

A Comparative Study of
Triquilar versus Lo-Femenal
in Quito, Ecuador

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I. Introduction

A comparative study of two low-dose combination oral contraceptives (OCs) was conducted by the Hospital Patronato San Jose in Quito, Ecuador. This study was designed to evaluate clinical performance by determining rates of continuation and reasons for termination, including pregnancy, between Triquilar (Schering AG) and Lo-Femenal (Wyeth). The studied oral contraceptives were selected so that a comparison could be made between pills with a triphasic regimen and a low dose monophasic regimen.

Triquilar is a triphasic OC patterned after the hormonal profile of a normal female menstrual cycle and which provides a high degree of pregnancy protection at a lower monthly progestogen dosage than conventional constant-dose preparations such as Lo-Femenal. Therefore, triphasic OCs such as Triquilar may be associated with a lower incidence of reported side effects than that of monophasic OCs. 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. With Triquilar, the women receive a different dosage schedule in each of three time sequences within the same cycle.

The women receive 50 mcg levonorgestrel and 30 mcg ethinyl estradiol (EE) for the first 6 days; for the next 5 days they receive 75 mcg levonorgestrel and 40 mcg EE. During the next 10 days, the women receive 125 mcg levonorgestrel and 30 mcg EE. This is followed by 7 days in which the women receive inert tablets containing iron. Lo-Femenal, a low-dose combination pill, has a composition of 150 mcg levonorgestrel and 30 mcg ethinyl estradiol. The iron tablets in each of the products contain 75 mg of ferrous fumarate.

Study Procedure

Each woman admitted to the study had to meet the following criteria: be between the ages of 18 and 35 years old; be sexually active; if not breastfeeding, have terminated her last pregnancy at least 42 days prior to admission to the study or if breastfeeding, have terminated her last pregnancy at least 4 months prior to admission to the study; have had at least one normal menstrual period since termination of her last pregnancy; be in good health; rely exclusively upon the pills as her only method of contraception throughout the course of the study unless advised otherwise by the investigator; give informed consent, and agree to be followed up for at least 12 months.

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

A total of 102 women were admitted to the study from April 1987 through October 1988. Women admitted to the study were randomly allocated to receive either Triquilar or Lo-Femenal according to preprinted sealed envelopes opened at the time of admission; 50 women were assigned Triquilar and 52 women were assigned 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 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 therefore reported at 1, 4, 7 and 11 months. All 102 women admitted were included in the analysis. All of these women were interval patients (\geq 42 days postpartum). Fifty-five women (53.9%) were breastfeeding at admission, and were included in the study because they had completed one normal menses. The study was not blind 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. Serious adverse events were recorded by the investigator on Adverse Experience

III. Results

Sociodemographic Characteristics

Selected patient characteristics are presented by pill group in Table I. The mean age of the Triquilar group was 25.5 years and of the Lo-Femenal group, 25.2 years. The mean education levels were 10.9 and 11.1 years for Triquilar and Lo-Femenal users, respectively. The mean total live births for the Triquilar group was 1.3 and for the Lo-Femenal group was 1.4. These differences are not statistically significant ($p > .05$).

Contraceptive Practices

Table I also presents a summary of the contraceptive practices of the women one month prior to admission into the study. Twenty women (40.0%) in the Triquilar group and 16 women (30.8%) in the Lo-Femenal group reported having used no contraception in the month before study admission. The predominant method used in both groups was condoms, by 10 women (20.0%) in the Triquilar group and 10 women (19.2%) in the Lo-Femenal group. Sixteen women (32.0%) in the Triquilar group and 14 women (27.0%) in the Lo-Femenal group reported ever having used oral contraceptives prior to the study.

