Colonic Crohn's disease and use of oral contraception

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Abstract

The prevalence of use of oral contraception before the onset of disease was established in 100 consecutive women attending follow up clinics for inflammatory bowel disease. A significant excess of women with Crohn's disease confined to the colon had taken oral contraceptives in the year before developing symptoms (10/16 (63%)) compared with women with small-intestinal Crohn's disease (12/49 (24%); $p < 0.02$) and women with ulcerative colitis (3/35 (9%); $p < 0.0005$). When the patient groups were matched for age and year of onset of disease usage of oral contraception before the onset of disease was still more common among women with isolated colonic Crohn's disease (9/12, 75%) than among those with ulcerative colitis (2/12 (17%); $p < 0.02$) and was also more common than would be expected from reported figures for oral contraception in England and Wales (31.4% of women aged under 41; $p < 0.005$). A survey of current patient records showed that isolated colonic disease was at least twice as common among women with Crohn's disease (63/218, 29%) compared with men (25/181, 14%; $p < 0.001$).

These data support the suggestion made previously that oral contraceptives may predispose to a colitis that resembles colonic Crohn's disease.

Introduction

Twenty six cases of colitis in women attributed to use of oral contraceptives have been reported.¹⁻⁸ All these reports noted that the colitis improved after the oral contraceptive treatment was stopped. Table I shows some of the features of

TABLE I—Details of case reports of colitis associated with use of oral contraceptives

Reference	No of cases	Rectal sparing	Granulomas	Colitis better when contraceptive stopped	Duration of follow up
Morowitz and Epstein ¹	2	no	no	yes	> 2 years
Bernadino and Lawson ²	1	yes	no	yes	8 months
Simon and Figus ³	4	yes (in 2/4)	no	yes	5-18 months
Bonfils <i>et al</i> ⁴	4	yes	no	yes	1-5 years
Favier ⁵	7	yes	no	yes	1 month
Conri <i>et al</i> ⁶	1	yes	yes	yes	2 years
Camilleri <i>et al</i> ⁷	2	yes	no	yes (in 1/2)	5 years
Tedesco <i>et al</i> ⁸	5	yes	no	yes	4 months-2 years

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these cases. Rectal sparing was noted in nearly all the cases, and this, together with evidence of segmental disease and the colonoscopic appearance of discrete ulcers separated by relatively normal mucosa, led several authors to suspect colonic Crohn's disease,^{3,4,6-8} but granulomas were found on biopsy in only one of the 26 cases. Four cases of ileocolonic or ileal Crohn's disease responding to withdrawal of oral contraceptives have also been reported.^{1,7,9,10} We had seen four cases of colitis in young women taking oral contraceptives, and this prompted us to carry out the present study.

Patients and methods

We asked 100 consecutive women with inflammatory bowel disease attending outpatient follow up at three hospitals whether they had taken oral contraceptives before the onset of symptoms and if so for how long. They comprised 16 patients with isolated colonic Crohn's disease, 36 with ileocolonic Crohn's disease, 13 with ileal Crohn's disease, and 35 with ulcerative colitis. The four index patients who had prompted this study were excluded. The medical records of 399 patients with Crohn's disease treated at Birmingham General Hospital were scrutinised and the site of disease as defined by barium studies or laparotomy, or both, noted. In all cases a diagnosis of ulcerative colitis or Crohn's disease had been established previously according to conventional criteria, an in no case was this diagnosis altered retrospectively on review.

Matching for age and year of onset—Among the 100 consecutive outpatients questioned about oral contraception those with ulcerative colitis were found to have presented earlier (median year of onset 1968) than those with colonic Crohn's disease (median year of onset 1975) (table II). Matching for year of onset between these

TABLE II—Median age at onset of symptoms and median year of onset of symptoms in 100 consecutive women attending follow up for inflammatory bowel disease (ranges given in parentheses)

	Age at onset (years)	Year of onset	Age at onset in corrected groups*
Crohn's disease:			
Colonic	28 (16-50)	1975 (1962-82)	25 (15-37)
Ileocolonic	21 (10-50)	1970 (1938-81)	19 (12-35)
Ileal	30 (13-51)	1971 (1938-81)	30 (15-32)
Ulcerative colitis	26 (5-68)	1968 (1940-83)	26 (15-39)

*Corrected so that 1975 was median year of onset, and excluding women aged >40 at onset.

groups was achieved by excluding consecutively the patients with the longest duration of ulcerative colitis so that the median year of onset in the remaining patients with ulcerative colitis was the same as that in the patients with colonic Crohn's disease. As prescription of oral contraceptives to patients aged over 40 is unusual, patients of this age were also excluded. After this adjustment patients with ulcerative colitis were well matched with patients with colonic Crohn's disease, both for year of onset (median 1975 in both groups; range 1969-81 in those with ulcerative colitis, 1965-81 in those with Crohn's disease) and for age at onset (table II).

