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Preventing stroke

High risk patients should receive ramipril irrespective of their blood pressure

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The Heart Outcomes Prevention Evaluation study (HOPE), has shown beneficial effects of the angiotensin converting enzyme inhibitor ramipril on cardiovascular events and disease progression.[1] In this issue the investigators describe the results of preventing stroke (p 699).[2] The findings clearly show that ramipril substantially decreased the risk of stroke and transient ischaemic attacks in 9297 patients with high cardiovascular risk. A 32% relative risk reduction was found, while the reduction in blood pressure was only 3.8 mm Hg (systolic) and 2.8 mm Hg (diastolic). This benefit was greater than expected from prior meta-analyses of epidemiological studies or trials in hypertension studies. The results have important implications for the primary and secondary prevention of stroke.

Firstly, it must be emphasised that hypertension is still the most important risk factor for stroke, as shown in all studies on hypertension in recent decades,[3] and more recently in the PROGRESS study, in which an average blood pressure reduction of 9/4 mm Hg decreased the risk by around 28%.[4] Also in HOPE the highest risk for stroke was found within patients in the placebo group with blood pressure greater than 140/90 mm Hg. A strict normotensive blood pressure adjustment should be crucial for the physician in primary and secondary prevention of stroke—a goal that is not achieved even in well developed countries.

Secondly, HOPE focused on patients with high cardiovascular risk and controlled blood pressure. Patients with uncontrolled hypertension were excluded; thus HOPE is not a hypertension study. The angiotensin converting enzyme inhibitor ramipril decreased the risk for stroke independent of reduction in blood pressure. There was a beneficial effect even in patients with blood pressure less than 129/79 mm Hg. The beneficial effects of the treatment were seen in all subgroups examined. This shows that high risk patients should be treated with ramipril in addition to other preventive measures irrespective of their initial blood pressure.

The underlying mechanisms by which angiotensin converting enzyme inhibitors prevent vascular events have been discussed widely. The protective effects of these drugs on the vascular wall are possibly explained by decreased oxidative stress and decreased proliferative and inflammatory responses resulting in a beneficial effect on the progression of atherosclerotic plaques.[5] The anti-inflammatory response of angiotensin converting enzyme inhibition may lead to more plaque stabilisation.[6]

These causal concepts are supported by the SECURE study, a substudy in which progression of atherosclerosis was significantly reduced by ramipril compared with placebo.[7] Importantly, the effect of a 10 mg dose, as used in the HOPE study, was better than 2.5 mg. This underlines the need for titrating ramipril to a higher dose to exploit its full preventive potential. One cannot assume, however, that similar outcomes would occur with other angiotensin converting enzyme inhibitors or with different dosages, although it is possible. Angiotensin 1 antagonists have yet to prove similar long term benefits.

Thirdly, patients who have previously been treated with acetylsalicylic acid tend to benefit from ramipril less than patients who have not been treated with acetylsalicylic acid. Similarly, patients with a history of cerebral events—who have the highest risk for stroke—benefit less from ramipril than patients without a similar history. It must be assumed that most of these patients were treated with acetylsalicylic acid. These differences were, however, not significant.

This raises the question of interaction of acetylsalicylic acid and angiotensin converting enzyme inhibitors. It is not possible to understand from the HOPE study the extent to which the subgroup of patients with stroke benefits from the combination of acetylsalicylic acid and ramipril, because of the small number of patients. However, it is already known from cardiovascular studies that the beneficial effect of angiotensin converting enzyme inhibitors can be weakened by acetylsalicylic acid.[8]

This raises a very important question. Since acetylsalicylic acid is one of the best documented treatments in secondary prophylaxis of stroke, the effectiveness of its combination with angiotensin converting enzyme inhibitors must be urgently proved. The positive effects in HOPE occurred in more than 70% of patients in the context of treatment with acetylsalicylic acid. The recommendation at present should be not to exclude acetylsalicylic acid or angiotensin converting enzyme inhibitors when there is an indication for both substances. Low dose acetylsalicylic acid appears to be more favourable. Adenosine diphosphate antagonists may constitute an alternative to acetylsalicylic acid but there are no studies yet to prove long term superiority.

