



CLINICAL ISSUES IN HYPERTENSION

CANADIAN COALITION FOR HIGH BLOOD PRESSURE PREVENTION AND CONTROL
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Putting Your Heart at Risk

Hypertension and Dyslipidemia

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Hypertension and dyslipidemia are two important risk factors for the development of coronary heart disease and cerebrovascular disease. In the Framingham Study, a link between dyslipidemia and hypertension was seen up to 50% of the time, twice the rate that can be expected by chance alone.¹

The most likely common denominator for the simultaneous presence of dyslipidemia and

hypertension is obesity. It is well documented that obesity in general, but particularly abdominal obesity, is associated with reduced sensitivity of insulin receptors and, consequently, increased resistance to the effect of insulin on peripheral glucose utilisation. The reduced sensitivity of insulin receptors results in an elevated level of plasma insulin. Hyperinsulinemia, in turn, increases hepatic, very low-density triglyceride synthesis, plasminogen activator inhibitor-1 synthesis, sympathetic nervous system activity, and sodium reabsorption. These changes contribute to simultaneous occurrence of hyperlipidemia and hypertension in obese patients.

Epidemiologic studies confirm the close association of hypertension and obesity. In the Nurses' Health Study, the body mass index at age 18 and at midlife was positively associated with the occurrence of hypertension.²

The metabolic syndrome

In recent years, particular attention has been paid to the metabolic syndrome, which is characterised by abdominal obesity, hyperinsuline-

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mia, and hypertension. The metabolically-active, visceral fat depot releases a large amount of free fatty acids, which enter the portal circulation and reach the liver to stimulate an increased production of very low-density and low-density lipoproteins. The combined effect of dyslipidemia and hypertension causes an exponential increase in the risk of coronary events.

This effect is well illustrated in two prospective epidemiologic studies of men in Finland.

Helsinki policemen study

The first study consisted of 970 men with no coronary artery disease who were followed for 22 years. The presence of hyperinsulinemia (defined as values in the highest quintile) was associated with an increased risk of a major coronary event (death or nonfatal myocardial infarction), although the predictive value of hyperinsulinemia did diminish with time. The hazard ratios, adjusted for other risk factors, at five, 10, 15, and 22 years were 2.3, 2.4, 1.8, and 1.3, respectively. Hyperinsulinemia was associated with increases in both cardiovascular and non-cardiovascular mortality.³

The metabolic syndrome and cardiovascular mortality in middle-aged men

This study, by Lakka et al, used both the Adult Treatment Panel (ATP) III and World Health Organisation (WHO) definitions of the metabolic syndrome.⁴ In this study,

4,209 men without cardiovascular disease, diabetes, or cancer were followed for an average of 11.4 years; 8.8% to 14.3% had the metabolic syndrome. Overall, the survival rate was 90% in patients without metabolic syndrome compared to 79% to 84% in those with the metabolic syndrome. After adjustment for conventional cardiovascular risk factors, coronary mortality was increased 2.9-fold to 4.2-fold according to the ATP III definition and 2.6-fold and 2.9-fold to 3.3-fold according to the WHO definition in men with the metabolic syndrome.⁴ The study's authors estimated that the metabolic syndrome accounted for 18% of the variance in cardiovascular risk.⁴

One study found a link between hypertension and dyslipidemia up to 50% of the time, twice the rate expected by chance alone.

What can be done?

A large database exists documenting the close association between dyslipidemia and hypertension. The combination of these two risk factors steeply increases the risk of developing coronary heart disease and stroke. The question is: what should be done with the patients who present with these risk factors?

The usual advice is to institute lifestyle changes, such as reducing weight by embarking on a low-fat diet and increasing physical activity. The problem with this





HYPERTENSION AND DYSLIPIDEMIA

Table 1

Antihypertensive drugs and their effects on plasma lipid levels

Diuretics (≥ 50 mg/day)

Increase LDL-C and total cholesterol by 5% to 10%.

Increase triglycerides.

Beta blockers

Decrease HDL-C by 10%.

Increase triglycerides by 20% to 40%.

Alpha blockers

Decrease total cholesterol.

Increase HDL-C moderately.

ACE inhibitors & CCBs

No measurable effect.

LDL-C: Low-density lipoprotein cholesterol
HDL-C: High-density lipoprotein cholesterol
ACE: Angiotensin-converting enzyme
CCB: Calcium channel blocker

advice is that the low-fat diet lacks scientific evidence for efficacy in reducing overall mortality.⁵ Counselling with respect to weight reduction is a failing technique in most patients. On the other hand, increased physical activity does have a documented benefit, but the effectiveness of counselling is ambiguous.⁶ Ultimately, the practicing physician will have to rely on drug treatment.

Different classes of antihypertensive drugs have different effects on plasma lipid levels (Table 1).

Diuretics

High doses of diuretics (≥ 50 mg/day) produce a 5% to 10% elevation in total and low-density lipoprotein cholesterol (LDL-C) and a lesser increase in triglycerides. Fortunately, these

doses are not used anymore and the present dose of 12.5 mg has little effect on levels of LDL-C or triglycerides.

Beta blockers

Beta blockers may cause a 10% fall in high-density lipoprotein cholesterol (HDL-C) and a 20% to 40% increase in plasma triglycerides.⁷ An exception is carvedilol, which has shown an 8% increase in HDL-C and a 20% reduction in triglycerides.


Alpha blockers

In general, alpha blockers, have a favourable effect on plasma lipids, lowering total cholesterol and moderately raising HDL-C.

Angiotensin-converting enzyme (ACE) inhibitors and calcium channel blockers

These drugs have no measurable effects on lipids. Administration of ACE inhibitors in the Heart Outcomes Prevention Evaluation (HOPE) study and angiotensin II receptor blockers in the Losartan Intervention For Endpoint reduction in hypertension (LIFE) study significantly reduced the onset of new diabetes and may, therefore, be considered suitable therapy, particularly in prediabetic situations, such as the metabolic syndrome.^{8,9}

Statins

There is evidence suggesting the treatment of dyslipidemia with statins may independently lower blood pressure and that the use of both antihypertensive medications and statins concurrently produces no unwanted drug interactions.¹⁰ Aggressive statin treatment in dyslipidemic patients with hypertension is a prudent strategy. 



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Take-home message

- Drugs are more effective than lifestyle changes as treatment for dyslipidemia.
- Diuretics, beta blockers, alpha blockers, ACE inhibitors, and calcium channel blockers have varying effects on plasma lipids (Table 1).
- Statins may independently lower blood pressure, and when used with antihypertensives, result in no unwanted side effects.

