ROLE OF LIFE-STYLE ON PLASMA AND ERYTHROCYTE MEMBRANE LIPID PROFILE IN GASTRIC CANCER PATIENTS

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(Received on August 20, 1996)

Abstract: The present study has examined the role of life-style on plasma and erythrocyte membrane lipid profile in 25 adult male gastric cancer patients as well as age and sex-matched controls. Total, free and LDL cholesterol were markedly elevated in plasma and erythrocyte membrane whereas HDL cholesterol and triglycerides were significantly reduced in gastric cancer patients. These changes can be attributed to alcohol consumption and cigarette smoking-risk factors in gastric carcinogenesis, associated with low levels of ascorbic acid and vitamin E.

Key words: gastric cancer, cholesterol, ascorbic acid, vitamin E

INTRODUCTION

Studies on the profiles of lipids and lipoproteins are of paramount importance due to their role in maintaining membrane integrity and in the regulation of cellular processes. The plasma lipid profile is labile and affected by dietary factors, smoking and alcohol consumption which may be reflected in the lipid composition of the membrane (1-3). The structure and functions of cell surfaces are affected by changes in membrane lipids, considered to be important aspects of malignant transformation (4). The erythrocyte membrane, a classic prototype of the plasma membrane, is highly responsive to changes in the surrounding lipid milieu, and is the most readily available source of pure membrane in the human body. Profound alterations in the composition and morphology of red cells have been observed in a variety of pathological conditions (5).

Adenocarcinoma of the stomach still remains a major cause of cancer death in developing countries (6). Epidemiological studies implicate nutritional factors and life-style in the development of stomach cancer. Ascorbic acid and vitamin E have been identified as protective factors in gastric carcinogenesis. Alcohol and cigarette smoking have been increasingly associated with the incidence of gastric cancer in several studies (7). Since similar risk factors influence lipid profile and the genesis of gastric carcinoma, it was of interest to analyse the concentration of plasma and erythrocyte membrane lipids in gastric cancer patients.

METHODS

Twenty five newly diagnosed gastric cancer patients from Rajah Muthiah Medical College Hospital, Annamalai University, India, who had not undergone any previous treatment for their
tumours were chosen for the study. All the patients were males, ranging in age from 45-60 years and in stage III of adenocarcinoma of the stomach. An equal number of control and normal subjects were investigated. Controls were age matched and sex-matched and had a lifestyle similar to that of the gastric cancer patients i.e., smoking and excessive alcohol consumption. Normals were healthy subjects not habituated to smoking and alcohol consumption and were of the same age and sex as the other two groups. Both control and normal subjects were diagnosed as being free from precancerous and cancerous lesions. A comparative study of normal versus controls was attempted to assess the role of risk factors in the etiology of gastric cancer.

Blood samples were obtained by venous arm puncture in heparinised tubes. Plasma was separated by centrifugation at 1000xg for 15 minutes. The buffy coat was removed and packed cells washed thrice with physiological saline. The erythrocyte membrane was prepared by the method of Dodge et al (18) modified by Quist (9). The erythrocyte membrane lipid fraction was extracted by the method of Folch et al (11). Lipids in both plasma and erythrocyte membrane were estimated by the method of Parekh and Jung (11) (total cholesterol), Sperry and Web (12), Gidez et al (13) (HDL cholesterol), Zilversmit and Davies (14) (phospholipid), Rice (15) (triglycerides). Erythrocyte membrane protein was estimated by the method of Lowry et al (16). Plasma ascorbic acid was determined by the method of Omaye et al (17) and vitamin E was measured according to the method of Desai (18).

Statistical analysis was done by Student's t-test.

RESULTS

The plasma lipid profile in normal, control and stomach cancer patients is shown in Table I. Total, free and LDL cholesterol were significantly increased whereas the plasma HDL cholesterol and triglyceride levels were significantly decreased and phospholipids unaltered in gastric cancer patients as compared to normals and controls. Although controls

<table>
<thead>
<tr>
<th>Parameters (mg/dl)</th>
<th>Normal</th>
<th>Control</th>
<th>Gastric cancer</th>
</tr>
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<tbody>
<tr>
<td>Total cholesterol</td>
<td>164.57 ± 18.9</td>
<td>203.5 ± 22.1*</td>
<td>260.64 ± 36.67*</td>
</tr>
<tr>
<td>Free cholesterol</td>
<td>48.3 ± 5.3</td>
<td>69.6 ± 6.4*</td>
<td>96.4 ± 11.2**</td>
</tr>
<tr>
<td>HDL</td>
<td>46.71 ± 4.51</td>
<td>39.1 ± 3.72*</td>
<td>32.65 ± 3.41**</td>
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<tr>
<td>LDL</td>
<td>96.61 ± 10.12</td>
<td>143.1 ± 12.5*</td>
<td>210.43 ± 19.95*</td>
</tr>
<tr>
<td>Phospholipids</td>
<td>169.04 ± 14.3</td>
<td>160.3 ± 14.1NS</td>
<td>159.54 ± 15.64NS</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>106.70 ± 11.2</td>
<td>100.3 ± 13.4NS</td>
<td>88.27 ± 9.1**</td>
</tr>
<tr>
<td>C/P ratio</td>
<td>0.98 ± 0.11</td>
<td>1.29 ± 0.16*</td>
<td>1.72 ± 0.21**</td>
</tr>
</tbody>
</table>

*- as compared with normal (P < 0.01; P < 0.001)

**- as compared with control (P < 0.01; P < 0.001)

NS – Not significant
showed a pattern similar to gastric cancer patients, the magnitude of the change was less pronounced.

