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A Comparative Study of Loestrin  
Versus Lo-Femenal  
in Alor Setar and Sungai Petani, Malaysia

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## I. Introduction

A comparative study of two low-dose combination oral contraceptives (OCs) was conducted at two clinics in Kedah State, Malaysia. (One clinic is in Alor Setar, the other in Sungai Petani.) 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 and long-term side effects.

## II. Study Design

### Oral Contraceptive 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 breast-feeding) or have terminated their last pregnancy at least four months prior to admission to the study (if breast-feeding), 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 criteria for contraindications to OC use were followed. In addition, 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 300 women were admitted to the study from March 1987 through January 1988. The women were randomly allocated to receive either Loestrin or Lo-Femenal according to preprinted sealed envelopes opened at the time of admission; 150 women were given Loestrin and 150 women were given Lo-Femenal. Follow-up visits were scheduled at 1, 4, 8 and 12 months after admission to the study. One woman was not included in the analysis due to a protocol violation. This woman was breast-feeding and was 11 weeks postpartum; protocol selection criteria state that if a woman is breast-feeding, she must be at least 4 months postpartum to be admitted to the study. All of the 299 women included in the

analysis were interval patients ( $\geq$  42 days since last pregnancy termination). Four women in the Loestrin group and 5 women in the Lo-Femenal group were breast-feeding without supplementation at admission; twenty-five women in the Loestrin group and 31 women in the Lo-Femenal group were breast-feeding with supplementation at admission; the remaining 120 women in the Loestrin group and 114 women in the Lo-Femenal group were not breast-feeding at admission. The study was not blind; because an evaluation of the products as they appear on the market was desired, study volunteers were given regularly labeled OC packs.

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 27.9 years and of the Lo-Femenal group, 27.8 years. The mean education level was 8.1 years for Loestrin users, and 7.9 years for Lo-Femenal users. The mean total live births was 2.6 for the Loestrin group and 2.4 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-nine women (26.2%) from the Loestrin group and 41 women (27.3%) from the Lo-Femenal group reported having used no contraception in the month before study admission. The predominant method used prior to admission in both groups was oral contraceptives; 108 women (72.5%) in the Loestrin group and 104 women (69.3%) in the Lo-Femenal group used

oral contraceptives in the month before study admission. A total of 112 women (75.2%) in the Loestrin group and 108 women (72.0%) 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, no women in the Loestrin group and 2 women (1.3%) in the Lo-Femenal group reported menstrual complaints (Table II); both menstrual complaints were for dysmenorrhea. Twenty-three women (15.4%) in the Loestrin group and 21 women (14.0%) in the Lo-Femenal group reported having one or more other minor physical complaints in the month prior to admission (Table II). Headaches were the most frequently reported physical complaint, being reported by 11 women (7.4%) in the Loestrin group and 11 women (7.3%) in the Lo-Femenal group.

#### Regularity of Use

Data on regularity of use were collected at 1, 4, 8 and 12 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 6 women (4.0%) in the Loestrin group and 2 women (1.3%) in the Lo-Femenal group missed one or more pills at some time during the study period. In the Loestrin group, one of the women who missed one or more pills was reported as "not taking (her) pills correctly." Specifics on how many pills she actually missed were not obtainable. This woman was discontinued for chest and abdominal pain at the same follow-up visit her pill misuse was reported. It appears that this woman took her pills irregularly when she was experiencing the above medical complaints. Her chest and abdominal

pains were diagnosed as not being pill-related.

#### Minor Medical Complaints During Follow-Up

Table III presents minor medical complaints reported at follow-up. Minor medical complaints were reported by 26 women (17.4%) in the Loestrin group and 21 women (14.0%) in the Lo-Femenal group. The most common minor medical complaints were weight gain and hypertension for both groups, and scanty menses for the Loestrin group.

