Effects of Biphasic Oral Contraceptives Containing Desogestrel (Oilezz) on Cycle Control Facial Acne and Seborrhea in Healthy Thai Women

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Objective: *To demonstrate the effects of a new biphasic oral contraceptive (Oilezz) on cycle control as well as mild to moderate acne and facial seborrhea of healthy fertile Thai women.*
Material and method: *The trial is a prospective, open, non-comparative, single center study. Fifty healthy, fertile Thai women with mild to moderate facial acne were recruited to study a specific drug (Oilezz) for 6 months.*
Results: *At the beginning, 66% of the subjects had mild acne and 34% had moderate acne. Significant improvements in facial seborrhea grades (as indicated by Sebutape assessments) were found after the first cycle. These improvements increased steadily and were much larger after the sixth cycle. There were no statistically significant changes in body weight or blood pressure during the study. No serious adverse events were reported. There were no mood changes, migraine, rash, abdominal discomfort, malaise, nausea and decrease in libido during the study period. The premenstrual symptoms at initiation were 21 cases (42%). The symptoms were 4 (8%) with headache, 8 (16%) with breast tenderness, 5 (10%) with dysmenorrhea and one (2%) with bleeding irregularity. These symptoms were improved in the third and the sixth cycles. The percentage of women with spotting or bleeding increased after first cycle, compared with baseline and gradually decreased during subsequent cycles. After the sixth cycle of treatment, all subjects had improvement of acne. 80% of cases recovered from acne and there were only 20% had mild acne.*
Conclusion: *Facial seborrhea and acne improved significantly with Oilezz .It is good to control cycle without change in body weight and blood pressure. Therefore, Oilezz can be used for treatment of seborrhea and acne and as a contraceptive.*

Keywords: *Biphasic oral contraceptive, Acne, Seborrhea grades, Sebutape*

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Acne is the most common dermatological condition. It affects 80-90% in age group of 13-18 years old[2] and still as many as 40% in women n age group of 25-40 years old [1]. Research indicates that both seborrhea and acne have negative effect on self-esteem and self-confidence of women[3].

Acne is a disease of androgenic effects[4], and usually develops at puberty due to an increase in androgen production. Androgen increase sebum production. Higher androgen level results in over-production of sebum by sebaceous glands. It causes greasy or oily skin and hair[3]. Seborrhea is also a major contributory factor in acne development and can be considered as a pre-condition for acne formation[5].

Oral Contraceptives (OCs) containing desogestrel provides a favorable balance between estrogenic and androgenic effects. Desogestrel is a highly selective progestogen with minimal androgenic activity compared with other synthetic progestogens[10]. These OCs have been shown to decrease circulating total testosterone and the amount of free testosterone[11],

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increasing Sex Hormone-Binding Globulin (SHBG)[6-8]. They have successfully been used in treating conditions associated with signs of hyperandrogenic activity such as acne[9].

Oilezz is the first biphasic oral contraceptive, with an estrogen-dominant (40 g ethinyl estradiol + 25 g desogestrel) phase of 7 days, followed by a progestogen-dominant (30 g ethinyl estradiol + 125 g desogestrel) phase of 15 days. Oilezz is a unique biphasic OC that has exceptionally good cycle control[12].

Oilezz has been shown to have beneficial effects on androgenic skin disorders such as seborrhea and acne[13,14]. It is because Oilezz significantly increases SHBG (+250%)[15,16] and reduces free testosterone (55%)[17] levels that results in an improvement in the incidence and severity of mild to moderate acne comparable to that of cyproterone acetate[18].

The official approved indications by Thai FDA for Oilezz are contraception and treatment of mild to moderate acne. Since there is no local data of Oilezz available, therefore, it is interesting to study the effect of Oilezz among Thai women on cycle control and acne treatment.

Material and Method

Participants

Fifty patients were selected to study the drug (Oilezz) for 6 months at Family planning unit, Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University.

Participants were healthy female, in good physical and mental condition, $\geq$ 18 and $\leq$ 30 years of age, body mass index (BMI) $\geq$ 18 and $\leq$ 29 kg/m^2, facial acne assessed by the investigator as mild to moderate, with three regular cycles of 28-35 days prior to the study, and not currently using systemic anti-acne and/or Diane. No history of allergy to estrogens, cardiovascular disease, renal disease, hepatic disorders, porphyria, haemoglobinopathies, hypertension, diabetic mellitus, and any other relevant disorders were noted.

Study design and material

The trial is a prospective, open, non-comparative, single center study. Oilezz is the first combiphasic oral contraceptive, with an estrogen-dominant (40 g ethinyl estradiol + 25 g desogestrel) phase of 7 days, followed by a progestogen-dominant (30 g ethinyl estradiol + 125 g desogestrel) phase of 15 days.

All patients gave written informed consent and gave their medical and obstetrics history. Subjects had physical and gynecological examination including cervical smear. Prior to the study, blood collection for hemoglobin, hematocrit, WBC, total platelet, BUN, creatinine, SGOT, SGPT, alkaline phosphatase, total bilirubin, fasting blood sugar, and urine for routine examination were done. They were instructed to fill the daily bleeding card as well as to take the medication properly. Follow up were done at 1, 3 and 6 months during the study period.

