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A Comparative Study of Triquilar  
Versus Marvelon  
in Kuala Lumpur, Malaysia

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## I. Introduction

A comparative study of two low dose combination oral contraceptives (OCs) was conducted at Pusat Kepakaron Reproductif, LPPKN in Kuala Lumpur, Malaysia. Triquilar is a triphasic OC patterned after the hormonal profile of a normal menstrual cycle which provides a high degree of pregnancy protection at a lower total monthly steroid dosage than conventional constant-dose preparations. Therefore, Triquilar may be associated with a lower incidence of reported side effects than that of conventional OCs. Marvelon is a low-dose monophasic, combined OC. The progestogen it contains, desogestrel, has no androgenic activity, with a minimal binding affinity for the androgen receptor and a high binding affinity for the progesterone receptor. Marvelon has been shown to be highly effective and to provide good cycle control while at the same time not inducing androgenic side effects such as acne or increasing overall body weight. This study was designed to determine if there were differences in the discontinuation rates between Triquilar (Shering AG) and Marvelon (Organon) as well as the frequency of selected symptoms contributing to method discontinuation. The studied oral contraceptives were selected so that a comparison could be made between pills with a low dose monophasic regimen and a triphasic regimen.

## II. Study Design

### Oral Contraceptive Evaluated

Each of the OCs administered in this study was provided in

packages of 21 active steroid tablets with no pills to be taken for 7 days. Each cycle of Triquilar, a triphasic low estrogen dose combination OC, has a composition of 6 tablets containing 50 mcg levonorgestrel and 30 mcg ethinyl estradiol (EE), followed by 5 tablets of 75 mcg levonorgestrel and 40 mcg EE, followed by 10 tablets of 125 mcg levonorgestrel and 30 mcg EE. Marvelon, a monophasic low dose combination pill, has a composition of 150 mcg desogestrel and 30 mcg ethinyl estradiol.

### 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 in good physical health, be sexually active, have terminated her last pregnancy at least 42 days prior to admission to the study and have had at least one menstrual period since termination of her last pregnancy, not to be breastfeeding, want to use oral contraceptives as a method of contraception, be willing to rely exclusively upon the pills as her only method of contraception throughout the course of the study, give informed consent and be followed-up for at least 12 months. Normal clinic criteria for contraindications to oral contraceptive use were to be followed. In addition, women with any of the following conditions were to be excluded from the study: pregnancy; thromboembolic disorders; history or evidence of cardiac failure, diabetes, renal dysfunction, epilepsy, hypertension or migraine, severe liver disorders or breast cancer; history of jaundice, severe pruritus or herpes gestationis during pregnancy or due to progestogen use;

undiagnosed vaginal bleeding; prior use of oral contraceptives within three months of admission or prior use of injectable contraceptives within six months of admission, or chronic use of internal medications, such as antibiotics and barbiturates, which could reduce pill effectiveness.

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

Women were admitted to the study from March 1986 through September 1986. A total of 200 women were randomly allocated to receive either Triquilar or Marvelon according to preprinted sealed envelopes opened at the time of admission; 100 women were given Triquilar and 100 women were given Marvelon. The study was not blinded because an evaluation of the products as they appear on the market was desired. Follow-up visits were scheduled at one, four, eight and twelve (most women came in at 11 months) months after admission to the study. Four of the women were breastfeeding with supplementation at admission, and were included in the study as they had completed one normal menses. One woman in the Triquilar group was excluded from the analysis because of pregnancy prior to her beginning her assigned OC (study admission). A second woman in the Triquilar group was excluded because she never began taking the pills. All of the 198 women included in the analysis were interval patients (42 days since last pregnancy termination).

### III. Results

#### Sociodemographic Characteristics

Selected patient characteristics are presented by group in Table I. The mean age of the Triquilar group was 27.0 years and of the Marvelon group, 27.2 years. The mean education levels were 9.2 and 8.8 years for Triquilar and Marvelon users respectively. The mean total live births was 2.2 for both the Triquilar and Marvelon groups.