#### 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 the two groups in reports of intermenstrual bleeding ( $p > .05$ ). There was a significantly greater proportion of Loestrin users who reported menstrual complaints, primarily scanty menses (12.1% vs. 1.3%) and amenorrhea (6.7% vs. 2.0%), compared to Lo-Femenal users ( $p < .001$ ).

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 33 women (22.1%) in the Loestrin group and 32 women (21.3%) 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 increase in complaints were for headaches, dizziness, and vaginal discharge for Loestrin users; and for nausea, dizziness, and headaches for Lo-Femenal users.

### Discontinuation Rates and Reasons

A summary of all reasons for discontinuation is presented in Table VII. A total of 32 women (21.5%) in the Loestrin group and 27 women (18.0%) in the Lo-Femenal group discontinued during the study period. In the Loestrin group, side effects such as headaches, menstrual problems such as amenorrhea, and medical reasons such as chest pain were the primary reasons given for discontinuation. In the Lo-Femenal group, medical reasons such as hypertension, personal reasons such as not needing the oral contraceptive any longer, and method unrelated reasons such as moving or travel were the primary reasons for discontinuation.

There were two accidental pregnancies that occurred in the Loestrin group. Both pregnancies were attributed by the Investigator to user failure because both women stopped taking the pills on their own. One woman stopped taking the pills because she decided to plan a pregnancy. The other woman stopped taking the pills when she traveled out of town and forgot to take her pills with her. Both women became pregnant after they stopped taking the pills.

Lost to follow-up and total discontinuation percentages, along with woman months are presented in Table VIII. The lost to follow-up percentages at 12 months for the two groups were 2.7 for Loestrin users and 3.3 for Lo-Femenal users. The 12-month total discontinuation percentages were 24.2 for the Loestrin group and 21.3 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 two clinics -one in Alor Setar, the other in Sungai Petani-in Kedah State, Malaysia. 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 299 women, all interval patients ( $\geq 42$  days since last pregnancy termination). Of the 299 women, 149 were in the Loestrin group and 150 were in the Lo-Femenal group. Follow-up visits were scheduled at 1, 4, 8 and 12 months after admission.

The lost-to-follow-up percentages were 2.7 for Loestrin and 3.3 for Lo-Femenal users. The 12-month total discontinuation percentage (including women lost to follow-up) was 24.2 and 21.3 for the Loestrin and Lo-Femenal groups, respectively. The primary reasons for discontinuation in the Loestrin group were for medical problems such as chest pain, menstrual problems such as amenorrhea, and side effects such as headaches. The primary reasons for discontinuation in the Lo-Femenal group were for method-unrelated reasons such as moving or travel, medical reasons such as hypertension, and personal reasons such as no longer needing the oral contraceptives. There were two accidental pregnancies, both in the Loestrin group. Both pregnancies were attributed to user failure and occurred after the women stopped taking the pills.

Table I  
Selected Sociodemographic Characteristics

Characteristic	Loestrin (N=149)		Lo-Femenal (N=150)	
	No.	% <sup>a</sup>	No.	% <sup>a</sup>
<b>Age (years)</b>				
Less than 20	2	1.3	4	2.7
20-24	37	24.8	39	26.0
25-29	61	40.9	59	39.3
30-34	44	29.5	42	28.0
35-39	5	3.4	6	4.0
Mean	27.9		27.8	
<b>Education (years)</b>				
None	9	6.0	10	6.7
1-6	47	31.5	50	33.3
7-12	83	55.7	84	56.0
13+	10	6.7	6	4.0
Mean	8.1		7.9	
<b>Total live births</b>				
1	30	20.1	35	23.3
2	48	32.2	54	36.0
3	40	26.8	35	23.3
4	20	13.4	15	10.0
5	8	5.4	8	5.3
6+	3	2.0	3	2.0
Mean	2.6		2.4	
<b>Contraceptive method used 1 month prior to admission</b>				
None	39	26.2	41	27.3
Oral contraceptives	108	72.5	104	69.3
Condoms	2	1.3	2	1.3
IUD	0	0.0	2	1.3
Injectables	0	0.0	1	0.7

