Blood cholesterol and coronary heart disease: changing perspectives

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Summary

There has been much controversy concerning the value of efforts to reduce blood cholesterol levels. In this contribution, the risks and benefits of interventions are discussed. Lowering cholesterol level by drugs is not recommended except in a small minority of subjects at very high risk of coronary heart disease (CHD), since it causes an excess of non-CHD deaths. Dietary intervention, by contrast, is safe. However, for it to be effective it must be sufficiently vigorous to achieve a drop in blood cholesterol of at least 6%, though considerably more is preferable. This action should be part of a more general effort aimed at the prevention of all Western diseases based on changes in lifestyle.

Introduction

Currently, there is controversy over the significance to health of high and low cholesterol level, whom should be tested, and over the short and long-term benefits of interventions[1-3]. Recent evidence has indicated that in Western populations there is an association between a low blood cholesterol level and death from various diseases, particularly stroke and certain types of cancer[4,5]. Among women there is actually no association between hypercholesterolaemia and cardiovascular deaths. This is because haemorrhagic stroke makes up a higher proportion of total cardiovascular deaths in women, due to their lower death rates from CHD[3].

Ravnskov[6] recently reviewed the results from 26 intervention trials in which blood cholesterol had been lowered by diet or by drugs. He reported that when all of the trials are taken into account, fatal CHD has been lowered by only 6% and non-fatal CHD by only 10%. Overall, there has been no change in total mortality since the fall in fatal CHD is offset by a rise in fatalities from other causes. Ravnskov contended that some authors of reviews and other contributions have been biased in the literature which they have cited, thereby leading to the conclusion that the impact of interventions on CHD has been more favourable than is actually the case.

The above observations raise the possibility that the whole strategy to prevent CHD by lowering the blood cholesterol will achieve, at best, only meagre benefits since a decrease in CHD will, to a greater or lesser extent, be offset by a rise in non-CHD deaths.

It is our belief, however, that the lowering of the blood cholesterol by diet can be recommended for the avoidance of CHD, particularly for the secondary prevention. Drugs should be reserved for the small minority of subjects at exceptionally high risk of CHD. With this approach the fall in CHD is not outweighed by an excess of non-CHD mortality. Of course, for maximal benefit, other aspects of lifestyle in addition to diet must be incorporated, for alterations in lifestyle must form part of a general preventive endeavour against Western diseases. It should be stressed that efforts in prevention are dwarfed by those for cure, a fact insufficiently appreciated. To exemplify, in the UK the health service spends 10 million pounds annually on the prevention of CHD, but 500 million pounds on treatment[7].

Blood cholesterol and CHD

To achieve a clinically meaningful impact on CHD occurrence there must be a significant reduction in blood cholesterol. The minimum should be about 6%, but a considerably higher fall is desirable. Unfortunately, many CHD prevention trials have achieved only an insignificant decrease in the blood cholesterol. The major reason for this, as pointed out by Ramsey *et al.*[8,9], is that a step I diet typically causes a drop in blood cholesterol of only about 2%. More rigorous alterations in diet reduce the intake of fat to supplying 20-30% of energy, and saturated fat to 5-7%. Such diets achieve a fall of from 6% to over 20%[8,10,11]. A step I diet is likely to be effective when strictly followed; but when supervision is minimal, as is usually the case in clinical trials, there is often insufficient compliance[12,13].

Regarding the dietary trials reviewed by Ravnskov[6], five of them achieved a drop in blood cholesterol of at least 6% and are therefore advantageous. Two others, that also achieved such a drop in blood cholesterol, are of limited value as in one of the trials there were only 80 subjects, and in another the trial lasted only 1.1 years. The odds ratio for CHD in each of the five key trials is shown in Table 1. In none was there a rise in non-CHD deaths. Taken together the trials indicate that lowering blood cholesterol does indeed reduce the risk of CHD. Evidence citable in support of this conclusion includes the following: (i) studies on non-human primates demonstrate that atherosclerosis develops in response to a high blood cholesterol level, and that lesions regress when the cholesterol level is lowered[19-21]; (ii) clinical studies using angiography indicate that this is also the case in humans[22]; (iii) in individuals there is a measure of association between blood cholesterol and the risk of CHD; (iv) populations or groups who habitually consume a diet (and persue a manner of life) that causes a low blood cholesterol have a low risk of CHD[23,24]; (v) in several European countries, at the

