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A Comparative Study of Noriday  
Versus Lo-Femenal  
in Bamako, Mali

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## I. Introduction

A comparative study of two combination oral contraceptives (OCs) was conducted through the Ministry of Health in Bamako, Mali. This study was designed to determine if there were differences in the discontinuation rates between a standard dose combined OC, Noriday (Syntex), and a low-dose combined OC, Lo-Femenal (Wyeth) as well as the frequency of selected symptoms possibly contributing to method discontinuation. This study compared two types of pills which are available in Mali and which differ in dosage and package design. While the sample size was small, the main purpose of the study was to give the study staff an opportunity to participate in a clinical study as well as to observe any differences in patient acceptance of the two pills.

## 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 inert tablets. Noriday, a standard dose combination OC, has a composition of 50 mcg mestranol and 100 mcg norethindrone. Lo-Femenal, a low dose combination pill, has a composition of 30 mcg norgestrel and 30 mcg ethinyl estradiol (EE).

### Study Procedure

Women were admitted to the study from July 1984 through April 1986. A total of 202 women were randomly allocated to receive either Noriday or Lo-Femenal according to preprinted sealed

envelopes opened at the time of admission; 101 women were give Noriday and 101 women were given Lo-Femenal. Follow-up visits were scheduled at one, four, eight and twelve months after admission to the study. Three women were not included in this analysis because of protocol violation. These protocol violations included two women who were non-interval (less than 15 days postpartum) at admission and a third woman who was older than 35 years of age at the time of admission.

Each woman admitted to the study had to meet the following criteria; be in good physical health, want to use oral contraceptives as a method of contraception, rely exclusively upon the pills as her only method of contraception throughout the study, be sexually active, have terminated her last pregnancy at least 42 days prior to admission to the study, be between the ages of 18 and 35 years old, not be breastfeeding or if breastfeeding have been breastfeeding for at least six months, give informed consent and be followed up for at least 12 months. Normal clinic criteria for contraindications to OC use were followed. In addition, women with any of the following conditions were excluded from the study: pregnancy; thromboembolic disorders or history of cardiac problems; history or evidence of diabetes, renal dysfunction, epilepsy, hypertension, migraine headache, pulmonary disease or gastrointestinal disorders; severe liver disorders; history of jaundice; rotor syndrome or Dubin-Johnson syndrome; undiagnosed vaginal disease. Of the 199 women included in the analysis, all

were interval patients (42 days since last pregnancy termination). Twenty-seven women in the Noriday group and 36 women in the Lo-Femenal were breastfeeding at admission, and were included in the study as they had been breastfeeding for at least six months.

Data from this study were recorded on standard forms by hospital staff 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 Noriday group was 24.4 years and of the Lo-Femenal group, 24.7 years. The mean education levels were 7.8 and 8.2 years for Noriday and Lo-Femenal users respectively. The mean total live births for the Noriday group was 1.9 and for the Lo-Femenal group 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. Seventy-eight women (78.8%) from the Noriday group and 87 women (87.0%) from the Lo-Femenal group reported having used no contraception in the month before study admission. The predominant method used in both groups prior to admission was oral contraceptives--by 15 women (15.2%) in the Noriday group and 11 women (11.0%) in the

Lo-Femenal group. A total of 16 women (16.2%) in the Noriday group and 11 women (11.0%) in the Lo-Femenal group reported ever having used oral contraceptives prior to the study.

#### Complaints at Admission

Ninety women (90.9%) in the Noriday group and 86 (86.0%) in the Lo-Femenal group reported minor complaints at admission, such as menstrual irregularities (dysmenorrhea and scanty menses), nausea, headache, dizziness, vaginal discharge, breast discomfort and back pain. There were no significant differences between the two groups in the incidence of any complaint ( $p > .05$ ).

#### Regularity of Use

Regularity of use data was evaluated at one, four, eight and twelve months after beginning oral contraceptive use. Follow-up visit data indicated that 2 women (2.2%) in the Noriday group and 2 women (2.2%) in the Lo-Femenal group missed at least one pill. One additional woman (1.1%) in the Noriday group and 7 women (7.9%) in the Lo-Femenal group reported missing more than one pill at some time during the study period.

