Recurrent pregnancies during oral contraception

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SUMMARY. The records of the Royal College of General Practitioners' Oral Contraception Study were examined for those women who had become pregnant while using combined oral contraceptive pills. Analysis reveals that these women are much more likely than average to have further failures if they resume taking the Pill (seven failures in 35 women-years, compared with one in 500 women-years for the whole study). This finding could occur through some factor in the patient's personality (patient failure) or through some factor in the patient's metabolism.

Introduction

There are three types of oral contraceptive: combined, sequential, and progestogen-only preparations. Sequential and progestogen-only preparations are little used, and most of them have higher failure rates than combined formulations. For this reason this article is concerned mainly with combined products.

The *FPA Reviewed List of Contraceptives* (1972) includes clinical trials of combined pills. The trials involved 2,905 women in over 47,074 cycles, with six involuntary pregnancies. One of these pregnancies was noted to have occurred in a woman who had had a previous pregnancy while taking a combined oral contraceptive. This suggested that it might be fruitful to investigate the failure rate of combined pills in women who had a history of becoming pregnant while being prescribed an oral contraceptive.

Aims

When a woman relying on the Pill becomes pregnant, she and her partner are likely to seek medical advice on how to avoid further unintended pregnancies. One of the aims of this investigation is to improve the quality of such advice.

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Method

I made a systematic search of other clinical trials of combined pills. Again the proportion of pregnancies where a history of previous failure with oral contraception was mentioned was higher than I should have expected had such a history been unimportant. I continued this search until June 1976 when the data involved 51,655 women over 42,068 women-years with 127 pregnancies. In two trials (Bye and Elstein, 1973; Bergstein *et al.*, 1974), a pregnancy was noted in a woman with a history of previous failure with oral contraception.

I also interviewed 104 women after termination of pregnancy at Birmingham. Forty-two of these women had tried combined oral contraceptives for a total of 94 women-years, with a total of six unintended pregnancies. Two women had relied on the Pill, after a previous failure, for 2·8 woman-years. One of these women had a second inadvertent pregnancy; both conceptions seemed to have occurred when the Pill was being taken according to directions. In view of the rarity of recurrent apparent method failures her case history is given as an appendix. The other four failures seemed to be patient failures.

Taken together the data seemed suggestive, but not conclusive, that women with a history of pregnancy while using combined pills were far more likely than average to have further failures if they resumed the Pill.

Oral Contraception Study

The Royal College of General Practitioners' Oral Contraception Study is a long-term prospective survey in which 23,000 pill users and 23,000 controls were enrolled in 14 months beginning in May 1968. The Royal College of General Practitioners (1974) described this study in detail in *Oral Contraceptives and Health*. I thought that material from this study might clarify the

risk of recurrent failure during oral contraception, and in early summer 1975 I approached the staff of the study for further data.

Methods

By April 1976 there were records of 166 women with inadvertent pregnancies during the RCGP study. Between October 1975 and June 1976 the staff of the RCGP study made four searches for these records, and sent me photostats of about 1,500 record sheets for 126 of the 166 women. The records of 40 women, about 600 record sheets, were not photocopied because in each case, apparently, one or more of the record sheets was out of file for special processing.

After June 1976 the staff of the RCGP study could not spare the time and effort to search again for the remaining records. However, they saw no reason why the missing material should bias the results analyzed here. They also provided me with additional data from the study.

Where a record stated that a woman had become pregnant while in the RCGP study, and taking an oral contraceptive, the event was classified as a 'failure'.

Failures

Failures were subdivided into:

1. *Apparent method failures* when the record stated that the Pill appeared to have been taken according to directions, and no misgivings on the trustworthiness of the history were expressed.

2. *Possible method failures* when there was no special evidence that the Pill had been taken according to directions, but no mention that tablets had been missed.

3. *Patient failures* where conception occurred in a month when the Pill had not been taken as directed.