Complaints at Admission

None of the women reported a pre-existing medical condition at admission. Seven women (14.0%) in the Triquilar group and 13 women (25.0%) in the Lo-Femenal group reported one or more menstrual complaints (Table II). The most frequently reported primary menstrual complaint in both groups was dysmenorrhea; reported by 5 women (10.0%) in the Triquilar group and 8 women (15.4%) in the Lo-Femenal group; this difference is not statistically significant ($p > .05$). Twenty-one

women (42.0%) in the Triquilar group and 29 women (55.8%) in the Lo-Femenal group reported one or more other minor physical complaints (Table II). Headaches and vaginal discharge were the most frequently reported physical complaints. Headaches were reported by 12 women (24.0%) in the Triquilar group and 17 women (32.7%) in the Lo-Femenal group, and vaginal discharge was reported by 11 women (22.0%) in the Triquilar group and 17 women (32.7%) in the Lo-Femenal group.

Regularity of Use

Information on regularity of use was collected at 1, 4, 7, and 11 months after beginning oral contraceptive use. Compliance was based on self-report and from the date the last pill was taken prior to the date of follow-up visit. Follow-up visit data indicated that of the 73 women ever followed up, 3 women (8.1%) in the Triquilar group and 4 women (11.1%) in the Lo-Femenal group missed more than one pill at some time during the study.

Side Effects

Of the 73 women who returned for at least one follow-up visit, 3 reported serious adverse events; 1 woman in the Triquilar group and 2 women in the Lo-Femenal group (Table III). Reports of serious adverse events were based on the clinician's interpretation of the severity of the problem. The woman in the Triquilar group reported severe headaches and severe leg pain in both thighs after 7 months of pill use. She did not discontinue from the study and this complaint was not reported at further follow-up visits. However, the investigator did not report if she remained under treatment for this adverse event after the initial report. One of the women in the Lo-Femenal group

reported gastric intolerance accompanied by diarrhea, nausea, vomiting, dizziness, and headaches after only 2 weeks of pill use. She was discontinued from the study for gastric intolerance. The investigator reported that she recovered from the adverse event after stopping pill use. The second woman reported abdominal pain accompanied by gastric intolerance, vomiting and diarrhea after 4 weeks of pill use. She discontinued for abdominal pain, however, there was no indication from the investigator if she completely recovered from the adverse event after stopping pill use.

Table III also lists minor medical complaints ever reported throughout the follow-up period. Seven women (18.9%) in the Triquilar group and 7 women (19.4%) in the Lo-Femenal group reported one or more of these minor medical complaints, with chloasma being reported most often.

A summary of primary menstrual complaints ever reported throughout the follow-up period is shown in Table IV. Six women (16.2%) in the Triquilar group and 10 women (27.8%) in the Lo-Femenal group reported one or more menstrual/bleeding complaints throughout the study period. Of the primary other menstrual complaints reported, 2 women (5.4%) in the Triquilar group reported dysmenorrhea, and 2 women (5.6%) in the Lo-Femenal group ever reported dysmenorrhea and intermenstrual pelvic discomfort. Five women (13.5%) in the Triquilar group and 9 women (25.0%) in the Lo-Femenal group reported intermenstrual bleeding at follow-up visits.

A summary of typical pill-related problems and complaints ever reported at all follow-up visits is presented in Table V, and a summary of the changes in complaints is reported in Table VI. A total of 27 women (73.0%) in the

Triquilar group and 25 women (69.4%) in the Lo-Femenal group reported one or more of these typical pill-related complaints (Table V). Overall, the largest increases in complaints were for headaches for both Triquilar and Lo-Femenal users (Table VI).

Discontinuation Rates and Reasons

A summary of all reasons for discontinuation is presented in Table VII. Eight women (21.6%) in the Triquilar group and 11 women (30.1%) in the Lo-Femenal group discontinued during the study period. The reasons provided most often by both the Triquilar and Lo-Femenal groups were for side effects such as headaches.

There was one accidental pregnancy in the Lo-Femenal group during the study period. The pregnancy was attributed to user failure by the investigator because the woman stopped taking her pills on her own accord after experiencing skin problems (3 months after initiating use).

