

A Comparative Study of Loestrin
Versus Lo-Femenal
in Bangkok, Thailand

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October 1990

19 pages
CR # 670

I. Introduction

A comparative study of two low-dose combination oral contraceptives (OCs) was conducted at the Pramongkutklao Army Hospital in Bangkok, Thailand. This study was designed to evaluate the clinical acceptability by determining rates of continuation and reasons for termination, including pregnancy, between Loestrin (Parke-Davis) and Lo-Femenal (Wyeth). The latter is currently provided in United States Agency for International Development (USAID) programs. A major reason for the selection of these two oral contraceptives was to compare combined OC pills with a low estrogen dose composition with differing progestogenic activity.

The incidence of some common side effects associated with combined oral contraceptives (e.g. nausea, vomiting, spotting, and breakthrough bleeding) varies for different formulations and for the same formulation when evaluated in different geographic areas. Oral contraceptives with lower estrogen doses may reduce short term and long-term side effects.

II. Study Design

Oral Contraceptives Evaluated

Each of the OCs administered in this study was provided in 28 day packs of 21 active steroid tablets and 7 iron tablets. Loestrin has a composition of 150 mcg norethindrone acetate and 30 mcg ethinyl estradiol (EE). Lo-Femenal has a composition of 300 mcg of the progestin, norgestrel, and 30 mcg EE. The iron tablets in each of the products contained 75 mg of ferrous fumarate.

Study Procedure

Women recruited into the study had to meet the following criteria: be between

the ages of 18 and 35 years old, be sexually active, have terminated their last pregnancy at least 42 days prior to admission to the study (if not breastfeeding) or have terminated their last pregnancy at least four months prior to admission to the study (if breastfeeding), have had at least one normal menstrual period since termination of their last pregnancy, be in good health, and rely exclusively upon the pills as their only method of contraception throughout the course of the study unless advised otherwise by the investigator; and give informed consent and be willing to be followed up for at least 12 months.

Normal clinical contraindications to OC use were followed. Specifically, women with any of the following conditions were to be excluded from the study: pregnancy; history or evidence of thromboembolic disorders; significant cardiovascular disease; diabetes; renal dysfunction; epilepsy; hypertension; migraine; severe liver disorders; breast cancer; undiagnosed vaginal bleeding; chronic use of internal medications, such as antibiotics and barbiturates, which could reduce pill effectiveness.

A total of 149 women were admitted to the study from December 1987 through December 1988. The women were randomly allocated to receive either Loestrin or Lo-Femenal according to preprinted sealed envelopes opened at the time of admission; 74 women were given Loestrin and 75 women were given Lo-Femenal. Follow-up visits were scheduled at 1, 4, 8, and 12 months after admission to the study although most women returned for their third follow-up visit at 7 months and for their last follow-up visit at 11 months. This was due to the fact that while pill cycles are 28 days, follow-ups are scheduled by calendar months (30-31 days). Women returning at 7 months for their third follow-up had

completed 8 pill cycles; women returning at 11 months for their last follow-up had completed 12 pill cycles. Rates are thus reported at 1, 4, 7, and 11 months. Two Loestrin users and two Lo-Femenal users were not included in the analysis due to protocol violations. The two Loestrin users and one Lo-Femenal user were determined to be protocol violations because they were breastfeeding and were all only 6 weeks postpartum. The other Lo-Femenal user was determined to be a protocol violation because she was 36 years old. All of the 145 women included in the analysis were interval patients (\geq 42 days since last pregnancy termination). Two women in the Loestrin group and no women in the Lo-Femenal group were exclusively breastfeeding (no supplementation) at admission; four in the Loestrin group and 4 women in the Lo-Femenal group were breastfeeding with supplementation at admission; the remaining 66 women in the Loestrin group and 69 women in the Lo-Femenal group were not breastfeeding at admission. The study was not blinded because an evaluation of the products as they appear on the market was desired.

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

III. Results

Sociodemographic Characteristics

Selected patient characteristics are presented by group in Table I. The mean age of the Loestrin group was 25.6 years and of the Lo-Femenal group, 26.2 years. The mean education level was 9.3 years for Loestrin users, and 9.0 years for Lo-Femenal users. The mean total live births was 1.0 for the Loestrin group and 1.2 for the Lo-Femenal group.