Statistical methods—Fisher's exact test (two tailed) was used to compare prevalences of oral contraceptive usage between the disease groups. An exact binomial test (two tailed) was used to compare the prevalence of oral contraceptive usage in colonic Crohn's disease with figures for England and Wales published by the Department of Health and Social Security.¹¹ The χ^2 test with Yates's correction was used to compare the proportions of women and men with colonic Crohn's disease attending Birmingham General Hospital.

Results

Ten of the 16 (63%) women with Crohn's disease confined to the colon had taken oral contraceptives within the year before they developed symptoms of Crohn's disease. This compared with nine out of the 36 (25%) with ileocolonic Crohn's disease ($p < 0.02$), three of the 13 (23%) with only small-bowel Crohn's disease (NS), and three of the 35 (9%) with ulcerative colitis ($p < 0.0005$).

In the groups matched for age and year of onset of disease nine of the 12 (75%) women with isolated colonic Crohn's disease were taking oral contraceptives at the onset of symptoms. This compared with nine of the 20 (45%) with ileocolonic Crohn's disease (NS), two of the five (40%) with small-bowel Crohn's disease (NS), and two of the 12 (17%) with ulcerative colitis ($p < 0.02$). The Department of Health and Social Security found that in England and Wales in 1975, 31.4% of a sample of 3068 women aged under 41 were taking oral contraceptives.¹¹ This proportion is significantly lower than that among our women with colonic Crohn's disease ($p = 0.005$), although the groups are not strictly comparable.

Of the 10 women with isolated colonic Crohn's disease who had taken oral contraceptives within the year before they developed symptoms, only three had granulomas on rectal biopsy; three others had rectal sparing on sigmoidoscopy, one had a chronic perianal fistula, and the other three had radiological evidence of skip lesions. The median duration of oral contraceptive usage before symptoms of colitis developed was 12 months (range six months to nine years). Eight of the 10 patients stopped taking oral contraceptives, and four of these, all with non-granulomatous colitis, subsequently remained completely asymptomatic for 12 months, 13 months, three years, and 10 years. One of the other four had a colectomy before stopping oral contraceptives, one died of renal failure due to amyloidosis, and two with granulomatous colitis had further relapses.

Scrutiny of Birmingham General Hospital records of current patients with Crohn's disease showed that isolated colonic Crohn's disease (as defined by the finding of a normal small intestine on barium examination or laparotomy, or both) was more than twice as common among women with Crohn's disease (63/218, 29%) than men with Crohn's disease (25/181, 14%; $p < 0.001$).

Discussion

We found a significantly higher prevalence of oral contraceptive usage before the onset of disease in patients with isolated colonic Crohn's disease compared with patients with ulcerative colitis who were well matched for age and year of onset of disease and were attending the same clinics. The Department of Health and Social Security's figures for oral contraceptive usage in 1975, while not strictly comparable, suggest that use of oral contraception before the onset of disease is greater than expected in women with colonic Crohn's disease rather than less than expected in women with ulcerative colitis. The association between usage of oral contraceptives and colonic Crohn's disease is supported by the finding that among patients with Crohn's disease in Birmingham isolated disease of the colon is at least twice as common among women than men.

Oral contraceptives may rarely predispose to ischaemic colitis,^{1 12-21} and this might be misdiagnosed as Crohn's disease. None of the barium studies in the patients reported on here, however, showed the typical radiological features of ischaemic colitis, although this does not exclude the possibility that the observed changes in colitis associated with use of oral contraceptives are a sequel to ischaemia. The rectal sparing would be consistent with this, but the other features of the colitis and the skip lesions are much more typical of Crohn's disease.

Almost all the reported cases of colitis associated with use of oral contraceptives have been cases of non-granulomatous colitis

with rectal sparing. It is interesting, therefore, that the four patients in this study whose disease went into remission when they stopped taking oral contraceptives had non-granulomatous colitis whereas the two patients with granulomatous colitis who stopped taking oral contraceptives continued to have symptoms. This suggests that usage of oral contraceptives, rather than causing Crohn's disease, probably predisposes to a form of non-granulomatous colitis that is otherwise indistinguishable from colonic Crohn's disease. Final proof of this association will require further case reports of colitis associated with use of oral contraceptives coupled with evidence of relapse on rechallenge. Until this evidence is available it seems sensible to recommend alternative forms of contraception to women who present with non-granulomatous colitis while taking oral contraceptives.

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