Contemporary Themes

Amenorrhoea after Discontinuing Combined Oestrogen-Progestogen Oral Contraceptives

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Summary

Out of 210 women seen at the Middlesex Hospital with secondary amenorrhoea the 63 who developed it after stopping oral contraceptives were fully investigated. Five had organic disease sufficient to account for the amenorrhoea (one had severe diabetes, one a pituitary tumour, and three premature ovarian failure); two patients had galactorrhoea (one of whom also had the pituitary tumour); two had anorexia nervosa.

Of the 63 women 40 (63%) had suffered from amenorrhoea or prolonged or irregular menstrual cycles before taking the pill, and this suggested that combined oestrogen-progestogen oral contraceptives should be used with caution for women with irregular menstruation.

Nineteen patients wished to become pregnant and 12 have so far done so after treatment with clomiphene or gonadotrophins.

In another study 204 women recorded when their first menstrual cycle occurred after stopping the pill. Seventy-four had a cycle longer than five weeks but only five exceeded three months, and only one of the five had more than six months' amenorrhoea. These results confirm that the incidence of amenorrhoea after stopping oral contraceptives is low.

Introduction

Amenorrhoea in women who have stopped taking combined oestrogen-progestogen oral contraceptives was first described in 1966. There has been a series of reports of a few cases, relating mainly to patients in Australia and the United States of America. Shearman and Smith¹ described 96 cases with over 12 months' amenorrhoea after stopping contraceptives, and Golditch² reported on 41 patients. Because amenorrhoea may be a symptom of serious disease and because of the implications for fertility this condition has caused patients and doctors some anxiety. The incidence appears to be small. Golditch² reported an incidence of 2.2 per thousand women. Nonetheless, it has been suggested that the incidence may be reduced by advising women with a history of amenorrhoea or irregular periods against the use of combined oral contraceptives.

The condition has been discussed twice in the *British Medical Journal*^{3,4} and more information is needed on the women affected, the prognosis, and the best management with particular reference to the United Kingdom since there may be geographical or racial variation. Several authors⁵⁻⁷ have described a high incidence of galactorrhoea but this has not been noted in Britain.

We record our experience with patients seen at the Middlesex Hospital since 1969 and compare this series with others already published. We have also conducted a prospective study on a series of women stopping oral contraceptives to ascertain the length of the first cycle.

Patients

Sixty-three patients were seen by one of us (S.J.S.) for investigation of amenorrhoea lasting longer than six months and after oral contraception (52 had over 12 months' amenorrhoea). All were interviewed and a careful history was taken with particular reference to the earlier menstrual history and to any other factors such as dieting, travel, and emotional disturbance which might relate to the amenorrhoea. A routine medical and gynaecological examination was carried out. All patients underwent a skull x-ray examination to exclude any lesion in the region of the pituitary fossa and this was repeated in one patient with galactorrhoea and a negative first x-ray result. Tests of pituitary, thyroid, and adrenal function and endometrial biopsy, laparoscopy, and ovarian biopsy were carried out in patients in whom spontaneous menstruation did not return and in those complaining of infertility who did not respond to treatment with clomiphene. If the husbands were apparently fertile patients wishing to become pregnant were treated with clomiphene initially and with human menopausal gonadotrophin (Pergonal) if there was no response to clomiphene and no contraindication to gonadotrophin therapy. In all patients the object was to exclude serious disease, and to treat the infertility or to obtain evidence that the patient was at least potentially fertile.

A total of 204 women seen at the Margaret Pyke Centre for the Study of Fertility kept a record of their first menstrual cycle after stopping oral contraceptives. Details of their age, parity, and previous cycle were recorded when they stopped the pill.

Results

These 63 patients represented 30% of the 210 patients seen by S.J.S. with secondary amenorrhoea during this period. The menarche, age, and parity of the patients are shown in table I, and the length of the menstrual cycle before taking the pill is given in table II. Nineteen women (30%) had previously had amenorrhoea and 33 (52%) had irregular or prolonged cycles or were amenorrhoeic at the time they started oral contraceptives. The contraceptive taken by each patient was recorded where

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possible but some were uncertain about the product they had taken and 32 had been given more than one preparation. No patient was noticeably hirsute but two had galactorrhoea.

Five patients had organic disease sufficient to account for the amenorrhoea. These included one patient with severe diabetes mellitus, one with a pituitary tumour, and three with premature ovarian failure. Four other patients had major changes of weight or emotional disturbances to which the amenorrhoea may have been related. Two of these had gained over a stone (6 kg) while taking the pill and one had subsequently dieted until she was diagnosed as having anorexia nervosa. Another had had a broken engagement and also appeared to have anorexia nervosa, while the fourth had worried excessively about examinations.

