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Review article

The expanding role of lipoprotein apheresis in the treatment of raised lipoprotein(a) in ischaemic heart disease and refractory angina

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ABSTRACT

It is increasingly recognised that lipoprotein(a) [Lp(a)], an inherited, genetically-determined form of LDL-cholesterol, is an independent cardiovascular risk factor and predictor of adverse cardiovascular outcomes. Lp(a) is felt to increase cardiovascular risk via its pro-thrombotic effect and by enhancing intimal lipoprotein deposition. Lipoprotein apheresis is currently the most effective treatment for raised Lp(a). There is a growing body of evidence suggesting that aggressively lowering raised Lp(a) may improve cardiovascular and clinical outcomes, although much more research is required in this field.

Angina which is refractory to conventional medical therapy and revascularisation, is extremely challenging to manage. Treatment options for such patients remain very limited. We describe the case of a patient with refractory angina and raised lipoprotein(a) in whom aggressive reduction of Lp(a) with lipoprotein apheresis successfully ameliorated the progression of coronary stenosis and provided effective and durable relief of angina symptoms. In our centre, we are currently conducting a prospective, randomised controlled cross-over study of patients with refractory angina and raised Lp(a), randomised to undergoing lipoprotein apheresis or 'sham' apheresis with assessment of myocardial perfusion, carotid atherosclerosis, endothelial vascular function, thrombogenesis, oxidised phospholipids and their antibodies, exercise capacity, angina symptoms and quality of life at the beginning and end of treatment.

Keywords: Lipoprotein(a), Lipoprotein Apheresis, Ischaemic heart disease, Refractory angina

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INTRODUCTION

Lipoprotein(a) [Lp(a)] was first discovered in the 1960s by Berg.[1] The exact physiological role of Lp(a) is not currently understood; however an elevated Lp(a) level (>600 mg/l) has emerged as an important independent cardiovascular risk factor and predictor of adverse outcome in atherosclerotic disease.[2,3]

Lp(a) is an inherited, genetically determined form of LDL-cholesterol. It is a plasma lipoprotein consisting of a cholesterol-rich LDL particle with one molecule of apolipoprotein B100 and an additional protein, apolipoprotein(a), attached via a disulphide bond (Figure 1). Elevated Lp(a) levels can potentially increase the risk of cardiovascular disease via (i) pro-thrombotic/anti-fibrinolytic effects as apolipoprotein(a) possesses structural homology with plasminogen and plasmin but has no fibrinolytic activity and (ii) via accelerated atherogenesis as a result of intimal deposition of Lp(a) cholesterol, or both.[4]

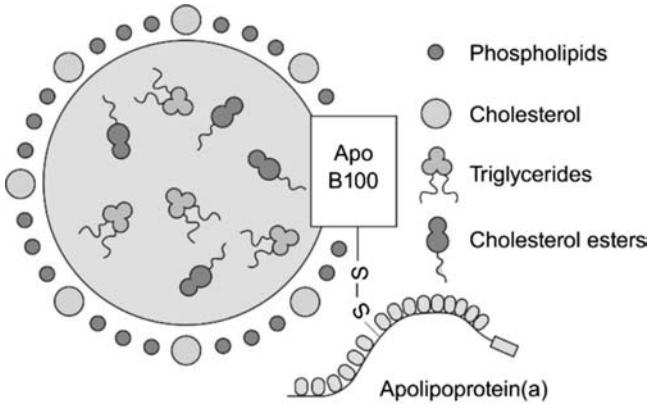

Figure 1. The structure of lipoprotein(a).

EPIDEMIOLOGY

The Göttingen Risk Incidence and Prevalence Study (GRIPS) evaluated the impact of Lp(a) on the basis of a large prospective cohort study (6002 men aged 40–59.9 years at baseline with data of a 5-year follow-up period). Multivariate logistic regression models for the estimation of MI risk confirm Lp(a) as an important risk factor for IHD, ranking fifth behind LDL cholesterol, family history of MI, plasma fibrinogen and HDL cholesterol (inverse relationship).[5]

