PEPTIC ULCERATION AND THE USE OF ORAL CONTRACEPTIVES

A NEGATIVE CORRELATION ATTRIBUTABLE TO THE DISEASE

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The development of active peptic ulceration during pregnancy is widely regarded as uncommon, and, in the case reports that have been published, ulcer activity occurred close to the time of delivery (Sandweiss, Saltzstein, and Farbman, 1939; Jones, 1947; Rider, Kirsner, and Palmer, 1953). Furthermore, pregnancy is believed to have a beneficial influence on the course of pre-existing acute peptic ulceration (Clark, 1953). These observations have prompted therapeutic trials using synthetic analogues of the hormones that are normally elevated during pregnancy, some of which appear to have shown that oestrogens may have a favourable effect on the healing of both gastric and duodenal ulcers (Truelove, 1960; Doll, Hill, and Hutton, 1965; Parbhoo and Johnston, 1966). It occurred to us that the use of oral contraceptives containing oestrogen might reduce the risk of peptic ulceration, and a pilot study was undertaken to examine this hypothesis.

SUBJECTS AND METHODS

A list of all married women aged 20 to 44 years who had been discharged from hospitals in the Oxford and Reading area during the years 1965-7 with a diagnosis of peptic ulcer was prepared from the files of the Oxford Record Linkage Study (Acheson, 1968). Additional names for the years 1968-9 were obtained from the central diagnostic index of the Radcliffe Infirmary and Churchill Hospital at Oxford.

In this way, 75 women recorded as having suffered from peptic ulcer were identified. The hospital records of each of these patients were reviewed by one of us (G.G.), and 10 were discarded because our diagnostic criteria were not fulfilled (that is, either confirmation of ulceration at operation or endoscopy, or demonstration of an ulcer niche in at least two separate barium meal examinations). A further 19 patients were excluded be-

cause they were postmenopausal (8); were widowed, divorced or separated (5); had experienced previous ulcer surgery (2); had died (2); or had left the country (2). Seven of the remaining 46 patients had been admitted for ulcer symptoms occurring during the week preceding hospital admission in the absence of earlier symptomatology, while the remainder had all had a more chronic illness.

Permission to visit the 46 patients was obtained from consultants and family doctors, and they were interviewed in their homes by a medical social worker experienced in research (Mrs. Eva Goldenberg). Questions were asked about each patient's medical, obstetrical, social, and contraceptive histories. An attempt was also made to ascertain whether any decision not to use contraception was related to ulcer symptoms.

For comparative purposes, two married premenopausal control patients were matched by age (within five-year groups), parity (within groups of 1-2, and 3 or more deliveries), and year of hospital admission, with each of the 46 patients with peptic ulceration, save for one for whom suitable controls could not be found. The 90 successfully matched controls were selected from hospitals in the same areas as those to which the patients with peptic ulceration had been admitted. All had undergone routine, non-gynaecological surgical procedures of which the most common were appendicectomy (35), cholecystectomy (19), dental extraction (12), E.N.T. operations (8), and repair of minor trauma (7). Eighty-eight of these controls were successfully interviewed while the remaining two completed postal questionnaires.

RESULTS

None of the 45 patients with peptic ulcer who were successfully matched with controls had been using oral contraceptives during the three months preceding admission to hospital, nor had the one remaining unmatched patient. In contrast, 12 (13.3%) of the 90 corresponding control patients had been

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TABLE I

USE OF CONTRACEPTION DURING 3 MONTHS BEFORE ADMISSION TO HOSPITAL BY PATIENTS WITH PEPTIC ULCER AND MATCHED CONTROLS

Method of Contraception	No. of Patients	
	Peptic Ulcer	Control
Oral	0 (0.0)*	12 (13.3)
Other	16 (35.6)	57 (63.4)
None	29 (64.4)	21 (23.3)
Total	45 (100.0)	90 (100.0)

*Percentages in parentheses.

Ten triads contributed to the test of significance for a difference between the use of oral contraceptives by the peptic ulcer patients and the controls by the method of Pike and Morrow (1970) referred to in the text. In two of these triads, both controls used oral contraceptives, while in eight triads only one did so.

doing so. This difference between the groups is statistically significant ($\chi^2 = 5.5$, D.F. = 1, $P = 0.02$) when tested by the method of Pike and Morrow (1970).

Further examination of the data, however, showed that the use of methods of contraception other than oral was also very much less frequent among the patients with peptic ulcer than among the controls (Table I). As a result, when the comparison of the frequency of use of oral contraceptives between the two groups was restricted to those patients who were using some method of birth control (that is 0/16 against 12/69), the difference between them was no longer statistically significant ($\chi^2 = 2.0$, D.F. = 1, $0.20 > P > 0.10$)*.

What is the explanation for the very high proportion of patients with peptic ulcer who were not using any method of contraception during the three months prior to admission to hospital? Clearly this finding cannot be attributed to marital status, age, or parity because the control patients were matched on these characteristics. The patients with peptic ulcer were also found to be comparable with the controls with respect to country of origin and religion. Social class differences between the groups, on the other hand, were large, many more of the peptic ulcer patients than the controls coming from the lower social classes. This difference, which is consistent with the known tendency for peptic ulceration (especially of the stomach) to occur in the semiskilled and unskilled rather than in the professional and managerial classes (Doll, 1964), does not, however, explain the infrequent use of contraceptive methods by the patients with peptic ulcer (Table II).