Table II shows the erythrocyte membrane lipid profile of normal, control and gastric cancer patients. The total cholesterol, and free cholesterol were markedly elevated in gastric cancer patients compared to normal and control subjects with no significant alteration in phospholipid levels. Marked decrease in erythrocyte count was found in gastric cancer patients as compared to the other two groups. Controls also showed a similar pattern.

Table III shows a significant decrease in the levels of vitamin E and ascorbic acid in plasma and erythrocyte membrane of gastric cancer patients in comparison with normals and controls. Controls also showed a similar pattern.

DISCUSSION

All the patients in the present study were found to be alcoholics and bidi or cigarette smokers. Epidemiological studies have implicated life-style and other environmental factors in the genesis of stomach cancer (8). We feel that the changes in lipid profile seen in

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<tbody>
<tr>
<td>Cholesterol</td>
<td>155.83 ± 21.70</td>
<td>176.96 ± 22.3*</td>
<td>220.22 ± 31.20**</td>
</tr>
<tr>
<td>Free cholesterol</td>
<td>132.64 ± 16.7</td>
<td>150.30 ± 18.3</td>
<td>190.32 ± 24.8**</td>
</tr>
<tr>
<td>Phospholipids</td>
<td>287.47 ± 18.53</td>
<td>279.31 ± 24.5NS</td>
<td>269.17 ± 29.46NS</td>
</tr>
<tr>
<td>C/P ratio</td>
<td>0.57 ± 0.07</td>
<td>0.64 ± 0.09*</td>
<td>0.83 ± 0.12**</td>
</tr>
<tr>
<td>RBC Count 10^6 / µL</td>
<td>5.59 ± 0.9</td>
<td>4.51 ± 0.4*</td>
<td>3.09 ± 0.5**</td>
</tr>
</tbody>
</table>

* - as compared with normal (P < 0.01; P < 0.001)
* - as compared with control (P < 0.01; P < 0.001)
NS - Not significant

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<tr>
<td>Plasma (mg/dl)</td>
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<tr>
<td>Ascorbic acid</td>
<td>1.12 ± 0.18</td>
<td>0.86 ± 0.16*</td>
<td>0.72 ± 0.14**</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>1.29 ± 0.22</td>
<td>1.01 ± 0.15*</td>
<td>0.83 ± 0.14**</td>
</tr>
<tr>
<td>Erythrocyte membrane (µg/mg protein)</td>
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<tr>
<td>Vitamin E</td>
<td>2.35 ± 0.51</td>
<td>1.96 ± 0.47*</td>
<td>1.71 ± 0.42**</td>
</tr>
</tbody>
</table>

* - as compared with normal (P < 0.01; P < 0.001)
* - as compared with control (P < 0.01; P < 0.001)
gastric cancer patients is strongly related to life-style.

Craig et al (2) have also reported profound alterations in blood lipids in smokers. The decrease in plasma triglycerides in gastric cancer patients may be related to tobacco smoke. Nicotine present in smoke can stimulate catecholamine secretion inducing depletion of adipose tissue triglycerides, leading to decreased plasma triglyceride levels. Increased total cholesterol with concomitant decrease in HDL has been reported in smokers (19). Alcohol is known to cause changes in the concentration of lipoprotein cholesterol (20). The enhanced plasma total cholesterol level in gastric cancer patients can cause an increase in plasma LDL with suppression of LDL receptor activity, resulting in a further increase in plasma cholesterol levels. The decrease in HDL cholesterol in gastric cancer patients in the present study may be due either to increased LDL cholesterol or diminished lecithin cholesterol acyltransferase activity.

We feel that the enhanced cholesterol and reduction in HDL cholesterol in gastric cancer patients is related to low levels of the micronutrients, ascorbic acid and vitamin E. These nutrients are known to modulate the pathway for cholesterol biosynthesis and lower plasma cholesterol levels (21, 22). Both ascorbic acid and vitamin E have a profound effect on the hepatic conversion of cholesterol to bile acids (23). Risk factors such as cigarette smoking and alcohol, associated with gastric cancer are known to deplete serum levels of these essential nutrients which have important effects on lipid and lipoprotein metabolism (24).

Changes in the cholesterol content of the erythrocyte membrane in gastric cancer patients may be a reflection of alterations in plasma cholesterol. Sakagami et al (25) have proposed that plasma and erythrocytes, exchange cholesterol and phospholipids. Hence, increased cholesterol content in erythrocyte membrane may be due to some defect in the exchange mechanism or a result of increased plasma LDL or decreased HDL cholesterol which may indirectly inhibit cholesterol removal from red cells causing its accumulation.

Membrane fluidity is known to be dependent on the type of cholesterol (free or esterified) and the molar ratio of cholesterol to phospholipid (26). In a previous report, we demonstrated increased fragility with consequent reduced erythrocyte count and anemia in gastric cancer patients.

The changes in the lipid profile observed in gastric cancer patients were also evident in controls, placing them in a "high risk" category. It is therefore felt that the alterations in lipid profile seen in gastric cancer patients and controls are strongly related to life-style.

REFERENCES