An early meta-analysis of 18 prospective studies which reported on a pooled analysis of 4000 coronary heart disease (CHD) cases, suggested that the combined relative risk of CHD for individuals in the top vs. bottom thirds of baseline Lp(a) concentrations was 1.7 (95% CI: 1.4–1.9).[3] A more recent meta-analysis of 31 prospective studies, involving a total of 9870 CHD cases suggested that the corresponding combined risk was more modest (relative risk: 1.5; 1.3–1.8).[6]

A very large epidemiological study on Lp(a) assessed individual records of 126 634 participants in 36 prospective studies.[7] The association of Lp(a) with CHD was broadly continuous in shape and curvilinear, with no evidence of a threshold. The relative risk of CHD per 3.5-fold higher Lp(a) level adjusted for age and sex only was 1.16 and 1.13 (95% CI: 1.09–1.18) following further adjustment for systolic blood pressure, smoking, history of diabetes and total cholesterol.[7] This suggests that the association is only minimally confounded by conventional risk factors. Accordingly, a recent prospective study found that the Lp(a)/CHD risk association did not depend on levels of other CVD risk factors, including LDL cholesterol levels.[8]

There are significant disparities between different ethnic groups, in terms of the prevalence of raised Lp(a). In a study performed by Enas et al., it was demonstrated that amongst Americans of different ethnic origins, Blacks have the highest median Lp(a) levels, followed by Asian Indians. Caucasians had substantially lower median Lp(a) levels, whilst Hispanics and American Indians had the lowest levels. The median Lp(a) level in Blacks was approximately three times higher than that in Whites.[9] Furthermore, Lp(a) confers less risk in Blacks than in Asian Indians or Whites.[10] This decreased risk may be due to their less atherogenic lipid profile (slightly lower LDL-C and triglyceride levels and higher

HDL-C levels compared with Whites), which may, in part, counterbalance the atherogenic potential of Lp(a).[11]

Asian Indians have high levels of Lp(a) second only to Blacks with more than 40% having Lp(a) levels >200 mg/L.[12] The high Lp(a) levels seen in Asian Indians are in sharp contrast to levels seen in other Asian populations, which are similar to or lower than those observed in Whites.[13] The adverse effects of Lp(a) in Asian Indians are significantly increased by the high prevalence of diabetes, low HDL-C levels, high TC/HDL-C ratio, high triglycerides, and hyper-homocystinemia.[14]

In conclusion, elevated Lp(a) levels correlate significantly and independently with CHD risk. The association is continuous in shape without a threshold and does not depend on high levels of LDL or non-HDL cholesterol, or on the levels or presence of other cardiovascular risk factors. There are significant differences between ethnic groups in relation to the prevalence of raised Lp(a) and its conferred risk.

PATHOPHYSIOLOGICAL ROLE OF LIPOPROTEIN(A) IN ATHEROTHROMBOTIC DISEASE

Elevated Lp(a) is believed to promote atherosclerosis via Lp(a)-derived cholesterol entrapment in the intima, via inflammatory cell recruitment and/or via the binding of pro-inflammatory-oxidised phospholipids. In addition, elevated Lp(a) is felt to be pro-thrombotic via the inhibition of fibrinolysis with enhancement of clot stabilisation as well as via enhanced coagulation via the inhibition of tissue factor pathway inhibitor.[4]

After transfer from plasma into the arterial intima, Lp(a) binds to the extra-cellular matrix not only through apolipoprotein(a), but also via its apolipotrotein B component, thereby contributing cholesterol to the expanding atherosclerotic plaque.[15] Lp(a) binds to several extra-cellular matrix proteins including fibrins[16] and defensins, a family of amino acid peptides that are released by neutrophils during inflammation and severe infections.[17] It is likely that defensins, like lipoprotein lipase, provide a bridge between Lp(a) and the extracellular matrix.[4]

It is also now recognised that Lp(a) binds pro-inflammatory-oxidised phospholipids and is the preferential carrier of oxidised phospholipids in human plasma.[18] This was demonstrated by Bergmark et al. via immunoprecipitation and ultra-centrifugation studies performed on human plasma.[18] In a prospective case-control study, it was shown that after adjusting for age, smoking, diabetes, low and high-density lipoprotein cholesterol, and systolic blood pressure, the highest tertiles of oxidised phospholipids on apolipoprotein B-100 particles and Lp(a) were associated with a significantly higher risk of CAD events (odds ratio 1.67 and 1.64 respectively; $p < 0.001$) compared with the lowest tertiles. The odds ratio of CAD events associated with the highest levels of oxidised phospholipids on apolipoprotein B-100 particles or Lp(a) was significantly potentiated by the highest tertiles of secretory phospholipase A2 activity and mass.[19]

