

Update on the Treatment of Hypertension

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CHEUNG: Update on the Treatment of Hypertension. Despite recognition of the dangers of untreated and uncontrolled hypertension, it is still widely and persistently under-treated in the community. Universal screening of all adults for hypertension is essential, as the probability of hypertension in any randomly chosen person is considerable, especially from middle age onwards. The level of blood pressure, the presence of other risk factors, target organ damage and overt cardiovascular disease allow the physician to estimate the cardiovascular risk of a patient. The urgency of treatment depends on the degree of risk. It is now believed that the control of hypertension is the primary goal. This may necessitate changing the class of antihypertensive drug or using a combination of different classes. The choice of drug class is also determined by co-morbidities. The control of blood pressure to the point of normalisation of blood pressure is safe and beneficial, especially in diabetics. In patients with mild hypertension, non-pharmacological treatment through lifestyle modification has a definite place. (J HK Coll Cardiol 2002;10:17-20)

Antihypertensive drugs, blood pressure, cardiovascular diseases, hypertension

摘要

儘管已認識到高血壓未治療或未得到控制的危險性，但社區中仍存在許多未得到持續性治療的高血壓患者。對所有成年人進行高血壓普查十分必要，因為在任何隨機抽取的人群中高血壓的概率比較大，特別是中年以上者。血壓水平、合併的其他危險因素、靶器官損害及明顯的心血管系統疾患有助於醫師評估患者的心血管危險性。治療的緊迫性有賴於疾病的危險程度。迄今得到認可的是高血壓的控制是首要目的。這有必要改換抗高血壓藥物的種類或採用聯合用藥。藥物種類的選擇同樣要受到伴發疾病的影響。把血壓控制在正常點是安全、有益的，尤其是糖尿病患者。輕度高血壓患者，通過改善生活方式的非藥物療法具有肯定的作用。

關鍵詞：抗高血壓藥物 血壓 心血管疾病 高血壓

Update on Hypertension

The risks of untreated hypertension are well known and well understood. Blood pressure has a direct relation with the risk of stroke and myocardial infarction. Hypertension may also lead to left ventricular hypertrophy, heart failure and renal failure. Despite

recognition of the dangers of untreated and uncontrolled hypertension, it is still widely and persistently under-treated in the community. Many hypertensives remain undiagnosed. Of those who have been diagnosed, many of them are not on treatment. Of those who are on treatment, many are not well controlled. This "rule of halves" has been demonstrated in many countries around the world, including even the United States.¹ As hypertension is an asymptomatic disease, screening in apparently healthy individuals is warranted. The probability of hypertension in an individual in the general population is around 20%; this increases to as high as 50% in the elderly.² Universal screening of all adults for hypertension is essential, as the probability of hypertension in any randomly chosen person is considerable, especially from middle age onwards.

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Screening for hypertension in first degree relatives is arguably mandatory in view of the clustering of hypertension in families due to shared genetics and environmental factors.

If high blood pressure is undesirable, we may ask what is the ideal blood pressure for normal people and what is the treatment target for hypertensives. We have little definite information on the former but we now have a partial answer for the latter. In the Hypertension Optimal Treatment (HOT) Study, an achieved diastolic blood pressure of 83 mmHg was associated with the lowest incidence of cardiovascular events (Table 1).³ However, there was scarcely any difference whether the target diastolic blood pressure was <80, <85 or <90 mmHg. The results of HOT allow a dual interpretation; aggressive blood pressure reduction is justifiable as there is no harm, but cautious and cost-conscious prescribing is also justified as there is little additional benefit from lowering the diastolic blood pressure below 90 mmHg. Instead of increasing the dose or adding on another drug if the diastolic blood pressure is already below 90 mmHg, one might consider addressing other modifiable risk factors. There is one subgroup of hypertensives who should have aggressive reduction of blood pressure; these are the diabetics. In HOT and the UK Prospective Diabetes Study (UKPDS),⁴ there were benefits in lowering the blood pressure beyond 140/90 mmHg. A target blood pressure of <130/85 mmHg is now recommended for diabetics.⁵

There is increasing recognition that elevated systolic blood pressure is of prognostic significance and treatment of systolic hypertension is beneficial, even if the diastolic blood pressure is normal as in isolated systolic hypertension. In the latest guidelines, a systolic blood pressure of 140 mmHg or above is considered abnormal.^{1,5,7} However, a large proportion of the elderly has a systolic blood pressure higher than this. Thus, a large section of the elderly population is at risk from the complications of hypertension and requires a combination of lifestyle modifications and drug treatment.

The role of other additional medications for hypertensive patients is unclear. Aspirin was shown to be beneficial in HOT in terms of reduction of cardiovascular events, but the incidence of gastrointestinal bleeding is also increased, so the risks and benefits have to be worked out for each patient. Antioxidants are less

promising than they have appeared to be; the Heart Outcome Prevention Evaluation (HOPE) did not show any cardiovascular benefit associated with vitamin E supplementation.⁶

