EDITORIAL

Live long and prosper: a mass strategy for treating the factors associated with ischaemic heart disease and stroke

In the 1950s and 1960s a debate raged between Professor (later Sir) George Pickering, Regius Professor of Medicine at Oxford, and Professor Robert (later Lord) Platt, Professor of Medicine in Manchester.[1] Pickering maintained that people with a high blood pressure were in the tail of a skewed normal distribution of blood pressures in the general population. Platt maintained that those with a high blood pressure formed a distinct distribution. Pickering is generally held to have won the debate. Platt accepted that blood pressure was multifactorial, while Pickering for his part conceded that there might be discrete subgroups of patients hidden in the unimodal distribution.

Now we have epidemiological evidence not only that blood pressure is unimodally distributed, but also, as Law, Wald, and Morris show in a recently published monograph,[2] that the risks of the complications of a raised blood pressure (ischaemic heart disease and stroke) are increased at all blood pressures, at least down to a diastolic pressure of 75 mmHg. In other words, no matter how high or low your blood pressure, a lower pressure is associated with a smaller risk of complications. And no matter what your blood pressure is to start with, if you reduce it by a fixed amount you will reduce your risk of vascular events by a fixed proportion. For example, in people aged 55–64 years, lowering the diastolic blood pressure from 85 to 80 mmHg produces a 34% reduction in the risk of stroke, and the same reduction in risk can be achieved by lowering the diastolic blood pressure from 105 to 100 mmHg. The corresponding reduction in the risk of ischaemic heart disease for a 5 mmHg drop in diastolic pressure is 21%. The effect is independent of the type of blood pressure lowering drug used. Furthermore, the beneficial effect of lowering the blood pressure extends below the currently recommended targets for diastolic blood pressure in patients with hypertension (85 mmHg; 80 mmHg in those with diabetes mellitus).[3]

IMPLICATIONS

Implications for screening for high blood pressure

The first major implication of these observations is that there is no practical threshold for lowering the blood pressure. Within the range of blood pressures found in the population, most people will benefit from having their blood pressure reduced by at least a small amount; at higher pressures greater reductions will be possible and the effects will be proportionately greater, although the risks are also greater to start with.

This in turn implies that it is not necessary to measure the blood pressure in order to identify those who will benefit from having their blood pressure lowered. Almost everyone will benefit from some reduction. Furthermore, Law *et al.* show that the blood pressure is in any case not a good screening test for those who are most at risk of developing the complications of high blood pressure.[2] This apparently paradoxical observation arises from the fact that at any age those in the top 10% of the blood pressure distribution suffer only about 25% of all vascular events. An adapted version of the section of the monograph that deals with blood pressure as a screening test is reproduced on pages 3–7.[3]

However, the risks of the complications of high blood pressure increase with age, and so age is a much better screening test than blood pressure. This in turn implies that a sensible strategy would be to use blood pressure lowering drugs in all those over a certain age, say 55 years, above which the risks increase markedly.

Implications for treatment of the risk factors for vascular disease

Traditionally doctors have screened their patients for defined abnormalities and have treated those in whom the abnormalities were found. But now the evidence regarding blood pressure suggests that they should instead treat everyone above a certain age, without carrying out any other screening test. They may regard this advice as heretical. However, that is precisely the strategy that they currently adopt when they give everyone at high risk a daily low dose of aspirin, without measuring the aggregability of their platelets. Giving a blood pressure lowering drug without measuring the blood pressure is in principle no different. And the principle extends further. For neither is there any difference in giving a statin without measuring the serum LDL cholesterol concentration, or folic acid without measuring the serum homocysteine concentration. In each case the lower the risk factor (blood pressure, platelet aggregability, serum LDL cholesterol, or serum homocysteine) at all values, the less the risk of vascular disease.[5]

