Myocardial Infarction in Patients Treated with Sippy and Other High-Milk Diets

An Autopsy Study of Fifteen Hospitals in the U.S.A. and Great Britain

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It has been reported that the incidence of myocardial infaracts is higher among persons with chronic peptic ulcers than among others.\(^1\)\(^2\) This higher incidence may be due to the type of diet consumed by these patients. Milk products are suspect because of their common use by ulcer patients. Butter fat is particularly suspect because it has an effect on blood coagulation\(^3\) and clot lysis,\(^4\) because it is a major constituent of diets that produce coronary thrombosis and myocardial infaracts in experimental animals,\(^5\) and because of its effect on blood cholesterol levels in man under certain conditions.\(^6\)

It occurred to us that we might obtain important information by dividing patients with chronic peptic ulcer who had come to autopsy into 2 groups: (1) those whose treatment included the use of milk or cream (such as the Sippy diet), and (2) those whose histories did not indicate that their therapy included the use of milk or cream. If the patients who consumed milk or cream as part of their therapy had a higher incidence of myocardial infaracts than those who had not been given this type of therapy, it would at least suggest that the higher incidence of infaracts was related to the therapy. Such an association would not constitute absolute proof of the relation of consumption of milk and cream to the higher incidence of myocardial infaracts in patients with peptic ulcer, since some unknown factor of selection may enter into the choice of patients to be placed on a diet including milk or cream; some other part of the therapy might play a role.

It seemed to us that the best way to minimize factors of selection would be to study autopsies of patients from many different medical centers and therefore probably treated for their peptic ulcers in many different ways. Also, by studying autopsies from various places, we could obtain a larger number of autopsies for analysis than would be available from a single institution, and it would be possible to use more rigid criteria in matching groups for comparison. It seemed important to match groups of patients by age, sex, race, and place and period of death.

Therefore, we have carried out a study of the incidence of myocardial infaracts among 3 matched groups of autopsied patients from 10 centers in various parts of the United States and in 5 centers in Great Britain. The groups are (1) patients with peptic ulcers of the stomach or duodenum found at autopsy who gave a history of having been treated with a Sippy diet or its equivalent (Sippy ulcer), (2) patients with a peptic ulcer found at autopsy who did not have a history of such dietary therapy (non-Sippy-ulcer), and (3) patients without ulcers chosen to match each patient of each of the above 2 groups by taking the next autopsy performed on a patient of the same age, sex, and race (non-ulcer). Patients with acute peptic ulcers were not included in the study because most of them would not have a history of dietary therapy. The pathologic diagnosis was used as the criterion of chronicity of an ulcer when it was definite; otherwise a microscopic description of fibrosis at the base of the ulcer was required before the ulcer was tabulated as "chronic."

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Supported by funds provided by the National Dairy Council. Dr. Zoe Anderson of the National Dairy Council suggested this study.

Mr. Briggs and Mr. Rubenberg were recipients of Summer Research Fellowships from Washington University at the time of the study.
The purpose of this report is to present the results of the study regarding the incidence of myocardial infarcts in the various groups. Both acute and healed myocardial infarcts were tabulated to determine the incidence of myocardial infarcts. The pathologic diagnosis on the autopsy protocol was accepted for the purposes of this study, and such diagnoses as "focal fibrosis" were not tabulated as infarcts.

Material and Methods

Clinical and autopsy records for the years 1940 to 1959 were examined from the following hospitals in the U.S.A.: Barnes Hospital, St. Louis; Massachusetts General Hospital, Boston; Charity Hospital of Louisiana, New Orleans; University of California, San Francisco; Western Reserve University, Cleveland; University of Illinois, Chicago; Johns Hopkins Hospital, Baltimore; Mt. Sinai Hospital, New York; Boston City Hospital, Boston; Cook County Hospital, Chicago.