#### Side Effects

Serious complications were reported by 2 women in the Noriday group and by 4 women in the Lo-Femenal group during the study period (Table II). These complications were based on the patient's interpretation as to the severity of the problem. In the Noriday group one woman reported severe abdominal pain and

discontinued for gastric pain. The other woman reported severe chest pains with severe headache, respiratory difficulty and dizziness. Through additional testing it was discovered that the woman was anemic. She was prescribed an iron supplement and continued in the study.

In the Lo-Femenal group two women reported severe abdominal pain. Both women were hospitalized for the complaint but only one woman discontinued for the complaint. Another woman reported vision problems along with palpitations and severe dizziness. She was discontinued from the study for this reason and was referred to a cardiologist. One woman reported mild continuous pelvic pain and discontinued from the study for this reason. Another woman was diagnosed to have jaundice and was discontinued from the study for this reason.

A summary of menstrual complaints ever reported at follow-up visits is shown in Table III. The total represents the number of women ever followed up. Sixty-one women (68.5%) in the Noriday group and 57 women (64.0%) in the Lo-Femenal group reported at least one menstrual complaint and this difference was not significant ( $p > 0.05$ ). The occurrence and distribution of menstrual complaints was similar between the two treatment groups.

A summary of typical pill-related problems and complaints ever reported at all follow-up visits is shown in Table IV. There was

not a significant difference ( $p>0.05$ ) between the two groups in the number of women (92.1% in the Noriday group and 88.8% in the Lo-Femenal group) who reported at least one pill-related problem or individual complaint. The two groups were not significantly different ( $p>0.05$ ) in reports of any complaint.

Other complaints were reported by 49 women (55.1%) in the Noriday group and 36 women (40.4%) in the Lo-Femenal group (Table IV). The most common complaints reported by women in both the Noriday and Lo-Femenal groups included those of general fatigue, increased appetite and mild pelvic pain.

A summary of the changes in complaints since admission is presented in Table V. Although users of Lo-Femenal generally (except for dizziness) had a smaller increase in complaints compared to Noriday users, there were no significant changes ( $p>.05$ ) in reports of menstrual or other complaints between the two groups. There were, however, significant changes in the percentage of women reporting complaints at admission and during follow-up in each treatment group (Table VI). In the Noriday group there were significant increases in reports since admission for intermenstrual bleeding ( $\chi^2=8.64$ ,  $p<.01$ ), primary other menstrual complaints ( $\chi^2=9.26$ ,  $p<.01$ ), nausea ( $\chi^2=13.14$ ,  $p<.01$ ), dizziness ( $\chi^2=4.76$ ,  $p<.05$ ) and vaginal discharge ( $\chi^2=6.04$ ,  $p<.05$ ). In the Lo-Femenal group there were significant increases in reports since admission for intermenstrual bleeding ( $\chi^2=5.82$ ,  $p<.05$ ), primary other menstrual complaints ( $\chi^2=4.45$ ,  $p<.05$ ),

nausea ( $x^2=10.32$ ,  $p<.01$ ) and dizziness ( $x^2=5.26$ ,  $p<.05$ ).

#### Discontinuation Rates and Reasons

A summary of all reasons for discontinuation is presented in Table VII. A total of 20 women (22.5%) in the Noriday group and 29 women (32.6%) in the Lo-Femenal group discontinued during the 12-month study period. One woman was discontinued for hospitalization after being hospitalized for two days for sickness. Method unrelated reasons such as "patient moved" or "unable to return to the clinic" were the primary reasons given for discontinuation in both groups followed by other personal and other medical reasons in the Lo-Femenal group.

Twelve month gross cumulative discontinuation and event rates are presented in Table VIII. Twelve month total discontinuation rates (including those lost-to-follow-up) were 60.6 for the Noriday group and 63.0 for the Lo-Femenal group. The corresponding lost-to-follow-up rates for the two groups were not significantly different ( $p>0.05$ ); 42.4 for the Noriday group and 39.0 for the Lo-Femenal group at 12 months.

One accidental pregnancy occurred during the study period in the Noriday group. The pregnancy was attributed to method failure because the woman reported to have taken her pills correctly when she became pregnant.

#### IV. Summary

A study of two combined oral contraceptives, Noriday and Lo-Femenal, was conducted through the Ministry of Health in Bamako, Mali, to determine if there were differences in discontinuation rates and reasons for discontinuation between a standard dose OC (Noriday) versus a low-dose OC (Lo-Femenal). This report includes an analysis of 199 women, all interval patients, randomly allocated to one of the above oral contraceptives between July 1984 and April 1986. Follow-up visits were scheduled at one, four, eight and twelve months after admission.

