Some Methodological Issues in Epidemiological Studies of Fat and Cancer

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Abstract

Three types of approach to the study of the possible relationship between fat and cancer are discussed, namely, correlational, case-control, and cohort studies. The advantages and limitations of each method are analyzed, and it is emphasized that a necessary prerequisite to direct observational studies in humans is the development of a satisfactory and uniform method of a diet assessment. Despite the problems, epidemiological research in this area offers considerable potential for cancer prevention.

Evidence concerning possible associations between dietary fat intake and risk for various cancers has to date been derived primarily from animal and correlational studies. The limitations of these methods with respect to establishing any possible causal relationship in humans are well known. Thus, it would appear that the establishment of causal associations will depend upon direct observational studies in humans. The Epidemiology Unit of the National Cancer Institute of Canada has been involved in a number of epidemiological studies of diet and cancer, and the experience gained has indicated a number of methodological issues which directly relate to future priorities for diet-related research in cancer epidemiology.

Correlational Studies

We have examined correlations among Canadian cancer incidence rates for 1969 to 1973 (data supplied by Health Division, Statistics Canada). Significant correlations exist between rates for female breast and colon cancers \( r = 0.40 \) and male colon and prostate cancers \( r = 0.29 \), at sites for which a common dietary etiological factor has been postulated. Although intra- as opposed to international comparisons have the advantage of more uniform reporting of cancer rates, their greater homogeneity inevitably leads to smaller correlation coefficients.

Case-Control Studies

We have conducted 2 case-control studies of diet and cancer. The first was of 400 pairs of individually matched breast cancer cases and controls (1). The primary focus of the study was fat intake, and some evidence of a weak association between total fat and breast cancer risk was observed.

If, in reality, this association is stronger than observed, there could be 2 possible explanations: the population is too homogeneous with respect to fat intake for an estimate to be made with sufficient precision; or the great majority of the sample of cases and controls have a level of fat consumption which places them all at high risk.

The second case-control study was of colorectal cancer (3). Table 1 shows the relative risks associated with various levels of daily intake of saturated and polyunsaturated fats. A dose-response relationship for saturated fat intake is seen for both males and females in contrast to the relative risks for polyunsaturated fat. Thus, it would appear that the problems of homogeneity or a population who all are at high risk do not apply to studies of colorectal cancer in Canadian populations, but 2 further problems do arise.

1. Inconsistency between the results from this and other studies indicates the need for dietary measurement by an instrument which, if not common to all studies, at least provides results which can be compared directly.

2. Measurements of specific nutrient intake, such as saturated fat, oleic acid, and cholesterol, are usually highly correlated both with each other and with total caloric intake. It may therefore be impossible to separate any differential effects of such nutrients even with the most sophisticated multivariate techniques of analysis.

Cohort Studies

Cohort studies have been little used in studies of diet and cancer. The major factor mitigating against such studies is the large sample size required. However, one possible route is to make use of existing data resources. One such study is the follow-up of a probability sample of 14,000 individuals from the Canadian population who were surveyed in 1972 as to their dietary habits by Nutrition Canada (6). Follow-up is being conducted by linking records from the survey to Canadian mortality records. Techniques for computerized record linkage have been extensively developed by ourselves in conjunction with the Health Division of Statistics Canada. These techniques are simple and inexpensive and could be applied to a number of other data resources which have been accumulated, for example, for the purposes of studying cardiovascular disease. The formation of a United States national death index is currently under way and should greatly facilitate any such studies. An alternative approach to cohort studies is to include dietary assessment information in a cohort formed for other purposes. We are currently planning on doing this in a large sample of women who are being enrolled in a Canadian trial of screening for breast cancer. Ascertainment dietary information from the large samples involved in cohort studies will require the development of a short self-administered instrument to minimize interviewing costs and maximize compliance rates.

Development of Dietary Instruments

We have used 3 instruments in our case-control studies: a 24-hr recall; a 4-day diet diary; and a diet history. Comparisons

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1 Presented at the Workshop on Fat and Cancer, December 10 to 12, 1979, Bethesda, Md.
Table 1

Relative risk estimates for colorectal cancer for daily fat intake

<table>
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<tr>
<th></th>
<th>Male</th>
<th>Female</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Relative risk</td>
<td>Relative risk</td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saturated fat</td>
<td>38-56 g: 2.0</td>
<td>26-39 g: 2.0</td>
</tr>
<tr>
<td></td>
<td>56 g: 2.4</td>
<td>39 g: 2.6</td>
</tr>
<tr>
<td></td>
<td>Unsaturated fat (linoleic acid)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10-17 g: 1.1</td>
<td>8-14 g: 0.8</td>
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<tr>
<td></td>
<td>17 g: 0.8</td>
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<tr>
<td>Female</td>
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</tr>
<tr>
<td>Saturated fat (linoleic acid)</td>
<td>26-39 g: 2.0</td>
<td>8-14 g: 0.8</td>
</tr>
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between the methods showed a number of discrepancies (5), and it was concluded that the most satisfactory instrument was the diet history, on which we have conducted a reliability study (2). Such reliability and validity studies are not easy because of the difficulty in measuring actual dietary intake, and they are also time consuming and expensive. A further consideration is the necessity for using a standardized source for the nutrient composition of various food items.

Conclusions

It would appear that the maximum amount of information per study subject in the immediate future will be obtained from case-control studies. However, it is essential that such studies be conducted in areas with heterogeneous dietary experiences, and the most practicable way of achieving this is international collaborative studies in areas with such heterogeneity and with varying risks for the cancers in question. Cancers of interest include breast, colorectal, prostate, and possibly pancreas. Control selection for such studies would ideally come from a random sample of the population of the area from which the cases were drawn and should be matched only for age and sex in order to avoid problems of overmatching. This would also enable interesting comparisons to be made between controls from low- and high-risk areas. For such studies to be conducted, it is necessary that a common instrument be developed which could, however, be appropriately modified, depending upon local requirements, but would nevertheless contain a core of dietary information which could be directly comparable between the study areas. The creation of a working group would be of great value in order to facilitate the development of such an instrument and possibly to initiate validation and reliability studies. A further function of such a group would be to advise as to requirements for data banks of nutritional information. Finally, it should be pointed out that epidemiological studies may serve only to indict certain dietary patterns and that, due to the high correlations which exist between many nutrients, one may be unable to identify a specific etiological factor. Nevertheless, in terms of preventive measures, identification of dietary patterns which lead to an increased risk may be of more immediate value than are such specific identifications.

References


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