The data recorded included site of chronic peptic ulcer, age, sex, race, year of death, height, body weight, history and duration of diabetes, history and duration of therapy with "Sippy" diet or similar diets including milk products, principal diseases at death, and presence or absence of a myocardial infarct, with the description of the anatomic characteristics of the infarcts as given in the autopsy protocol.

Each ulcer patient was matched with the nearest non-ulcer patient in the autopsy records of the same age (decade of life), race, hospital, and period of death (± 5 years). The data from the non-ulcer control were attached permanently to the data from its ulcer mate.

After the survey was completed, the records were accumulated from all hospitals and divided into a Sippy-ulcer group and a non-Sippy-ulcer group. Patients in these 2 groups were matched by age, sex, race, hospital, and period of death. Since the non-ulcer control for each patient in the above groups remained attached, 3 groups matched for the above characteristics were thus available. Cases that could not be matched were discarded from the study.

After the matching was complete, the incidence of myocardial infaracts and other characteristics were tabulated for each of the 3 groups (tables 1 and 2).

A study identical in design to the one in the U.S.A. was carried out in the following British hospitals: Bristol Royal Infirmary, Bristol; Western Infirmary, Glasgow; Royal Victorian Infirmary, Newcastle-on-Tyne; St. Mary’s Hospital, London; and the British Postgraduate Medical School at Hammersmith Hospital, London. Although the Sippy diet per se is used infrequently in Britain, patients with a history of increased intake of milk for treatment of an ulcer were placed in the Sippy-ulcer group. Milk and alkali powders constitute a common form of treatment for ulcers in Britain.

Results

The results are presented in tables 1 and 2 and in figure 1. It is apparent from table 1 that the average heights and weights differ little for the 3 groups. The incidence of diabetes mellitus was too low in all groups to be of importance. Removal of all diabetic patients from the study does not significantly alter the results. Deaths of the patients were due primarily to complications of the ulcer in 34 of the Sippy-ulcer patients and 23 of the non-Sippy-ulcer patients.

The incidence of myocardial infaracts (table 2) among the ulcer patients in the United States not treated with the Sippy diet is identical with that in the non-ulcer group (15 per cent). The 36 per cent incidence of myocardial infarcts in the ulcer groups treated with the Sippy diet is significantly higher than that in the other 2 groups (p<0.01). If the 21 patients who had been on the Sippy diet for a year or less are eliminated, the incidence of myocardial infarcts rises to 42 per cent.
Table 1

Some Characteristics of Three Matched Groups of Autopsied Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>U.S.A. (average age—60 ± 10)</th>
<th>Great Britain (average age—59 ± 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sippy-ulcer</td>
<td>Non-Sippy-ulcer</td>
</tr>
<tr>
<td>Average height (cm.) with standard deviation</td>
<td>168 ± 8</td>
<td>166 ± 11</td>
</tr>
<tr>
<td>Average weight (Kg.) with standard deviation</td>
<td>67 ± 16</td>
<td>64 ± 13</td>
</tr>
<tr>
<td>History of diabetes</td>
<td>1 patient</td>
<td>3 patients</td>
</tr>
<tr>
<td>Diabetic subjects with myocardial infarcts</td>
<td>1 patient</td>
<td>2 patients</td>
</tr>
</tbody>
</table>