Wald and Law have calculated that the simultaneous administration of aspirin, a statin, folic acid, and three blood pressure lowering drugs (the 'Polypill') could reduce the risks of heart attack or stroke by about 85%.[6] This means, for example, that if 100 men adopted this strategy from the age of 55 years, 37 of them would benefit by avoiding or delaying a vascular event, each gaining on average 12 years of life in so doing. This policy of simultaneously treating several risk factors for vascular disease is discussed in the World Health Organization's 'Health Report 2002'.[7]

Implications for the definition of disease

Finally, these observations on blood pressure suggest that the disease that we call essential hypertension is not a disease at all, since everyone above a certain age will benefit from blood pressure reduction. The same is true of other conditions in which a risk factor that causes complications has been labelled as the source of a disease, such as hyper-

cholesterolaemia – no matter what the serum cholesterol concentration is, it can generally be beneficially lower.[5] And although we do not (yet) regard hyperhomocystinaemia or platelet hyperaggregability as defined diseases, the same principles apply to lowering serum homocysteine concentrations with folic acid supplements and reducing platelet aggregability with aspirin.

The idea that hypertension is not a discrete disease is by no means new.[8] However, it has not previously informed drug therapy in this way. For example, when Geoffrey Rose suggested what he called the mass strategy of treating the whole population in order to reduce the mean blood pressure by just a few mmHg,[9] he concluded that lowering the mean blood pressure in the population would not benefit individuals (the effect in each would be too small) but would reduce the overall burden of strokes and heart attacks in the community (because of the large reduction in the area under the population distribution curve). But although the strategy was sound, his conclusion was wrong. A mass strategy of achieving even quite small reductions in blood pressure benefits not only the community but each individual as well; treating everyone over a certain age makes sense.

BENEFITS VERSUS HARMS

No analysis of the benefits of drug therapy is complete without an analysis of the potential harms, in other words the risks of adverse drug reactions. Here too the news is good. The risk of an adverse effect from any blood pressure lowering drug is less than 10% and the risk of an adverse effect severe enough to require withdrawal is 1.4% or less. The prevalence of adverse effects can be substantially reduced, moreover, with little loss of efficacy, by using the drugs in half the current doses: three blood pressure lowering drugs in low-dose combination are safer and more effective than two at standard doses.[10] The combination of aspirin, a statin, folic acid, and three blood pressure lowering drugs in half standard doses (the 'Polypill') would cause symptoms in 8–15% of people, depending on the precise formulation.[6]

COSTS

Cost estimates were not presented in the blood pressure monograph or the 'Polypill' papers. The financial cost per year of life gained would be low with therapy based on inexpensive generic (off-patent) drugs. But counting overall costs is more complicated than this.[11] We are currently witnessing an increase in the average ages of the populations of Western countries, and changes in the proportions of elderly people. Governments are already considering extending the retirement age to make good use of this resource, and there is no doubt that a healthy ageing population can continue to contribute to the economic welfare of a country, and indeed will need to. Retraining those who want to embark on new careers and providing companies with financial incentives to employ older people should enhance this. The costs of taking care of the sick elderly will of course increase, but they will be sick for shorter periods of time, and it is likely that the costs of caring for them will be outweighed by the extra value that they will have given to the community before they require care.

CONCLUSIONS

Doctors will continue to measure blood pressure and to treat those whose pressure is considered to be inappropriately high for their age, perhaps paying attention only to the systolic pressure, as has been suggested.[12] And increasing understanding of the genetic components of high blood pressure will slowly whittle away at the label 'essential hypertension',[13] perhaps affording new therapies as a result.

But doctors' attitudes to preventing ischaemic heart disease and strokes should be radically revised in the light of the current epidemiological evidence and its analysis. Everyone over a certain age (say 55 years) should be given at least a small dose of one or more blood pressure lowering drug, a statin to reduce the serum LDL cholesterol concentration, folic acid to reduce the serum homocysteine concentration, and aspirin to reduce platelet aggregability. This strategy, if properly implemented, could almost eradicate strokes and heart attacks. Many of us will then have to find other ways to die.

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