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HYPERTENSION AND CORONARY HEART DISEASE

Jean-Philippe Baguet and Jean-Michel Mallion, Cardiology and Hypertension Department, Grenoble University Hospital, BP 217, 38043 Grenoble cedex 09, France

Correspondence: Jean-Philippe Baguet, Cardiologie et Hypertension artérielle, CHU de Grenoble - BP 217, 38043 Grenoble Cedex 09, France, tel +33476765440, fax +33476765559, JPBaguet@chu-grenoble.fr

Introduction

Hypertension (HT) is a major risk factor for coronary heart disease (CHD). Among the numerous risk factors associated with CHD, HT plays a major role given its high frequency and its physiopathogenesis. Thus, roughly 15% of the general adult population manifest HT with a net male predominance, and 25% of patients with CHD have HT [1]. CHD is the first cause of morbidity and mortality in hypertensive patients.

Numerous other risk factors for CHD, such as dyslipidaemia, insulin resistance, diabetes, obesity, lack of physical exercise and certain genetic mutations are frequently associated with HT [2]. Furthermore, hypertensive patients have a greater number of cardiovascular risk factors than normotensive patients.

Epidemiological studies have shown that the two other reversible risk factors for CHD, namely smoking and hypercholesterolaemia, increase the risk associated with HT in a multiplicative rather than in an additive manner [3]. Furthermore, although HT alone is weakly predictive of individual risk for the occurrence of CHD but the association between the level of blood pressure (BP) and the risk of CHD is independent of other factors.

Level of BP and risk of CHD

Numerous epidemiological studies have shown that the presence of HT increases the risk of CHD, not only in at risk populations but also in the general population. The prevalence of CHD is closely related to the BP level, especially systolic BP. This has been shown in studies of clinical BP and also in studies using ambulatory BP measurements (ABPM) [4]. Otherwise, the increase in pulse pressure is a predictive factor of coronary mortality [5]. The relationship between BP level and CHD seems linear, continuous and independent [6]. Indeed, the J-shaped curve of relationship between BP level and the risk of CHD comes from retrospective studies in patients with cardiovascular antecedents before anti-hypertensive treatment was instituted. Prospective therapeutic trials did not show an increase in risk of CHD in the lower levels of BP. In reference to ABPM studies, it has been reported that non-dipper hypertensive patients (night-time fall in BP <10%) have a cardiovascular risk, in particular a CHD risk, multiplied by three [7].

The fall in BP under treatment is associated with a reduction in cardiovascular events, more so for stroke than for coronary events. Thus, a reduction by 5 mmHg in diastolic BP reduces by one fifth the risk of CHD and a reduction of 10 mmHg leads to nearly a one third reduction on CHD risk [1]. According to a meta-analysis of 37,000 patients followed up over 5 years, treatment of moderate HT reduced by 14% the coronary morbidity and mortality by primary prevention [8]. Likewise, the meta-analysis by MacMahon et al. showed that a fall in BP in hypertensive subjects over 60 years reduced by 19% major coronary events [9].

Physiopathogenesis of myocardial ischaemia in HT

There is a multiplicity of mechanisms related to HT that lead to the development of myocardial ischaemia. These act by leading to an inequality between the transport and consumption of oxygen by the myocardium.

Acceleration of atherosclerosis

HT is an important risk factor for atherosclerosis and in particular in the coronary bed. The reduction in the lumen of the coronary arteries by atheromatous plaques reduces myocardium blood flow thereby favouring ischaemia. These plaques may eventually break and thus form peripheral emboli or especially thrombus in situ by means of platelet aggregation that is responsible for acute coronary syndromes.

Left ventricular hypertrophy

Left ventricular hypertrophy (LVH) is one of the most important risk factors for CHD and sudden death independently of the level of BP [10]. This is the case whether LVH is diagnosed by ECG or by echocardiography. LVH reduces coronary flow reserve and favours the development of ventricular arrhythmias. This reduction in coronary flow reserve is secondary to structural and functional modifications in the myocardium (myocardial component), and in the arteries (vascular component), and also to anomalies in the control of coronary blood flow (nervous component) [11]. LVH increases metabolic and oxygen demands of the myocardium, increase coronary flow and coronary vascular resistances but diminish coronary flow reserve. This is associated with disturbance of diastolic function of the left ventricle that leads to a fall in perfusion of the myocardium. Furthermore, LVH is responsible for dysfunction of the mecano-receptors in the left ventricle thereby leading to anomalies in coronary vascular tone.

