Prospective Study of a Monophasic Oral Contraceptive Pill Containing 20 mcg Ethinyl Oestradiol and 150 mcg Progestrel (Mercilon ™)

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Abstract

Oral contraceptive pill registered 72 - 75% of the overall contraceptive usage ever since it was introduced in Malaysia. Most of the oral contraceptive pills available contain 30 mcg of Ethinyl Oestradiol and a standard progestogen, which ranges from Levanogestrel, Desogestrel and Gestoden. Mercilon™ however is an oral contraceptive containing the progestogen, Desogestrel and 20 mcg of Ethinyl Oestradiol which has recently been introduced in the Malaysian market. A similar concentration known as Marvelon which contains Desogestrel and 30 mcg of Ethinyl Oestradiol has already been available in Malaysia since 1982 and has already been evaluated. Therefore it is imperative that Mercilon™ be put on trial as well. In this prospective, open and non-comparative study 200 women in the reproductive age group who asked for oral contraceptives were given Mercilon™. They were counselled on when to start the first and the subsequent packet of pills and were informed to come for a scheduled 1,2,3 and 6th cycle follow-ups. The duration of the study was 6 months. At follow-ups, cycle efficacy, cycle control and side effects were assessed. Body weight and blood pressure were also measured. 190 women completed the study. There was no pregnancy. The incidences of irregular bleeding were minimal and stabilised towards subsequent cycles. Subjective side effects like nausea, giddiness and headache were few. Blood pressure and body weights were not affected. Mercilon™ is well accepted by the study group.

Introduction

Oral contraceptives have been modified considerably over the past 30 years they have been in use. Epidemiologial research into the incidence of the thromboembolic side effects of oral contraceptives [1-4] led to the lowering of the oestrogen portion of the pill from 150 mg in the 70's to 30 mcg in the most currently available preparations. Further epidemiological studies demonstrated a relationship between the risk of ischaemic heart disease and the concentration of lipoproteins in serum [5-6]. This subsequently led to the development of a new generation of highly selective progestogens of which desogestrel is the first and the most commonly used. Further changes have been made to the formulation of combined oral contraceptive pills to improve their safety, the result of which is the formulation of combined oral contraceptive pills containing 20 mcg Ethinyl

Oestradiol and 150 mcg of Desogestrel known as Mercilon™. Mercilon™ has been introduced in 1988 and made available in Malaysia since 1992.

Clinical studies on this new ultra-low dose oral contraceptive have shown it to be reliable with good cycle control and low incidences of side effects [7-8]. The acceptability and reliability of this new formula among Asian women need to be evaluated. This paper presents a Malaysian report of a multicentre, multinational, prospective non-comparative study of Mercilon™.

Materials and Methods

Two hundred women who requested for oral contraception participated in the trial. They were recruited through the National Population and Family Development Board's Clinics at the Maternity Hospital, University Hospital, Selayang, Kepong and Salak South. Both starters and switchers from other oral contraceptives were included, in addition to which the number of switchers would not be more than half of the total of investigated women. All women were healthy and between 18 - 40 years of age. At screening, the usual contraindications to oral contraceptive use were included and verbal informed consent was obtained and clients were counselled on the method accordingly.

Clients were advised to take one Mercilon™ tablet per day preferably at the same time in the morning or evening, for 21 consecutive days followed with 7 days pill free interval before starting on the next packet. Starters were instructed to take the first pill on the first day of menstruation or up to day 5. Late starters were advised to use an additional contraceptive method (e.g. barrier) during the first week. Switchers were instructed not to use any active tablets for 7 days after the last tablet of the strip of their previous oral contraceptive and to then start with the trial medication. The total study period was for 6 cycles.

After inclusion in the study, clients were instructed to return to the clinic after 1,2,3 and 6 treatment cycles. Cycle control was assessed with a daily card on which clients had to fill their daily tablet intake and occurrence of any vaginal bleeding. Irregular bleeding was defined as bleeding which occur during pill intake, which include all patterns of breakthrough bleeding (BTB). Vaginal spotting is defined as requiring a pad, moderate bleeding as requiring 2-3 pads and heavy bleeding that needed more than 3 pads per day.

At each follow-up visits the women were asked if they had experienced any side effects during the fast cycle (s). Blood pressure and weight were recorded during each visit. Clients were instructed to return to the clinics if they had any problem. During the course of the trial 10 case records were found to be irregular and the patients could not be traced.

The study ran from February 1992 to the end of September 1992. A standard protocol (N.V. Organon) was used. The information on the diary cards and other details were transferred to computerised forms. These data were analysed by the Population Research Division of the National Population and Family Development Board.