Table 2

Incidence of Myocardial Infarcts among the Three Groups of Patients

<table>
<thead>
<tr>
<th></th>
<th>U.S.A.</th>
<th>Great Britain</th>
<th>Non-ulcer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sippy-ulcer</td>
<td>Non-Sippy-ulcer</td>
<td>Non-ulcer</td>
</tr>
<tr>
<td>No. of cases</td>
<td>97 (85M, 12F)</td>
<td>97 (85M, 12F)</td>
<td>194 (170M, 24F)</td>
</tr>
<tr>
<td>No. with myocardial infarcts</td>
<td>35</td>
<td>15</td>
<td>30</td>
</tr>
<tr>
<td>% with myocardial infarcts</td>
<td>36</td>
<td>15</td>
<td>15</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Sippy-ulcer</th>
<th>Great Britain</th>
<th>Non-ulcer</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases</td>
<td>95 (74M, 21F)</td>
<td>95 (74M, 21F)</td>
<td>190 (148M, 42F)</td>
</tr>
<tr>
<td>No. with myocardial infarcts</td>
<td>17</td>
<td>3</td>
<td>16</td>
</tr>
<tr>
<td>% with myocardial infarcts</td>
<td>18</td>
<td>3</td>
<td>8</td>
</tr>
</tbody>
</table>

*If the 21 patients in this group who had been on the Sippy diet for only 1 year or less (average age of these 21 patients was 62 years) are eliminated, the percentage of infarcts in the 76 remaining patients rises to 42 per cent. Many of these 76 had been on the Sippy diet for over 10 years.

†The number of patients of each sex is given here for easy reference.

§In this group of British patients only 11 patients' diets were actually called "Sippy," and 3 of these 11 patients had infarcts. However, all patients in the Sippy-ulcer group had a history of therapy with milk.

The incidence of myocardial infarcts (table 2) among the ulcer patients in Great Britain with a history of treatment with milk was 18 per cent, significantly higher (p<0.01) than the 3 per cent incidence in the non-Sippy-ulcer group and the 8 per cent incidence in the non-ulcer controls (p<0.05). The difference in incidence between the latter 2 groups is not statistically significant.

Discussion

The results of this study show clearly that there is a much higher incidence of myocardial infarcts among autopsied individuals with peptic ulcers who have been treated with the Sippy or similar diets than among ulcer patients not treated in this way or among non-ulcer controls. This association might indicate some conscious or unconscious factors of selection in determining which patients should be placed on the Sippy regimen. However, it seems unlikely that this is the real explanation. In some of the centers the Sippy diet was used commonly but in others very seldom, suggesting that its use is influenced by local therapeutic philosophies and backgrounds.

A more likely explanation is that something
in the diet associated with medication increases the incidence of infarcts. One possibility is that it has something to do with antacids such as the commonly used aluminum hydroxide or magnesium trisilicate. There is no evidence at present that they have anything to do with myocardial infarction.

Another possibility is that the dairy products that form a prominent part of the diet are responsible. Considerable experimental evidence has been reported that butter has an effect on blood coagulation and clot lysis in man and animals,\textsuperscript{3, 4, 7, 8} also, a diet containing a large proportion of saturated fat such as is found in butter tends to increase the cholesterol level in the blood over the levels obtained with certain other fats.\textsuperscript{9} In addition, arterial thrombi and myocardial infarcts have been produced in large numbers of rats given diets containing, among other ingredients, large quantities of butter.\textsuperscript{5, 9}

Even if the increased intake of milk is responsible for the high incidence of myocardial infarction in ulcer patients, the identity of the specific constituent of milk that is important in this respect has not yet been established. The mineral component of milk, for example, may be as important as the fat content.

Although at present the butter-fat content of the Sippy diet would seem to be the most likely culprit, it must be emphasized that proof beyond reasonable doubt has not yet been presented in this study. The association certainly warrants suspicion, but it does not constitute proof. Further investigation will be necessary, such as studies of coagulation, fibrinolysis, and cholesterol levels in the blood of living patients with peptic ulcers who are being treated with and without the use of milk products.

An incidental observation of the present study was a lower incidence of myocardial infarcts among the patients in England than in comparable groups in the U.S.A. This is consistent with the results of other studies of clinical and autopsy material, as well as vital statistics.\textsuperscript{10, 11} The incidence of myocardial infarcts among the Sippy-ulcer patients in England, although much higher than in the British non-ulcer controls, was essentially the same as the incidence in the non-ulcer controls in the U.S.A. This could be interpreted as evidence that the comparatively high incidence of myocardial infarcts in the control groups in the U.S.A. might be due to the high over-all consumption of milk products, but there are too many uncontrolled variables for this interpretation to be warranted.