The assessment of the overall cardiovascular risk for each patient is the cornerstone in the latest World Health Organisation (WHO) guidelines⁴ as well as the British Hypertension Society guidelines⁷ for the management of hypertension. As hypertension is only one of a number of risk factors for cardiovascular disease, it is desirable to address all these risk factors rather than to consider the level of blood pressure in isolation. Hence, in the new paradigm, the level of blood pressure, the presence of other risk factors, target organ damage and overt cardiovascular disease allow the physician to estimate the cardiovascular risk of a patient. The urgency of treatment depends on the overall degree of cardiovascular risk as well as the level of blood pressure. This new mode of thinking, although initially complicated, is an improvement on treating the blood pressure with disregard of actual cardiovascular risk. A pre-menopausal woman with mild hypertension, e.g. 150/100 mmHg, but no other risk factors has a very low immediate risk of cardiovascular events and should probably have lifestyle changes to lower blood pressure as far as possible. The same level of blood pressure in a 60-year-old male smoker with multiple risk factors requires treatment and aggressive modification of other risk factors to lower the cardiovascular risk. However, a major disadvantage of using cardiovascular risk in treatment decisions is that it makes no distinction between a cardiovascular event in the young and in the elderly. In the very elderly, treatment might only prolong life marginally whereas it is disastrous if a young person

Table 1. Recent major clinical trials

Trial objective	Name of Trial
Optimal blood pressure target	HOT ³
Hypertension in diabetics	UKPDS ⁴
CCB vs. placebo	Syst-Eur, ¹⁰ Syst-China ¹¹
CCB vs. other drugs	INSIGHT, ¹³ NORDIL ¹⁴
ACEI vs. placebo	HOPE, ⁶ PROGRESS ¹⁸
Comparing several drug classes	STOP-2, ¹² ALLHAT ¹⁷
Diet	DASH, ^{19,20} TONE ²¹

has a debilitating stroke. It is therefore important to consider the potential benefits of treatment as well as the risks of no treatment.⁸

The relative merit of different classes of antihypertensive drugs is always a controversial area, not least because of commercial interests. The WHO,⁵ British⁷ and JNC-VI¹ guidelines have all attempted to address this issue. It is now believed that the control of hypertension is the primary goal. This may necessitate changing the class of antihypertensive drug or using a combination of different classes. Following some adverse findings about calcium channel blockers (CCBs) mainly from case control studies,⁹ randomised controlled trials such as Systolic Hypertension in Europe (Syst-Eur),¹⁰ Systolic Hypertension in China (Syst-China),¹¹ the Swedish Trial in Old Patients with Hypertension-2 (STOP-Hypertension-2),¹² the International Nifedipine GITS Study Intervention as a Goal in Hypertension Treatment (INSIGHT)¹³ and Nordic Diltiazem (NORDIL) Study¹⁴ have shown that this drug class also reduces cardiovascular events. This underlines the paramount importance of blood pressure control. However, two meta-analyses of hypertension trials have recently been published with somewhat conflicting conclusions regarding CCBs. One reported a significantly higher risk of myocardial infarction and heart failure associated with CCBs,¹⁵ whereas the other regarded these differences to be of borderline significance.¹⁶ In Asia, the incidence of stroke is higher than that of myocardial infarction. As CCBs are effective in lowering blood pressure and reducing the risk of stroke, they have an important place in the formulary.

The merits of alpha-blockers are put in doubt by the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), in which a higher rate of cardiovascular events, mainly heart failure and strokes, was observed in the alpha-blocker arm.¹⁷ However, there was no difference in the primary endpoint, which was the occurrence of fatal and non-fatal myocardial infarction. Alpha-blockers may not be the first-line drug for the treatment of hypertension, but they remain useful for the control of blood pressure, especially in elderly male patients with prostatic symptoms.

The latest guidelines have also incorporated clinical trial evidence to support the use of certain classes in certain situations. For example, a hypertensive with

angina should receive beta-blockers. ACEIs have emerged as an important drug class, preventing cardiovascular events in those who are at risk, as shown in the HOPE study.⁶ On the other hand, both the STOP-Hypertension-2 and the UKPDS failed to show that ACEIs are superior to conventional antihypertensive agents.

In the HOPE study, subjects randomised to treatment with an ACEI had lower cardiovascular events even if they were normotensive.⁶ It has been argued that the degree of blood pressure lowering did not fully explain the benefits observed. It was postulated that ACEIs might have a protective effect beyond blood pressure reduction. Interestingly, in the Perinodopril pROtection aGAINst Recurrent Stroke Study (PROGRESS), a decrease in stroke rate was observed in normotensive as well as hypertensive patients randomised to treatment with an ACEI.¹⁸

The cost-effectiveness of antihypertensive medications varies enormously because of the tremendous differences in the price of drugs. At the same time, the efficacies of antihypertensive drugs are remarkably similar. Large clinical trials have shown that, in terms of cardiovascular outcome, the newer classes are not superior to beta-blockers and diuretics.^{12,13,17} In patients at high risk from cardiovascular disease, use of expensive medications may be acceptable. Yet, in patients with mild hypertension and at low risk from cardiovascular disease, cost-effectiveness should not be ignored, especially in the public sector. Nevertheless, patients respond differently to antihypertensive medications and some may require newer and more expensive medications to control their blood pressure or to avoid side effects.

In the approach to treating patients with mild hypertension, non-pharmacological treatment has a definite place. Factors leading to hypertension in Hong Kong include ageing, family history, obesity and diabetes. The Dietary Approaches to Stop Hypertension (DASH) study showed that a healthy diet rich in fruits and vegetables and low in fat and sodium lowers blood pressure.^{19,20} The Trial of Non-pharmacologic intervention in the Elderly (TONE) showed that weight loss and reduction in salt intake resulted in decreased blood pressure and need for antihypertensive medications.²¹ We have also identified sodium intake as a strong determinant of diastolic blood pressure.²²

Obesity and sodium intake are modifiable risk factors. In patients with mild hypertension, lifestyle measures may be sufficient to control blood pressure or at least ameliorate it. For the whole population, universal screening for hypertension and a healthier lifestyle are likely to bring about the largest amount of benefit to the greatest number of people with the minimum of risks.

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