EDITORIAL REVIEW

Approaches to reducing cardiovascular disease risk: food or pills?

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Dietary modification to reduce the risk of developing cardiovascular disease (CVD) is a key component of guidelines developed by such organizations as the National Cholesterol Education Program (NCEP), the American Heart Association (AHA) and the World Health Organization [1–3], and is commonly accepted by the scientific community at large. These recommendations are intended for the general population and most individuals at moderately increased risk of developing CVD. They focus primarily on limiting saturated fat and cholesterol intake and routinely engaging in physical activity. In contrast, other recommendations to decrease the risk of developing CVD, such as nutrient supplementation, are not commonly accepted by the scientific community at large but rather are areas of research activity and debate. The uncertainty with respect to the benefit of nutrition supplement to decrease the risk of developing CVD is due, in part, to the discordant nature of the literature to date. Unfortunately, all too often, these uncertainties surface in the popular press, causing confusion for the lay public. The intent of this editorial is to raise issues regarding the wisdom, at this time, of recommending the broad based use of nutrient supplements to decrease the risk of developing CVD. Hopefully, it will stimulate debate and discussion. It is not intended to come to any resolution on the topic.

Nutrient intakes versus food patterns

In order to better understand why the value of supplementing diets with individual nutrients to decrease the risk of developing CVD still remains unresolved it is helpful to consider the genesis of some of the purported relationships between individual nutrients and CVD risk. Many of the relationship were first derived from epidemiological data, for example, beta-carotene. Strong epidemiology data supported an inverse association between diets high in fruits and vegetables, and CVD incidence [4–7]. When the dietary data were translated into nutrient intakes beta-carotene was inversely associated with CVD risk. Another example is vitamin E. Epidemiological data suggested a protective effect of vitamin E intake on CVD [8–10]. Whether this protective effect could be attributed to food derived or supplemental vitamin E remains controversial [8–10]. Yet in both the case of beta-carotene and vitamin E, the intervention studies, to date, have been disappointing and in the case of beta-carotene supplementation may, in some cases, be detrimental [11–15]. Clearly, these two examples do not suggest that assertions made from observational studies are wrong or that supplemental nutrients are not efficacious in the prevention of CVD. The evidence to date simply suggests that we have insufficient data on which to set policy at this time. There are a number of reasons for this conundrum.

Nature of the data available

Most of the initial relationship(s) between the incidence of CVD and individual nutrients were derived from dietary (food pattern) data. In order to estimate nutrient intakes, food intake data were collected and from these data nutrient intakes approximated using databases to translate the food intake data into quantitative nutrient intakes. These databases are limited in completeness and accuracy. Variation among common food items attributable to differences in plant varieties, variations in the growing conditions, circumstances of food storage (length of time, temperature), and method of food preparation contribute uncertainties to the estimated nutrient intakes. Additionally, nutrient analysis of the dietary data is limited to the nutrients for which sufficient data are available, thereby allowing the potentially biologically active compound(s) to go unassessed.

Selective or biased reporting contributes to the uncertainty of data interpretation, regardless of how diligent the researchers are in collecting the data. Subjects wanting to put their best foot forward or demonstrating to the investigator that they know what they should be eating is difficult to distinguish from actual behavior. It also may be easier for subjects to accurately report, for example, vitamin supplements or a specific type of milk, rather than type of cooking oil used to prepare foods

eaten outside the home. It may be difficult for subjects to adequately distinguish and report intent to use versus actual use.

To complicate interpretation of the data further, intakes of individual nutrients are not always independent. For example, nutrient X usually occurs in the same foods as nutrient Y. Nutrient X may be quantifiable and nutrient Y may not, or both nutrient X and Y may be quantifiable. However, unclear is whether to attribute a health outcome to only X or only Y, to X and Y, or to the synergistic effect of both together. Similarly, specific dietary patterns are frequently associated with certain lifestyle behaviors. Individuals who eat diets high in fruits and vegetables have been reported, at various times, to be more likely to smoke less, engage in more regular vigorous physical activity, eat diets containing less total and saturated fat, use multivitamin supplements and in females, use of hormone replacement therapy [8,9,16,17]. These behaviors themselves may be the major determinant of disease risk rather than a co-varying nutrient intake(s). From the opposite perspective, supplement users have been reported to consume more nutrient rich diets, notably higher levels of vitamins A and C, calcium, iron and fiber, and diets with lower levels of total and saturated fat [18–21]. The most rigorous attempts to control for factors other than the nutrient of interest may not always be sufficient, making interpretation of the data difficult.

Biological factors

Another perspective from which to understand why the value of supplementing the diet with individual nutrients for CVD risk reduction is yet unresolved is to consider the biological data currently available to support a particular relationship. The best scenario would be to have a control and experimental group, institute an intervention, wait 20 to 30 years and after that time assess an outcome. Accepting the impracticality of such an approach the scientific community has elected to either rely on surrogate measures of disease risk, i.e. low density lipoprotein cholesterol levels or total cholesterol/high density lipoprotein cholesterol ratios; intervene in a high risk group in which outcomes can be anticipated to occur in a relatively short period of time, i.e. secondary prevention trials; or study a group of individuals with a relatively high risk of developing the disorder, i.e. older individuals. Disadvantages of each approach are numerous. For example, measures other than the surrogate one(s) monitored might be better predictors of the intervention outcome. The relative importance of each surrogate measure of disease risk has yet to be determined. Secondary prevention trials may be handicapped by the presence of existing disease which may prevent the putative factor from exerting its effect.

Impact of a population-wide nutrient supplement recommendation

The impact of a population-wide recommendation to use nutrient supplements to reduce the risk of developing CVD has yet to be determined. An obvious issue of concern is long-term compliance. More difficult issues relate to the impact of the message on food intake patterns. Little data are available on the effect of a shift in the message from *rely on food to get your nutrient(s)* to *rely on supplements to get your nutrient(s)*. If the message perceived is that supplements provided an 'insurance' against an imperfect diet we must consider what impact this message would have on the balance of food choices, hence, overall nutritional status. This becomes particularly important for the case of fruits and vegetables. If taking a nutrient supplement containing, for example, beta-carotene (vitamin A) or vitamin C were made would it be interpreted as *in addition to fruits and vegetables* or *in place of fruits and vegetables*? The outcome would directly impact on the intake of nutrients not supplied by the nutrient supplement but normally present in fruits and vegetables (i.e. phytochemicals, fiber) and potentially other life-style factors. Little is known about issues surrounding the area of determinants of food intake and lifestyle behaviors. Individuals complying with a nutrient supplementation recommendation might feel 'empowered' and strive to improve the general quality of their diets and increase activity levels or, alternatively, might kick off their running shoes, sit back, and let the pill do the work.

Conclusions

At this time it is difficult to find intervention data to support a recommendation to supplement the diet of the general population or high risk individuals with a specific nutrient rather than to provide dietary and lifestyle guidance. This lack of data may be because there is, in fact, no biological advantage for most individuals to consume levels of a specific nutrient in excess of that available via dietary means. Alternatively, it may be that our limited knowledge of the etiology of CVD has precluded us, to date, from asking the right questions and/or collecting the right types of data to assess the effect of nutrient supplementation adequately and accurately. At this point we need to be mindful to heed the age old adage, *primum non nocere*, and remember what our mothers told us, 'eat your vegetables'!

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