concentrations of plasma immunoreactive atrial natriuretic peptide and that concentrations rise further with the severity of the disease. Notwithstanding reports that atrial natriuretic peptide is released into the plasma in response to increased atrial pressure our results imply that this is not the principal stimulus for the raised concentrations of the peptide in pre-eclampsia.

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Influence of non-steroidal anti-inflammatory drugs on the outcome of faecal occult blood tests in screening for colorectal cancer

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Abstract

Non-steroidal anti-inflammatory drugs have been accused of causing false positive results in faecal occult blood tests for colorectal cancer. A study was therefore performed in 10 931 people undergoing faecal occult blood screening tests to assess the effect of these drugs on the predictive value of a positive test result. Those with a positive result were interviewed and a full drug history was taken before they underwent a full colorectal examination. Of the 455 people with a positive result, 50 were taking non-steroidal anti-inflammatory drugs: 10 (20%) had colonic neoplasia. Of the 405 who were not taking non-steroidal anti-inflammatory drugs, 129 (32%) had colonic neoplasia. These detection rates were not significantly different, and the predictive value of a positive result for an adenoma larger than 1 cm was 14% in the group not taking anti-inflammatory drugs and 26% in the group taking them (not significant).

These results suggest that a finding of occult faecal blood cannot be attributed to upper gastrointestinal tract bleeding caused by non-steroidal anti-inflammatory drugs and should be followed by a thorough colorectal examination.

Introduction

There is much evidence linking the ingestion of non-steroidal anti-inflammatory drugs with chronic gastrointestinal bleeding.[1] These drugs inhibit the synthesis of prostaglandins, which have cytoprotective effects on the upper gastrointestinal tract, as well as suppressing gastric acid secretion.[2] Testing stool for occult blood is becoming an important means of screening for colorectal neoplasia in individuals over the age of 50,[3] for whom non-steroidal anti-inflammatory drugs are widely prescribed. A small study conducted on patients attending a rheumatology clinic suggested that treatment with non-steroidal anti-inflammatory drugs does not lead to false positive faecal occult blood test results,[4] but another study showed an increase in false positive results in such patients compared with those taking a placebo.[5] The aim of this study was to establish the effect of ingestion of non-steroidal anti-inflammatory drugs on the predictive value of a positive faecal occult blood test result in population screening for colorectal neoplasia.

Patients, methods, and results

A total of 10 931 asymptomatic individuals (aged 50-74 years) underwent faecal occult blood tests in a screening study for colorectal neoplasia. Either a standard guaiac, pseudoperoxidase based test (Hemoccult) or an immunological test (Feca EIA) was completed over a three or six day period. Individuals with positive faecal occult blood test results were interviewed and a full drug history was taken to establish drug ingestion at the time of the test. They then underwent full colonic assessment either by flexible sigmoidoscopy and double contrast barium enema or colonoscopy.

Of the 10 931 individuals who completed the faecal occult blood test, 455 had positive results and underwent full colonic investigation. Fifty of these were taking non-steroidal anti-inflammatory drugs at the time of the test, 10 of whom (20%) were found to have colonic neoplasia (three carcinomas, seven adenomas more than 1 cm in size). Of the 405 patients not taking non-steroidal anti-inflammatory drugs at the time of the test, 129 (32%) had neoplastic disease (23 carcinomas, 106 adenomas more than 1 cm in size) (table). These detection rates were not significantly different ($\chi^2=2{\cdot}9$, $p>0{\cdot}05$). The predictive value of a positive test result for a colorectal adenoma more than 1 cm in size was 14% (7/50) in the group not taking non-steroidal anti-inflammatory drugs and 26% (106/405) in the group taking them ($\chi^2=3{\cdot}5$, $p>0{\cdot}05$).

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Results of investigation of patients with positive test results

	Patients not taking non-steroidal anti-inflammatory drugs (n=405)	Patients taking non-steroidal anti-inflammatory drugs (n=50)
No disease	276	40
Total No (%) with neoplasia (carcinoma or adenoma >1 cm)	129 (32)	10 (20)
No (%) with carcinoma	23 (5·7)	3 (6)
No (%) with adenoma (>1 cm)	106 (26·1)	7 (14)

Discussion

Although treatment with non-steroidal anti-inflammatory drugs may cause upper gastrointestinal bleeding, any blood loss will be subject to digestion during its passage through the proximal gut to the colon. The pseudoperoxidase activity of the haematin necessary to render the Hemoccult test positive and the immunological properties of the haemoglobin molecule required for the Feca EIA may thereby be reduced or lost completely.

The number of carcinomas detected in our study was similar in both groups. The group taking non-steroidal anti-inflammatory drugs had fewer adenomas than the non-treatment group; nevertheless, there were enough patients with adenomas in the treated group to warrant appropriate investigation.

A positive faecal occult blood test result in patients taking non-steroidal anti-inflammatory drugs cannot safely be attributed to upper gastrointestinal bleeding and should be followed by a thorough colorectal examination.

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Deoxyribonucleic acid (DNA) polymorphism of the α_1-antitrypsin gene in chronic lung disease

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Abstract

Specific gene probes were used to study restriction fragment length polymorphisms of the human α_1-antitrypsin gene. A polymorphism due to loss of a recognition site for the restriction enzyme Taq I was identified in eight of 42 patients with bronchiectasis and nine of 49 patients with pulmonary emphysema, none of whom had α_1-antitrypsin deficiency. Among a control group without lung disease the polymorphism was significantly less frequent, being found in only five of 101 apparently healthy blood donors. The deoxyribonucleic acid (DNA) polymorphism was also present in two of 14 unrelated patients with α_1-antitrypsin deficiency, indicating a lack of association with any specific α_1-antitrypsin protein phenotype.

The polymorphism identified in this study may be a new marker for genetic predisposition to chronic lung disease.

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Introduction

People with substantially reduced concentrations of α_1-antitrypsin in serum (<35% of normal) are predisposed to developing pulmonary emphysema.[1,2] Hitherto, some 30 variants of the proteins have been defined conventionally by isoelectric focusing.[3] People with two common variants have reduced concentrations in serum and are at risk of developing disease; ZZ homozygotes have about 20% and SZ heterozygotes about 40% of the mean serum concentrations found in normal MM homozygotes. This risk is greatly increased if the subject also smokes.[4]

Fewer than 5% of patients with emphysema have α_1-antitrypsin deficiency.[5] With specific deoxyribonucleic acid (DNA) probes we have identified DNA variants of the human α_1-antitrypsin gene that are not detected by isoelectric focusing and defined one potentially useful DNA polymorphism in relation to pulmonary emphysema.[6] This paper examines whether the frequency of this DNA polymorphism is increased in patients with pulmonary emphysema and bronchiectasis.

Subjects and methods

Four groups were studied: 101 healthy white blood donors (49 women, 52 men aged 18-59 (mean 31) years); 49 patients with pulmonary emphysema unrelated to α_1-antitrypsin deficiency (13 women, 36 men aged 38-80 (mean 56) years); 14 patients with pulmonary emphysema due to homozygous deficiency (eight women, six men aged 24-68 (mean 42) years); and 42 patients with bronchiectasis (20 women, 22 men aged 36-73 (mean 56) years). All the patients were white and assessed by physical examination, chest radiography, and physiological tests of lung function.

All 63 patients with pulmonary emphysema (14 with α_1-antitrypsin deficiency) had features compatible with emphysema with or without evidence of chronic bronchitis. Eighteen of these patients were smokers, 42