Lost to follow-up and total discontinuation percentages, along with woman months of use are presented in Table VIII. The lost to follow-up percentages at 11 months for the two groups were 56.0 for Triquilar users and 55.8 for Lo-Femenal users. The 11 month total discontinuation percentages (including lost to follow-up) were 70.0 for the Triquilar group and 76.9 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, Triquilar and Lo-Femenal, was conducted at the Hospital Patronato San Jose in Quito, Ecuador. The objectives of this study were to compare and evaluate the effectiveness, side effects, and continuation rates of the aforementioned oral contraceptives. This report includes an analysis of 102 women; all of whom were interval patients (\geq 42 days since last pregnancy termination). 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 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 therefore reported at 1, 4, 7 and 11 months.

The lost to follow-up percentages at 11 months were 56.0 for Triquilar users and 55.8 for Lo-Femenal users. The 11 month total discontinuation percentages (including women lost to follow-up) were 70.0 and 76.9 for the Triquilar and Lo-Femenal groups, respectively. The rate at 11 months for method-related discontinuations was 13.0 ± 6.2 for Triquilar users and 20.6 ± 8.1 for Lo-Femenal users; this is an indicator of clinical acceptability. Their reasons for termination were generally for side effects such as headaches. One accidental pregnancy was reported in the Lo-Femenal group; it was attributed to user failure by the investigator.

Table I
Selected Sociodemographic Characteristics

Characteristic	Triquilar (N=50)		Lo-Femenal (N=52)	
	No.	% ^a	No.	% ^a
Age (years)				
18-20	6	12.0	4	7.7
20-24	18	36.0	20	38.5
25-29	18	36.0	22	42.3
30-34	8	16.0	6	11.5
Mean	25.5		25.2	
Education (years)				
4-6	5	10.0	8	15.4
7-12	33	66.0	28	53.8
13+	12	24.0	16	30.8
Mean	10.9		11.1	
Total live births				
0	1	2.0	3	5.8
1	31	62.0	29	55.8
2	18	36.0	18	34.6
3	0	0.0	2	3.8
Mean	1.3		1.4	
Contraceptive method used one month prior to admission				
None	20	40.0	16	30.9
Condoms	10	20.0	10	19.2
Foam/Diaphragm/Jelly	8	16.0	9	17.3
Oral contraceptives	5	10.0	7	13.5
IUD	3	6.0	8	15.4
Withdrawal/Rhythm	4	8.0	2	3.8

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	Triquilar (N=50)		Lo-Femenal (N=52)	
	No.	%	No.	%
Intermenstrual bleeding				
None	49	98.0	47	90.4
Staining/Spotting	1	2.0	4	7.7
Severe (Clots)	0	0.0	1	1.9
Primary Other Menstrual Complaints ¹				
None	44	88.0	40	76.9
Dysmenorrhea	5	10.0	8	15.4
Menorrhagia	1	2.0	1	1.9
Intermenstrual pelvic discomfort	0	0.0	3	5.8
Total women with one or more menstrual/bleeding complaints	7	14.0	13	25.0
Other complaints reported in past month				
Headaches	12	24.0	17	32.7
Vaginal discharge	11	22.0	17	32.7
Dizziness	3	6.0	7	13.5
Nausea	2	4.0	3	5.8
Breast discomfort	2	4.0	3	5.8
Vomiting	0	0.0	2	3.8
Total women with one or more complaints	21	42.0	29	55.8

N represents the number of women in the analysis.
Multiple complaints may be reported per woman.

Table III
Medical Complaints Since Admission

Characteristic	Triquilar (N=37)		Lo-Femenal (N=36)	
	No.	%	No.	%
Serious complications				
Severe abdominal pain	0	0.0	1	2.8
Combination: Severe headaches and intense pain in thighs	1	2.7	0	0.0
Combination: Severe headaches, nausea and vomiting	0	0.0	1	2.8
Total women with serious complications	1	2.7	2	5.6
Minor complaints ¹				
Loss of appetite	1	2.7	0	0.0
Vaginal discharge	1	2.7	0	0.0
Dyspnea	1	2.7	0	0.0
Weakness	1	2.7	0	0.0
Insomnia	1	2.7	0	0.0
Chloasma	2	5.4	3	8.3
Skin problems	0	0.0	1	2.8
Epigastric pain	0	0.0	1	2.8
Gastric intolerance	0	0.0	1	2.8
Gastric pain	1	2.7	0	0.0
Photosensitivity	1	2.7	0	0.0
Burning in legs	1	2.7	0	0.0
Sweating	0	0.0	1	2.8
Lactation decrease	1	2.7	0	0.0
Total women with one or more minor medical complaints	7	18.9	7	19.4

N represents number of women ever followed up.