The patients in the U.S.A. weighed an average of 8 to 10 Kg. more than the British patients and were a few centimeters shorter. The difference in height may be due to different technics of measurement; in Great Britain the measurement in some hospitals is taken from the ball of the foot instead of the heel.\textsuperscript{12} In both the American and British groups, the Sippy-ulcer patients who had a high incidence of infarcts weighed no more than the non-ulcer controls with a low incidence of myocardial infarcts.

Diabetes mellitus is a well-known factor in the production of myocardial infarcts. In this study elimination of the patients with a history of diabetes did not significantly alter the results.

It occurred to us that the severity of the ulcers might be different in the patients treated with Sippy diet and the non-Sippy-ulcer patients. In the patients in the U.S.A., 38 of the patients on the Sippy diet and 23 of the ulcer patients not on the Sippy diet died of complications of the ulcer, either hemorrhage, perforation, obstruction, or following operation. This would appear to indicate that, in general, the patients on the Sippy diet had a somewhat more severe disease than those not treated with the Sippy regimen, but we are unable to see how this difference would alter the interpretation of our results.

**Summary**

A study has been made of the incidence of myocardial infarcts among 3 groups of autopsied patients who were matched for age, sex, race, and place and period of death: (1) patients with peptic ulcers who had been treated with a Sippy diet or milk products,
(2) patients with peptic ulcers who were not known to have been so treated, (3) a group consisting of non-ulcer patients matched with the other 2 groups.

In the U.S.A. the incidence of myocardial infarcts was more than twice as high in the ulcer patients treated with Sippy diet than it was in either of the other 2 groups. The differences in each case were statistically highly significant. There was no significant difference in the incidence of myocardial infarcts between the ulcer patients not treated with the Sippy diet and the non-ulcer controls.

Differences and similarities of the same degree were noted among corresponding groups from Great Britain. It is tempting to think that the high incidence of myocardial infarcts among the Sippy-treated patients was a result of the butter-fat content of their diets. Mere association, however, does not constitute proof and further study is needed before definitive conclusions are drawn.

Acknowledgment

We wish to thank the hospital authorities, and particularly the pathologists at the various hospitals visited, for their kindness in allowing us to use their material.

Summario in Interlingua

Esseva effectuate un studio del incidentia de infarimento myocardial in tres gruppos de necropsiate patientes qui esseva comparabile ab i le punctos de vista del etate, del sexo, del raccia, e del placa e del tempore de lor morte. Le tres gruppos esseva (1) patientes con ulceres peptic qui habeva esiste tractate con le dieta de Sippy o un altere dieta de productos de lacte, (2) patientes con ulceres peptic qui non habeva cognoscimente recipite un tal tractamento, e (3) un gruppo de patientes sin ulceres.

In le Statos Unite le incidentia de infarimento myocardial esseva plus que duo veces plus alte in le patientes tractate con le dieta de Sippy que in tanto le un como etiam le alte del 2 gruppos sin ille tractamento. In ambe casos, le differentia esseva statisticamente significativissime. Il non existeva un differentia significative in le incidentia de infarimento myocardial inter le patientes con ulceres non tractate con le dieta de Sippy e le patientes de controlo sin ulceres.

Differentias e similitudes del mesme grados esseva notate inter correpondente gruppis de patientes in Grande Britannia. Es seduttive le notion que le alte incidentia de infarimentos myocardial inter le patientes tractate secundo Sippy esseva le resultato del alte contento de grassia butyris in lor dietas. Tamen, un simple association non es un prova de un interrelatation causal, e studios additional es requirite ante que conclusiones definitive pote esser formulate.

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Circulation. 1960;21:538-542
doi: 10.1161/01.CIR.21.4.538

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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