The lost-to-follow-up rates were 42.4 and 39.0 at 12 months for the Noriday and Lo-Femenal groups, respectively. The rate for total discontinuations (including women lost-to-follow-up) was 60.6 and 63.0 for the Noriday and Lo-Femenal groups, respectively and this difference was not significant ( $p > 0.05$ ).

No significant differences between the two groups were reported in complaints or reasons for discontinuation. In both groups there were significant changes in reports since admission of intermenstrual bleeding, primary other menstrual complaints, nausea and dizziness, and of vaginal discharge in the Noriday group. There was one accidental pregnancy during the study period in the Noriday group which was attributed to method failure.

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Table I  
Selected Sociodemographic Characteristics

Characteristic	Noriday (N=99)		Lo-Femenal (N=100)	
	No.	%	No.	%
<b>Age (years)</b>				
Less than 20	4	4.0	4	4.0
20-24	57	57.6	57	57.0
25-29	28	28.3	27	27.0
30-34	8	8.1	10	10.0
35-39	2	2.0	2	2.0
40+	0	0.0	0	0.0
Mean	24.4		24.7	
<b>Education (years)</b>				
0	6	6.1	6	6.0
1-6	22	22.2	20	20.0
7-12	64	64.7	68	68.0
>12	7	7.1	6	6.0
Mean	7.8		8.2	
<b>Total live births</b>				
0	10	10.1	5	5.0
1-2	63	63.7	73	73.0
3-4	18	18.2	15	15.0
5+	8	8.1	7	7.0
Mean	1.9		1.8	
<b>Contraceptive method used during month before admission</b>				
None	78	78.8	87	87.0
IUD	3	3.0	1	1.0
Orals	15	15.2	11	11.0
Injectables/implants	1	1.0	0	.0
Condoms	0	0.0	1	1.0
Withdrawal/rhythm	0	0.0	0	0.0
Foam/diaphragm/jelly	2	2.0	0	0.0

Table II  
Complications Since Admission

Characteristic	Noriday (N=89)		Lo-Femenal (N=89)	
	No.	%	No.	%
Serious complications				
Severe abdominal pain	1	1.1	2	2.2
Jaundice	0	0.0	1	1.1
Blurred vision	0	0.0	1	1.1
Continuous mild pelvic pain	0	0.0	1	1.1
Combination of severe headache, respiratory difficulty, chest pain and dizziness	1	1.1	0	0.0
Total women with 1+ complications	2	2.2	4	4.5

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

Table III  
Menstrual Complaints Since Admission

Complaint	Noriday (N=89)		Lo-Femenal (N=89)	
	No.	%	No.	%
Intermenstrual bleeding				
None	76	85.4	79	88.8
Staining/spotting	4	4.5	4	4.5
Moderate	9	10.1	5	5.6
Severe	0	0.0	1	1.1
Other menstrual complaints				
Amenorrhea	4	4.5	3	3.4
Dysmenorrhea	27	30.3	25	28.1
Menorrhagia	4	4.5	6	6.7
Scanty menses	22	24.7	12	13.5
Intermenstrual pelvic pain	2	2.2	4	4.5
Dysmenorrhea and scanty menses	0	0.0	1	1.1
Heavy menses	1	1.1	1	1.1
Premenstrual pain	1	1.1	0	0.0
Premenstrual pelvic pain	0	0.0	1	1.1
Pain 2 days prior to menses	1	1.1	0	0.0
Slight menstrual pain	0	0.0	1	1.1
Painful breasts during menses	1	1.1	0	0.0
Periods are more painful	0	0.0	1	1.1
Longer periods	1	1.1	0	0.0
Shortened menstrual cycles	3	3.4	1	1.1
Total women with 1+ menstrual complaints	61	68.5	57	64.0

