Male fertility in Crohn's disease

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Summary: The fertility of 70 men with Crohn's disease and a group of age matched controls were compared. Crohn's disease was associated with a significant reduction in family size independent of steroid or sulphasalazine treatment.

Introduction

Impaired fertility is sometimes a problem in both men and women with Crohn's disease. The fertility of men with Crohn's disease (Birnie *et al.*, 1981; Freeman *et al.*, 1982; Levi *et al.*, 1979; O'Morain *et al.*, 1984; Summers *et al.*, 1979; Toth, 1979; Toovey *et al.*, 1981) may be reduced by sulphasalazine due to its effect on sperm, or simply as a consequence of the disease itself. We have examined fertility in a group of male patients from South Wales and have attempted to assess the effect of various drug treatments.

Methods

Patients and controls

Seventy men with Crohn's disease aged between 19 and 79 were interviewed, as well as healthy controls who were matched for the same year of birth. Forty-eight patients had been married and 45 of them were married at the time of the interview (Table I).

Controls were healthy subjects who were either hospital administrative staff or orthopaedic out-patients with fractures. Medical and nursing staff were specifically excluded as controls. None of the controls had previously received treatment with sulphasalazine or azathioprine for periods greater than 6 months. They were matched exactly for year of birth with a patient and were asked the same questions about marital status, reproductive history and drug treatment.

Details of the site of disease were recorded for the 48 married men and the largest group (22 patients) had ileocaecal involvement. Nine patients had colorectal disease, five small bowel and 12 had extensive disease

involving two or more sites. The mean age at marriage and diagnosis was similar in all groups, as was the age at the time of the survey.

Details of treatment with sulphasalazine, corticosteroids and azathioprine or combinations of these drugs for periods greater than 6 months were also recorded (Table III).

Marital status and family size

Fifty-three of the controls had been married and 44 of them remained married. Forty-two matched pairs of patients and controls were married at the time of the survey. Although not specifically matched for age at marriage, this was 24 years (± 5 years) for both patients and controls and the mean interval since marriage was 18 years. Single subjects were analysed as well as married couples as such patients may have cohabited and fathered children while not married. Their single status may also be a reflection of the disease.

To study family size a 'critical date' was determined for each subject. In the patients this was the year of diagnosis. Each patient's critical date was also assigned to his individually matched control. For each patient and control a note was made of the number of children before and after the critical date.

Statistical analysis

The main analyses related to differences between the 42 married patients with their married controls; in addition the total groups of married patients (48) and married controls (53) were compared. Paired *t* tests were used to compare age at marriage in these groups, Wilcoxon tests and Mann U Whitney tests and paired *t* tests were used to compare numbers of children. The number of offspring of patients using steroids or

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sulphasalazine for longer than 6 months were compared by χ^2 with continuity correction (Table III).

Results

Patients with Crohn's disease were married, on average, 6 years before the diagnosis of their disease and this study of fertility took place a mean of 12 years after diagnosis (Table I). Consequently, family size before and after diagnosis could be recorded. In both cases and controls the majority of children were born before the critical date (Figure 1). Before diagnosis, all married patients had a mean of 1.2 children compared with 1.5 children for the married controls. However, after diagnosis, patients had significantly fewer children than controls (0.4 children compared with 0.8;

$t = -2.06$; $P < 0.04$; non-parametric tests $P < 0.05$). When only the 42 married pairs were considered the difference was highly significant (Table II and Figure 1, $P < 0.008$; non-parametric tests $P < 0.05$). This significant reduction in family size was independent of the site of disease. The 12 married men with extensive disease had seven children, the 22 men with ileocaecal disease had 6 children, the nine men with colorectal disease three children and the five married men with small bowel disease had three children after diagnosis. The reduction in family size was also independent of sulphasalazine and steroid therapy (Table III). The mean number of children fathered by men on steroids was 0.2 ± 0.5 compared with 0.5 ± 0.9 in those who had received steroids for less than 6 months but this difference was not statistically significant (Table III). It is clear that the decrease in fertility is unlikely to be due solely to drug therapy.

Table I Details of marital status in 70 men with Crohn's disease and age-matched controls. Forty-eight patients and fifty-three controls had been married at some time.