Contraceptive Practice

Table I also presents a summary of the contraceptive practices of the women one month prior to admission to the study. Thirty-seven women (51.4%) from the Loestrin group and 43 women (58.9%) from the Lo-Femenal group reported having used no contraception in the month before study admission. The predominant method used was oral contraceptives by 25 women (34.7%) in the Loestrin group and 20 women (27.4%) in the Lo-Femenal group. A total of 53 women (73.6%) in the Loestrin group and 45 women (61.6%) in the Lo-Femenal group reported ever having used oral contraceptives prior to the study; this difference was not statistically significant ($p > .05$).

Complaints at Admission

None of the women reported a pre-existing medical condition at admission. At admission, one woman (1.4%) from each group reported having intermenstrual bleeding; both complaints were for staining/spotting. Eleven women (15.3%) in the Loestrin group and 11 women (15.1%) in the Lo-Femenal group reported having a menstrual complaint other than intermenstrual bleeding; the majority of these complaints were for dysmenorrhea (Table II). Twenty-eight women (38.9%) in the Loestrin group and 25 women (34.2%) in the Lo-Femenal group reported having one or more other minor physical complaints in the month prior to admission (Table II). Vaginal discharge was the most frequently reported physical complaint, being reported by 15 women (20.3%) in the Loestrin group and 12 women (16.4%) in the Lo-Femenal group.

Regularity of Use

Data on regularity of use were collected at 1, 4, 7 and 11 months after beginning oral contraceptive use. Compliance was assessed by self-report and

from the date the last pill was taken prior to the date of follow-up visit. Follow-up visit data indicate that 19 women (28.4%) in the Loestrin group and 15 women (22.4%) in the Lo-Femenal group missed one or more pills at some time during the study period.

Medical Complaints During Follow-Up

One serious complication was reported by a woman in the Lo-Femenal group. (Table III) The woman reported (at her one and four month follow-up visits) that her thighs and legs felt tired while she was menstruating but that after her menses ended, her symptoms disappeared. This woman completed the 12 months of study.

Table III also presents medical complaints reported at follow-up. Minor medical complaints were reported by 3 women (4.5%) in the Loestrin group and 6 women (9.0%) in the Lo-Femenal group. The most common minor medical complaints were skin problems such as facial chloasma or rash.

Side Effects

A summary of menstrual complaints ever reported throughout the follow-up period is shown in Table IV. There were no significant differences between groups in reports of intermenstrual bleeding. With regard to primary other menstrual complaints, a significantly larger proportion of Loestrin users reported menstrual complaints, primarily scanty menses and amenorrhea ($p < .05$). For women who ever reported a menstrual/bleeding complaint, significantly more Loestrin users reported complaints during follow-up, specifically, 38 Loestrin users (56.7%) versus 26 Lo-Femenal users (38.8%) ($p < .05$).

A summary of pill-related problems and complaints ever reported at all follow-up

visits is shown in Table V, and a summary of the changes in complaints is reported in Table VI. A total of 32 women (47.8%) in the Loestrin group and 35 women (52.2%) in the Lo-Femenal group reported at least one of these common pill-related complaints. The two groups were not significantly different ($p > .05$) in reports of these complaints. Overall, the largest increases in complaints were for intermenstrual bleeding, vaginal discharge, and nausea in the Loestrin group and for intermenstrual bleeding and headaches in the Lo-Femenal group.

Discontinuation Rates and Reasons

A summary of all reasons for discontinuation is presented in Table VII. A total of 8 women (11.9%) in the Loestrin group and 10 women (14.9%) in the Lo-Femenal group discontinued during the study period. In the Loestrin group, pregnancy (both user failure and method failure) and forgetfulness in taking the pill were the primary reasons given for discontinuation. In the Lo-Femenal group, forgetfulness and side effects such as nausea, headaches, and acne were the primary reasons for discontinuation.

There were three accidental pregnancies that occurred in the Loestrin group. Two of the pregnancies occurred when the subject missed one or more pills and therefore were attributed to user failure. The third pregnancy was attributed to method failure because the subject was reported to have taken all pills regularly.

Lost to follow-up and total discontinuation percentages, along with woman months are presented in Table VIII. The lost to follow-up percentages at 11 months for the two groups were 30.6 for Loestrin users and 20.6 for Lo-Femenal users. The

11-month total discontinuation percentages were 41.7 for the Loestrin group and 34.2 for the Lo-Femenal group. Gross cumulative life table discontinuation rates are presented in Table IX.