<sup>a</sup>Percentages 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=149)		Lo-Femenal (N=150)	
	No.	%	No.	%
Menstrual Complaints	0	0.0	2*	1.3
Other Complaints (Reported in Past Month) <sup>1</sup>				
Headaches	11	7.4	11	7.3
Vaginal Discharge	7	4.7	5	3.3
Dizziness	6	4.0	4	2.7
Nausea	5	3.4	4	2.7
Breast Discomfort	0	0.0	3	2.0
Vomiting	2	1.3	1	0.7
Total women with one or more complaints	23	15.4	21	14.0

\*Both menstrual complaints were for dysmenorrhea.

<sup>1</sup>Multiple complaints may be reported per woman for this category.

Table III  
Medical Complaints Since Admission

Characteristic	Loestrin (N=149)		Lo-Femenal (N=150)	
	No.	%	No.	%
Minor complaints				
Weight gain	5	3.4	9	6.0
Hypertension	2	1.3	4	2.7
Scanty menses	5	3.4	0	0.0
Abdominal pain	2	1.3	1	0.7
Rash	1	0.7	2	1.3
Chest pain	2	1.3	0	0.0
Hair loss	2	1.3	0	0.0
Breakthrough bleeding	1	0.7	0	0.0
Nausea	0	0.0	1	0.7
Loss of appetite	1	0.7	0	0.0
Dizziness	1	0.7	0	0.0
Vaginal discharge	1	0.7	0	0.0
Fever	1	0.7	0	0.0
Epigastric pain	1	0.7	0	0.0
Wheezing and breathlessness	1	0.7	0	0.0
Back pain	0	0.0	1	0.7
Numbness of hands	0	0.0	2	1.3
Asthmatic attacks	1	0.7	0	0.0
Combination: slight chest discomfort and pimples	0	0.0	1	0.7
Combination: general weakness of hands; white discharge and pruritus vulvae	0	0.0	1	0.7
Combination: numbness of fingers; irritability; pimples	1	0.7	0	0.0
Respiratory tract infection	1	0.7	0	0.0
Total women with minor medical complaints	26	17.4	21	14.0

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=149)		Lo-Femenal (N=150)	
	No.	%	No.	%
Intermenstrual bleeding <sup>1</sup>				
None	138	92.6	142	94.7
Staining/spotting	6	4.0	6	4.0
Moderate	5	3.4	2	1.3
Primary other menstrual complaints* <sup>2</sup>				
None	120	80.5	144	96.0
Scanty menses	18	12.1	2	1.3
Amenorrhea	10	6.7	3	2.0
Dysmenorrhea	0	0.0	1	0.7
Intermenstrual pelvic discomfort	1	0.7	0	0.0
Total women with one or more menstrual/bleeding complaints*	40	26.8	13	8.7

N represents number of women ever followed up.

<sup>1</sup>Most severe complaint ever reported

<sup>2</sup>Multiple complaints may be reported per woman for this category.

\*  $p < .001$ , using chi-square,  $df=1$

Table V  
Other Complaints Ever Reported Since Admission

Complaint	Loestrin (N=149)		Lo-Femenal (N=150)	
	No.	%	No.	%
Dizziness	13	8.7	12	8.0
Headaches	15	10.1	10	6.7
Nausea	8	5.4	15	10.0
Vaginal discharge	9	6.0	6	4.0
Vomiting	5	3.4	1	0.7
Breast discomfort	2	1.3	3	2.0
Total women with one or more complaints	33	22.1	32	21.3