#### 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 (79.6%) from the Triquilar group and 85 women (85.0%) from the Marvelon group reported having used no contraception in the month before study admission. The predominant method used in both groups prior to admission was condoms, by 12 women (12.2%) in the Triquilar group and 8 women (8.0%) in the Marvelon group. A total of 6 women (6.1%) in the Triquilar group and 13 women (13.0%) in the Marvelon group reported ever having used oral contraceptives prior to the study; this difference was not significant (not shown).

#### Complaints at Admission

None of the women reported a preexisting medical condition at admission. One woman in the Triquilar group, however, was later diagnosed with thyrotoxicosis and was discontinued for this

reason. The woman had had this condition previously and had been stabilized by medication but had failed to return for follow-up visits. At admission, 3 women (3.1%) in the Triquilar group and 4 women (4.0%) in the Marvelon group reported minor physical complaints. These seven women reported dysmenorrhea, and one woman in the Marvelon group reported headache, dizziness and vaginal discharge at admission (not shown).

#### Regularity of Use

Regularity of use data were collected at one, four, eight and eleven 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 contact. Follow-up visit data indicate that 5 women (5.1%) in the Triquilar group and 2 women (2.0%) in the Marvelon group missed at least one pill, and that 15 women (15.3%) in the Triquilar group and 9 women (9.1%) in the Marvelon group missed more than one pill at some time during the study period. One woman in the Triquilar group was unable to take the pills correctly and was discontinued for this reason. In addition, 6 women (6.1%) in the Triquilar group and three women (3.0%) in the Marvelon group were discontinued for "forgetfulness", missing three or more consecutive pills.

#### Side Effects

Serious complications were reported by 2 women in the Triquilar group and by 2 women in the Marvelon group during the study period (Table II). These complications were based on the

patient's interpretation and on the medical opinion of the investigator as to the severity of the problem. In the Triquilar group, one woman reported severe headache and discontinued for a combination of headache and vomiting. The other woman was diagnosed with symptoms of thyrotoxicosis (heavy tremors and palpitations). She had had this condition before and had been stabilized on medication but had failed to return for follow-up visits. In the Marvelon group, one woman reported severe headaches and discontinued for this complaint. The other woman reported a "black out," giddiness and a fainting spell at her office. She discontinued for a combination of nausea and giddiness which had increased during her second month of pill use.

Other complaints were reported by 7 women (7.1%) in the Triquilar group and two women (2.0%) in the Marvelon group (Table II). The women in the Triquilar group had complaints of dryness of the vagina, weight gain, allergy, dyspepsia, generalized itchiness and numbness of fingers and toes. The women in the Marvelon group had complaints of generalized itchiness and dyspepsia.

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. Fourteen women (14.3%) in the Triquilar group and 9 women (9.1%) in the Marvelon group reported at least one menstrual complaint; this difference was not statistically significant ( $p > 0.05$ ).

A summary of the changes in complaints and new reports of complaints since admission is presented in Table IV. A total of 20 women (20.4%) in the Triquilar group and 20 women (20.0%) in the Marvelon group reported one or more of these complaints. The two groups were not significantly different ( $p>0.05$ ) in changes or new reports of other complaints. An analysis of changes in the percentage of women reporting complaints at admission and at the one month follow-up contact showed no significant change ( $p>.05$ ) in reports of menstrual or common complaints from baseline data.

#### Discontinuation Rates and Reasons

A summary of all reasons for discontinuation is presented in Table V. A total of 41 women (41.8%) in the Triquilar group and 33 women (33.3%) in the Marvelon group discontinued use during the 12 month study period. Personal reasons such as "desires method change" were the primary reasons given for discontinuation in both groups followed by method unrelated reasons.

Eleven month gross cumulative discontinuation event rates are presented in Table VI. Eleven month total discontinuation rates were 46.9 for the Triquilar group and 40.0 for the Marvelon group. The corresponding lost-to-follow-up rates for the two groups were 5.1 for the Triquilar group and 7.0 for the Marvelon group. Neither differences were statistically significant ( $p>.05$ ).

