SHORT REPORTS

Gastrointestinal endoscopy in the young

The clinical value of standard procedures such as upper gastrointestinal endoscopy needs periodic scrutiny, preferably audit rather than debunking. Open access to endoscopy has been questioned and criteria for selection suggested.¹ We do not believe that the elderly should be excluded from endoscopy, because our diagnostic yield in 100 patients over 70 was 77%, and management was changed in over half of those with appreciable abnormalities.² Should the young be excluded because malignancy is unlikely and precise diagnosis might be unnecessary?

benefit of endoscopy simply divided 1526 patients at 40 years.³ In Uppsala endoscopy was successful in only 153 of 162 patients younger than 25 years old, and although 75 (49%) of these were normal, "Undisputable pathological findings with relevance for treatment were made in 37 patients (24%)."⁴ We found more abnormalities, consistent with our results in the over 70s,² perhaps because of different populations and patterns of referral.

Spiro may ask, "What good to see the hole in the duodenum if we ignore the ambitions, the passions, the frustrations and failures, even the hopes of the patient with a duodenal ulcer?"⁵ A controlled, blind, randomised prospective study of the outcome of management is needed for a valid evaluation of endoscopy. Meanwhile our data suggest that neither the young

Diagnoses and changes in management by indication for endoscopy

	Total	Dyspepsia	Indication		
			Upper gastrointestinal bleed	Anaemia	Foreign body
No patients	100	78	18	3	1
No (%) of abnormal findings	64 (64)	48 (62)	13 (72)	2 (67)	1 (100)
Hiatus hernia with or without reflux	19	15	3	1	1?
Oesophagitis	6	4	1	1	
Oesophageal tear	3	1	2		
Erosive gastritis	8	6	2		
Gastric ulcer	3	2	1		
Gastric ulcer scar	1				
Gastric ulcer other	4	1	2	1	
Duodenal ulcer	10	7	3		
Duodenal ulcer scar	10	10			
Duodenal ulcer other	4	4			
Duodenitis	6	5	1		
Removal of foreign body	1				1
No with normal endoscopic results (one technical failure)	36	30	5	1	
No with abnormal findings whose management was changed	38	31	6		1
As % of total group	38	40	33		100
As % of total abnormal findings	59	65	46		100

Methods and results

We reviewed retrospectively 106 consecutive and unselected patients aged 25 or younger who had been referred for endoscopy by hospital doctors. The endoscopists did not give clinical or therapeutic advice, except if specifically asked. Records were inadequate for six patients, which left 100: 68 men and 32 women with a mean age of 22.2 years (range 5-25). There was one technical failure and no complications.

Endoscopic abnormalities were seen in 64 patients, and some had more than one abnormality (table). The diagnosis before endoscopy was confirmed in 48 patients only.

Endoscopy was considered to have altered management if a new drug was prescribed, an operation was performed, or a new and relevant investigation was performed.³ Ulcers or erosions were treated by H₂ antagonists in 15 patients (two while awaiting vagotomy and two after acid secretion tests) and by antacids in six patients (four of whom underwent acid studies). Six patients with hiatus hernia were given metoclopramide and seven an alginate-antacid mixture. One patient taking an H₂ antagonist was referred for vagotomy. Four other patients had acid secretion tests: two had normal output of acid (one had recurrent symptoms but normal findings on endoscopy, the other had had treatment with an H₂ antagonist), and two had hypersecretion of acid (one was being treated with antireflux treatment only and was therefore given an H₂ antagonist as well, the other was taking an H₂ antagonist in standard dosage and this dose was doubled). There were 26 emergency endoscopies: 13 for gastrointestinal bleeding (10 abnormal), 12 for epigastric pain (nine abnormal), and one to remove a 5 pence piece swallowed by a 5 year old boy (the only patient under 15).

Management was changed in 38 out of 64 (59%) patients with endoscopic abnormalities. Of the 36 with no endoscopic abnormalities management was changed in two (6%) patients; no further tests were done in either patient and H₂ antagonists were discontinued for both.