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

Table IV
Menstrual Complaints Ever Reported Since Admission

Complaint	Triquilar (N=37)		Lo-Femenal (N=36)	
	No.	%	No.	%
Intermenstrual bleeding ¹				
None	32	86.5	27	75.0
Staining/spotting	2	5.4	5	13.9
Moderate	3	8.1	4	11.1
Primary other menstrual complaint ²				
None	35	94.6	34	94.4
Dysmenorrhea	2	5.4	1	2.8
Intermenstrual pelvic discomfort	0	0.0	1	2.8
Total women with one or more menstrual/bleeding complaints	6	16.2	10	27.8

N represents number of women ever followed up.

¹Most severe ever reported.

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

Table V
Other Complaints Ever Reported Since Admission

Complaint	Triquilar (N=37)		Lo-Femenal (N=36)	
	No.	%	No.	%
Headaches	20	54.0	17	47.2
Vaginal discharge	9	24.3	12	33.4
Dizziness	9	24.3	5	13.9
Nausea	8	21.6	5	13.9
Breast discomfort	7	18.9	4	11.1
Vomiting	5	13.5	3	8.4
Total women with one or more complaints	27	73.0	25	69.4

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

Table VI¹

Changes in Severity of Complaints Since Admission

Changes in Complaints	Triquilar (N=37)		Lo-Femenal (N=36)	
	No.	%	No.	%
Intermenstrual bleeding				
Never reported	31	83.6	25	69.4
No change	0	0.0	1	2.8
Decrease	1	2.7	2	5.6
Increase	5	13.5	8	22.2
New reports	5	13.5	8	22.2
Nausea				
Never reported	28	75.7	31	86.1
No change	0	0.0	0	0.0
Decrease	1	2.7	0	0.0
Increase	8	21.6	5	13.9
New reports	7	18.9	4	11.1
Vomiting				
Never reported	32	86.5	33	86.1
No change	0	0.0	0	0.0
Decrease	0	0.0	0	0.0
Increase	5	13.5	3	8.3
New reports	5	13.5	2	5.6
Headaches				
Never reported	13	35.1	15	41.7
No change	2	5.4	2	5.6
Decrease	4	10.8	4	11.1
Increase	18	48.6	15	41.7
New reports	14	37.8	14	38.9
Dizziness				
Never reported	25	67.6	29	80.6
No change	0	0.0	1	2.8
Decrease	3	8.1	2	5.6
Increase	9	24.3	4	11.1
New reports	9	24.3	4	11.1

(cont.)

Table VI (cont.)

Changes in Severity of Complaints Since Admission

Changes in Complaints	Triquilar (N=37)		Lo-Femenal (N=36)	
	No.	%	No.	%
Vaginal discharge				
Never reported	21	56.8	16	44.4
No change	3	8.1	2	5.6
Decrease	7	18.9	8	22.2
Increase	6	16.2	10	27.8
New reports	6	16.2	10	27.8
Breast discomfort				
Never reported	29	78.4	31	86.1
No change	1	2.7	0	0.0
Decrease	1	2.7	1	2.8
Increase	6	16.2	4	11.1
New reports	6	16.2	4	11.1

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. 4 months from the 4 to 8 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 and 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
Reasons for Discontinuation

Complaint	Triquilar (N=37)		Lo-Femenal (N=36)	
	No.	%	No.	%
Accidental pregnancy				
User failure	0	0.0	1	2.8
Side effects				
Vomiting	1	2.7	0	0.0
Loss of appetite	1	2.7	0	0.0
Headaches	1	2.7	3	8.3
Vaginal discharge	0	0.0	1	2.8
Chloasma	0	0.0	2	5.6
Combination: Nausea & headaches	1	2.7	0	0.0
Other medical				
Gastric intolerance	0	0.0	1	2.8
Epigastric pain	0	0.0	1	2.8
Planning pregnancy	1	2.7	1	2.8
Other personal				
Forgetfulness	1	2.7	0	0.0
Method unrelated				
Moving/travel	2	5.4	1	2.8
Total Discontinuations	8	21.6	11	30.1

N represents number of women ever followed up.