Three accidental pregnancies occurred in the Triquilar group during the study period. All were attributed by the investigator

to method failure because the women reported taking their pills correctly when they became pregnant. Duration of pill use at estimated date of conception was different (<1 month, 3 months, 4 months) in each case. For the woman who conceived after less than one month of pill use the contraceptive method used prior to study admission was condoms. There was no information available as to the outcome of these pregnancies. No accidental pregnancies were reported in the Marvelon group.

#### IV. Summary

A study of a low dose triphasic oral contraceptives, Triquilar and a low-dose monophasic OC, Marvelon, was conducted at the Pusat Kepakaron Reproductif, LPPKN Kuala Lumpur, Malaysia to determine if there were differences in discontinuation rates and reasons for discontinuation. This report includes an analysis of 198 women, all interval patients, randomly allocated to one of the above oral contraceptives between March 1986 and September 1986. Follow-up visits were scheduled at one, four, eight and twelve months after admission. Most of the women that returned for the final visit returned during the eleventh month rather than at the scheduled twelve month visit.

The lost-to-follow-up rates were 5.1 for the Triquilar group and 7.0 for the Marvelon group. The rate for total discontinuations (all discontinuations including women lost-to-follow-up) was 46.9 and 40.0 for the Triquilar and Marvelon groups, respectively. The primary reason for discontinuation was for personal reasons such

as "desires method change", in both groups. There were three accidental pregnancies in the Triquilar group during the study period. All three were attributed to method failure.

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## Data Quality Statement

The overall data quality of this study was very good. Of the 200 women admitted to this study, two women in the Triquilar group were excluded. One woman was excluded for pregnancy prior to study admission and one woman never began taking the pills. Lost-to-follow-up rates at 11 months were low at approximately 6% - an above average level. There were three accidental pregnancies attributed to method failure in the Triquilar group. There were no accidental pregnancies in the Marvelon group. A total of six women (6.1%) in the Triquilar group and three women (3.0%) in the Marvelon group were discontinued for "forgetfulness", for missing five or more consecutive pills. Additionally, in the Triquilar group two women discontinued because the "method was troublesome". Overall data quality was good; the investigator was very conscientious and queries were answered with adequate speed.

Table I  
Selected Sociodemographic Characteristics

Characteristic	Triquilar (N=98)		Marvelon (N=100)	
	No.	%	No.	%
<b>Age (years)</b>				
Less than 20	6	6.1	4	4.0
20-24	19	19.4	27	27.0
25-29	51	52.0	44	44.0
30-34	21	21.4	22	22.0
35-39	1	1.0	3	3.0
40+	0	0.0	0	0.0
Mean	27.0		27.2	
<b>Education (years)</b>				
0	1	1.0	1	1.0
1-6	20	20.4	20	20.0
7-12	67	68.4	78	78.0
>12	10	10.2	1	1.0
Mean	9.2		8.8	
<b>Total live births</b>				
0	0	0.0	0	0.0
1-2	67	68.4	66	66.0
3-4	25	25.5	31	31.0
5+	6	6.1	3	3.0
Mean	2.2		2.2	
<b>Contraceptive method used 1 month prior to admission</b>				
None	78	79.6	85	85.0
IUD	6	6.1	7	7.0
Orals	1	1.0	0	0.0
Injectables/implants	0	0.0	0	0.0
Condoms	12	12.2	8	8.0
Withdrawal/rhythm	0	0.0	0	0.0
Foam/diaphragm/jelly	0	0.0	0	0.0
Other (traditional medicine)	1	1.0	0	0.0

Table II  
Complications and Complaints Since Admission

Characteristic	Triquilar (N=98)		Marvelon (N=99)	
	No.	%	No.	%
Serious complications				
Severe headache	1	1.0	1	1.0
Thyrotoxicosis	1	1.0	0	0.0
"Black out" (giddiness, fainting spell)	0	0.0	1	1.0
Total women with serious complications	2	2.0	2	2.0
Other complaints				
Itchiness	1	1.0	0	0.0
Generalized itchiness	1	1.0	1	1.0
Epigastric pain (dyspepsia)	1	1.0	1	1.0
Weight gain	1	1.0	0	0.0
Dryness of vagina	2	2.0	0	0.0
Numbness of fingers and toes	1	1.0	0	0.0
Total women with 1+ other complaints	7	7.1	2	2.0

N represents number of women followed up.