Fourthly, the main target of treatment is not only to reduce quantitatively the risk of stroke and fatal events but to improve the quality of life for survivors of strokes by reducing disability, cognitive impairment, and dementia. This would also entail substantial financial savings due to reduced need for care.

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In HOPE, fatal stroke was reduced by 61%, non-fatal stroke was reduced by 24%, and functional and cognitive outcomes improved with ramipril. Significantly fewer patients on ramipril experienced functional impairment, impaired consciousness, speech, and swallowing. Thus the two main goals of treatment for stroke prevention were achieved in HOPE.

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Africa can solve its own health problems

But first, the continent must reorder its priorities and commit to distributive justice

On the evidence of such archaeological finds as Lucy, the australopithecine female unearthed in Ethiopia's Hadar region, Africa is the cradle of the human race. Africa was also home to notable ancient civilisations—the Egypt of the Pharaohs, the Ashanti Empire of the Gold Coast, and the Zimbabwe settlements in the south. Given such a head start, it is ironic that Africa should now find itself at the bottom of the ladder in terms of human development. Most of the countries in sub-Saharan Africa lag far behind other developing nations with respect to critical health indicators such as maternal and infant mortality and life expectancy.

Granted, Africa's legacy of particularly exploitative colonial occupation by European powers is partly to blame. However, Africans themselves must bear the responsibility for failing to create an enabling environment for better health—safe water and sanitation, secure supply of food and nutrition, education, and higher status of women—in the period since the continent's political emancipation that began with Ghana's independence in 1957.[1] Instead, many countries have seen both opportunity and resources squandered on political adventurism, civil wars, misguided macroeconomic policies, and greed.

Nevertheless, with sufficient will, commitment, and vision, and by making the right choices, Africa can successfully address its own health challenges and start to contain the morbidity and mortality from diarrhoeal diseases, childhood infections, parasites, and maternal and perinatal morbidity, as well as emerging and re-emerging infections of HIV, malaria, and tuberculosis. Africa's health challenges are not insurmountable. In most cases, the solutions are straightforward and inexpensive, requiring only that the right political choices be made.

The World Health Organisation has identified poverty in Africa as "the single biggest threat to health."[2] And in an unpublished speech to Kenya's Medical Research Foundation on 19 January 2001, Britain's minister for the Department for International Development, Baroness Amos, warned that "in the short term and in the long run, African governments, leaders, and individuals will need to exercise more leadership, set agendas, and mobilise far more resources, for a sustained response to lift people out of poverty."

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Africa's top priority must therefore be to grow the economy, which in the view of the World Bank means buying into the global economic movement. David Dollar of the World Bank cites the example of Vietnam, where the proportion of the population in poverty fell from 75% in 1988 to 37% in 1999 as the country "opened up to foreign trade."[3] This view is not universal, however, as has been evident in the "anticapitalism" protests spanning the globe from Seattle to Genoa. Certainly, globalisation has been responsible for crises in banking and currency, steep rises in poverty rates, and widening income inequalities in many countries.[4]

While African countries cannot escape the global movement, they must embrace it with the necessary circumspection. Two harms of globalisation come to mind. The first is the use of Africans to test drugs from which they will never benefit, either because the drugs are too costly or because they are designed to treat conditions that largely affect industrialised nations.[5] The second is the global proselytising of first world values that are detrimental to Africa. The ban on dicophane (DDT)—a cheap and highly effective weapon against malaria—because it was thought to be harmful to US bird species cost millions of African lives, whereas no African has ever died from the normal use of dicophane.[6]

The mere accumulation of national wealth is not sufficient to deal with poverty as a health risk. Africa must commit to equity and economic distributive justice in order to address national health needs. With this approach, the poor Indian state of Kerala has achieved health indicators almost comparable to those of the United States despite its per capita income being 99% less and its spending on health being $28 per capita compared with $3925 in the United States.[7] China, Costa Rica, and Sri Lanka have made similarly impressive gains.[8]

This means that African countries must address the highly unequal access to personal health care that exists between rich and poor, between urban and rural populations, and between ethnic groups. They must

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