	Patients with Crohn's disease n = 70	Controls n = 70
Marital status:		
Single	22	17
Married	45	44
Divorced	2	9
Widowed	1	0
Mean age at marriage (mean $\pm$ s.d.)	24 $\pm$ 5	24 $\pm$ 5
Mean age at diagnosis (mean $\pm$ s.d.)	30 $\pm$ 12	
Mean age at survey (mean $\pm$ s.d.)	42 $\pm$ 13	42 $\pm$ 13

Discussion

Between 1975 and 1980 married people in Great Britain were reported to have between 1.9 and 2.1 children (Wermer, 1984). Our controls had a total of 2.3 children compared with 1.6 for men with Crohn's disease. In a separate multicentre study (Mayberry & Weterman, 1986) of women with Crohn's disease, 224 patients in South Wales had a mean of 1.6 children compared with a mean of 1.9 children born to 208 matched control subjects. The fertility of our controls is similar to that of the general population but Crohn's disease is associated with reduced fertility, which may be due to ill health or a direct manifestation of the disease. Chronic ill health itself may result in a desire not to increase family size and lead to increased use of contraception. This was not the case in the multicentre study of women with Crohn's disease. The

Table II Fertility before and after the diagnosis of Crohn's disease

	Before diagnosis		After diagnosis		Significance		
	Patients with Crohn's disease	Controls	Patients with Crohn's disease	Controls	t	t test	Non- parametric
All subjects (n = 70)	0.8 $\pm$ 1.1‡	1.1 $\pm$ 1.4	0.3 $\pm$ 0.7	0.6 $\pm$ 1.0	- 2.85	$P < 0.006$	$P < 0.05$
Married pairs (n = 42)	1.2 $\pm$ 1.1	1.5 $\pm$ 1.4	0.3 $\pm$ 0.7	0.7 $\pm$ 1.1	- 2.79	$P < 0.008$	$P < 0.05$
Ever married* (n = 48 patients; n = 53 controls)	1.4 $\pm$ 1.1	1.6 $\pm$ 1.4	0.4 $\pm$ 0.8	0.8 $\pm$ 1.1	- 2.06	$P < 0.04$	$P < 0.05$

‡ The numbers refer to mean numbers of children ($\pm$ s.d.)/patient or control
* In the case of controls, this refers to the comparable period after diagnosis in their age matched patients six of whom remained single.

Figure 1 Family size (a) before and (b) after the critical date in 42 patients with Crohn's disease (■; $n = 42$) compared with their age matched controls (□; $n = 42$) who were also married.

Table III Effect of drug therapy on the fertility of 48 men with Crohn's disease who had been married at some time. Eighteen had received no drugs since diagnosis, 12 had received steroids and sulphasalazine, 9 sulphasalazine alone, 6 steroids alone, 2 steroids, sulphasalazine azathioprine and in one case azathioprine and steroids ($n = 48$). The three men given azathioprine had no children after diagnosis. None of the differences between these groups reached statistical significance on parametric or non-parametric testing.

	Steroids ($n = 48$)		Sulphasalazine ($n = 48$)	
	Treatment for 6 months or longer ($n = 21$) (Mean $\pm$ s.d.)	No treatment with steroids or treatment for less than 6 months ($n = 27$) (Mean $\pm$ s.d.)	Treatment for 6 months or longer ($n = 23$) (Mean $\pm$ s.d.)	No treatment with sulphasalazine or treatment for less than 6 months ($n = 25$) (Mean $\pm$ s.d.)
Age:				
At diagnosis	33 $\pm$ 9	32 $\pm$ 11	33 $\pm$ 11	31 $\pm$ 10
At marriage	25 $\pm$ 5	25 $\pm$ 4	25 $\pm$ 4	25 $\pm$ 4
At survey	43 $\pm$ 12	47 $\pm$ 10	44 $\pm$ 12	47 $\pm$ 11
No. of children:				
Before diagnosis	1.1 $\pm$ 1.1	1.3 $\pm$ 1.2	1.2 $\pm$ 1.2	1.3 $\pm$ 1.2
After diagnosis	0.2 $\pm$ 0.5	0.5 $\pm$ 0.9	0.4 $\pm$ 0.9	0.4 $\pm$ 0.6

role of drugs and surgery needs to be assessed in a larger survey, preferably involving several countries. There is clear evidence that sulphasalazine reduces sperm motility (Toth, 1979), increases the proportion

of abnormal forms (O'Morain *et al.*, 1984) and increases oligospermia (Birnie *et al.*, 1981), but its role in the reduced fertility of men with Crohn's disease needs further elucidation.

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