

PN-ABF-790

CR #630

67627

A Study of a Progestogen-Only Oral Contraceptive
for Lactating Women in São Paulo, Brazil

Prepared for
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March 1989

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I. Introduction

A non-comparative study of a progestogen-only oral contraceptive was conducted at the Centro de Estudos de Oncologie e Reproducao, São Paulo, Brazil. This center was part of a multicenter trial. This trial was designed to evaluate in breastfeeding women the discontinuation rate, reasons for discontinuation, the frequency of selected symptoms contributing to method discontinuation and contraceptive efficacy of the progestogen-only oral contraceptive (OC), Ovrette. Several studies have shown that lactation may be impaired by combined estrogen-progestogen oral contraceptives, including those with relatively low doses of estrogen.

Progestogen-only OCs offer an alternative to combination OCs for lactating women who desire steroidal contraception. Progestogen-only OCs may minimize a reduction in milk volume and length of lactation, and relative to combined OCs may have a lower incidence and lesser severity of non-menstrual, estrogen-related side effects associated with combined OCs. Progestogen-only OCs have been associated with disrupted menstrual cycles, mainly manifested as a higher incidence of both intermenstrual bleeding and amenorrhea.

II. Study Design

Oral Contraceptive Evaluated

The OC administered in this study was provided in 28-day packs of

28 active steroid tablets. Ovrette has a composition of 0.075 mg of the progestin, norgestrel.

Study Procedure

A total of 150 women were admitted to the study from January 1985 to April 1986. Women in good physical health with none of the standard contraindications for use of steroidal contraceptives were recruited for study participation. Due to the increased risk of irregular bleeding and possible ectopic pregnancy among progestogen-only pill users, undiagnosed abnormal genital bleeding or a history of ectopic pregnancy were considered as contraindications for admission to this study. In addition, each woman had to meet the following criteria: be 18 years of age or older, be sexually active, be recruited within 6 months (26 weeks) of delivery, be breastfeeding, desire to use oral contraceptives as a method of contraception, rely exclusively upon the pills as her only method of contraception throughout the course of the study, give informed consent and be accessible for regular follow-up through scheduled clinic appointments and home visits for at least 12 months. Each woman could be terminated from the study if she became pregnant, if any of the reasons for initial exclusion of patients from the study had occurred (except cessation of breastfeeding), if she missed three or more consecutive pills, or if she discontinued use of the progestogen-only OC for any reason.

Follow-up visits were scheduled at two, six and twelve months after admission to the study. Four women were not included in

this analysis because of protocol violations. Two patients were excluded from the analysis because they never began taking the pills. One patient was excluded for being 17 years old while the protocol specifies the age to be 18 years or older. One patient was excluded due to being pregnant before admission.

Of the 146 women included in the analysis, 100 women (68.5%) were interval patients, 42 days or greater since last pregnancy termination but within 26 weeks postpartum, and 46 (31.5%) were less than 42 days postpartum. All women were breastfeeding at admission.

Data from this study were recorded on standard forms by the clinic staff and were sent to Family Health International (FHI) for processing and analysis.

III. Results

Sociodemographic Characteristics

Selected patient characteristics are presented in Table I. Women admitted to the study had a mean age of 25.7 years. The mean education level was 6.0 years, and the mean total live births was 1.8.

Contraceptive Practice

Table I also presents a summary of the contraceptive practices of the women, one month prior to admission to the study for interval patients and one month prior to conception for postpartum

patients. Seventy-five women (51.4%) reported having used no contraception immediately prior to admission or conception. The predominant method employed was oral contraceptives--by 55 women (37.7%). Seventy-five women (51.4%) reported ever having used oral contraceptives prior to the study.

Complaints at Admission

None of the women reported a preexisting medical condition at admission. At admission, 127 women (87.0%) reported minor physical complaints (Table II). The most frequently reported complaints were headaches by 78 women (53.4%), vaginal discharge by 66 women (45.2%), and dizziness by 41 women (28.1%).

Regularity of Use

Regularity of use data were collected at two, six and twelve months after beginning oral contraceptive use. Compliance was assessed by self-report and from the date last pill taken prior to the date of follow-up visit contact. Follow-up visit data indicate that 25 women (18.2%) reported missing at least one pill during the study period. One woman was discontinued for incorrect pill use for having taken the pill twice a day.