4. *Dubious failures* if there was any doubt that pregnancy had occurred, or if there was some likelihood that the woman had not been in the study or had not taken the Pill at all during the month of conception.

When analysis was restricted to combined products, any experience a woman had taking another type of oral contraceptive was classified as if she were not on the Pill at that time.

The tests of statistical significance made were based on the Poisson distribution.

Results

In the RCGP study there were 166 'inadvertent pregnancies' with oral contraceptives. The time at risk was 63,705 women-years for combined preparations, and 1,183 women-years for other oral contraceptives.

My copies of record sheets from the RCGP study included details of 90 women who had had 97 failures with combined pills: the estimated time at risk was $63,705 \times 126/166 = 48,354$ women-years, equivalent to one failure in about 500 women-years.

The RCGP data contained records of a further 14 women who had each had a failure with other types of oral contraceptives (mainly sequentials): the estimated time at risk was $1,183 \times 126/166 = 898$ women-years. The difference in failure rates between the combined and other types of pills is unlikely to have happened by chance alone ($p<0.01$).

The records of the remaining 22 women, although classified as containing details of inadvertent pregnancies in the RCGP study, did not mention any failures as defined in the methods section. This remainder included 12 women in whom the start of the last menstrual period before the pregnancy, occurred after oral contraception had been stopped; four women who had conceived before entry into the study; and four women who became inadvertently pregnant before starting the Pill.

Reverting to combined preparations, Table 1 shows that the risk of pregnancy was far greater where there was a history of previous failure. It made surprisingly little difference whether the previous failure had been definite or doubtful.

There were seven failures in 35 women-years. If the history of previous failure was unimportant, and there were no uncertainties over classification, the likelihood of the observed figures happening by chance is extremely remote ($p < 0.000001$).

Table 2 shows that a history of failure increases the risk of failure in each subgroup.

Discussion

One of the assumptions made in the statistical interpretation was that there were no uncertainties in classifying

Table 1. Women who resumed Pill after failure classified according to type of their first failure.

	Number who resumed Pill	Failures	Years method at risk
Experience after apparent method failure	4	0	5.75
Experience after possible method failure	17	4	16.28
Experience after patient failure	6	1	2.42
Experience after dubious failure	9	2	10.67
Total	36	7	35.12

Table 2. Experience with each subgroup of first and second failures.

	First failures (Exposure 48,319 women/years		*Second failures (Exposure 35.1 women-years)*	
	Numbers	Failures/woman-year × 100 (99 per cent confidence limits)	Numbers	Failures/woman-year × 100 (99 per cent confidence limits)
Apparent method failures	9	0.019 (0.0065—0.041)	1	2.8 (*0.014—21)
Possible method failures	34	0.070 (0.043—0.11)	2	5.7 (0.29—26)
Patient failures	25	0.052 (0.029—0.085)	2	5.7 (0.29—26)
Dubious failures	22	0.046 (0.024—0.077)	2	5.7 (0.29—26)
Total of failures	90	0.19 (0.14—0.24)	7	20 (5.8—48)

*This lower limit becomes 0.072 if 95 per cent confidence limits are used.

failures. This assumption is not fully justified even where as much care has been taken over the case histories as in the RCGP study. The diagnosis of oral contraceptive failure depends on the history given by the patient. People are sometimes inaccurate and occasionally deliberately misleading when giving a contraceptive history. Further possible sources of error include difficulties in distinguishing early miscarriage from other causes of vaginal bleeding, and ambiguities and inaccuracies in the records, or their interpretation.

Seven recurrent failures were mentioned in my photostats of record sheets from the RCGP study. If one had perfect knowledge of the populations involved, and found there were only two recurrent failures in 35 woman-years and that the total failure rate was unchanged, then the increased tendency to recurrent failure would still be significant at the one per cent level.

Thus the data described give strong empirical evidence for some women having accident-proneness with combined pills. This would remain true even if none of the 'missing' inadvertent pregnancy records had involved a recurrent failure with combined pills.

