Gut, 1977, 18, 670-672

Carbohydrate content of endoscopic gastric biopsies in carcinoma of the stomach

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SUMMARY An investigation of the glycoproteins of gastric mucus from biopsies of patients with gastric cancer has shown a change in certain carbohydrate components. There is a significant increase (p < 0.001) in mannose and a significant decrease in N-acetylgalactosamine in both secretors and non-secretors from cancer-free and cancer-bearing regions of the stomach as compared with normal stomachs. The possible reasons for this change and its relation to two possible glycoprotein fractions are discussed.

Endoscopic gastric biopsies are mainly composed of the superficial layer of the stomach because of the limited size of the forceps. Histochemical studies conducted by Doberneck and Engle (1966) showed that mucus is the major carbohydrate-containing component of this layer. Barton et al. (1972) and Brown et al. (1972) have demonstrated that the carbohydrate composition of these biopsies is almost exclusively contributed by mucous glycoproteins within cells or adherent to the epithelial surface. Gastric biopsies were, therefore, used as a convenient screening procedure in order to investigate, firstly, the mucous glycoproteins from normal individuals and from patients with carcinoma of the stomach, and, secondly, the mucous glycoproteins from cancer-bearing and cancer-free areas of the same diseased stomachs.

Methods

All patients studied were referred to the Digestive Endoscopy Unit, University Department of Medicine, Bristol Royal Infirmary.

Endoscopic examinations were performed and gastric biopsies were taken from 37 subjects in whom barium meal and upper gastrointestinal endoscopy were normal, and from 27 patients with carcinoma of the stomach.

In patients with gastric carcinoma, biopsies were taken from the tumour (cancer-bearing area) and from an area free of tumour (cancer-free area). As far as possible, biopsies were taken from each area in duplicate. One specimen was placed in 10% formol saline solution for histopathology. The paraffin embedded biopsy tissue was treated as described elsewhere (Machado et al., 1975) and the final diagnosis was made by histopathological examination. The second specimen was placed in absolute ethanol for 24 hours at 4°C, then transferred to a previously weighed 2 ml ampoule and dried in a vacuum desiccator to constant weight. The internal standards mannitol and perseitol were added according to the dry weight of the samples, so that approximately 0.1 µmol was added for each milligram of sample.

The ampoules were dried once more and stored in a desiccator until ready for analysis.

The method described by Clamp (1974) was used for the analysis of the following monosaccharides, L-fucose (Fuc); D-mannose (Man); D-galactose (Gal); N-acetylgalactosamine (GlcNAc); N-acetylgalactosamine (GalNAc); N-acetylneuraminic acid (sialic acid; SA).

Blood-group activity (A, B, and H) of all patients was determined using methods based on those of Boorman and Dodd (1970).

Results

Of the 37 normal individuals 12 were non-secretors, whereas the 27 patients with carcinoma of the stomach contained 15 non-secretors. This difference has been noted previously (Doll et al., 1961).

The monosaccharide contents of the mucous glycoproteins in the biopsies were analysed and the results were examined according to the blood-group activity and secretor status of each individual.
Carbohydrate content of endoscopic gastric biopsies in carcinoma of the stomach

Table 1 Carbohydrate content of gastric biopsies from individuals who were secretors of ABH blood-group substances

<table>
<thead>
<tr>
<th></th>
<th>Fuc Mean (SD)</th>
<th>Man Mean (SD)</th>
<th>Gal</th>
<th>GlcNAc Mean (SD)</th>
<th>GalNAc Mean (SD)</th>
<th>NeuNAc Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Normal group (n = 25)</td>
<td>4-1 (0-8)</td>
<td>1-0 (0-2)</td>
<td>6-0</td>
<td>4-6 (0-4)</td>
<td>4-0 (0-8)</td>
<td>0-5 (0-2)</td>
</tr>
<tr>
<td>II. Carcinoma group (n = 12)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Cancer-bearing area</td>
<td>3-7 (0-4)</td>
<td>1-7 (0-4)</td>
<td>6-0</td>
<td>4-8 (0-2)</td>
<td>2-6 (0-3)</td>
<td>0-6 (0-3)</td>
</tr>
<tr>
<td>2. Cancer-free area</td>
<td>3-8 (0-4)</td>
<td>1-5 (0-4)</td>
<td>6-0</td>
<td>4-8 (0-5)</td>
<td>2-8 (0-4)</td>
<td>0-4 (0-2)</td>
</tr>
</tbody>
</table>

The results are given as mean (standard deviation) and are expressed as residues of monosaccharide relative to a galactose content of 6-0 residues. A comparison between normal subjects and those with carcinoma of the stomach with their significance (p value) is also given. Abbreviations are as follows: Fuc, fucose; Man, mannose; Gal, galactose; GlcNAc, N-acetylgalcosamine; GalNAc, N-acetylgalactosamine; NeuNAc, N-acetylenuraminic acid; n, number of patients; NS, not significant.