IV. Summary

A study of two low dose oral contraceptives, Loestrin and Lo-Femenal, was conducted at the Pramongkutklao Army Hospital in Bangkok, Thailand. The study was designed to determine if there were differences in discontinuation rates and reasons for discontinuation between the aforementioned oral contraceptives. This report includes an analysis of 145 women, all interval patients (\geq 42 days since last pregnancy termination). Of the 145 women, 72 were in the Loestrin group and 73 were in the Lo-Femenal group. Follow-up visits were scheduled at 1, 4, 8, and 12 months after admission to the study although most women returned for their third follow-up visit at 7 months and for their last follow-up visit at 11 months. This was due to the fact that while pill cycles are 28 days, follow-ups are scheduled by calendar months (30-31 days). Women returning at 7 months for their third follow-up had completed 8 pill cycles; women returning at 11 months for their last follow-up had completed 12 pill cycles.

The 11-month lost-to-follow-up percentages were 30.6 for Loestrin and 20.6 for Lo-Femenal users. The 11-month total discontinuation percentage (including women lost to follow-up) was 41.7 and 34.2 for the Loestrin and Lo-Femenal groups, respectively. The primary reasons for discontinuation in the Loestrin group were for forgetfulness and pregnancy (both user and method failure). The primary reasons for discontinuation in the Lo-Femenal group were for forgetfulness and for side effects such as nausea, headaches, and acne. There were three accidental pregnancies, all in the Loestrin group. Two pregnancies were attributed to user failure and one pregnancy was attributed to method failure.

Table I
Selected Sociodemographic Characteristics

Characteristic	Loestrin (N=72)		Lo-Femenal (N=73)	
	No.	% _a	No.	% _a
Age (years)				
Less than 20	3	4.2	3	4.1
20-24	28	38.9	29	39.7
25-29	34	47.2	29	39.7
30-34	5	6.9	12	16.4
35-39	2	2.8	0	0.0
Mean	25.6		26.2	
Education (years)				
None	0	0.0	0	0.0
1-6	17	23.6	25	34.2
7-12	41	56.9	34	46.6
13+	14	19.4	14	19.2
Mean	9.3		9.0	
Total live births				
0	12	16.7	9	12.3
1	47	65.3	44	60.3
2	12	16.7	18	24.7
3	1	1.4	2	2.7
Mean	1.0		1.2	
Contraceptive method used 1 month prior to admission				
None	37	51.4	43	58.9
Oral contraceptives	25	34.7	20	27.4
Condoms	10	13.9	9	12.3
IUD	0	0.0	1	1.4

N represents the total number of women included in the analysis.
^aPercentages may not always add to 100 due to rounding errors; this holds true for all subsequent tables in this report.

Table II
Complaints at Admission

Complaints	Loestrin (N=72)		Lo-Femenal (N=73)	
	No.	%	No.	%
Intermenstrual bleeding				
None	71	98.6	72	98.6
Staining/Spotting	1	1.4	1	1.4
Primary other menstrual complaints ¹				
None	61	84.7	62	84.9
Dysmenorrhea	8	11.1	8	11.0
Scanty menses	2	2.8	3	4.1
Amenorrhea	1	1.4	0	0.0
Total women with one or more menstrual/bleeding complaints	11	15.3	12	16.4
Other complaints (reported in past month) ¹				
Vaginal discharge	15	20.8	12	16.4
Headaches	11	15.3	12	16.4
Breast discomfort	10	13.9	9	12.3
Dizziness	11	15.3	8	11.0
Nausea	2	2.8	2	2.7
Vomiting	1	1.4	1	1.4
Total women with one or more complaints	28	38.9	25	34.2

N represents the total number of women included in the analysis.

¹Multiple complaints may be reported per woman for this category.

Table III

Medical Complaints Since Admission

Characteristic	Loestrin (N=67)		Lo-Femenal (N=67)	
	No.	%	No.	%
Serious complications				
Fatigue in thighs and legs during menses	0	0.0	1	1.5
Minor complaints				
Chloasma	1	1.5	2	3.0
Rash	0	0.0	1	1.5
Dysmenorrhea	1	1.5	0	0.0
Weight gain	0	0.0	1	1.5
Appetite decrease	1	1.5	0	0.0
Fatigue during menses	0	0.0	1	1.5
Combination dyspareunia, weight gain, and chloasma	0	0.0	1	1.5
Decreased menses	0	0.0	1	1.5
Total women with minor medical complaints	3	4.5	6	9.0

N represents number of women ever followed up.

Multiple complaints may be reported per woman.