In most cases of apparent method failure with combined pills no special reason for the failure, such as drug interaction or persistent diarrhoea, was recorded. Such cases might be explained if a few women possessed metabolic peculiarities that make the Pill less effective in ways that are unrecognized at present.

Such metabolic peculiarities might also explain recurrent failures with combined pills. According to this explanation some patient failures may be due more to unusual metabolisms than forgetfulness in tablet taking.

Alternatively, it can be argued that a failure with oral contraception is usually a patient failure, and that a woman who is careless on one occasion is more likely than average to make the same mistake again. According to this view, any recurrent failure with oral contraception is virtually certain to be a patient failure. It could be further argued that such a patient and her partner might be less reliable than average with other contraceptive methods.

Advice for patients

What advice may be given to a woman after contraceptive failure with a combined pill? She might be warned that such pills may not give her and her partner very good protection against pregnancy, and that other methods, particularly sterilization if their family is complete, are likely to be more suitable.

It should be remembered that, except for effectiveness, the factors that made them decide on the Pill may be unchanged.

Case history

Mrs A. gave a detailed history. She gave me permission to examine her FPA clinic records and to discuss her case with her general practitioner. The histories from all sources agreed, and her general practitioner regarded the case as a genuine method failure.

Mrs A. was born in 1937, her general health was good, her periods had been regular, 5-7/28, when not on the Pill, and there was no history of serious illness. Her husband was a bus driver, they had married in 1958 and had two children born July 1964 and February 1967. She conceived within a month of trying for the first pregnancy. The second pregnancy was not intended and followed a condom bursting. In July 1968 she was prescribed 'Orthonovin'. Her weight was 56·7 kg (8 st 13 lb), and her blood pressure was 120/70 mm Hg. In January 1969 she changed to 'Orthonovin 1/80'; her blood pressure was 130/80. In April 1969 she came off the Pill because of headaches during the week between packs, and because of weight gain.

The couple relied on coitus interruptus until November 1971 when Mrs A. was prescribed 'Minovlar', to start December 1971. In January 1973 she was found to be pregnant after three months' amenorrhoea. The pregnancy was terminated on 19 January 1973, and she was prescribed 'Ovulen 50'.

In November 1974 she "missed a period". Her periods usually started the day before she finished her pack of pills, but two months before this amenorrhoea her period had been a week early. On 20 November a 'Prepurex' pregnancy test was positive. The pregnancy was terminated on 28 November; placental tissue was noted at the operation.

She was of average physique and unremarkable appearance. Her weight was recorded on ten occasions be-

tween July 1968 and October 1974; it varied between 56·7 and 69·9 kg (8 st 13 lb and 11 st).

She was sure that at the time of her two most recent conceptions she had taken her pills according to directions, and had taken no other form of medication.

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Pharmaceutical evidence to the Royal Commission on the NHS

Great emphasis is placed upon the need to recognize pharmacists' potential contribution to primary health care. Thus, it is suggested to the Commission that the general public should be encouraged to seek advice on the treatment of minor ailments from persons with knowledge of the health sciences, and that all advertisements for proprietary medicines should be banned. Moreover, it is pointed out that if pharmacists could supply certain prescription-only medicines, subject to suitable conditions, they would be helped to extend their contribution to primary health care and thus reduce the cost of medicine provided by the NHS.

It is argued that pharmacists' NHS remuneration should include a significant element to recognize their contributions to primary health care, in terms of advice to the general public and allied professions, and to their attendance at the pharmacy throughout opening hours. It is also urged that each health care planning team should include a representative of general-practice pharmacy and that domiciliary health care teams should include pharmacists. Emphasis is also laid on the role of pharmacists in the health education of the public.

Again they stress that dispensing should be the responsibility of pharmacists, except where the public would have difficulty obtaining prescriptions in this way.

They urge limitation of prescribing to 28 days' supply.

Reference

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