Side Effects

Serious complications were reported by five women during the study period. Serious complications are based on the patients' interpretation as to problem severity. Three women reported severe headaches, one woman complained of visual problems and one of a skin rash/allergy. Of the three women who reported severe

headaches, one woman discontinued for headaches. The second woman discontinued for running out of pills and not being able "to come and get more". The third did not discontinue--but did not return for the subsequent follow-up visit. The woman who complained of visual problems discontinued for high blood pressure. The woman who complained of skin rash/allergy discontinued for that reason.

A summary of menstrual problems and complaints ever reported at all follow-up visits is shown in Table III. One hundred and thirty-seven women returned for at least one follow-up visit. One hundred and fourteen women (83.2%) reported at least one menstrual complaint during the study period. Of the 136 women who reported no intermenstrual bleeding at admission and returned for a follow-up visit, 61 (44.5%) reported it at some time during the study period. The one person who reported intermenstrual bleeding at admission did not report it at follow-up. One hundred and twenty-five women did not report other menstrual problems at admission. Of these women, 77 (56.2%) reported other menstrual problems (amenorrhea and dysmenorrhea in particular) at sometime during the study period.

A summary of other complaints ever reported at follow-up visits is presented in Tables IV and V and changes in complaints since admission in Table VI. A total of 116 women (84.7%) complained of the more common complaints--nausea through breast discomfort--in Table IV. Thirty-four women (24.8%) reported one or more less common complaints (Table V), the most often-cited

complaint was nervousness--reported by 8 women (5.8%). Thirty-eight women (27.7%) who had not reported nausea at admission reported the complaint at follow-up (Table VI). Other new reports include thirty-seven women (27.0%) who reported dizziness, 31 women (22.6%) who reported headaches, 26 women (19.0%) who reported vaginal discharge, and 18 women (13.1%) who reported breast discomfort.

A summary of significant changes in the percentage of women reporting complaints at admission and during follow-up is presented in Table VII. There were significant increases ($p < .01$) in reports since admission for intermenstrual bleeding ($\chi^2 = 56.1$), other menstrual complaints ($\chi^2 = 72.6$), nausea ($\chi^2 = 20.0$), and dizziness ($\chi^2 = 8.4$). Since the time periods for reporting a complaint since admission (e.g. 6 months from 6 to 12 months follow-up visit) were longer than the time period to report a complaint at admission (1 month prior to admission), there is a bias towards an increased reporting of complaints since admission.

One infant death occurred during the study. The child was approximately 4 months old and no Infant Death Report was completed. No further information is known about this incident.

Discontinuation Rates and Reasons

A summary of all reasons for discontinuation is presented in Table VIII. A total of seventy-six women (55.5%) discontinued from the study. The reason for discontinuation provided most

often was other personal reasons such as "desires change of method" and "fears method".

There were two pregnancies reported during the study period. One pregnancy occurred approximately two months after study admission and was attributed to method failure because the woman had reportedly taken Ovrette as scheduled. The second pregnancy occurred approximately three months after admission to the study. This pregnancy was also attributed to method failure because the woman reported taking the Ovrette as scheduled. The outcomes of both pregnancies were full term live births.

Two women returned to the clinic suspecting that they were pregnant. One woman was amenorrheic at her 12 month follow-up, but upon gynecological exam she was found to have an ovarian cyst of \pm 5 cm. The second woman suspected pregnancy at her 6 month follow-up, but a pregnancy was not confirmed by pregnancy test or ultrasound.

Gross cumulative life table discontinuation and event rates are presented in Table IX. The twelve month total discontinuation rate was 80.8, including a lost-to-follow-up rate of 30.8 at 12 months.