Another possible explanation that occurred to us was that the patients with peptic ulcer might

*In this instance, the test of significance used was the standard χ^2 test for 2×2 tables since restricting the comparison to those patients using some method of birth control disrupted the matched triads.

TABLE II

USE OF CONTRACEPTION DURING 3 MONTHS BEFORE ADMISSION TO HOSPITAL BY PATIENTS WITH PEPTIC ULCER AND MATCHED CONTROLS IN RELATION TO SOCIAL CLASS

Social Class	Method of Contraception	No. of Patients	
		Peptic Ulcer	Control*
I-II	Oral	0 (0.0)†	2 (8.7)
	Other	1 (25.0)	14 (60.9)
	None	3 (75.0)	7 (30.4)
	Total	4 (100.0)	23 (100.0)
III	Oral	0 (0.0)	6 (12.7)
	Other	9 (34.6)	31 (66.0)
	None	17 (65.4)	10 (21.3)
	Total	26 (100.0)	47 (100.0)
IV-V	Oral	0 (0.0)	3 (21.4)
	Other	6 (40.0)	9 (64.3)
	None	9 (60.0)	2 (14.3)
	Total	15 (100.0)	14 (100.0)

*6 wives of servicemen and students omitted.

†Percentages in parentheses.

have felt too ill to have sexual intercourse during the three months preceding hospital admission and would not, therefore, have required any contraception. Accordingly, we examined the reasons given by the peptic ulcer patients and the controls who were using no method of birth control as to why this was their practice. Table III shows that only 4 of the 29 peptic ulcer patients specifically stated that they were too ill to have intercourse, but it may be noted that another 11 commented that their illness had been sufficiently severe to interrupt their normal pattern of living and to disturb their family relationships (of these 11, the reason given as to why contraception was not being used was infertility or subfertility in 4, infrequent intercourse in 2, religious convictions in 1, and 'no special reason' in 4). Table III also suggests that an unexpectedly high proportion of the patients with peptic ulcer were not using contraception because they were infertile or subfertile. However, the parity distribution of the ulcer patients (no deliveries, 3; one or two deliveries, 31; three or

TABLE III

REASONS GIVEN BY PEPTIC ULCER PATIENTS AND CONTROLS AS TO WHY NO METHOD OF BIRTH CONTROL WAS BEING USED

Reason given	No. of Patients	
	Peptic Ulcer	Control
Infertile or subfertile	9	6
Infrequent intercourse	5	3
Religious convictions	2	1
Too ill for intercourse	4	0
No special reason	9	11
Total	29	21

more deliveries, 11) is unremarkable and suggests that this difference between the groups may be a chance finding.

DISCUSSION

At first sight, the results of this investigation appeared to be compatible with the hypothesis that oral contraceptives offer some protection against peptic ulceration. Closer examination of the data, however, showed that the most likely explanation for the findings is that patients with peptic ulceration are less likely to use oral contraceptives (and other methods of birth control) than other women, probably because the severity of the disease reduces the frequency of sexual intercourse.

An interesting contrast to these findings is provided by the study of Vessey and Doll (1968, 1969) into the relationship between oral contraceptives and deep vein thrombosis and pulmonary embolism. The relevant data are shown in Table IV. Among the patients who were not using oral contraceptives, the use of other methods of contraception, or of no method, was closely similar in the group of patients with thromboembolism and in the controls.

SUMMARY

Of 45 married female patients aged 20 to 44 years, discharged from hospitals in the Oxford area during 1965-9 with a diagnosis of peptic ulceration,

TABLE IV
CONTRACEPTIVE PRACTICES OF PATIENTS INCLUDED IN STUDY OF VESSEY AND DOLL (1968, 1969) DURING MONTH PRECEDING ONSET OF ILLNESS

Method of Contraception	No. of Patients	
	Thromboembolism	Control
Oral	42	23
Non-oral		
Otherwise no information	14 (33.3)*	35 (24.1)
Other methods	19 (45.3)	84 (58.0)
No method	9 (21.4)	26 (17.9)
Total	42 (100.0)	145 (100.0)
Total	84	168

*Percentages in parentheses.

All women were asked about their use of oral contraceptives. In the early stages of the study, however, no woman was asked about her use of methods of contraception other than oral, and throughout the study this question was not asked of women completing postal questionnaires. This accounts for the 49 women in the 'not oral—otherwise no information' category. It may be noted that if the 35 controls in this category are allocated proportionately to the 'other methods' and 'no method' categories, it is then estimated that 13.7% of the controls were using oral contraceptives, 65.9% were using other methods, and 20.4% were using no method, percentages almost identical to those shown for controls in Table I.

none had been using oral contraceptives during the three months prior to admission. By contrast, 12 of 90 control patients had been doing so. This difference, however, may be attributed to reduced sexual activity among women suffering from peptic ulceration and it is not necessary to postulate any protective effect of oral contraceptives against the disease.

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