The lipid risk factor in hypertension and cardiovascular disease

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In the Framingham Study, coronary disease developed in every fifth man and every 17th woman by the age of 60 years (Castelli *et al.*, 1977). The level of total cholesterol proved to be an excellent predictor of coronary disease in those aged less than 50 years. However, in those aged over 50 years, more accurate predictors of coronary disease risk were lipoprotein measurements, including low-density lipoproteins (LDL), very low density lipoproteins (VLDL), triglycerides and high density lipoproteins (HDL). Both LDL and VLDL have a linear association with coronary disease. LDL cholesterol and HDL cholesterol are independently related to coronary disease risk in both sexes. In women, but not in men, the VLDL cholesterol and triglycerides levels are independent risk factors. HDL is the most important fraction for predicting coronary disease risk in both sexes. One of the most reliable profiles in this regard is the ratio of total cholesterol to HDL cholesterol, which should be under 4.5. In an important constellation of lipid factors, including elevated levels of both triglyceride and LDL along with average ('normal') levels of total cholesterol, LDL cholesterol has been found to be a risk factor not only for coronary disease, but also for diabetes mellitus.

The Framingham Study found that a person's risk of coronary disease rose 2 to 3% with every 1% increase of plasma cholesterol. Diet and drug intervention studies confirm this finding by showing that for every 1% decrease in cholesterol level there is a 2% decrease in coronary disease. Furthermore, studies using repeated arterial angiography have shown that by controlling lipid levels (independent of blood pressure control or smoking) progression of the arteriosclerotic lesions, which occurs in 80% of the patients studied, can be stopped.

However, elevations in both systolic and diastolic blood pressure are also established risk factors for coronary disease: the higher the levels of pressure, the greater the incidence of coronary disease (Veterans Administration Cooperative Study Group, 1970). Blood pressure and serum

cholesterol are also correlated; patients with higher blood pressure values tend to have higher serum cholesterol levels (Gordon *et al.*, 1977). Half of the women and more than half of the men who present with treatable hypertension have an abnormal lipid profile. Intervention should include therapies to reduce blood pressure and lower lipoproteins and triglycerides.

Most physicians agree that treatment is advisable when cholesterol levels are above 300 mg dl⁻¹; some believe therapy is necessary when levels are more than 250 mg dl⁻¹. However, 50% of the patients who eventually develop coronary disease have cholesterol values under 250 mg dl⁻¹. The National Institutes of Health Consensus Development Conference on Lipid Lowering has recommended that cholesterol levels be reduced to 200 mg dl⁻¹ in all persons. The problem lies in deciding which patients with cholesterol levels between 200 and 250 mg dl⁻¹ actually have a lipid abnormality. The answer may be in the patient's ratio of total cholesterol to HDL cholesterol which, as noted above, should be below 4.5.

Since many antihypertensive agents have an adverse effect on lipids, considerable thought should be given to those drugs which represent a therapeutic alternative. While most antihypertensive drugs increase blood lipids, some do not. The mechanism by which these latter drugs exert a more favourable effect on lipids may be related to capillary blood flow. If blood flow is curtailed the availability of lipase at the LDL cholesterol receptor is also reduced. This may adversely affect the three most important lipoproteins (LDL, VLDL and HDL) for coronary disease risk. Maintaining good capillary perfusion and low peripheral resistance, along with adequate cardiac output should be the goal of blood pressure control. Improved perfusion will not only prevent adverse lipid changes, but will also have beneficial effects on silent ischaemia and will diminish the unfavourable effects of the heart's reaction to increased total peripheral resistance.

References

- Castelli, W. P., Doyle, J. T., Gordon T., Hames, C. G., Hjortland, M. C., Halley, S. B., Kagan, A. & Zuckel W. J. (1977). HDL cholesterol and other lipids in coronary heart disease. The cooperative lipoprotein phenotyping study. *Circulation*, **55**, 767–772.
- Gordon, T., Castelli, W. P., Hjortland, M. C., Kannel, W. B. & Dawber, T. R. (1977). High density lipoprotein as a protective factor against coronary heart disease. The Framingham study. *Am. J. Med.*, **62**, 707–714.
- Veterans Administration Cooperative Study Group on Antihypertensive Agents (1970). Effects of treatment on morbidity in hypertension II. Results in patients with diastolic blood pressure 90 through 114 mm Hg. *J. Am. med. Ass.*, **213**, 1143–1152.