TABLE I—Menarche, Age and Parity in 63 Patients with Amenorrhoea

Menarche Age in Years	No.	Age in Years	No.	Parity	No.
11	5	Less than 20 ..	8	0	57
12	10	20-24	37	1	5
13	13	25-29	13	2 or more ..	1
14	20	30-34	3		
15	7	35 and over ..	2		
16 or over ..	8				

TABLE II—Cycle before Pill

	No. of Patients
Amenorrhoeic	6
Prolonged or Irregular	19
5 weeks-3 months (3 with previous amenorrhoea)	3
3-6 months (1 with previous amenorrhoea)	5
Gross irregularity (up to 1 year)	4
Regular (less than 5 weeks)	3
Previous amenorrhoea	23
Previously irregular	
Regular cycle	
A regular cycle is one which does not exceed 35 days. Amenorrhoea = more than six months without a period.	

Nineteen patients complained of infertility. The results of their treatment and the follow-up of the remaining 44 are shown in table III. Of the 19 patients treated 12 became pregnant.

The 204 patients in the prospective study were divided according to the length of their previous menstrual cycle. After stopping oral contraception seventy-four women (36.3%) had a cycle longer than five weeks, only 5 (2%) waited longer than three months, but only one of the five had more than six months' amenorrhoea (table IV).

TABLE III—Follow-up

	No. of Patients
Untreated	11
Spontaneous period	30
Continuing amenorrhoea	3
Ovarian failure	10
Treated with Clomiphene	7
No response	2
Pregnancy	
Ovulation	
Treated with Pergonal (no response to clomiphene)	5
Pregnancy	1
Ovulation	

TABLE IV—Length of First Spontaneous Cycle after Oral Contraception

Cycle after Pill	Cycle before Pill				Amenorrhoeic
	Up to 35 Days	35-90 Days	3-6 Months	6-12 Months	
Up to 35 days ..	116	11	1	—	—
35-90 days ..	50	16	—	2	—
3-6 months ..	4	—	—	—	1
Over 6 months ..	1	—	—	—	—
Pregnant	2	—	—	—	—

Discussion

The incidence of amenorrhoea after discontinuing contraceptives appears to be low. Golditch² reported a crude incidence of 2.2 per thousand in almost 20,000 women, Larsson-Cohn⁸ found only four patients with more than six months' amenorrhoea in a prospective study of 516, and Rice-Wray⁹ reported that 98% of patients started to ovulate within three months of stopping oral contraceptives. The low incidence in our series (one patient out of 204 with amenorrhoea persisting more than six months) agrees with the accepted low incidence of amenorrhoea after stopping the pill. The increased length of the first cycle seen in 36% of our patients is well recognized by obstetricians as a source of error in calculating the date of delivery when conception occurs during this cycle.

The low incidence of amenorrhoea is reassuring in view of the many patients now taking oral contraceptives. The fact that it occurs at all, however, is worrying to patients, and gynaecologists and endocrinologists are seeing more patients in this category. Shearman and Smith¹ reported that 41.7% of their patients with secondary amenorrhoea had developed it after taking the pill compared with 30% in our series.

Bender¹⁰ reported that what appeared to be amenorrhoea after discontinuing the pill might be a symptom of a pituitary tumour. We found a patient who, like Bender's, had galactorrhoea and a pituitary tumour. Nine of our 63 patients (14%) had amenorrhoea which was probably not or certainly not related to the pill, and possibly the pill-amenorrhoea sequence may be coincidental in other cases. The most significant feature in relation to future fertility is ovarian failure. Shearman¹¹ found two cases of premature menopause in 69 patients and we have found three cases in a series of 63. Two cases of anorexia nervosa in our series may be related to the pill since excessive dieting was started in an attempt to reduce weight which had increased by a stone (6 kg) or more while the patients took oral contraceptives. Clearly amenorrhoea after the pill is not necessarily caused by it. Serious disease such as a pituitary tumour must be excluded and other causes for the amenorrhoea eliminated. Finally, it is important for the patient to know whether she is potentially fertile even if she does not wish to become pregnant immediately. We ascertained this by measuring urinary or serum gonadotrophin levels and laparoscopy or by treatment with clomiphene.

It is desirable to identify women who may have a higher risk of amenorrhoea after taking oral contraceptives so that they may be warned of the possibility. The presence in our series of eight women who did not menstruate until after they were 16 is noteworthy and a late menarche may suggest caution in prescribing the pill.