Results

Case records of 190 study clients were analysed. Demographic profile of the acceptors (Table 1) showed that 70.5% of the acceptors belong to the 25-34 years age group and less than 17% were in the 15-24 years of age. 98% of the acceptors have at least one child and only 4 acceptors were childless. In terms of previous contraceptive method everused 63.7% have never used any method before, 26.3% had taken pills before and the rest IUCD, condoms and others.

Table I : Distribution of Acceptors by Selected Demographic Characteristics

Demographic Characteristics	Percentage
Age Groups (Years)	1.6
15-19	14.7
20-24	38.4
25-29	32.1
30-34	13.2
35-40	
Parity	2.1
0	60.5
1-2	30.0
3-4	7.4
5 +	
Previous Contraceptive Method	26.3
Pill	3.2
IUCD	6.3
Condom	0.5
Other	63.7
None	

The side effects were minimal the most common side effects (nausea, giddiness, rashes) were slightly increased during the first treatment cycle, but later ceased to minimal on subsequent use (Table II).

Table II : Side-effects experienced by women according to the cycles

	Cycle				
Side-Effects	**1** **190**	**2** **175**	**3** **169**	**4** **165**	**6** **163**
Mild nuisance medical side-effects	34	10	8	2	3
Bleeding problems	12	2	3	1	2
Total	46	12	11	3	5

The bleeding side-effects (BTB, spotting. heavy bleeding) were slightly increased during the first treatment cycle, which later reduced to almost pretreatment levels (Table II). Fifteen acceptors dropped out of the study due to personal reasons, while 12 acceptors dropped out due to medical reasons (Table III).

Table III : Reasons for Termination of MERCILON™ use according to cycle

Cycle	No. of cases	Personal	Medical
0	190	7	0
1	183	3	5
2	175	3	3
3	169	1	3
4	165	1	1
5	163	0	0
6	163	0	0

Details, of the dropout due to medical reasons are as listed in Table IV.

Table IV : Reasons for Termination

Bleeding	3
Breakthrough bleeding	1
Continous Spotting	1
Heavy bleeding	**5**
Total	
Other Medical Reasons	2
Pruritus and rashes	2
Giddiness	1

Nausea, headache	1
Nausea, weight gain	1
Extreme weight gain (10 kg)	7
Total	

One acceptor experienced extreme weight gain (10 kg) after 3 months of taking Mercilon™, which was considered rather unusual. There was no effect on either the systolic or diastolic blood pressure at pre- or post-treatment. (Table V).

Table V : Blood pressure and weight gain before and after 6 cycle of MERCILON™

	Pretreatment n = 189	**After 6 cycles n = 163**
Mean Systolic	110.8	110.4
Mean diastolic	72.3	71.5
Mean weight (kg)	52.9	53.3

There was also no difference in the weight gain before treatment as compared to post treatment in acceptors who completed the study period (Table V).

Discussion

Mercilon™ has been shown to give an excellent cycle control with very few side effects in women. The registration (Phase III) trial of this oral contraceptive which was conducted in 12 European countries at 72 centres (with the same definitions for irregular bleeding and method of analysis) showed that 87.8% of the women experienced regular withdrawal bleeding and 26.4% breakthrough bleeding and spotting during the first treatment cycle which later tapered off after subsequent use (8). In Malaysia on the other hand, the evidence of BTB and spotting was minimal. The high acceptability of Mercilon™ is also reflected in the low dropout rate.

The small average increase in body weight (0.3 kg over 6 cycles) is comparable to body weight demographics in non-oral contraceptive using women. This increase occurs mainly in adolescent women who still show a tendency to grow. One acceptor that dropped out after 3 cycles of Mercilon™ due to excessive weight gain of 10 kg was rather unusual. Since she was still under our follow-up, her weight was monitored and the tendency to increase in weight was still present. The reason for the excessive weight gain was difficult to establish.

The blood pressure profiles before and after treatment were normal. Mercilon™ could be considered in women having borderline hypertension if hormonal methods are still required. Metabolic studies have shown that Mercilon™ has no adverse side effects on carbohydrate or lipid metabolism. Most of the studies showed an increase in HDL-cholesterol [9-12]; an increase, which can be regarded as favourable since HDL-cholesterol, has been recognised as a negative risk factor for ischaemic heart disease.

In conclusion, Mercilon™ has a low incidence of bleeding irregularities good cycle control and low minor side effects. Mercilon™ can be a good choice for women who are keen to start family planning with oral contraceptives with low cardiovascular risk.

Acknowledgements

This study was made possible by the cooperation of physicians and the nursing staff working at the National Population and Family Development Board Clinics in Kuala Lumpur. This study was coordinated by Dr. Kwa Siew Kim and was sponsored by N. V. Organon, P.O. Box 20, 5340 BH. OSS, The Netherlands.

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