Apolipoprotein(a), a homologue of the fibrinolytic pro-enzyme plasminogen, impairs fibrinolysis.[20] It is believed that Lp(a)/apolipoprotein(a) can competitively inhibit tissue-type plasminogen activator mediated plasminogen activation on fibrin surfaces, although the mechanism of this inhibition remains controversial.[4] It has also been shown that Lp(a) through its apo(a) moiety may promote thrombosis by binding and inactivating tissue factor pathway inhibitor (TFPI).[21]

GENETICS

Elevation in Lp(a) has been demonstrated to be highly inheritable.[22] Clarke et al. used a novel gene chip containing 48,742 single-nucleotide polymorphisms (SNPs) in 2100 candidate genes to test for associations in 3145 case subjects with coronary disease and 3352 control subjects.[22] Three chromosomal regions (6q26-27, 9p21, and 1p13) were strongly associated with the risk of coronary disease. The LPA locus on 6q26-27 encoding Lp(a) lipoprotein had the strongest association. They identified a common variant (rs10455872) at the LPA locus with an odds ratio for coronary disease of 1.70 (95% confidence interval [CI], 1.49 to 1.95) and another independent variant (rs3798220) with an odds ratio of 1.92 (95% CI, 1.48 to 2.49). Both variants were strongly associated with an increased level of Lp(a) lipoprotein, a reduced copy number in LPA (which determines the number of kringle IV-type 2 repeats), and a small Lp(a) lipoprotein size.[22]

A meta-analysis showed that with a genotype score involving both LPA SNPs, the odds ratios for coronary disease were 1.51 (95% CI, 1.38 to 1.66) for one variant and 2.57 (95% CI, 1.80 to 3.67) for two or more variants.[22] In conclusion, two LPA variants were strongly associated with both an increased

level of Lp(a) lipoprotein and an increased risk of coronary disease. These findings provide support for a causal role of Lp(a) lipoprotein in coronary disease.

TREATMENT AND CURRENT GUIDELINES

Most patients with raised LDL-cholesterol levels can be adequately treated with appropriate dietary measures and lipid-lowering drug therapy.[23] On the other hand, the conservative therapy of elevated Lp(a), in most cases, is unsatisfactory.[24] Statins are ineffective in lowering Lp(a). Niacin (nicotinic acid) reduces Lp(a) levels by up to 30–40% in a dose-dependent manner and in addition exerts other potential beneficial effects by reducing LDL cholesterol, total cholesterol, triglycerides, and remnant cholesterol and by raising HDL cholesterol.[25] However, there is a reasonably high incidence of side effects experienced with niacin, including flushing and gastro-intestinal effects. In a study assessing niacin therapy on the lipid profile of diabetic patients, 21% of the patients were unable to tolerate niacin owing to reversible side-effects, and 14% were unable to adhere to the niacin dosing regimen of three times daily.[26] Tredaptive (a nicotinic acid based treatment also containing laropiprant) was previously felt to be modestly effective at lowering Lp(a), however the European Medicines Agency have withdrawn this drug based on preliminary findings from the HPS2-THRIVE trial showing that this drug does not reduce major adverse cardiac events and causes a higher incidence of serious non-fatal side effects.[27]

Lipoprotein Apheresis

Lipoprotein apheresis is a selective lipid-lowering extracorporeal treatment by which excess atherogenic ApoB100-containing lipoproteins, including Lp(a) and LDL cholesterol, are removed from blood or plasma. Currently it remains the most effective means of lowering Lp(a) levels.[28] Stefanutti et al. compared the efficacy of lipoprotein apheresis with standard lipid-lowering therapy such as statins in patients with raised levels of Lp(a) and angiographically documented coronary artery disease.[29] They found that the lipoprotein apheresis group averaged an Lp(a) reduction of 57.8 ± 9.5% ($p < 0.001$) compared to the group treated with standard lipid-lowering therapy in whom Lp(a) increased in a year by 14.7% ± 36.5% ($p = 0.66$).[29] Lipoprotein apheresis may improve myocardial perfusion[30] and attenuate the progression of coronary artery disease.[31] It has also been demonstrated to improve various haemo-rheological parameters including plasma viscosity, native blood viscosity, red cell aggregation, and red cell deformability.[32]

