MIXED BAG

THE POLYPILL – IS THIS AN EFFECTIVE APPROACH TO PREVENTION OF CARDIOVASCULAR DISEASE?

The past 2 or 3 years have seen increasing interest, overseas at least, in the idea of a polypill – one combination pill that will take care of all aspects of cardiovascular disease. When first put forward as an idea by Wald and Law in 2003, the intention was to combine lipid-lowering medication, antihypertensive medication and antiplatelet therapy with folic acid. They proposed this as an approach not only to secondary prevention but for primary prevention as well, targeting those with pre-existing cardiovascular disease as well as everyone over the age of 55. The underlying assumption concerning the efficacy of this strategy is that the 6 individual ingredients of the polypill (thiazide diuretic, angiotensin-converting enzyme inhibitor, β-blockers, statin, aspirin, and folic acid) when combined together have synergistic treatment effects – calculated by multiplying the relative risk reductions on each class of treatment. The idea has definitely generated interest around the world, although some critics have questioned the assumption that the effects of these drugs will be synergistic and multiplicative.

Julia Hippisley-Cox and Carol Coupland, writing in a recent *British Medical Journal*, decided to look at the effect of combinations of statins, aspirin, β-blockers and angiotensin-converting enzyme inhibitors in the secondary prevention of all-cause mortality in patients with ischaemic heart disease. Using a database of 1.18 million patients registered with general practices across 23 health areas in Britain, they examined all patients with a first diagnosis of ischaemic heart disease between January 1996 and December 2003. Cases were patients with ischaemic heart disease who died. Controls were patients with ischaemic heart disease who were matched for age, sex and year of diagnosis and were alive in the year that their matched case died.

Hippisley-Cox and Coupland found 13 029 patients with a first diagnosis of ischaemic heart disease. A total of 2 266 cases were matched to 9 064 controls. The drug combinations that were associated with the greatest reduction in all-cause mortality were statins, aspirin and β-blockers; β-blockers and angiotensin-converting enzyme inhibitors; and statins, aspirin and angiotensin-converting enzyme inhibitors. The treatments that were associated with the least reduction in all-cause mortality were β-blockers alone, angiotensin-converting enzyme inhibitors alone, and combined statins and angiotensin-converting enzyme inhibitors. This trial is the first large-scale, long-term community-based study to report the effect of different combinations of drugs in the secondary prevention of all-cause mortality in patients with ischaemic heart disease. They included patients with multiple comorbidity, elderly people and women – who may have been excluded from previous trials.

Their findings were that combinations of statins, aspirin and β-blockers improve the survival of high-risk patients with ischaemic heart disease. They also found that adding an angiotensin-converting enzyme inhibitor did not have any additional benefit, even for those patients with congestive cardiac failure. This latter finding is consistent with the results of another recent trial. The evidence is compelling that a combination of these drugs, but not with an angiotensin inhibitor, does play a role in the secondary prevention of ischaemic heart disease. But what of primary prevention? This trial does not address this issue and there are still many concerns about what has been called a scatter-shot approach to primary prevention. There is already evidence that the effects of aspirin are different in men and women. The role of folic acid in the proposed polypill is far from established, particularly with the conflicting evidence of the proposed efficacy of antioxidants in preventing cardiovascular disease. There is also the problem of giving life-long treatment that has known side-effects to people who are not actually ill. On another front there is the issue of medicalising the population – potentially relieving people of having to take responsibility for their own health through lifestyle adjustment. I would also like to see a trial in which combined treatments for those with established ischaemic heart disease are compared with lifestyle interventions. Difficult ethically perhaps, but in a situation where health care costs are escalating alarmingly, possibly a more practical approach than yet more pills.

Hippisley-Cox J, Coupland C. *BMJ* 2005; **330:** 1059-1063.

MORE ON THE MILLION WOMEN STUDY

The Million Women Study hit the headlines in 2003 when it was published in the *Lancet* and changed the prescribing habits of doctors treating postmenopausal women. Many people feel that the study was flawed, unrepresentative of all women, did not provide consistent follow-up and used an inaccurate classification of hormone replacement therapy (HRT). There was also the issue of the public's understanding of what constitutes risk – highlighted by what became a generally accepted idea that using HRT increases the absolute, rather than the relative, risk of developing breast cancer. However, the fact remains that fewer people are currently willing to prescribe HRT and certainly not for long periods of time.