Cardiology in the Young

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Lipoprotein[a]: a novel therapeutic target for cardiovascular disease management

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Letter to the Editor

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Dear Editor,

We were intrigued by the study conducted by Björnson et al.[1] which highlighted the considerably higher atherogenicity of lipoprotein[a] (Lp[a]) compared to low-density lipoprotein. The researchers employed a unique technique to measure the concentration of Lp[a] in patients, addressing the challenge of accurately measuring Lp[a] due to the repetitive structure of its component, apolipoprotein[a] (apo[a]). Each apo[a] is covalently bound to an apo[B] molecule on low-density lipoprotein particles to form Lp[a]; therefore, quantifying the contained apo[B] enabled them to measure Lp[a] indirectly. This approach allowed them to determine the relative atherogenicity of apo[B] in Lp[a] versus low-density lipoprotein. The results revealed a significant disparity in atherogenicity between Lp[a] and low-density lipoprotein, with Lp[a] being 6.6 times more atherogenic per particle compared to low-density lipoprotein.[1]

Lp[a] is a complex plasma lipoprotein like low-density lipoprotein, but with the addition of apo[a]. Apo[a] is a protein like plasminogen that is covalently bonded to the apolipoprotein B-100 (apoB-100) of an low-density lipoprotein particle.[2] The serum levels of Lp[a] are primarily determined by genetic factors rather than lifestyle choices. Understanding the relative atherogenicity of Lp[a] and low-density lipoprotein holds crucial implications for risk assessment and therapeutic interventions in coronary heart disease. Studies have shown that elevated Lp[a] levels are independently linked to an increased risk of cardiovascular disease regardless of traditional risk factors.[3,4] This establishes Lp[a] as a significant risk factor for multiple cardiovascular endpoints, each with varying levels of association. Additionally, individuals with high levels of both Lp[a] and low-density lipoprotein, such as those with familial hypercholesterolaemia, are at an even greater risk of cardiovascular events.[3] This highlights the importance of comprehensive risk assessment in clinical practice. A study conducted by Wohlfahrt et al.[5] found an association between mortality and recurrent cardiovascular events after myocardial infarction, both in individuals with high and very low levels of Lp[a]. The association of low Lp[a] levels with increased mortality raises interesting questions that warrant further research.[5] Apart from its role in atherosclerosis, Lp[a] also has prothrombotic effects.

Traditional lipid-lowering therapies, such as statins, ezetimibe, nicotinic acid, and lipoprotein apheresis, have limited effectiveness in lowering Lp[a] levels. In fact, statin therapy is associated with increased Lp[a] levels, making Lp[a] an even stronger predictor of cardiovascular events in patients on this therapy.[6] Therefore, there is a pressing need for more effective and safer treatments. Recently, emerging therapies specifically aimed at lowering Lp[a] levels have garnered significant attention. One such approach involves using antisense apo[a] and/or apo[B] inhibitors to suppress the production of atherogenic proteins in the liver.[7] This novel approach has the potential to significantly lower Lp[a] levels by 35–80%, with the added decrease if low-density lipoprotein levels by 6–16%.[7] thereby mitigating cardiovascular risk.

In conclusion, recent evidence emphasises the importance of addressing elevated levels of Lp[a] as a major target for managing cardiovascular disease. Since Lp[a] levels remain stable throughout life and are primarily determined by genetics, it is advisable to measure Lp[a] at least once in the lifetime of all individuals. This can provide a more accurate evaluation of cardiovascular disease risk, enabling the initiation of a more effective therapeutic approach. This would be a significant stride towards preventing the estimated 29% of global deaths caused by cardiovascular disease.

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