IV. Summary

A non-comparative study of the progestogen-only oral contraceptive, Ovrette, in breastfeeding women was conducted at

the Centro de Estudios de Oncologie e Reproducao, São Paulo, Brazil. The study was designed to evaluate the discontinuation rate, reasons for discontinuation and contraceptive efficacy of Ovrette in breastfeeding women. This report includes an analysis of 146 women, all of whom were less than 26 weeks postpartum at admission; 100 women were interval patients and 46 were less than 42 days postpartum. Follow-up visits were scheduled at two, six and twelve months after admission. Overall, women experienced increases in most of the common complaints associated with oral contraceptive use, with the greatest increases in nausea and dizziness. A total of 76 women (55.5%) discontinued from the study. The most common reasons for discontinuation were other personal reasons, such as "desires change of method" and patient "fears method". The total discontinuation rate (including those lost-to-follow-up) at 12 months was 80.8. The lost-to-follow-up rate was 30.8 at 12 months. There were two intrauterine pregnancies reported during the study period.

Table I
Selected Sociodemographic Characteristics

Characteristic	No. (N=146)	%
Age (years)		
Less than 20	27	18.5
20-24	48	32.9
25-29	42	28.8
30-34	18	12.3
35+	11	7.5
Mean		25.7
Education (years)		
None	3	2.1
1-6	76	52.0
7-12	62	42.5
13+	5	3.4
Mean		6.0
Total Live Births		
1	80	54.8
2	46	31.5
3	7	4.8
4	8	5.5
5	1	0.7
6+	4	2.7
Mean		1.8
Contraceptive method used in the month prior to admission or conception		
None	75	51.4
Orals	55	37.7
Withdrawal/rhythm	6	4.1
Condoms	4	2.7
Injectables	2	1.4
IUD	2	1.4
Foam/diaphragm/jelly	1	0.7
Other barrier methods	1	0.7

Table II
Complaints at Admission

Complaint	No. (N=146)	%
Intermenstrual bleeding		
None	145	99.3
Staining/spotting	1	0.7
Other menstrual complaints		
None	133	91.1
Amenorrhea	9	6.2
Dysmenorrhea	1	0.7
Scanty menses	1	0.7
Irregular menses	1	0.7
Lochia (continuing from childbirth)	1	0.7
Nausea	17	11.6
Vomiting	9	6.2
Headaches	78	53.4
Dizziness	41	28.1
Vaginal discharge	66	45.2
Breast discomfort	27	18.5
Total women with 1+ complaints	127	87.0

Multiple symptoms may be reported per woman.

Table III
Menstrual Complaints Since Admission

Complaint	No. (N=137)	%
Intermenstrual bleeding		
None	76	55.5
Staining/spotting	24	17.5
Moderate	30	21.9
Severe	7	5.1
Other menstrual complaints		
Amenorrhea	59	43.1
Dysmenorrhea	14	10.2
Irregular menses	11	8.0
Scanty menses	9	6.6
Late menses	2	1.5
Menorrhagia	1	0.7
Polymenorrhea	1	0.7
Intermenstrual pelvic discomfort or cramps	1	0.7
Total women with 1+ menstrual complaints	114	83.2

Multiple symptoms may be reported per woman.
N represents number of women followed up.

Table IV
Other Complaints Since Admission

Complaint	No. (N=137)	%
Nausea	47	34.3
Vomiting	17	12.4
Headaches	83	60.6
Dizziness	59	43.1
Vaginal Discharge	69	50.4
Breast Discomfort	27	19.7
Total women with 1+ of the above complaints	116	84.7

Multiple symptoms may be reported per woman.
N represents number of women followed up.

Table V
Other Complaints Since Admission

Complaint	No. (N=137)	%
Weight gain	2	1.5
Headaches	1	0.7
Vaginal monilia	1	0.7
Fever	1	0.7
Allergy/Rash	1	0.7
Epigastric pain	3	2.2
Hypertension	1	0.7
Leg pain	2	1.5
Increase in hair	1	0.7
Hair loss	2	1.5
Dyspareunia	2	1.5
Nervousness	8	5.8
Frigidity	1	0.7
Mood changes	2	1.5
Insomnia	1	0.7
Muscular pains throughout body	1	0.7
Milk volume decreased	2	1.5
Baby had colic	1	0.7
Baby had gastroenteritis	1	0.7
Total # of women with 1+ other complaints	34	24.8