Lipoprotein apheresis can be carried out using several methods. The most commonly used are dextran sulphate cellulose adsorption (DSA), heparin-induced extracorporeal LDL-cholesterol precipitation (HELP), immunoadsorption, double filtration plasmapheresis (DFPP) and direct adsorption of lipoproteins (DALI). In the DSA, HELP, immunoadsorption and DFPP systems, plasma is separated from red blood cells prior to removal of LDL-cholesterol and Lp(a), whereas in DALI and direct haemoperfusion (DHP), these lipoproteins are removed directly from whole blood.[33] Figure 2 shows a patient undergoing lipoprotein apheresis using the Kaneka whole blood system (DX21).

Figure 2. A patient undergoing lipoprotein apheresis using the Kaneka whole blood system (DX21).

The European Atherosclerosis Society Consensus Panel, in its recent statement regarding the role of Lp(a) as a cardiovascular risk factor, recommended that Lp(a) levels should be reduced below 500 mg/l, in extreme cases, by lipoprotein apheresis.[4] The HEART UK guidelines recommend lipoprotein apheresis for patients with Lp(a) levels >600 mg/L with progressive coronary heart disease despite treatment with maximally tolerated combined drug therapy.

A potential treatment that holds some promise for the future are antisense oligonucleotides (ASO) directed to apolipoprotein (a) [apo(a)], thereby reducing apo(a) and Lp(a) levels. So far, animal studies have shown that this may provide an effective approach to lower elevated Lp(a) levels.[34] However, human studies are needed to determine the safety and efficacy of this treatment before it can be established for widespread use.

Recently the impact of AMG145, a monoclonal antibody against proprotein convertase subtilisin kexin type 9 (PCSK9), on Lp(a) was assessed as part of the LDL-C Assessment With PCSK9 Monoclonal Antibody Inhibition Combined With Statin Therapy (LAPLACE)-Thrombolysis in Myocardial Infarction (TIMI) 57 trial.[35] 631 patients with hypercholesterolaemia receiving statin therapy were randomised to receive AMG145 at 1 of 3 different doses every 2 weeks or 1 of 3 different doses every 4 weeks, versus placebo. Lp(a) and other lipid parameters were measured at baseline and at week 12. Compared with placebo, AMG145 70 mg, 105 mg, and 140 mg every 2 weeks reduced Lp(a) at 12 weeks by 18%, 32% and 32% respectively ($p < 0.001$ for each dose versus placebo).[35] It is however worth noting that the mean baseline level of Lp(a) in this study was 43 nmol/L or 172 mg/L, hence a substantial portion of the patients did not have raised Lp(a) levels to start with. Also, the mean LDL-C level at baseline was 3.2 mmol/L, hence the patients did not have exclusively raised Lp(a). Nonetheless, this data does lend further support to studying the impact of PCSK9 inhibition on Lp(a) in a phase 3 clinical outcomes trial.

LDL reduction in the context of raised Lp(a)

Brown has reported that, based on an analysis by Maher et al. of the Lp(a) data in the FATS trial, lowering LDL levels in those with high LDL and high Lp(a) levels, dramatically reduced risk. Without treatment, these patients had a 42% risk of a major clinical event, including myocardial infarction, the need for revascularization, or cardiovascular death over the 2.5-year study. When LDL levels were lowered aggressively, even though the Lp(a) levels remained high, the risk of this group was reduced to less than 10%, for a roughly 75% reduction in the risk of a major cardiovascular event.[36]

Recent evidence supporting the link between treatment of lipoprotein(a) and improvement of clinical parameters in ischaemic heart disease

Although it is now well established that Lp(a) is an important independent cardiovascular risk factor and predictor of adverse cardiovascular events, more research is required to demonstrate that vigorously treating it can improve clinical outcomes. The body of evidence supporting this notion is growing slowly, but is still limited.

