Case Report: Lysine/Ascorbate-Related Amelioration of Angina Pectoris

Linus Pauling[1]

Abstract

It is gratifying to report the first observation of the amelioration of effort angina by the use of high-dose L-lysine and ascorbate in a man with severe coronary artery disease (CAD). This regimen was based on the hypothesis that, in thrombotic atherosclerosis, lipoprotein(a) [Lp(a)] — size-heterogeneous, LDL-like particles displaying independent risk activity for CAD — initiates plaque formation by binding to fibrin in the damaged arterial wall. This postulated mechanism correlates with the findings that apoliprotein(a) [apo(a)] has a striking homology to plasminogen, and the Lp(a) accumulates in atherosclerotic lesions in the arteries of man (Rath et al., 1989) and the hypoascorbic guinea pig (Rath and Pauling, 1990a, 1990b) and in occluded bypass venous grafts (Gushing et al., 1989). It is hoped that the remarkable outcome in this single case will motivate clinicians to examine the efficacy of lysine and ascorbate in additional cases of refractory angina.

Coronary Heart Disease Case History

In late April 1991, a biochemist National Science Medalist* with a familial trait of CAD told me that he experiences effort angina, in spite of medication and three coronary bypass operations. His father and a brother both died of CAD at age 62; he had his first angina attack at age 38. Now aged 71, this biochemist has fought CAD also by reducing risk factors (i.e., not smoking, exercising moderately, and diet/ weight control — 134 lbs. at 5'5"). His first operation in 1978 (two vein grafts and one LIMA graft) precipitated a second operation (a parallel vein graft) five months later. Stripping of saphenous veins in the first operation induced massive swelling, thrombi, and infection in his leg; bilateral pulmonary emboli; and loss of patency in a vein graft. In 1987, following an attack of unstable angina, he was hospitalized for coronary angiography, adjustment of medications, and a T1-stress test. A third operation in April 1990 followed attacks of unstable angina, a small MI,and angiography that revealed total occlusion of his right coronary artery and all bypass grafts except for a patent LIMA graft. Unfortunately, this LIMA was lacerated while freeing dense adhesions early in the third operation and required urgent heart-lung bypass cannulation and vein-patch repair; additionally, three venous grafts were made to left coronary arteries. The operation, which diminished but did not eliminate effort angina, left him with 1.8 liters of left-sided pleural effusate that was resistant to diuretics and tapping, and took 10 months to reabsorb. Medication with beta-receptor and calcium-channel blockers and lovastatin was reinstated; also, 325 mg of aspirin given initially was reduced to 81 mg following bilateral eye hemorrhages and adhesions that impair his peripheral vision. To this medication, he added 6g of ascorbate (acid form), 60 mg CoQ-10; a multivitamin tablet with minerals; additional vitamins A, E and a B-complex; lecithin; and niacin, on advice of his cardiologist to try to raise his HDL level. Nevertheless, he still had to take nitroglycerin sublingually to suppress angina during a daily two mile walk and when working in his yard. This effort angina continued to worsen, imparting a feeling of impending doom that was reinforced by his cardiologist's admonition during a check-up in March 1991 that a fifth angiographic test and a fourth bypass operation were no longer options. Also, the saphenous veins from his groin regions and legs had all been used for previous grafts.

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Effect of the Addition of Lysine

In this predicament and with his history of restenosis, I suggested that he continue ascorbate and add 5g of L-lysine daily *(ca.,* six times the lysine derived from dietary protein) to try to mitigate the atherosclerotic activity of Lp(a). After reading the 1990 Rath and Pauling reports and their manuscript titled "Solution to the puzzle of human cardiovascular disease", he began taking 1g of lysine in early May 1991 and reached 5g (in divided doses eight hours apart) by mid-June. In mid-July, his HDL was, as usual, a low 28 mg/dl. A low-normal 0.9 mg/dl blood creatinine indicated that lysine could be increased, if needed. He could now walk the same two miles and do yard work without angina pain and wrote, "the effect of the lysine borders on the miraculous". By late August, he cut up a tree with a chain saw, and in early September started painting his house. By late September, possibly from over-exertion, he again began to have angina symptoms during his walks, but after stopping strenuous work and increasing lysine to 6g — calculated to provide a peak 280,000 molar excess in the blood over his then 6 mg/dl of Lp(a) to help compensate for the relatively high dissociation constant of lysine-Lp(a) — these symptoms stopped entirely by mid-October. His blood creatinine was still a normal 1.2 mg/dl. He attributes his newfound well being to the addition of lysine to his other medications and vitamins. His wife and friends comment on his renewed vigor.

Discussion

This severe case of restenosing CAD was a difficult challenge to try to ameliorate by the addition of lysine. While a positive effect was anticipated, lysine had not been tested for activity in inhibiting or reversing Lp(a)-laden atherosclerotic plaques in hypoascorbemic guinea pigs (Rath and Pauling, 1990b). However, it was known that Lp(a) binds to lysine-Sepharose; immobilized fibrin and fibrinogen (Harpel et al., 1989); and the epithelial-cell receptor for plasminogen (Gonzalez-Gronow et al., 1989). This binding specificity correlates with the genetic linkage on chromosome six and striking homology of apo(a) and plasminogen — highly conserved multiple kringle-four domains, a kringle-five domain, and a protease domain (McLean et al., 1987). Moreover, using the molecular evolutionary clock, the loss in primates of the ability to synthesize ascorbate (Zuckerkandl and Pauling, 1962; Rath and Pauling, 1990a) and acquisition of Lp(a) (Maeda et al., 1983) both appear to have occurred about 40 million years ago. These observations and the presence of Lp(a) in sclerotic arteries (Rath et al., 1989; Rath and Pauling, 1990b) and in venous grafts (Cushing et al., 1989) indicate that atherosclerosis may be initiated by excess binding of Lp(a) to fibrin in vascular wall clots, thus interfering with normal fibrinolysis by plasmin. This thrombogenic activity, which is postulated to reside in plasmin-homologous domains of Lp(a), may help to stabilize the damaged vascular wall, especially in ascorbate deficiency (Scanu, Lawn, and Berg, 1991; Rath and Pauling, 1990a). Once bound to fibrin, the LDL-like domain of Lp(a) could promote atheromas (Scanu, Lawn, and Berg, 1991). In this scenario, high-dosage lysine could inhibit or reverse plaque accretion by binding to Lp(a). Independently, lysine benefits the heart as a precursor with methionine in the synthesis of L-carnitine, the molecule that carries fat into mitochondria for the synthesis of adenosine triphosphate (ATP) bond energy needed for muscular and other cellular activities (Cederblad and Linstedt, 1976). While his intake of 60 mg of CoQ-10, also required for ATP synthesis, prior to the addition of lysine improved his sense of well being, it did not suppress his angina. Ascorbate without lysine also did not ameliorate angina, but it is needed as an antioxidant to protect the vascular wall against per-oxidative damage and in hydroxylation reactions both in the synthesis of carnitine and in the conversion of procollagen to collagen (hydroxylation of prolyl and lysyl residues) (Myllyla et al., 1984) to strengthen the extracellular matrix of the wall.

Whatever the pathomechanisms of atherosclerosis, the addition of lysine to medications and vitamins, including ascorbate, markedly suppressed angina pectoris in this intractable case of CAD. While a single case is anecdotal, it is hoped that its remarkable success will motivate

clinicians to commence studies as soon as possible of the general applicability of lysine and ascorbate in relieving angina pectoris, so as to decrease greatly the amount of human suffering with less dependence on surgical intervention.

Footnote (p. 144)

* He made a major contribution to this report, but wishes anonymity.

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