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

Table VI<sup>1</sup>

## Changes in Severity of Complaints Since Admission

Changes in Complaints	Loestrin (N=149)		Lo-Femenal (N=150)	
	No.	%	No.	%
<b>Intermenstrual bleeding</b>				
Never reported	138	92.6	142	94.7
No change	0	0.0	0	0.0
Decrease	0	0.0	0	0.0
Increase	11	7.4	8	5.3
New reports	11	7.4	8	5.3
<b>Nausea</b>				
Never reported	138	92.6	133	88.7
No change	2	1.3	2	1.3
Decrease	3	2.0	2	1.3
Increase	6	4.0	13	8.7
New reports	6	4.0	13	8.7
<b>Vomiting</b>				
Never reported	143	96.0	148	98.7
No change	0	0.0	0	0.0
Decrease	1	0.7	1	0.7
Increase	5	3.4	1	0.7
New reports	4	2.7	1	0.7
<b>Headaches</b>				
Never reported	124	83.2	132	88.0
No change	1	0.7	3	2.0
Decrease	10	6.7	8	5.3
Increase	14	9.4	7	4.7
New reports	14	9.4	7	4.7
<b>Dizziness</b>				
Never reported	131	87.9	135	90.0
No change	1	0.7	1	0.7
Decrease	5	3.4	3	2.0
Increase	12	8.1	11	7.3
New reports	12	8.1	11	7.3
<b>Vaginal discharge</b>				
Never reported	134	89.9	141	94.0
No change	1	0.7	1	0.7
Decrease	6	4.0	3	2.0
Increase	8	5.4	5	3.3
New reports	8	5.4	4	2.7

(cont.)

Table VI (cont.)

## Changes in Complaints Since Admission

Changes in Complaints	Loestrin (N=149)		Lo-Femenal (N=150)	
	No.	%	No.	%
Breast discomfort				
Never reported	147	98.7	145	96.7
No change	0	0.0	1	0.7
Decrease	0	0.0	2	1.3
Increase	2	1.3	2	1.3
New reports	2	1.3	2	1.3

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.

<sup>1</sup>Reports 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=149)		Lo-Femenal (N=150)	
	No.	%	No.	%
Accidental pregnancy				
User failure	2	1.3	0	0.0
Menstrual problems				
Breakthrough bleeding	1	0.7	1	0.7
Scanty menses	1	0.7	0	0.0
Amenorrhea	5	3.4	2	1.3
Side effects				
Nausea	2	1.3	0	0.0
Vomiting	1	0.7	0	0.0
Weight gain	0	0.0	1	0.7
Headaches	3	2.0	1	0.7
Dizziness	0	0.0	1	0.7
Skin problems	0	0.0	1	0.7
Other medical reasons				
Abdominal pain	1	0.7	1	0.7
Breathlessness	1	0.7	0	0.0
Hypertension	2	1.3	3	2.0
Chest pain	3	2.0	0	0.0
Pain in the heel	0	0.0	1	0.7
Combination of chicken pox and appendectomy	0	0.0	1	0.7
Numbness of both hands	0	0.0	1	0.7
Numbness of fingers	1	0.7	0	0.7
Hair loss	1	0.7	0	0.0
Planning pregnancy	2	1.3	1	0.7
Other personal				
Forgetfulness	2	1.3	0	0.0
Desires change	1	0.7	0	0.0
Method not needed	0	0.0	5	3.3
Method unrelated				
Can't return	0	0.0	1	0.7
Moving/Travel	2	1.3	6	4.0
Disinterest in study	1	0.7	0	0.0
Total terminations	32	21.5	27	18.0

N represents number of women ever followed up.

Table VIII

## Lost To Follow-up And Total Discontinuation Percentages

Event	Loestrin (N=149)	Lo-Femenal (N=150)
Lost-to-follow-up percentage <sup>1</sup>		
1 month	0.0	0.0
4 month	0.0	6.7
8 month	0.7	1.3
12 month	2.7	3.3
Total discontinuation percentage <sup>2</sup>		
1 month	0.7	2.0
4 month	7.4	5.3
8 month	18.8	16.7
12 month	24.2	21.3
Woman months		
1 month	149.0	149.5
4 month	575.0	577.5
8 month	1087.5	1103.0
12 month	1496.0	1533.0