Table 2 Carbohydrate content of gastric biopsies from individuals who were non-secretors of ABH blood-group substances

<table>
<thead>
<tr>
<th></th>
<th>Fuc Mean (SD)</th>
<th>Man Mean (SD)</th>
<th>Gal</th>
<th>GlcNAc Mean (SD)</th>
<th>GalNAc Mean (SD)</th>
<th>NeuNAc Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Normal group (n = 12)</td>
<td>1-2 (0-3)</td>
<td>1-3 (0-4)</td>
<td>6-0</td>
<td>4-3 (0-3)</td>
<td>3-8 (0-7)</td>
<td>0-4 (0-1)</td>
</tr>
<tr>
<td>II. Carcinoma group (n = 15)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Cancer-bearing area</td>
<td>1-6 (0-3)</td>
<td>2-2 (0-5)</td>
<td>6-0</td>
<td>4-6 (0-5)</td>
<td>2-2 (0-4)</td>
<td>1-4 (0-5)</td>
</tr>
<tr>
<td>2. Cancer-free area</td>
<td>1-6 (0-2)</td>
<td>2-0 (0-2)</td>
<td>6-0</td>
<td>4-5 (1-2)</td>
<td>2-6 (0-3)</td>
<td>0-8 (0-5)</td>
</tr>
</tbody>
</table>

The results are given as mean (standard deviation) and are expressed as residues of monosaccharide relative to a galactose content of 6-0 residues. A comparison between normal subjects and those with carcinoma of the stomach with their significance (p value) is also given. Abbreviations are as in Table 1.

Tables 1 and 2 show that there are statistically significant (p < 0.001) differences between normal and carcinomatous stomachs in both secretors and non-secretors. The significant changes are an increase in mannose and a reduction in N-acetylgalactosamine. There is also a significant increase in N-acetylenuraminic acid in the tumour area of cancerous stomachs of non-secretors. However, this change is not seen elsewhere and, as the glycosidic linkage of this monosaccharide is very labile, the significance of such differences is difficult to assess.

In both secretors and non-secretors, the changes in mannose and N-acetylgalactosamine are found in the cancerous tissue as well as in the non-malignant parts of the stomach. It was not found possible to quantify satisfactorily the degree of gastritis found in the biopsies from the cancer-free areas. Chronic gastritis was, however, found to some degree in all specimens.

Discussion

There are a number of advantages in using biopsy material for monitoring changes in mucous glycoproteins. Thus, the material collected is less contaminated by other secretions such as saliva or bile, the mucous glycoproteins are less likely to have been degraded by enzymes than those present in aspirated gastric juice, and finally the analyses can be carried out on material from defined areas of the stomach.

Gas-liquid chromatography was the method used for the determination of the monosaccharide content of glycoproteins throughout this study. This technique can handle, in a single procedure, all the monosaccharides likely to be present in mucous glycoproteins and related materials, or in possible contaminants. These monosaccharides include ribose, xylose, fucose, mannose, galactose, glucose, N-acetylglucosamine, N-acetylgalactosamine, sialic and glucuronic acids, as well as fatty acids and a number of other substances.

When comparing the carbohydrate content of mucous glycoproteins from different individuals it is important to assess the results in relation to secretor status because of the changes in monosaccharide content—for example, fucose—associated with this (Clarke et al., 1959; Doll et al., 1961; Schrager and
biochemical support for the histological findings of Håkkinen et al. (1968) that there are glycoprotein changes in apparently normal areas of cancer-bearing stomachs.

These changes could perhaps be of diagnostic help, as, with refinement in techniques, isolation and carbohydrate analysis of adherent gastric mucus could, by indicating areas of altered carbohydrate content, possibly indicate a susceptibility to cancer even before histological change has occurred.

References