Table VIII

Lost To Follow-up And Total Discontinuation Percentages

Event	Triquilar (N=50)	Lo-Femenal (N=52)
Lost-to-follow-up percentage ¹		
1 month	26.0	30.8
4 month	38.0	40.4
7 month	42.0	46.2
11 month	56.0	55.8
Total discontinuation percentage ²		
1 month	28.0	36.5
4 month	46.0	53.8
7 month	56.0	61.5
11 month	70.0	76.9
Woman months		
1 month	41.5	42.0
4 month	125.5	118.5
7 month	191.5	181.0
11 month	256.0	244.0

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	Triquilar (N=50)		Lo-Femenal (N=52)	
	At Risk	Rate \pm S.E.	At Risk	Rate \pm S.E.
Accidental Pregnancy				
1 month	40.0	0.0 \pm 0.0	39.5	0.0 \pm 0.0
4 month	25.0	0.0 \pm 0.0	23.5	3.7 \pm 3.6
7 month	22.0	0.0 \pm 0.0	20.0	3.7 \pm 3.6
11 month	13.5	0.0 \pm 0.0	10.5	3.7 \pm 3.6
Side effects				
1 month	40.5	2.5 \pm 2.4	41.0	7.3 \pm 4.1
4 month	26.0	13.0 \pm 6.2	23.5	10.9 \pm 5.2
7 month	22.0	13.0 \pm 6.2	20.0	15.1 \pm 6.5
11 month	13.5	13.0 \pm 6.2	10.5	20.6 \pm 8.1
Other medical reasons				
1 month	40.0	0.0 \pm 0.0	40.5	4.9 \pm 3.4
4 month	25.0	0.0 \pm 0.0	23.5	4.9 \pm 3.4
7 month	22.0	0.0 \pm 0.0	20.0	4.9 \pm 3.4
11 month	13.5	0.0 \pm 0.0	10.5	4.9 \pm 3.4
Planning pregnancy				
1 month	40.0	0.0 \pm 0.0	39.5	0.0 \pm 0.0
4 month	25.0	0.0 \pm 0.0	23.5	0.0 \pm 0.0
7 month	22.0	0.0 \pm 0.0	20.0	0.0 \pm 0.0
11 month	13.5	0.0 \pm 0.0	10.5	6.5 \pm 6.2
Other personal reasons				
1 month	40.5	2.5 \pm 2.4	39.5	0.0 \pm 0.0
4 month	25.5	2.5 \pm 2.4	23.5	0.0 \pm 0.0
7 month	22.0	2.5 \pm 2.4	20.0	0.0 \pm 0.0
11 month	13.5	2.5 \pm 2.4	10.5	0.0 \pm 0.0

(cont.)

Table IX (cont.)

Gross Cumulative Life Table Discontinuation Rates

Event	Triquilar (N=50)		Lo-Femenal (N=52)	
	At Risk	Rate \pm S.E.	At Risk	Rate \pm S.E.
Method unrelated reasons				
1 month	40.5	2.5 \pm 2.4	39.5	0.0 \pm 0.0
4 month	25.5	6.3 \pm 4.4	23.5	0.0 \pm 0.0
7 month	22.0	6.3 \pm 4.4	20.0	0.0 \pm 0.0
11 month	13.5	6.3 \pm 4.4	10.5	5.1 \pm 5.0
Method related reasons				
1 month	40.5	2.5 \pm 2.4	41.0	7.3 \pm 4.1
4 month	26.0	13.0 \pm 6.2	23.5	10.9 \pm 5.2
7 month	22.0	13.0 \pm 6.2	20.0	15.1 \pm 6.5
11 month	13.5	13.0 \pm 6.2	10.5	20.6 \pm 8.1

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