Lipoprotein (a)

Lipoprotein (a) (or Lp(a) for short) is a large "sticky" lipoprotein particle which is made in the liver and found in the blood plasma, assembled from a cholesterol-rich LDL like particle and two protein molecules, apolipoprotein B100 and apolipoprotein (a).

Apolipoprotein B100 provides the framework for LDL and is important for recognition and removal of LDL cholesterol by receptors on the surface of body cells. The size of apolipoprotein B100 is the same in everyone but the size of apolipoprotein (a) is genetically determined and differs between individuals and can vary widely. The function of apolipoprotein (a) is unknown but it is a "sticky" protein which is analogous to adding a "patch of velcro" to normal LDL. Plasma levels of Lp(a) depend on the size of the apolipoprotein (a) isoforms which explain most of the variability seen in different populations and ethnic groups. Many large population studies have shown a strong independent relationship between high Lp(a) levels and heart disease. This has led to the consensus agreement that it is a very important risk factor for cardiovascular disease, even when cholesterol levels and other classical risk factors such as elevated cholesterol, hypertension and diabetes have been taken into account. It is thought to increase the risk of cardiovascular disease by two different mechanisms:

1. Causing atherosclerosis (narrowing of arteries): research studies have shown that Lp(a) may accelerate atherosclerotic damage (atheroma). It is thought to increase the size of plaque/atheroma in artery walls, causing inflammation, instability and growth of smooth muscle cells. It is retained in the artery wall more than LDL cholesterol as it binds to the artery lining through its "sticky" apolipoprotein (a) as described earlier.
2. Triggering blockage of arteries by formation of clots: Lp(a) is thought to increase risk of heart attacks by interfering with clotting mechanisms and therefore promoting clot development on the inner surface of blood vessels. Apolipoprotein (a) appears similar to proteins involved in clotting, such as plasminogen. It is thought to form a link between lipids and the coagulation system by preventing clot breakdown (fibrinolysis).

Some experts currently believe it has a greater effect on the clotting system than on the promotion of atherosclerosis.

Measurement of Lp(a)

Lp (a) is not routinely measured in general practice and reported in several different ways, as mass (either mg/dl or mg/l) or as particle numbers (nmol/L) which is now recommended. Patients who have levels greater than 500mg/L or 120nmol/L are at increased risk of developing cardiovascular disease. These elevations are present from birth and may potentially contribute to an increased cardiovascular disease risk, starting early in life.

Lp(a) levels are similar in men and women but have been found to be lower in some populations e.g. Chinese and Japanese, and higher in others e.g. Africans. It has been estimated that levels between 60 and 75nmol/L (250 to 300mg/L) are present in 30% of Caucasians and 60-70% of Africans. The desirable levels for LDL cholesterol are based on sound clinical evidence from meta analysis of randomised controlled intervention trials documenting the benefit of treatment (i.e. clinical trials with statins). For Lp (a) the evidence is less clear but those with levels in the top 10% of each population studied seem to be at particularly high risk.

Consensus Recommendations for Lp (a) Testing

The European Atherosclerosis Society currently recommends patients with an intermediate, moderate or high risk of cardiovascular disease should have their Lp (a) levels measured. This should include those with premature cardiovascular disease, familial hypercholesterolaemia (FH), family history of premature cardiovascular disease, family history of elevated Lp(a) and those with recurrent cardiovascular disease despite optimum medical treatment.

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Treatment of Lp (a)

Levels of Lp(a) do not change throughout life and are usually unaffected by lifestyle or environment.

Effects of medications: commonly prescribed lipid lowering medication such as statins have little effect on Lp(a). Results using statin medications have been mixed in most research trials, although a meta-analysis published in 2012 suggested that atorvastatin may be beneficial. Other agents reported to reduce Lp(a) to a minor degree include calcium antagonists, ACE inhibitors, androgens, oestrogen and thyroid replacement in hypothyroid patients. Co-enzyme Q-10 and fish oils have been suggested as beneficial but have not been proven in clinical trials. Nicotinic Acid (niacin or Vitamin B3) in high doses, was shown to reduce Lp(a) levels by about 25% in some patients, but has been withdrawn following results of a recent research trial which showed an increased risk of serious but non fatal side effects in those taking it.

Current advice from medical experts for the treatment of those known to have a high Lp(a) level is to treat other modifiable risk factors maximally, particularly non HDL-cholesterol. Aspirin may be added if there are no contra-indications, in order to reduce the risk of thrombosis. Once levels of Lp(a) have been determined, they do not usually need to be checked again, but it is important to continually monitor the other identified risk factors. There are several new medications currently in development, which may have an effect on Lp(a) levels, which include cholesterol-ester-transfer protein inhibitors (CETP inhibitors), anti-sense oligonucleotides and PCSK9 inhibitors. Results of clinical trials are awaited.

Treatment with apheresis

Apheresis may be considered for patients who have familial hypercholesterolaemia (FH) or treatment resistant hypercholesterolaemia with elevated Lp(a) levels and evidence of progressive coronary disease. Apheresis is a process which removes cholesterol carrying particles including Lp(a) and LDL by selective filtration of blood or plasma, and can achieve dramatic reductions in those with elevated levels. It is a highly specialized procedure and is currently available in 8 designated centres in the UK. Please see our section on apheresis on our website at the following link for more information:

www.heartuk.org.uk/cholesterol-and-health/ldl-apheresis

Summary of technical terms

Apheresis: filtration process which removes Lp(a) and LDL cholesterol from the blood or plasma

Apolipoprotein: found on the surfaces of lipoproteins and are involved in receptor recognition at the cell surface

Familial Hypercholesterolaemia: an inherited form of high cholesterol due to an abnormal gene resulting in exceptionally high levels between 7.5 – 12mmol/l with LDL-cholesterol greater than 5mmol/L

Fibrinolysis: the process of the breakdown of clots

Thrombogenesis: generation or production of clots