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

Table IV  
Other Complaints Since Admission

Complaint	Noriday (N=89)		Lo-Femenal (N=89)	
	No.	%	No.	%
Nausea	23	25.8	25	28.1
Vomiting	4	4.5	3	3.4
Headaches	48	53.9	39	43.8
Dizziness	19	21.3	20	22.5
Vaginal discharge	80	89.9	73	82.0
Breast discomfort	11	12.4	10	11.2
Total women with 1+ complaints	82	92.1	79	88.8
Other complaints				
Constipation	3	3.4	0	0.0
Mild pelvic pain	8	9.0	5	5.6
Vertigo (dizziness)	2	2.2	2	2.2
Weight gain	4	4.5	1	1.1
Pruritus vulva	2	2.2	3	3.4
General fatigue	14	15.7	12	13.5
Jaundice	1	1.1	1	1.1
Malaria	1	1.1	0	0.0
Increased appetite	8	9.0	5	5.6
Loss of appetite	1	1.1	3	3.4
Painful coitus	1	1.1	0	0.0
Slight abdominal pain	1	1.1	1	1.1
Breast tenderness	0	0.0	1	1.1
Dysuria	1	1.1	0	0.0
Rheumatic-like pain	2	2.2	0	0.0
Bloating	2	2.2	1	1.1
Back pain	3	3.4	1	1.1
Vulvo-vaginitis	3	3.4	4	4.5
Pain in the tip of breasts	3	3.4	1	1.1
Lower back pain	2	2.2	0	0.0
Palpitation	3	3.4	2	2.2
Fever	0	0.0	1	1.1
Weight loss	1	1.1	1	1.1
Generally felt bad (vomiting)	1	1.1	0	0.0
Decrease in breast milk	1	1.1	0	0.0
Engorged breasts	1	1.1	1	1.1

Table IV cont'd

## Other Complaints Since Admission

Characteristic	Noriday (N=89)		Lo-Femenal (N=39)	
	No.	%	No.	%
Anxiety	1	1.1	0	0.0
Anemia	0	0.0	1	1.1
Combination of fatigue and general anemia	1	1.1	0	0.0
Combination of cystitis and vaginal itching	0	0.0	1	1.1
Excessive saliva	1	1.1	1	1.1
Itching in the tip of breasts	0	0.0	1	1.1
Combination of general fatigue and fever	0	0.0	1	1.1
Muscular soreness on the left side of face	1	1.1	0	0.0
Minor discomfort in the joints	1	1.1	0	0.0
Excessive thirst	1	1.1	0	0.0
Total women with 1+ other complaints	49	55.1	36	40.4

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

Table V  
Changes in Complaints Since Admission

Changes in Complaints	Noriday (N=89)		I.O-Femenal (N=89)	
	No.	%	No.	%
<b>Intermenstrual bleeding</b>				
Never reported	75	84.3	78	87.6
No change	0	0.0	0	0.0
Decrease	1	1.1	1	1.1
Increase	13	14.6	10	11.2
<b>Nausea</b>				
Never reported	64	71.9	59	66.3
No change	2	2.2	0	0.0
Decrease	2	2.2	5	5.6
Increase	21	23.6	25	28.1
<b>Vomiting</b>				
Never reported	85	95.5	86	96.6
No change	0	0.0	0	0.0
Decrease	0	0.0	0	0.0
Increase	4	4.5	3	3.4
<b>Headaches</b>				
Never reported	22	24.7	30	33.7
No change	26	29.2	20	22.5
Decrease	22	24.7	22	24.7
Increase	19	21.3	17	19.1
<b>Dizziness</b>				
Never reported	65	73.0	65	73.0
No change	1	1.1	4	4.5
Decrease	5	5.6	4	4.5
Increase	18	20.2	16	18.0
<b>Vaginal discharge</b>				
Never reported	2	2.2	7	7.9
No change	37	41.6	38	42.7
Decrease	14	15.7	14	15.7
Increase	36	40.4	30	33.7
<b>Breast discomfort</b>				
Never reported	76	85.4	76	85.4
No change	2	2.2	2	2.2
Decrease	2	2.2	3	3.4
Increase	9	10.1	8	9.0

N represents the number of women ever followed up.

