Gastric luminal epidermal growth factor is affected by diet

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Objective. Diet is an area of major interest to those investigating the causes of cancer of the oesophagus in the Transkei. This study looked at the associations between intragastric epidermal growth factor level, diet and intragastric pH.

Setting and subjects. A dietary survey was co-ordinated with studies of gastric luminal epidermal growth factor and gastric fluid pH in 120 rural Transkeians.

Results. Gastric fluid epidermal growth factor was associated with low dietary intake of animal products \( (p = 0.002) \) and vegetables \( (p = 0.026) \). There was no association with pH.

Conclusion. A dietary subgroup has been identified in the Transkei population with high levels of epidermal growth factor in the upper gastrointestinal lumen. This adds to previously demonstrated diet-related changes in the upper gastrointestinal tract in Transkei. These changes may affect the disease pattern of the population.

A food frequency questionnaire was used which included 23 items identified as the most frequently eaten foods in rural Transkei (Fig. 1). These included 5 broad categories, viz. maize-based foods, animal products, fats and oils, fruit, and vegetables.

Consumption was recorded as daily, several times per week, weekly, monthly, yearly or never. For statistical calculations, "several times per week" was assumed to be 3 times per week.

Gastric juice was obtained from each volunteer, after an overnight fast, using a fine-bore nasogastric tube. The fluid obtained was transported in liquid nitrogen, and stored at \(-40^\circ C\) before analysis. The pH was measured by glass electrode. EGF was measured using an enzyme-linked

Patients and methods

Ethical permission was obtained from the Ethics Committee of the Faculty of Health Sciences, University of Transkei. One hundred and twenty volunteers were recruited from among patients attending a rural health clinic, and informed consent was obtained. Patients who were smokers, who had symptoms of upper gastrointestinal disease, or who were receiving non-steroidal anti-inflammatory drugs were excluded from the study.

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immunosorbent assay (ELISA) (R and D Systems, Minneapolis, Minn., USA, #DEGOO).

The relationships between individual dietary components, EGF and pH were studied using Spearman's rank correlation, and SPSS software (Chicago, Ill., USA).

Results

Results were available for all patients (Fig. 1). Gastric fluid EGF was associated with low dietary intake of foods of animal origin \( (p = 0.002) \) and vegetables \( (p = 0.026) \) (Figs 2 and 3). There was a non-significant association with low total fat intake \( (p = 0.076) \), but no significant association with any individual food. There was no association with intragastric pH (Table 1).

<table>
<thead>
<tr>
<th>Food groups</th>
<th>Spearman's correlation coefficient</th>
<th>Significance (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fruit</td>
<td>0.012</td>
<td>0.894</td>
</tr>
<tr>
<td>Animal products</td>
<td>-0.283</td>
<td>0.020</td>
</tr>
<tr>
<td>Maize</td>
<td>-0.129</td>
<td>0.158</td>
</tr>
<tr>
<td>Vegetables</td>
<td>-0.202</td>
<td>0.026</td>
</tr>
<tr>
<td>Fats</td>
<td>-0.182</td>
<td>0.076</td>
</tr>
<tr>
<td>pH</td>
<td>0.056</td>
<td>0.540</td>
</tr>
</tbody>
</table>

Discussion

The radioimmunoassay method used in this study does not distinguish between the different forms of EGF, and so the molecular levels detected do not equate accurately to EGF activity.

EGF is very labile, for instance rising to 10 times basal value in response to histamine stimulation. This may explain why the literature is not clear on what constitutes a 'normal' gastric luminal EGF level. Several studies support a level between 300 and 600 pg/ml, while other studies support a level nearly 10 times higher than this.

In this study it would be reasonable to think that 'normal' included those on a broad-based diet with a good intake of protein, fruit and vegetables. EGF levels in such individuals were mostly below 1 000 pg/ml. 'Abnormal' may have included individuals with low protein and vegetable intake, with EGF levels over 1 000 pg/ml.

The strongest association in this study was with animal products – milk, chicken, mutton and beef. These all contain fat in addition to protein. These fats are significant in quantity and quality. It is worthy of note that other dietary fats may have had an effect on EGF since a non-significant difference was seen. Vegetable content includes vitamins and some fatty acids. On a marginal diet such as is eaten in Transkei the amounts of these substances derived from vegetables may be enough to influence EGF production or regulation.

With both meat and vegetables, the association shown might be spurious, and the true association may be with some other aspect of the adoption of a more westernised diet or way of life. The lack of association between EGF levels and fruit makes this explanation unlikely since increased fruit consumption normally accompanies increased meat as part of a more westernised diet.

There was no association with pH levels. The first half of this study showed a strong association between maize intake and pH. It is of considerable interest that the diet of rural
Transkeians has now shown a second major diet-related phenomenon in the gastric lumen, not directly associated with the first.

The evidence presented suggests that there is a subsection of the population which has a high EGF, and in which that high EGF is not cleaved by pepsin activity. This subsection includes those who have a high intake of maize (and therefore a high intragastric pH), and a low consumption of animal products, vegetables and fats (and therefore a high EGF).

The group in South Africa susceptible to cancer of the oesophagus is poor but not very poor, and has a narrow diet highly dependent on maize, pumpkin and beans, and low in fats. This susceptible group appears to be the same as the subsection of the population which has raised pH and EGF.

Overexpression of transforming growth factor (TGF)-alpha, EGF and epidermal growth factor receptor (EGFR) is closely correlated with tumour invasion and prognosis.

The subsection of the Transkeian population with a high pH and EGF will have a strong mitogenic, possibly mutagenic drive from EGF activity.

Statistical analysis was carried out by Mr Chris Foy, medical statistician, Research and Development Support Unit, Gloucestershire, UK.