The high incidence before taking the pill of prolonged or irregular cycles in 40 patients (63%), with amenorrhoea in 19 (30%), confirms the conclusion of Larsson-Cohn⁸ that "oral contraceptives should be used with caution in women who have irregular menstruation." It contrasts with the report by Shearman¹¹ that 45 of his 69 patients had a history of regular menstruation. Halbert and Christian⁶ found a history of menstrual abnormality in 25 of their 35 patients.

Nineteen of our patients (30%) had had amenorrhoea of more than six months' duration at some time, though only six were actually amenorrhoeic at the time they started oral contraception. Only 23 (37%) had had consistently regular cycles not longer than 35 days, while 40 (64%) had suffered amenorrhoea or irregular cycles.

It is usually stated that over half of potentially fertile patients treated to induce ovulation will respond. In our series 13 out of 19 responded by ovulating and 12 have so far become pregnant. Six of the 10 patients who did not respond to clomiphene were treated with human menopausal gonadotrophin and five achieved pregnancy.

Shearman¹¹⁻¹³ included patients in his series only when amenorrhoea had lasted longer than 12 months. Fifty-two of our 63 patients had more than 12 months' amenorrhoea but we

think that investigation and treatment may be justified before this. Amenorrhoea is a source of great anxiety to women and this is increased if a pregnancy is desired. The need to exclude serious disease, assess future fertility prospects, and reassure the patient indicates that six months is an appropriate interval, since not more than 1-2% will have amenorrhoea after discontinuing the pill at this time. The investigation need not be unduly extensive but should include an x-ray examination of the pituitary fossa, gonadotrophin measurements unless there is a satisfactory response to clomiphene, and any other tests indicated by the history or examination findings in individual patients.

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Female Narcotic Addicts: A Follow-up Study of Criminal and Addiction Careers

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Summary

A sample of 66 female narcotic addicts first examined in prison in 1967-8 was followed-up four years later. At the end of the period of follow-up 36% were off narcotics, 32% were still addicted, and 15% had died. Altogether 62% committed further offences. Drug offences and offences against property were almost equally frequent and accounted for over two-thirds of all convictions. There was no evidence of a link between prostitution and narcotic addiction. A significant association was found between continued delinquency and continued addiction during the period of follow-up. Addiction career and criminal career coincided in over three-quarters of the subjects, who tended either to continue manifesting both forms of deviant behaviour (46%) or to relinquish both (30%). The findings are in keeping with the view that narcotic addiction and crime are not causally related but may be parallel effects of common underlying factors leading to social deviance.

Introduction

The relation between narcotic addiction and crime is controversial and there has been much argument about its nature. One of the reasons for this controversy is the wide variation in the crime rates of narcotic addicts in different countries. Even within one country relatively rapid changes may occur in the social patterns of drug abuse,¹ with a consequent change in the relation to crime. In Britain there is much evidence that during the past decade delinquency has become a prominent characteristic of young narcotic addicts,²⁻³. A similar trend has occurred in the United States, where addicts are recruited more and more from persons with a criminal record.⁴ Vaillant⁵⁻⁶ noted

some of the similarities in the long-term careers of narcotic addicts and recidivist criminals, including the rate at which they give up delinquent activity. Long-term follow-up studies of delinquent addicts are of special interest when attempting to elucidate the natural history of crime and addiction and the relation between their criminal and addiction careers. The present study describes a four-to-five year follow-up of 66 female narcotic addicts first examined in Holloway Prison during the 18-month period January 1967 to June 1968.

Subjects and Methods

The sample comprised all women (whether on remand or serving a sentence) who were found on admission to be physically dependent on narcotics. Their social characteristics, history of drug abuse, and patterns of delinquency were described in the original study.⁷ A baseline follow-up was carried out in September 1968, three months after the collection of the sample. In September 1972 data were again obtained from the Drugs Branch of the Home Office on the addiction status of the subjects, deaths that had occurred, and admissions notified by hospitals. Data on continued delinquency were obtained from criminal records. The register of deaths at Somerset House was searched for the names of 31 subjects who at the end of the follow-up period were no longer on the Home Office index; no additional deaths were discovered through this source. Continued personal contact during the period of follow-up was possible with 31 subjects who were readmitted to Holloway. The mean length of follow-up from the time of entry into the cohort was four years 11 months, with a range of four years three months to five years nine months.

Results

ADDICTION CAREERS

The status of the subjects was assessed in September of each year during the period of follow-up (tables I and II). Several subjects were not at risk of being addicted owing to death, emigration, or institutional care (table I).

At the time of the baseline follow-up in 1968, 18 subjects

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