Comment

In this series of young patients three fifths of the results from endoscopy were abnormal, and the results influenced clinical management in three fifths of these patients. Even when we excluded the emergency endoscopies for haemorrhage, with which few would disagree, these proportions were little changed (54/87 (62%) abnormal results, management influenced in 33/54 (61%)). Unfortunately the largest and most recent study of the clinical

nor the old should be denied appropriate investigation of their upper gastrointestinal tracts.

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- 4 Nyren O, Nilsson F. Is gastroscopic examination of young patients worthwhile? *Scand J Gastroenterol* 1982;17(suppl 78):27.
- 5 Spiro HM. Visceral viewpoints. Moynihan's disease? The diagnosis of duodenal ulcer. *N Engl J Med* 1974;291:567-9.

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Adverse reactions to sulphadoxine-pyrimethamine in Swedish travellers: implications for prophylaxis

Fansidar (500 mg sulphadoxine and 25 mg pyrimethamine tablets) has been widely used for malaria prophylaxis. The risk of severe cutaneous adverse reactions has been debated and, in particular, whether the high risk of such reactions among American travellers (1/5000-8000) compared with that among Swiss travellers (1/150 000) might be explained by concomitant

treatment with chloroquine.¹⁻³ Our analysis suggests that there is also a high risk of severe cutaneous adverse reactions when Fansidar is used as monophylaxis.

Reactions to Fansidar

Seventy eight reactions in 52 Swedish travellers occurring between 1978 and the end of June 1985 were considered by the Swedish Adverse Drug Reactions Advisory Committee to have had a probable or possible causal relation with Fansidar. During the same period roughly 1.2 million tablets were sold in Sweden. All 52 travellers used Fansidar as monophylaxis, and only four took any other drugs. All except three took one tablet weekly. Four travellers had previously experienced adverse reactions to sulphonamides. Only three went to chloroquine resistant areas in Africa.

Skin reactions were reported in 24 travellers after a median of 13 days (range 1-45 days). Seven patients experienced severe cutaneous adverse reactions (table).

Characteristics of seven Swedish travellers with severe cutaneous adverse reactions associated with Fansidar prophylaxis

Age (years)	Sex	Dose (tablets/week)	Diagnosis	Time to reaction (days)	Concomitant drugs	Outcome
50	F	1	EM	15	No	Recovered
48	F	1	SJS	21	No	Recovered
68	F	1	SJS	7	No	Recovered
41	M	1	SJS	7	No	Recovered
24	F	1	SJS	13	Levothyroxine	Recovered
31	M	1	TEN	23	No	Died
39	M	1	TEN	18	No	Died

EM=Erythema multiforme; SJS=Stevens-Johnson syndrome; TEN=toxic epidermal necrolysis (Lyell's syndrome).

Three cases of photosensitivity and 14 of exanthema were reported. None of the travellers who suffered cutaneous reactions had previously experienced adverse reactions to sulphonamides. Liver reactions occurred in 15 travellers (12 women), developing after a median of 52 days (range 16-91 days). Five had increased liver enzyme activities alone, while the others were also icteric. One of the eight travellers with respiratory symptoms (seven men) complained of dyspnoea and one had pleuritis, while the remaining six also suffered pulmonary infiltrations and fever. Symptoms occurred 1-30 days after treatment was started.

Two men developed severe generalised vasculitis. One became ill with fever, orchitis, jaundice, cutaneous vasculitis, and gastrointestinal bleeding after two weeks. The other developed cutaneous vasculitis and rapidly progressive nephritis after three weeks. Severe megaloblastic anaemia was noted in one traveller after six weeks, one traveller experienced reversible hyperaesthesia, and one reported itching.

Comment

The true risk of adverse reactions is difficult to estimate. The duration of prophylaxis varies and many tablets are never used and some are prescribed for self treatment. In addition, many adverse reactions are never reported.⁴ Despite these difficulties, however, a rough estimate can be made.