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Table 1. Results from clinical trials

	CHD Odds ratio	
*Trial**	*Fatal*	*Non-fatal*
Research Committee (Ref 14)	0.85	1.17
Leren (Ref 15)	0.68	0.74
MRC soya bean (Ref 16)	0.97	0.72
Dayton *et al.* (Ref 17)	0.80	–
Oslo Study Group (Ref 18)	0.44	0.61

*The Oslo Study Group trial was multifactorial, the others were unifactorial

time when wartime changes caused, *inter alia*, a reduction in fat and a rise in fibre intake, there was a fall in mortality from CHD[25,26]. The evidence cited constitutes strong support for the concept of a cause and effect relationship between a high blood cholesterol and the occurrence of CHD.

There are, however, many perplexing situations which imply that our understanding of the relationship between diet, blood cholesterol and CHD is still inadequate. The results of some population studies appear to conflict with a cause-and-effect relationship between fat intake, particularly saturated fat, and CHD[27]. For instance, France has a mortality rate from CHD one third of that in Scotland, although the mean cholesterol levels are the same in each country; this cannot be satisfactorily explained by known risk factors[28]. Similarly, Mormons, a religious group who advocate good health practices but have a typical American meat intake, have a surprisingly low mortality from CHD[29,30]. In a contrasting context, in a group of elderly African women, 5% had a blood cholesterol about 6.5 mmol/l, yet CHD is unknown among them[31]. These discrepant reports emphasize the need for more research and for caution in making recommendations. Nevertheless, the desirability of reducing cholesterol levels would seem a fair decision from the evidence available.

Non-CHD deaths

Why is the lowering of blood cholesterol often associated with an increase in non-CHD deaths? The most likely explanation lies in the use of drugs. Davey Smith *et al.*[32] reexamined recent evidence and concluded that drug trials lead to an increase in non-CHD deaths. In marked contrast, there is no evidence that adoption of diets which evoke a decrease in cholesterol level cause an increase in non-CHD deaths[32]. This indicates that lowering the blood cholesterol is not intrinsically dangerous, but rather that the increase in non-CHD deaths, so often reported, can be attributed specifically to the use of drugs.

The safety of a low blood cholesterol level is strongly supported by other evidence. All traditionally living Third World populations have a low average blood cholesterol level but there is no evidence that on this account they have an increased risk of stroke, cancer or of other diseases[33,34]. Similarly, vegetarians in Western countries have not only a low incidence of CHD but also have a reduced risk of other degenerative diseases. In Germany, for example, in a recent 11-year prospective study it was reported that the mortality rate for CHD in vegetarians was only a third of that in the general population[35]. Total mortality was lowered by half. Diseases that were markedly reduced in frequency were stroke and cancer. The subjects in that study, beside being vegetarian, were almost all non-smokers; they tended to be health conscious and were of a higher socio-economic class. A study of vegetarians in South Wales yielded similar observations[36]. A further example is provided by the experience of Seventh-Day Adventists, who, besides being largely vegetarian, are also non-smokers and largely non-drinkers of alcohol. They have lower rates, not only of CHD, but also of stroke and several cancers which are common in Western countries (lung and colon in men; lung, breast and colon in women)[37,38].

Clearly, therefore, lowering the blood cholesterol by dietary means can lower the occurrence of CHD while at the same time preventing other diseases and, as a result, reducing the overall mortality. Why then do some studies carried out on Western populations report that individuals who have a low blood cholesterol also have a raised risk of stroke and of certain types of cancer? One reason could be the existence of preclinical disease[5]. However, this is unlikely to explain more than a small fraction of cases[4]. Another possibility is that such people have metabolic differences in the manner in which they process cholesterol. There is also the possibility that a common factor might cause both a low blood cholesterol and non-CHD deaths.

