a statin alone in a dose equivalent to that of a statin combined with ezetimibe, of the same class or with similar hypolipidemic potency. We observed that in the group that received statins there were patients with type 2 diabetes and a history of coronary artery disease, compared with the group without these metabolic and inflammatory alterations. It is already known that in this patient population the response to hypolipidemic strategies may differ substantially, as diabetic patients have

increased cholesterol absorption.

The results were presented by grouping the two treatment arms and were quoted as the general effects of ezetimibe, an issue that can affect the findings, since it does not control for other variables, beyond statin effects, such as diet, intensity and volume of exercise performed by the study patients. These interventions can also alter triglycerides and oxLDL concentrations⁵⁾.

The conclusion that ezetimibe can reduce markers of atherosclerosis and be a potential therapeutic agent for the reduction of lipoprotein (a), and to modify other markers still needs to be confirmed in larger studies addressing its direct effect or the effect of the combination of hypolipidemic therapies.

References

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