

## PAPERS AND SHORT REPORTS

## Non-steroidal anti-inflammatory drugs and benign oesophageal stricture

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### Abstract

Drug histories were obtained from 76 patients at the time of initial Eder-Puestow dilatation for benign oesophageal stricture. Six patients had consumed drugs known to cause oesophageal ulceration (emepromium bromide and potassium preparations). Of the remaining 70 patients, 22 had regularly taken a non-steroidal anti-inflammatory drug before the onset of dysphagia compared with 10 patients in a control group matched for age and sex; this difference was significant ( $p < 0.02$ ).

Non-steroidal anti-inflammatory drugs may have a causative role in the formation of oesophageal stricture in patients with gastro-oesophageal reflux, in whom they should be prescribed with caution.

### Introduction

Aspirin and other non-steroidal anti-inflammatory drugs have long been recognised as causing gastric erosions and ulceration, but only in recent years have reports of drug-induced oesophageal damage appeared. Oesophageal ulceration has been described after emepromium bromide, potassium preparations, antibiotics including tetracycline and doxycycline,<sup>1</sup> and indomethacin.<sup>2</sup> Severe oesophageal damage may cause a fibrous stricture, and this has been reported after emepromium bromide,<sup>3</sup> alprenolol, doxycycline, iron preparations, and analgesic drugs.<sup>4</sup>

To examine the possible importance of drug-induced oesophageal injury in fibrous oesophageal stricture we carried out a prospective study of the consumption of non-steroidal anti-inflammatory drugs and other drugs in 76 patients presenting with oesophageal stricture.

### Patients and methods

After the diagnosis of benign oesophageal stricture had been established by means of radiology, endoscopy, and endoscopic biopsy 76 patients (27 men) with strictures severe enough to require Eder-Puestow dilatation were questioned about their drug consumption before the onset of dysphagia. Regular consumption was defined as taking a drug daily for three months or more immediately before the onset of dysphagia. The patients' ages ranged from 39 to 89 (mean 69.6) years. Fifty-three patients gave a characteristic history of gastro-oesophageal reflux with postural heartburn; at the time of the initial endoscopy all had ulceration in the strictured area. Radiology disclosed gastro-oesophageal reflux in 57 patients and a hiatal hernia in 55. Six patients had established rheumatoid disease.

A control group was obtained from patients admitted to general medical wards but excluding those who had oesophageal symptoms or were unable to give a medical history. After each patient with oesophageal stricture had been admitted a control was selected of the same sex and differing in age by no more than a year. Five control patients had rheumatoid disease.

The  $\chi^2$  test was used for statistical analysis.

*Number of patients who had consumed non-steroidal anti-inflammatory drugs*

Drug	Patients with stricture	Controls
Aspirin	8	4
Benorylate	2	0
Indomethacin	8	2
Ibuprofen	11	5
Phenylbutazone	2	0
Naproxen	5	2
Fenclofenac	1	0
Flurbiprofen	1	1

### Results

Of the 76 patients studied, 28 had regularly consumed drugs that might cause oesophageal damage, of whom three had taken emepromium bromide and three potassium preparations. Thus, excluding these six patients, 22 (31%) of the remaining 70 patients had regularly consumed non-steroidal anti-inflammatory drugs compared with 10 of the 70 controls; this difference reached significance ( $p < 0.02$ ). The incidence of antecedent symptoms of gastro-oesophageal reflux did

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not differ significantly between those patients who had taken non-steroidal anti-inflammatory drugs (20 out of 22; 91%) and those who had not (33 out of 48; 69%). The relative frequency of consumption of individual non-steroidal anti-inflammatory drugs did not differ between the patients with stricture and the controls (table), and ibuprofen, indomethacin, and aspirin were the drugs most often used by both groups.

### Discussion

We found an association between prior consumption of non-steroidal anti-inflammatory drugs and the development of benign oesophageal stricture. Before dysphagia occurred most of our patients had had symptoms of gastro-oesophageal reflux, and almost all had evidence of reflux at the time the stricture was diagnosed. This suggests that such drugs may aggravate reflux oesophagitis and so increase the risk of formation of stricture.

Swallowed tablets may remain in the oesophagus for considerable periods; Evans and Roberts<sup>5</sup> found that in 57 out of 98 patients without organic obstruction barium sulphate tablets remained in the oesophagus for five minutes or longer during recumbency. Oesophageal emptying is slow in the elderly, and clearing is impaired in the presence of gastro-oesophageal reflux with resulting disorder of motility. For these reasons passage of the non-steroidal anti-inflammatory drugs might have been slow even before stricture developed, resulting in prolonged exposure of the oesophageal mucosa to their irritant action.

Prostaglandins are believed to have a cytoprotective action

on the gastric mucosa,<sup>6</sup> and non-steroidal anti-inflammatory drugs may exert their ulcerogenic effect by reducing generation of mucosal prostaglandins. A similar action in the oesophagus might contribute to mucosal damage and aggravate reflux oesophagitis.

The proportion of patients suffering from rheumatoid disease did not differ significantly between the patients with peptic stricture and the controls, which suggests that rheumatoid disease in itself does not predispose to the formation of stricture.

These findings indicate that non-steroidal anti-inflammatory drugs should be prescribed with caution in the presence of symptomatic gastro-oesophageal reflux; if they are used endoscopic monitoring for oesophageal damage would seem advisable.

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## Pregnancy after surgical correction of tetralogy of Fallot

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### Abstract

**Forty pregnancies have been documented in 27 patients with surgically corrected tetralogy of Fallot. Infertility was uncommon and there were no premature births and few abortions or small-for-dates babies; this suggests that surgery that corrects cyanosis improves the outcome of pregnancy by correcting the fetal environment. Pregnancy was well tolerated and there were no serious cardiac complications. Thirty of the 31 infants examined were normal, the one abnormal infant having pulmonary atresia.**

**A patient with no major residual defects after surgery for tetralogy of Fallot may be reassured that pregnancy will be well tolerated and that delivery may be managed in the normal manner.**

### Introduction

"Total" or radical surgical correction of tetralogy of Fallot has become standard practice, and of those patients surviving radical surgery about 95% are alive five to 10 years later.<sup>1-3</sup> About half the deaths occurring after the perioperative period are in the first postoperative year and are caused by heart failure resulting from residual abnormalities. These include ventricular septal defects, pulmonary hypertension, and abnormalities of conduction or rhythm. Survivors of surgery show an improvement in effort tolerance and loss of cyanosis.<sup>2,4</sup>

Uncorrected cyanotic heart disease carries a high risk in pregnancy for both mother and fetus: a review of 57 pregnancies in women with uncorrected tetralogy of Fallot showed a fetal mortality of 22% and a maternal mortality of 7%.<sup>5</sup> The high fetal mortality was caused by poor fetal growth, leading to a high incidence of abortion, prematurity, and small-for-dates babies. Pregnancy in patients with surgically corrected tetralogy of Fallot is increasing, but no large, detailed series of such pregnancies has been reported.

### Patients and methods

All women who had had a total correction of tetralogy of Fallot at Hammersmith Hospital during the period 1958-74 and who were now aged 16 or over were considered for the study. Of the original group of 100 patients, 23 had returned abroad. In these and a further 25 patients insufficient follow-up information was obtained and they were therefore not included in the study.

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