Table III  
Menstrual Complaints Since Admission

Complaint	Triquilar (N=98)		Marvelon (N=99)	
	No.	%	No.	%
Intermenstrual bleeding				
None	87	88.8	93	93.9
Staining/spotting	6	6.1	4	4.0
Moderate	5	5.1	2	2.0
Severe	0	0.0	0	0.0
Primary other menstrual complaint				
None	91	92.9	96	97.0
Amenorrhea	3	3.1	2	2.0
Dysmenorrhea	1	1.0	1	1.0
Menorrhagia	1	1.0	0	0.0
Scanty menses	1	1.0	0	0.0
Intermenstrual pelvic pain or discomfort	1	1.0	0	0.0
Total women with 1+ menstrual complaints	14	14.3	9	9.1

N represents number of women ever followed up.

Table IV

## Changes in Complaints Since Admission

Changes in Complaints	Triquilar (N=98)		Marvelon (N=99)	
	No.	%	No.	%
<b>Intermenstrual bleeding</b>				
Never reported	87	88.8	93	93.9
No change	0	0.0	0	0.0
Decrease	0	0.0	0	0.0
Increase	0	0.0	0	0.0
New reports <sup>+</sup>	11	11.2	6	6.1
<b>Nausea</b>				
Never reported	90	91.8	93	93.9
No change	0	0.0	0	0.0
Decrease	0	0.0	0	0.0
Increase	0	0.0	0	0.0
New reports	8	8.2	6	6.1
<b>Vomiting</b>				
Never reported	94	95.9	96	97.0
No change	0	0.0	0	0.0
Decrease	0	0.0	0	0.0
Increase	0	0.0	0	0.0
New reports	4	4.1	3	3.0
<b>Headaches</b>				
Never reported	92	93.9	83	83.8
No change	0	0.0	0	0.0
Decrease	0	0.0	1	1.0
Increase	0	0.0	0	0.0
New reports	6	6.1	15	15.2
<b>Dizziness</b>				
Never reported	95	96.9	92	92.9
No change	0	0.0	0	0.0
Decrease	0	0.0	1	1.0
Increase	0	0.0	0	0.0
New reports	3	3.1	6	6.1

N represents the number of women ever followed up.

+ New reports = complaints reported by women at sometime during follow-up which were not previously reported at admission.

Table IV Cont'd  
Changes in Complaints Since Admission

Changes in Complaints	Triquilar (N=98)		Marvelon (N=99)	
	No.	%	No.	%
Vaginal discharge				
Never reported	95	96.9	95	96.0
No change	0	0.0	0	0.0
Decrease	0	0.0	1	1.0
Increase	0	0.0	0	0.0
New reports	3	3.1	3	3.0
Breast discomfort				
Never reported	95	96.9	99	100.0
No change	0	0.0	0	0.0
Decrease	0	0.0	0	0.0
Increase	0	0.0	0	0.0
New reports	3	3.1	0	0.0
Total women with 1+ complaints	20	20.4	20	20.0

N represents the number of women ever followed up.