The intended duration of Fansidar prophylaxis was stated for 30 of the 52 travellers. Assuming that they were representative of all users and taking into account the package sizes, the average number of tablets taken by each traveller was 17, giving an estimated number of around 70 000 users. Fatal reactions were thus reported for one in 35 000 and severe cutaneous adverse reactions for one in 10 000. These figures are well in accordance with the estimated risks in American travellers taking Fansidar in combination with chloroquine.² Thus our data do not support the theory that an interaction with chloroquine might increase the frequency and severity of adverse reactions to Fansidar.³

In South America and South East Asia the risk of contracting *Plasmodium falciparum* malaria is smaller than that in Africa and resistance to Fansidar is more common. Fansidar should therefore generally not be recommended for prophylaxis outside areas with chloroquine resistance in Africa.

All the severe cutaneous adverse reactions and the two cases of generalised vasculitis developed within less than one month of treatment. Fansidar therefore cannot be unequivocally recommended for short term prophylaxis, but it might be justified for non-immune subjects who have been taking Fansidar for some time and live in areas of Africa with a high risk of chloroquine resistant *P. falciparum* to continue using it.

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Immune haemolytic anaemia induced by glibenclamide in selective IgA deficiency

Glibenclamide is a widely prescribed and well tolerated oral antidiabetic drug. We report a case of immune haemolytic anaemia associated with glibenclamide treatment in a patient with selective IgA deficiency.

Case report

A 48 year old mentally retarded man with mild diabetes was given glibenclamide for two months. He had been taking zuclopenthixol for several years. During treatment with glibenclamide he became jaundiced and increasingly fatigued. Anaemia and a raised bilirubin concentration led to admission to hospital.

On examination he had icteric scleras but no fever, hepatosplenomegaly, or lymphadenopathy. Haemoglobin concentration was 85 g/l and red cell count $2.67 \times 10^{12}/l$ with 58% reticulocytes. Erythrocyte sedimentation rate was 108 mm in the first hour, serum bilirubin concentration 59 $\mu\text{mol}/l$, lactate dehydrogenase activity 696 IU/l, haptoglobin concentration $<0.25 \text{ mg}/l$, and ferritin concentration 113 $\mu\text{g}/l$. A peripheral blood smear showed polychromasia, spherocytosis, anisocytosis, and some nucleated red blood cells. The white cell morphology was normal except for 16% eosinophils. A bone marrow specimen showed erythroid hyperplasia. A Paul-Bunnell test and a complement fixation test for mycoplasma antibodies gave negative results and cold agglutinins were not found. A direct Coombs test gave strongly positive results with anti-IgG and weakly positive results with anti-C₃ and anti-C₄. Serum IgG concentration was 8.9 g/l, IgM 1.7 g/l, C₃ 0.75 g/l, C₄ 0.24 g/l, and IgE $<5 \times 10^3 \text{ U}/l$. IgA could not be shown in the serum ($<0.006 \text{ g}/l$). Tests for antinuclear and rheumatoid factors gave negative results.

After one week in hospital the patient's haemoglobin concentration had fallen to 78 g/l, and he received three units of blood. As this resulted in only a temporary increase in haemoglobin concentration glibenclamide was stopped. A few days later the blood variables began to improve, and on follow up examination five weeks later haemoglobin concentration was 132 g/l, erythrocyte sedimentation rate 24 mm in the first hour, and red cell count $4.62 \times 10^{12}/l$ with 23% reticulocytes. His diabetes was well controlled by diet alone.

His serum did not agglutinate normal red cells *in vitro*, and no agglutination occurred when glibenclamide at various concentrations was added to the serum. Six months later, a Coombs test with anti-IgG still gave strongly positive results, but negative results were obtained with anti-C₃ and anti-C₄. There was no haemolysis.

Comment

The rapid and complete recovery when glibenclamide was stopped strongly suggests that this drug caused the immune haemolytic anaemia. The neuroleptic treatment was continued, and the patient had not received any other drugs before admission. Although a wide variety of drugs may induce haemolysis,¹ sulphonylureas have seldom been found responsible.^{2,3} The Committee on Safety of Medicines and the manufacturer have not received any reports of a possible association between glibenclamide and haemolytic anaemia (personal communication). Logue *et al* described