Jaeger et al. conducted a longitudinal cohort study to assess whether combined lipid apheresis and lipid-lowering medication can reduce extremely high levels of Lp(a) and thus prevent major adverse coronary events (MACE) more efficaciously than lipid-lowering medication alone.[37] Eligible patients had coronary artery disease and Lp(a) levels ≥2.14 μmol/l or >600 mg/L (95th percentile). All patients received lipid-lowering medications alone until maximally tolerated doses were no longer effective, followed by combined lipid apheresis and lipid-lowering medication. The rates of the primary outcome, MACE, were recorded for both periods. A total of 120 patients were included. The mean duration of lipid-lowering therapy alone was 5.6 ± 5.8 years, and that of apheresis was 5.0 ± 3.6 years. Median Lp(a) concentration was reduced from 4.00 μmol/l to 1.07 μmol/l or 1120 mg/L to 300 mg/L with apheresis treatment ($P < 0.0001$); the corresponding mean annual MACE rate per patient was 1.056 versus 0.144 ($P < 0.0001$).[37] They concluded that lowering of Lp(a) levels by apheresis is efficacious and safe and they recommend apheresis for patients in whom maximally tolerated doses of medication alone have failed to control coronary artery disease-associated events.

Bohl et al. explored the effects of a single lipoprotein apheresis session on myocardial perfusion in patients with elevated Lp(a) and coronary artery disease using cardiac magnetic resonance imaging.[24] Twenty patients with Lp(a) >600 mg/L and coronary artery disease were randomized into a control or a treatment group. Both groups underwent cardiac magnetic resonance imaging with assessment of left ventricular function, perfusion and viability, and the treatment group underwent lipoprotein apheresis immediately afterwards. Repeat magnetic resonance imaging was performed at 24 h for both

groups and at 96 h for just the treatment group. The trans-myocardial perfusion gradient (i.e. endo-epi ratio [EER]) was determined and a comprehensive parameter of resting and adenosine-induced stress perfusion was derived (EER-S/R). The EER-S/R at 24 h was lowered by therapy (ΔEER-S/R 5%; $p < 0.03$), whereas this effect disappeared at 96 h. The ejection fraction (EF) was slightly improved at 24 h (67.07 ± 6.28% vs. 64.89 ± 6.39%; ΔEF 2.2%, $p < 0.05$) and returned to baseline at 96 h.[24] In the control group no corresponding changes were detected. They concluded that cardiac magnetic resonance imaging detects subtle treatment-related changes in regional myocardial perfusion in patients with elevated Lp(a) and coronary artery disease undergoing lipoprotein apheresis.

Safarova et al. assessed the impact of specific Lp(a) apheresis versus statin therapy on coronary atherosclerosis regression in stable CHD patients with high Lp(a) levels.[38] A total of 30 subjects with CHD verified by angiography, Lp(a) >500 mg/L, and low density lipoprotein cholesterol (LDL-C) ≤2.5 mmol/L on chronic statin treatment were prospectively evaluated for 18 months. Patients were allocated to receive specific weekly Lp(a) apheresis ($n = 15$), or atorvastatin only ($n = 15$). Blinded quantitative coronary angiography analyses of percent diameter stenosis and minimal lumen diameter (MLD) were performed at baseline and after the 18-month treatment period. Median percent diameter stenosis was reduced by −2.0 (95% confidence interval [CI], −5.0–0.0) with apheresis ($p < 0.01$ in comparison with baseline), and increased by 3.5 (0.0–6.9) with atorvastatin ($p < 0.001$ between the groups).[38] The effect on MLD was more favourable with apheresis than with atorvastatin: 0.20 ± 0.39 mm, as compared with 0.01 ± 0.34 mm, $p = 0.04$.(38) This suggests that specific Lp(a) apheresis may produce coronary atherosclerosis regression in stable CHD patients with high Lp(a).