Table IV

Menstrual Complaints Ever Reported Since Admission

Complaint	Loestrin (N=67)		Lo-Femenal (N=67)	
	No.	%	No.	%
Intermenstrual bleeding ¹				
None	35	52.2	45	67.2
Staining/spotting	27	40.3	17	25.4
Moderate	5	7.5	5	7.5
Primary other menstrual complaints* ²				
None	50	74.6	61	89.6
Scanty menses	1	10.4	2	3.0
Dysmenorrhea	5	7.5	2	3.0
Amenorrhea	5	7.5	0	0.0
Menorrhagia	2	3.0	1	1.5
Intermenstrual pelvic discomfort	0	0.0	1	1.5
Total women with one or more menstrual/bleeding complaints**	38	56.7	26	38.8

N represents number of women ever followed up.

¹For this category, the complaint reported is the most severe complaint ever reported..

²Multiple complaints may be reported per woman for this category.

* p<.05, using chi-square, df=1 (These values were collapsed in order to perform significance testing.)

** p<.05, using chi-square, df=1

Table V
Other Complaints Ever Reported Since Admission

Complaint	Loestrin (N=67)		Lo-Femenal (N=67)	
	No.	%	No.	%
Vaginal discharge	19	28.4	15	22.4
Headaches	12	17.9	14	20.9
Nausea	12	17.9	11	16.4
Dizziness	8	11.9	4	6.0
Breast discomfort	4	6.0	7	10.4
Vomiting	2	3.0	3	4.5
Total women with one or more complaints	32	47.8	35	52.2

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

Table VI¹

Changes in Severity of Complaints Since Admission

Changes in Complaints	Loestrin (N=67)		Lo-Femenal (N=67)	
	No.	%	No.	%
Intermenstrual bleeding				
Never reported	34	50.7	44	65.7
No change	0	0.0	0	0.0
Decrease	1	1.5	1	1.5
Increase	32	47.8	22	32.8
New reports	32	47.8	22	32.8
Nausea				
Never reported	53	79.1	56	83.6
No change	0	0.0	1	1.5
Decrease	2	3.0	0	0.0
Increase	12	17.9	10	14.9
New reports	12	17.9	9	13.4
Vomiting				
Never reported	64	95.5	64	95.5
No change	0	0.0	0	0.0
Decrease	1	1.5	0	0.0
Increase	2	3.0	3	4.5
New reports	2	3.0	2	3.0
Headaches				
Never reported	47	70.1	44	65.7
No change	3	4.5	1	1.5
Decrease	8	11.9	9	13.4
Increase	9	13.4	13	19.4
New reports	9	13.4	13	19.4
Dizziness				
Never reported	50	74.6	58	86.6
No change	2	3.0	1	1.5
Decrease	9	13.4	5	7.5
Increase	6	9.0	3	4.5
New reports	6	9.0	3	4.5
Vaginal discharge				
Never reported	39	58.2	48	71.6
No change	6	9.0	5	7.5
Decrease	9	13.4	4	6.0
Increase	13	19.4	10	14.9
New reports	13	19.4	10	14.9

(cont.)

Table VI (cont.)

Changes in Complaints Since Admission

Changes in Complaints	Loestrin (N=67)		Lo-Femenal (N=67)	
	No.	%	No.	%
Breast discomfort				
Never reported	55	82.1	54	80.6
No change	2	3.0	3	4.5
Decrease	8	11.9	6	9.0
Increase	2	3.0	4	6.0
New reports	2	3.0	4	6.0

N represents the number of women ever followed up.

New reports are complaints reported during the follow-up period by women who did not report the complaint at admission.

N.B. Since the time periods for reporting a complaint since admission (e.g. 6 months from the 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 toward an increased reporting of complaints since admission.

¹Reports of complaints were ranked by severity, with the most severe complaints ever reported throughout the study being given priority. For example, if a woman reported experiencing breast discomfort "sometimes" at admission, "often" at her first follow-up, and "sometimes" at her last follow-up, then the most severe report (here, "often") would be recorded. As represented in this table, the report would be an increase in severity of complaint since admission. The same rationale is true for decreases reported here, therefore, a decrease would only be reported if the complaint at admission was the most severe complaint ever reported by the patient throughout the study.