Anomalies of the microcirculation

HT is associated with anomalies of the coronary microcirculation with a peri-vascular fibrosis, a thickening of the media, a reduction in the number of capillaries per gram of muscular tissue and a diminution of the vascular lumen [12].

Endothelial dysfunction

The endothelium-dependent vascular relaxation is altered in HT [13]. This has been well demonstrated by the reduction in the vasodilator response after an intra-arterial injection of acetylcholine in the hypertensive subject while the response to nitrate derivatives is not altered [14]. This endothelial dysfunction brings into function numerous mediators such as nitric oxide (NO), prostacyclines, factors acting on the differentiation and the growth of vascular smooth muscle cells or cyclo-oxygenase dependent contraction factor. The anomalies in endothelial function explain in part the increase in the risk of CHD in HT since they favour vasoconstriction, thrombogenesis and the action of proliferative substances.

Insulin resistance

Insulin resistance is frequently found in essential HT. This leads to hyperinsulinism that is an independent predictive factor of CHD. This insulin resistance is often associated with low levels of HDL cholesterol and elevated levels of triglycerides. These may result in an acceleration of the atherosclerotic process.

Sympathetic activation

The regulation of myocardial blood flow is, in part, mediated by the sympathetic nervous system. HT is accompanied by an exaggerated sympathetic response to physiological stimuli that favours myocardial ischaemia.

Detection of CHD in the hypertensive patient

Repolarisation anomalies are frequently found on the ECG in hyper-

tensive patients, in particular negative T waves in the lateral leads indicating systolic overload of the left ventricle, frequently associated with LVH. The exercise ECG is difficult to interpret in HT since a ST depression in V5 and V6 is frequent especially in the presence of LVH. These findings are of low specificity for myocardial ischaemia. Myocardial scintigraphy is also often abnormal in HT because of LVH and anomalies of coronary microcirculation [15]. If diagnostic doubt persists after an exercise test or a myocardial scintigraphy in hypertensive subjects with chest pain, coronary angiography is often necessary.

It has been shown that roughly 30% of hypertensives have silent episodes of myocardial ischaemia due to a reduction in coronary flow reserve, to endothelial dysfunction and anomalies in the autonomic nervous system.

Treatment of HT and CHD

An isolated fall in BP with treatment does not completely reduce the risk of CHD in essential HT. This confirms the complexity of the relationship between CHD and HT since numerous factors other than HT are implicated as previously discussed. Treatment of HT in patients with CHD must be more aggressive that in the absence of CHD. Indeed, the risk of a recurrent coronary event in this population is very high and all efforts should be expended in order to lower BP, especially since we may expect a better compliance with treatment after a coronary event.

In primary prevention, successive studies have shown the benefit of thiazide diuretics and beta-blockers on cardiovascular events. Subsequently, calcium blockers and angiotensin converting enzyme (ACE) inhibitors have been shown to be effective in the same situation, and more recently angiotensin 2 receptors antagonists in the LIFE study [16]. All these treatments have an identical effect on the fall in BP and in the percentage of responders [17, 18]. The thiazide diuretics, beta-blockers, calcium blockers and ACE inhibitors have a similar effect of reduction in cardiovascular morbidity and mortality. The same drugs lead to a modest reduction in coronary events, of the order of 20%. Although it has not been definitively proven, the regression in LVH by antihypertensive treatment allows improvement in myocardial perfusion thereby reducing the risk of CHD. In this context, ACE inhibitors may have a more marked effect than the other therapeutic classes as regards regression in LVH. [19].

As regards secondary prevention, there are no studies of diuretics. The only therapeutic classes which have been proven to prevent recurrence of coronary events, whether associated with HT or not, are beta blockers [20-22], ACE inhibitors [23-26] and calcium blockers such as verapamil in case of contraindication of beta blockers or in association with trandolapril [27-28]. In patients with postmyocardial infarction, ACE inhibitors, beta blockers, and aldosterone antagonists have proven to be most beneficial [29-30]. Intensive lipid management and aspirin therapy are also indicated [30].

Conclusion

The prevalence of HT is very high in the general population and more so in patients with CHD. The mechanisms by which HT favours the development of CHD are multiple and are not simply limited to the presence of atheroma in the coronary arteries. Non-invasive diagnostic tests for CHD are often inadequate in HT. HT, as a major risk factor for CHD, can be partially reversed by anti-hypertensive treatment that has a vital role both in primary and secondary prevention.

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