REFRACTORY ANGINA

Cardiovascular disease remains a leading cause of death in the western world.[33] Most patients with angina, resulting from coronary heart disease (CHD) are successfully treated with conventional medical therapy and revascularisation techniques such as coronary artery bypass graft (CABG) surgery or percutaneous coronary interventions (PCI).[39] There is however a group of patients who have severe disabling angina from coronary artery disease which is refractory to conventional therapy.[40] The management of these patients is particularly challenging.

Refractory angina, as defined by Mannheimer and colleagues in 2002, is 'a chronic condition characterised by the presence of angina caused by coronary insufficiency in the presence of coronary artery disease which cannot be controlled by a combination of medical therapy, angioplasty and coronary bypass surgery'.[40] There are no accurate figures on the occurrence or frequency of refractory angina, though there is universal agreement that its prevalence is increasing. Estimates based on rejection rates for further intervention among angina patients in Europe suggest that between 30,000 to 50,000 patients per year develop the condition.[40] Most of these patients are relatively young and have a moderately impaired left ventricular ejection fraction.[41]

Several adjunctive therapies are available to patients with refractory angina, including stellate ganglion blockade,[42] electrical neuromodulation devices such as transcutaneous electrical nerve stimulation (TENS)[43] and spinal cord stimulation (SCS),[44] enhanced external counter-pulsation(EECP)[45] and transmyocardial laser revascularisation (TMLR).[46] However previous studies indicate such interventions fail to provide a universal impact on the chest pain and dyspnoea associated with refractory angina.

THE IMPACT OF LIPOPROTEIN APHERESIS ON REFRACTORY ANGINA WITH RAISED LIPOPROTEIN(A): A CASE HISTORY

In our centre, we have experience of treating a patient with refractory angina and raised lipoprotein(a) with lipoprotein-apheresis and demonstrated that aggressive reduction of Lp(a) successfully ameliorated the progression of coronary stenosis and provided effective and durable relief of angina symptoms.[47] At the age of 42, this gentleman presented with unstable angina. He had no previous cardiac history, had a balanced diet and had never smoked. Coronary angiography revealed diffuse multi-vessel coronary artery disease. Subsequently, in the context of ongoing angina he was treated with quadruple coronary artery bypass grafts and a total of 12 stents over a three-year period. He averaged a new coronary stent every four to six weeks. During this period, there was no evidence of myocardial infarction, but there was severe and dynamic progression of the native coronary disease and venous grafts. Despite these multiple and extensive coronary interventions and despite being treated with optimal medical therapy throughout, he continued to experience ongoing angina which

was adversely affecting his quality of life. At this point, his Lp(a) was screened and was found to be significantly elevated at 1200 mg/L (normal range: 0–300). The remainder of his fasting lipid profile revealed normal total cholesterol (TC) (3.2 mmol/L, LDL-C (1.5 mmol/L) and plasma triglycerides (TG) (1.4 mmol/L). As lipoprotein apheresis is the most effective means of reducing Lp(a) levels, the patient was started on a bi-weekly regimen of lipoprotein apheresis using the Kaneka whole blood system (DX21). Lipoprotein apheresis drastically reduced the plasma levels of LDL-C, TC, TG and most importantly Lp(a). Figure 3 demonstrates his pre- and post-treatment Lp(a) levels. Since the institution of regular apheresis, the patient has shown improvement in his functional status, with significant improvement of his angina chest pain and quality of life. The patient is now active and able to walk unrestricted and is engaged in fulltime employment. Lipoprotein apheresis has also slowed the rate of progression of his coronary disease, with a reduction in the rate of revascularisation procedures since the institution of lipoprotein apheresis. During the five-year period the patient has been undergoing lipoprotein apheresis, in terms of revascularisation, the patient has had four prophylactic stents to an in-stent stenosis in the distal right coronary artery; in contrast to the multiple frequent interventions he was requiring prior to starting apheresis.