Table VI
Changes in Complaints Since Admission

Complaint	No. (N=137)	%
Intermenstrual Bleeding		
Never reported	75	54.7
No change	0	0.0
Decrease	1	0.7
Increase	0	0.0
New Reports	61	44.5
Nausea		
Never reported	83	60.6
No change	6	4.4
Decrease	7	5.1
Increase	3	2.2
New Reports	38	27.7
Vomiting		
Never reported	112	81.8
No change	1	0.7
Decrease	8	5.8
Increase	0	0.0
New Reports	16	11.7
Headaches		
Never reported	33	24.1
No change	31	22.6
Decrease	28	20.4
Increase	14	10.2
New Reports	31	22.6
Dizziness		
Never reported	63	46.0
No change	13	9.5
Decrease	17	12.4
Increase	7	5.1
New Reports	37	27.0
Vaginal Discharge		
Never reported	48	35.0
No change	29	21.2
Decrease	28	20.4
Increase	6	4.4
New Reports	26	19.0
Breast Discomfort		
Never reported	96	70.1
No change	7	5.1
Decrease	15	10.9
Increase	1	0.7
New Reports	18	13.2

N represents number of women followed up.

Table VII
Significant Changes in the Percentage of Women Reporting
Complaints at Admission and Since Admission

Complaint	Ovrette	
	At Admission (N=146) %	Since Admission (N=137) %
Intermenstrual Bleeding*	0.7	44.5
Other Menstrual Complaints*	8.9	60.6
Nausea*	11.6	34.3
Dizziness*	28.1	43.1

*p<.01 using McNemar's non-parametric test

Table VIII
Primary Reasons for Discontinuation

Termination Reason	No. (N=137)	%
Accidental Pregnancy		
Method Failure	2	1.5
Menstrual Problems		
Spotting	1	0.7
Intermenstrual bleeding	2	1.5
Heavy bleeding	3	2.2
Scanty menses	1	0.7
Amenorrhea	10	7.3
Polymenorrhea	5	3.6
Side Effects		
Nausea	2	1.5
Headaches	3	2.2
Dizziness	2	1.5
Vaginal discharge	1	0.7
Combination discharge and inflammation of the uterus	1	0.7
nausea, headaches and "heavy head"	1	0.7
Other Medical		
Allergy, rash	1	0.7
Cardiac arrhythmia	1	0.7
Hypertension	2	1.5
Visual problems	1	0.7
Decrease in milk volume	1	0.7
Dyspareunia	1	0.7
Other Personal		
Fears method	8	5.8
Forgetfulness	2	1.5
Nervousness	2	1.5
Mood changes	1	0.7
Desires change of method	10	7.3
Method not needed	1	0.7
Method Unrelated		
Can't return	2	1.5
No supply	4	2.9
Disinterest in study	4	2.9
Family reasons	1	0.7
TOTAL DISCONTINUATION	76	55.5

N represents number of women followed up.

Table IX

Gross Cumulative Life Table Discontinuation Rates

Event	Rate \pm S.E. (N=146)
Accidental Pregnancy	
2 month	0.0 \pm 0.0
6 month	1.4 \pm 1.4
12 month	3.7 \pm 2.7
Menstrual Problems	
2 month	6.1 \pm 2.2
6 month	19.4 \pm 4.3
12 month	27.7 \pm 6.0
Side Effect	
2 month	4.9 \pm 2.0
6 month	11.5 \pm 3.4
12 month	11.5 \pm 3.4
Other Medical Reasons	
2 month	2.5 \pm 1.4
6 month	3.6 \pm 1.8
12 month	7.4 \pm 4.1
Other Personal Reasons	
2 month	9.7 \pm 2.7
6 month	23.8 \pm 4.6
12 month	32.6 \pm 5.8
Method Unrelated Reason	
2 month	6.1 \pm 2.2
6 month	7.4 \pm 2.5
12 month	11.1 \pm 4.4
Lost-to-Follow-up Rate	
2 month	6.2
6 month	22.6
12 month	30.8
Total Discontinuation Rate*	
2 month	15.8
6 month	63.0
12 month	80.8
Woman Months	
2 month	268.0
6 month	578.0
12 month	797.5

* Total discontinuation rate includes all women discontinuing from the study including those women lost-to-follow-up.