Table VI

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

Complaint	Noriday		Lo-Femenal	
	At Admission (N=99) %	Since Admission (N=89) %	At Admission (N=100) %	Since Admission (N=89) %
Intermenstrual bleeding	1.0	14.6**	1.0	11.2**
Other menstrual complaints	47.5	66.3**	43.0	56.2*
Nausea	6.1	25.8**	7.0	28.1**
Dizziness	10.1	21.3*	10.0	22.5*
Vaginal discharge	72.7	89.9*	71.0	82.0

\* p<.05 using McNemar's non-parametric test

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

Table VII  
Reasons for Discontinuation

Complaint	Noriday (N=89)		Lo-Femenal (N=89)	
	No.	%	No.	%
Accidental pregnancy				
Method failure	1	1.1	0	0.0
Menstrual problems				
Intermenstrual bleeding	0	0.0	1	1.1
Amenorrhea	1	1.1	0	0.0
Side effects				
Dizziness	0	0.0	1	1.1
Combination of nausea and vomiting	1	1.1	0	0.0
Other medical				
Pelvic pain	0	0.0	1	1.1
Palpitations	0	0.0	1	1.1
Jaundice	1	1.1	1	1.1
Stomachache	1	1.1	1	1.1
Anemia	0	0.0	1	1.1
Malaria	0	0.0	2	2.2
Planned pregnancy	0	0.0	1	1.1
Other personal				
Lost pills	0	0.0	1	1.1
Taking exams at school	0	0.0	1	1.1
Method not needed	1	1.1	2	2.2
Baby died	0	0.0	1	1.1
Method unrelated				
Relative ill	1	1.1	3	3.4
Couldn't return to clinic	1	1.1	0	0.0
Disinterest in study	1	1.1	0	0.0
Family reasons	1	1.1	0	0.0
Studying for exams	1	1.1	0	0.0
Resupplied elsewhere	1	1.1	0	0.0
Travel	8	9.0	10	11.2
Patient hospitalized	0	0.0	1	1.1
Total terminations	20	22.5	29	32.6

N represents number of women ever followed up.

Table VIII  
Gross Cumulative Life Table Rates

Event	Noriday (N=99) Rate ± S.E.	Lo-Femenal (N=100) Rate ± S.E.
<b>Accidental pregnancy</b>		
1 month	0.0 ± 0.0	0.0 ± 0.0
4 month	1.3 ± 1.3	0.0 ± 0.0
8 month	1.3 ± 1.3	0.0 ± 0.0
12 month	1.3 ± 1.3	0.0 ± 0.0
<b>Menstrual problems</b>		
1 month	0.0 ± 0.0	1.2 ± 1.2
4 month	1.6 ± 1.6	1.2 ± 1.2
8 month	1.6 ± 1.6	1.2 ± 1.2
12 month	1.6 ± 1.6	1.2 ± 1.2
<b>Side effects</b>		
1 month	1.1 ± 1.1	1.2 ± 1.2
4 month	1.1 ± 1.1	1.2 ± 1.2
8 month	1.1 ± 1.1	1.2 ± 1.2
12 month	1.1 ± 1.1	1.2 ± 1.2
<b>Other medical</b>		
1 month	1.1 ± 1.1	3.5 ± 2.0
4 month	1.1 ± 1.1	4.9 ± 2.4
8 month	1.1 ± 1.1	6.8 ± 3.0
12 month	3.5 ± 2.5	6.8 ± 3.0
<b>Planned pregnancy</b>		
1 month	0.0 ± 0.0	0.0 ± 0.0
4 month	0.0 ± 0.0	0.0 ± 0.0
8 month	0.0 ± 0.0	1.9 ± 1.9
12 month	0.0 ± 0.0	1.9 ± 1.9
<b>Other personal</b>		
1 month	0.0 ± 0.0	0.0 ± 0.0
4 month	0.0 ± 0.0	1.6 ± 1.6
8 month	2.0 ± 2.0	3.6 ± 2.5
12 month	2.0 ± 2.0	9.9 ± 4.2
<b>Method unrelated</b>		
1 month	3.4 ± 1.9	3.5 ± 2.0
4 month	13.6 ± 4.0	11.0 ± 3.7
8 month	15.4 ± 4.3	12.7 ± 4.0
12 month	20.5 ± 5.4	16.6 ± 4.7

Table VIII, continued

Event	Noriday (N=99) Rate	Lo-Femenal (N=100) Rate
Lost-to-follow-up		
1 month	10.1	12.0
4 month	23.2	25.0
8 month	39.4	32.0
12 month	42.4	39.0
Total discontinuations <sup>+</sup>		
1 month	10.1	14.0
4 month	30.3	34.0
8 month	55.6	50.0
12 month	60.6	63.0

+ Includes lost-to-follow-up

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