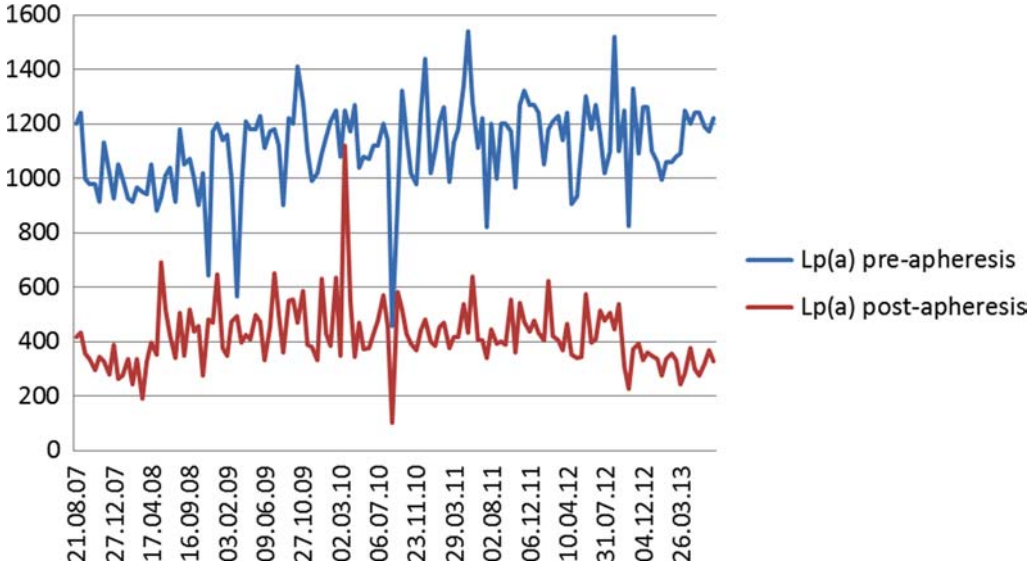

Figure 3. Case Study Lp(a) levels pre- and post-apheresis.

This case highlights several noteworthy lessons regarding the management of refractory angina in the context of raised lipoprotein(a). Firstly, the important role of Lp(a) as a risk factor for refractory angina and the progression of coronary artery disease. Lp(a) measurement is often a missed feature of the biochemical profile of these challenging patients.[47] Secondly, it shows that lipoprotein apheresis is a powerful tool in normalizing Lp(a), which can impact on the rate of progression of dynamic coronary artery disease and lead to an improvement in angina symptoms. Further studies at the clinical and the mechanistic level are needed to validate and understand this phenomenon.

FURTHER RESEARCH IN PROGRESS

The European Atherosclerosis Society Consensus Panel stated that further international effort is required to assess the atherothrombotic risk due to Lp(a) and unravelling the mechanisms by which Lp(a) contributes to cardiovascular disease.[4] Good quality lab-based research and well-designed prospective randomised controlled intervention trials with selective reduction of plasma Lp(a) are urgently needed to assess the clinical benefit of treating raised Lp(a) and determining the role of Lp(a) treatment in the primary and secondary prevention of coronary disease and its sequelae. In addition, as our case example highlights, further research is needed to explore raised Lp(a) as a risk factor for refractory angina or accelerated coronary artery disease and to determine the clinical and symptomatic benefit of aggressively lowering Lp(a) in such individuals.

We are currently conducting a single centre prospective, randomised controlled cross-over study of patients with refractory angina and raised Lp(a) in the absence of raised LDL cholesterol, randomised to undergo lipoprotein apheresis or 'sham' apheresis with assessment of myocardial perfusion, carotid atherosclerosis, endothelial vascular function, thrombogenesis, oxidised phospholipids and their antibodies, exercise capacity, angina symptoms and quality of life at the beginning and end of treatment. Our study aims to address whether lowering Lp(a) is beneficial in patients with refractory angina and raised Lp(a) and will the assess the mechanisms of this treatment effect on numerous clinical parameters.

CONCLUSION

Elevated lipoprotein(a) is an important and under-recognised risk factor for cardiovascular disease and accelerated atherosclerosis. Currently lipoprotein apheresis remains the most effective means of lowering Lp(a) levels, although alternative therapies are currently being assessed. There is increasing evidence that demonstrates that lowering plasma Lp(a) levels leads to an improvement in clinical outcomes. Further research is required to determine which patients will benefit most from treatment and when and how they should be treated. Lp(a) deserves further attention from cardiologists and may provide scope for a novel therapeutic approach in the primary and secondary treatment of coronary artery disease and its burden.

CONFLICTS OF INTEREST

None

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