Table V  
Reasons for Discontinuation

Complaint	Triquilar (N=98)		Marvelon (N=99)	
	No.	%	No.	%
Accidental pregnancy				
Method failure	3	3.1	0	0.0
Menstrual problems				
Spotting	1	1.0	0	0.0
Intermenstrual bleeding	1	1.0	0	0.0
Combination of intermenstrual bleeding and menorrhagia	1	1.0	0	0.0
Side effects				
Weight gain	1	1.0	0	0.0
Headaches	0	0.0	2	2.0
Combination of giddiness and nausea	0	0.0	1	1.0
Combination of vomiting and nausea	0	0.0	1	1.0
Combination of vomiting and headache	1	1.0	0	0.0
Other medical reason				
Itchiness, rash over body	1	1.0	0	0.0
Thyrototoxicosis	1	1.0	0	0.0
Generalized itchiness	0	0.0	1	1.0
Planned pregnancy	1	1.0	1	1.0
Other personal				
Forgetfulness	6	6.1	3	3.0
Desires method change	11	11.2	14	14.1
Method not needed	1	1.0	3	3.0
Other personal	0	0.0	1	1.0
Method troublesome	2	2.0	0	0.0
Husband objects	1	1.0	0	0.0
Method unrelated				
Can't return to clinic	1	1.0	1	1.0
Moving/travel	5	5.1	4	4.0
Disinterested in study	3	3.1	1	1.0
Total terminations	41	41.8	33	33.3

N represents number of women ever followed up.

Table VI  
Gross Cumulative Life Table Rates

Event	Triquilar (N=98) Rate $\pm$ S.E.	Marvelon (N=100) Rate $\pm$ S.E.
<b>Accidental pregnancy</b>		
1 month	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
4 month	1.2 $\pm$ 1.2	0.0 $\pm$ 0.0
8 month	4.2 $\pm$ 2.4	0.0 $\pm$ 0.0
11 month	4.2 $\pm$ 2.4	0.0 $\pm$ 0.0
<b>Menstrual problems</b>		
1 month	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
4 month	1.4 $\pm$ 1.3	0.0 $\pm$ 0.0
8 month	2.8 $\pm$ 2.0	0.0 $\pm$ 0.0
11 month	2.8 $\pm$ 2.0	0.0 $\pm$ 0.0
<b>Side effects</b>		
1 month	1.1 $\pm$ 1.1	2.1 $\pm$ 1.5
4 month	2.3 $\pm$ 1.6	4.4 $\pm$ 2.1
8 month	3.8 $\pm$ 2.2	4.4 $\pm$ 2.1
11 month	5.5 $\pm$ 2.7	4.4 $\pm$ 2.1
<b>Other medical reasons</b>		
1 month	0.0 $\pm$ 0.0	1.1 $\pm$ 1.1
4 month	1.2 $\pm$ 1.2	1.1 $\pm$ 1.1
8 month	1.2 $\pm$ 1.2	1.1 $\pm$ 1.1
11 month	1.2 $\pm$ 1.2	1.1 $\pm$ 1.1
<b>Planned pregnancy</b>		
1 month	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
4 month	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
8 month	1.7 $\pm$ 1.7	1.5 $\pm$ 1.5
11 month	1.7 $\pm$ 1.7	1.5 $\pm$ 1.5
<b>Other personal reasons</b>		
1 month	10.4 $\pm$ 3.1	8.2 $\pm$ 2.8
4 month	18.3 $\pm$ 4.0	15.8 $\pm$ 3.8
8 month	23.6 $\pm$ 4.5	22.8 $\pm$ 4.4
11 month	23.6 $\pm$ 4.5	22.8 $\pm$ 4.4
<b>Method unrelated reasons</b>		
1 month	1.1 $\pm$ 1.1	0.0 $\pm$ 0.0
4 month	6.3 $\pm$ 2.7	1.3 $\pm$ 1.3
8 month	12.4 $\pm$ 3.9	8.2 $\pm$ 3.2
11 month	12.4 $\pm$ 3.9	8.2 $\pm$ 3.2

Table VI, continued

Event	Triquilar (N=98) Rate	Marvelon (N=100) Rate
Lost-to-follow-up Rate		
1 month	0.0	1.0
4 month	3.1	2.0
8 month	3.1	5.0
11 month	5.1	7.0
Total discontinuations <sup>+</sup>		
1 month	1.0	4.0
4 month	25.5	22.0
8 month	41.8	36.0
11 month	46.9	40.0
Woman months		
1 month	97.0	99.0
4 month	340.5	350.0
8 month	592.5	644.5
11 month	740.5	811.0

+ Total discontinuations includes all women who discontinued for a specific reason and those women lost-to-follow-up