The prevention of CHD

Efforts to lower blood cholesterol should continue to play a major role in the prevention of CHD. But endeavours, in the great majority of cases, should be based on rigorous dietary intervention[8,10,11], and not on drugs. This means that the diet should contain as little as 20-30% of energy as fat, with 5-7% as saturated fat. The diet should also include a generous intake of plant foods rich in soluble dietary fibre, such as oats and beans[39], unfortunately, both currently unpopular foods. Such dietary advice can be given both by physicians to their patients as well as presented as a public health measure.

The study by Davey Smith *et al.*[32] indicated that drugs should be used only for those subjects at exceptionally high risk of CHD. A typical candidate would be a man with a blood cholesterol exceeding 7.8 mmol/l plus clinically evidence CHD. The proportions who smoke and have hypertension will increase the numbers at major risk. In brief, drugs should normally be reserved for the secondary prevention of CHD, since in primary prevention an excess of non-CHD deaths is likely to exceed the number of lives saved from CHD. As evidence increases from the use of more modern drugs this position may need to be revised.

It must be reiterated that there are other major factors involved in the causation of CHD. Davey Smith *et al.*[32] insisted that cholesterol levels should not remain the principal focus of clinical guidelines aimed at preventing CHD. These factors include hypertension, smoking, lack of exercise and, to a lesser extent, obesity. Tunstall-Pedoe and Smith[40] have stressed that an elevated cholesterol is far more noxious in the presence of smoking and hypertension, since risks are multiplicative, not additive. Unfortunately, in comparison with the emphasis placed on lowering the blood cholesterol, the other factors mentioned have been relatively neglected.

To repeat, the successful prevention of CHD demands a concerted attack on all of these factors, i.e., a changed lifestyle approach.

The previously mentioned study on German vegetarians also indicated the superiority of the lifestyle approach[35]. In that investigation, the combination of diet plus a generally healthy lifestyle was associated with a CHD mortality rate only one-third of that in the general German population.

It is significant that of the trials listed in Table 1 the multifactorial trial[18] was clearly the most successful. Also illuminating are the results of the World Health Organization European Collaborative Trial, which included the study of nearly 61 000 men[41]. This trial involved several lifestyle changes, chiefly of diet, smoking, weight control and exercise. In addition, drug treatment was given for hypertension. After six years of intervention a 10% decrease in CHD was achieved. Total mortality was reduced by 5.3%. Yet, even with a trial of this magnitude the resulting changes were not significant. Bearing in mind the modest extent of risk factor reduction (1.2% for plasma cholesterol, 8.9% for cigarette consumption, 2% for systolic blood pressure and 0.4% for weight[42], it may be inferred that a far more pronounced fall in CHD would have been achieved had the population been more compliant.

As already emphasized, the altered lifestyle approach has the outstanding advantage that it is also effective in preventing other Western diseases in addition to CHD[43]. Diseases potentially preventable include obesity, diabetes, stroke and various cancers. Because the cost/benefit ratio of a lifestyle approach is so advantageous, this is likely to make it far more acceptable to the general public than changes focused solely on the avoidance of CHD. Unfortunately, efforts to persuade the general public to make significant dietary changes have so far met with very limited success. As examples, in the Framingham Offspring Spouse Study[44], only 6% to 9% of subjects met total fat, 9% to 14% saturated fat, and fewer than 3% met dietary fibre guidelines. In Glasgow, in the MONICA Study[45], only 2% of 'council renters' were eating the 400 g daily of vegetables and fruit recommended by World Health Organization[46]. Perhaps the greatest challenge facing those involved in medicine and public health is to devise means of influencing people to change their lifestyle. Endeavours in this respect should not be abandoned simply because of strong resistance to change.

Conclusion

A population approach to CHD prevention based on lowering the blood cholesterol by dietary means is recommended. There is little to suggest that this will cause an increase in non-CHD deaths. To achieve a clinically significant impact on CHD demands a statistically significant impact on blood cholesterol. This requires rigorous dietary intervention. To obtain maximum benefits, the dietary approach must be combined with a more general intervention targeting hypertension, obesity, cigarette smoking and lack of exercise. Such a lifestyle approach should be 'marketed' as a general preventive of Western diseases.

Dedication: This paper is dedicated to Denis Burkitt MD FRS FRCS, who died on 23 March 1993.

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