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

<sup>2</sup>Percentage 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=149) Rate $\pm$ S.E.	Number at Risk	Lo-Femenal (N=150) Rate $\pm$ S.E.
Accidental pregnancy				
1 month	147.5	0.0 $\pm$ 0.0	146.5	0.0 $\pm$ 0.0
4 month	137.5	0.0 $\pm$ 0.0	141.5	0.0 $\pm$ 0.0
8 month	121.5	0.0 $\pm$ 0.0	125.5	0.0 $\pm$ 0.0
12 month	59.5	0.0 $\pm$ 0.0	65.5	0.0 $\pm$ 0.0
Menstrual problems				
1 month	148.0	0.7 $\pm$ 0.0	146.5	0.0 $\pm$ 0.0
4 month	138.0	2.8 $\pm$ 1.4	141.5	0.0 $\pm$ 0.0
8 month	122.5	5.8 $\pm$ 2.0	125.5	2.3 $\pm$ 1.3
12 month	59.5	5.8 $\pm$ 2.0	65.5	2.3 $\pm$ 1.3
Side effects				
1 month	148.0	0.7 $\pm$ 0.7	147.0	0.7 $\pm$ 0.7
4 month	138.5	3.5 $\pm$ 1.5	141.5	0.7 $\pm$ 0.7
8 month	121.5	4.3 $\pm$ 1.7	125.5	2.9 $\pm$ 1.4
12 month	59.5	4.3 $\pm$ 1.7	65.5	2.9 $\pm$ 1.4
Other medical reasons				
1 month	147.5	0.0 $\pm$ 0.0	147.5	1.4 $\pm$ 1.0
4 month	137.5	0.7 $\pm$ 0.7	141.5	1.4 $\pm$ 1.0
8 month	122.0	5.2 $\pm$ 1.9	125.5	4.3 $\pm$ 1.7
12 month	59.5	6.8 $\pm$ 2.2	65.5	5.1 $\pm$ 1.9
Planning pregnancy				
1 month	147.5	0.0 $\pm$ 0.0	146.5	0.0 $\pm$ 0.0
4 month	137.5	0.0 $\pm$ 0.0	141.5	0.0 $\pm$ 0.0
8 month	121.5	0.8 $\pm$ 0.8	125.5	0.0 $\pm$ 0.0
12 month	60.0	2.5 $\pm$ 1.8	65.5	0.8 $\pm$ 0.8
Other personal reasons				
1 month	147.5	0.0 $\pm$ 0.0	147.0	0.7 $\pm$ 0.7
4 month	137.5	0.7 $\pm$ 0.7	142.0	2.1 $\pm$ 1.2
8 month	121.5	1.4 $\pm$ 1.0	126.0	3.6 $\pm$ 1.6
12 month	59.5	2.3 $\pm$ 1.3	65.5	3.6 $\pm$ 1.6
Method unrelated reasons				
1 month	148.0	0.7 $\pm$ 0.7	147.5	1.4 $\pm$ 1.0
4 month	137.5	1.4 $\pm$ 1.0	141.5	1.4 $\pm$ 1.0
8 month	121.5	2.9 $\pm$ 1.4	125.5	3.5 $\pm$ 1.5
12 month	59.5	2.9 $\pm$ 1.4	65.5	5.1 $\pm$ 1.9

(cont.)

Table IX (cont.)

## Gross Cumulative Life Table Discontinuation Rates

Event	Number at Risk	Loestrin (N=149) Rate $\pm$ S.E.	Number at Risk	Lo-Femenal (N=150) Rate $\pm$ S.E.
Method related reasons				
1 month	148.5	1.4 $\pm$ 0.9	147.0	0.7 $\pm$ 0.7
4 month	139.0	6.2 $\pm$ 2.0	141.5	0.7 $\pm$ 0.7
8 month	122.5	9.8 $\pm$ 2.5	125.5	5.1 $\pm$ 1.9
12 month	59.5	9.8 $\pm$ 2.5	65.5	5.1 $\pm$ 1.9

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