Table VII

Primary Reasons for Discontinuation

Complaint	Loestrin (N=67)		Lo-Femenal (N=67)	
	No.	%	No.	%
Accidental pregnancy				
User failure	2	3.0	0	0.0
Method failure	1	1.5	0	0.0
Menstrual problems				
Breakthrough bleeding	0	0.0	1	1.5
Scanty menses	0	0.0	1	1.5
Side effects				
Nausea	1	1.5	2	3.0
Headaches	0	0.0	1	1.5
Acne	0	0.0	1	1.5
Planning pregnancy	0	0.0	1	1.5
Other personal				
Forgetfulness	2	3.0	2	3.0
Method unrelated				
Relative ill	0	0.0	1	1.5
Incorrect use	1	1.5	0	0.0
Patient hospitalized	1	1.5	0	0.0
Total Discontinuations	8	11.9	10	14.9

N represents number of women ever followed up.

Table VIII

Lost To Follow-up And Total Discontinuation Percentages

Event	Loestrin (N=72)	Lo-Femenal (N=73)
Lost-to-follow-up percentage ¹		
1 month	6.9	8.2
4 month	12.5	12.3
7 month	15.3	17.8
11 month	30.6	20.6
Total discontinuation percentage ²		
1 month	6.9	11.0
4 month	18.1	17.8
7 month	22.2	24.7
11 month	41.7	34.2
Woman months		
1 month	67.5	68.5
4 month	247.5	247.0
7 month	414.5	413.5
11 month	590.0	604.5

¹Percentage of women lost to follow-up among the total number who entered the study.

²Percentage of women not returning to the clinic among the total number who entered the study (including lost to follow-up).

Table IX

Gross Cumulative Life Table Discontinuation Rates

Event	Number at Risk	Loestrin (N=72) Rate \pm S.E.	Number at Risk	Lo-Femenal (N=73) Rate \pm S.E.
Accidental pregnancy				
1 month	66.5	0.0 \pm 0.0	66.5	0.0 \pm 0.0
4 month	58.5	1.7 \pm 1.7	58.0	0.0 \pm 0.0
7 month	54.5	1.7 \pm 1.7	54.0	0.0 \pm 0.0
11 month	34.5	5.6 \pm 3.2	39.5	0.0 \pm 0.0
Menstrual problems				
1 month	66.5	0.0 \pm 0.0	67.0	1.5 \pm 1.5
4 month	58.0	0.0 \pm 0.0	58.0	1.5 \pm 1.5
7 month	54.5	0.0 \pm 0.0	54.5	3.3 \pm 2.3
11 month	34.5	0.0 \pm 0.0	39.5	3.3 \pm 2.3
Side effects				
1 month	66.5	0.0 \pm 0.0	67.5	3.0 \pm 2.1
4 month	58.5	1.7 \pm 1.7	58.5	4.6 \pm 2.6
7 month	54.5	1.7 \pm 1.7	54.5	6.4 \pm 3.1
11 month	34.5	1.7 \pm 1.7	39.5	6.4 \pm 3.1
Planning pregnancy				
1 month	66.5	0.0 \pm 0.0	66.5	0.0 \pm 0.0
4 month	58.0	0.0 \pm 0.0	58.0	0.0 \pm 0.0
7 month	54.5	0.0 \pm 0.0	54.0	0.0 \pm 0.0
11 month	34.5	0.0 \pm 0.0	40.0	2.5 \pm 2.5
Other personal reasons				
1 month	67.0	1.5 \pm 1.5	67.0	1.5 \pm 1.5
4 month	58.0	1.5 \pm 1.5	58.0	1.5 \pm 1.5
7 month	55.0	3.3 \pm 2.3	54.0	1.5 \pm 1.5
11 month	34.5	3.3 \pm 2.3	39.5	3.4 \pm 2.4
Method unrelated reasons				
1 month	67.0	1.5 \pm 1.5	66.5	0.0 \pm 0.0
4 month	58.0	3.1 \pm 2.2	58.0	0.0 \pm 0.0
7 month	54.5	3.1 \pm 2.2	54.0	0.0 \pm 0.0
11 month	34.5	3.1 \pm 2.2	39.5	1.9 \pm 1.9

(cont.)

Table IX (cont.)

Gross Cumulative Life Table Discontinuation Rates

Event	Number at Risk	Loestrin (N=72) Rate \pm S.E.	Number at Risk	Lo-Femenal (N=73) Rate \pm S.E.
Method related reasons				
1 month	68.0	4.4 \pm 2.5	66.5	0.0 \pm 0.0
4 month	58.5	6.1 \pm 2.9	58.5	1.7 \pm 1.7
7 month	55.0	9.5 \pm 3.7	54.5	1.7 \pm 1.7
11 month	39.5	9.5 \pm 3.7	34.5	1.7 \pm 1.7

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