Assessment

Assessments were performed at baseline and at treatment cycle 1, 3 and 6 month. Medical, skin and gynecological histories were taken and physical and gynecological examinations. Bleeding data, Sebutape[21,22] assessments, a nonvalidated skin/hair questionnaire and counting skin lesions, and drug and concomitant medication assessments were done at each follow up. Adverse events were noted. Sebum output was assessed on the forehead using Sebutape strip, sampling sites were cleansed with detergent (chula soap), and allowed to dry before the tapes were gently pressed onto the facial sites. After 1 hour the strips were gently removed and placed on black storage cards. Acne was assessed by counting the acne lesions (comedones, papules, pustules, nodules) on the face and divided into three severity categories: none (no visible lesions); mild (maximum of 5 comedones or papules) and no inflamed lesions (pustules and/or nodule); moderate (6-15 comedones or papules and/or a maximum of 3 inflamed lesions); severe(more than 15 comedones or papules and/or more than 3 inflamed lesions).

Statistical analysis

Statistical analysis was performed with SPSS software package version 11.0 (SPSS Inc., Chicago, IL, USA). Mean $\pm$ Standard Deviation (SD) of mean for the age, height, body weight, Body Mass Index (BMI) and percentages were used where appropriated. A p-value of less than 0.05 was considered to be statistical significant.

Results

Study population

Fifty women enrolled in the study. Their age ranged from 18 to 30 years, with a mean of 24.54 years, body weight was 54.87 kgs, BMI was 22.04kg/m^2, height was 157.80 cms., normal blood pressure, normal blood and urine laboratory examination. There were no statistically significant changes in body weight or blood pressure during the study.

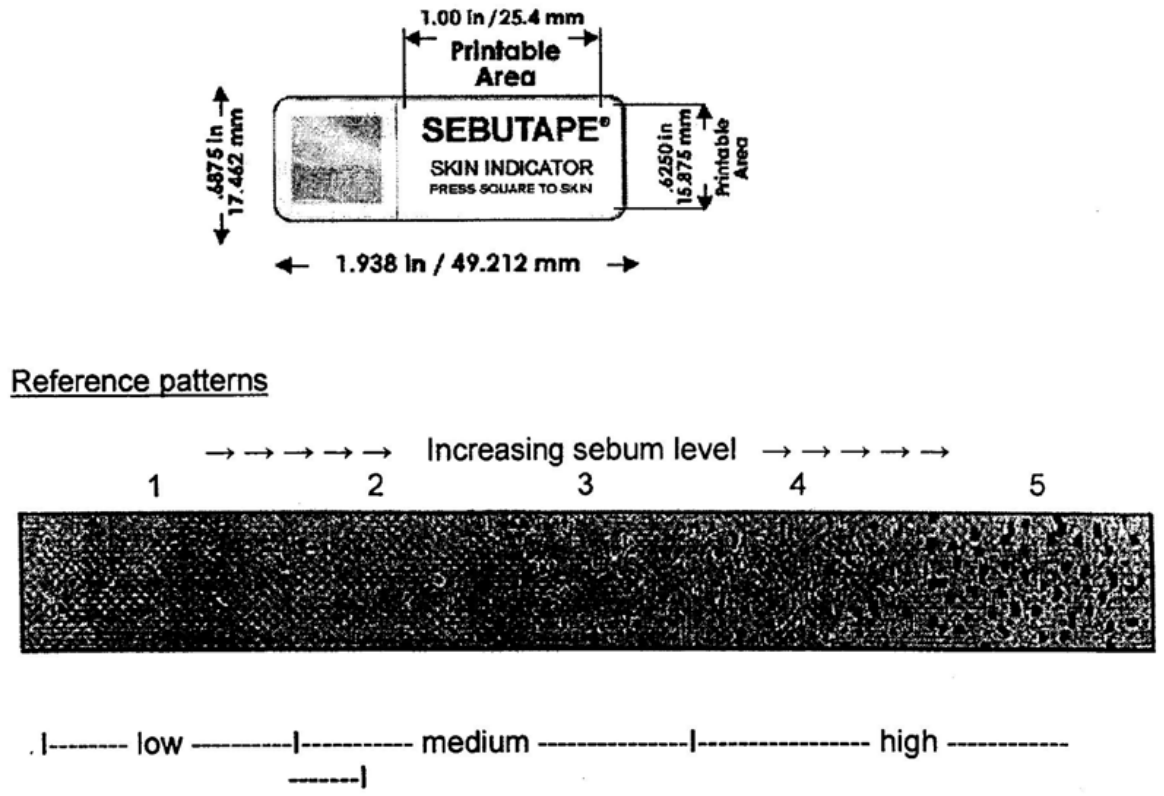

Fig. 1 Sebutape assessment

Vaginal bleeding pattern

The percentage of women with spotting or bleeding increased after cycle 1, compared with baseline and gradually decreased during subsequent cycles. At the cycle1, one patient had early withdrawal bleeding, the difference between cycle 1 and 6 was not statistically significant.

Skin and acne data

Statistically significant improvements on acne severity were observed. At the beginning, there were 66% of mild acne and 34% of moderate acne. After the sixth cycle of treatment, all subjects had improvement of acne as 80% of cases recovered from acne completely and the other 20% had only mild acne. The details were shown in Table 1.

Statistically significant improvements in facial seborrhea grades (as indicated by Sebutape assessments) were found after the first cycle, and obvious in the third cycles. These improvements increased steadily and were much larger after the sixth cycle (Table 2).

Adverse events

No serious adverse events were reported. In total 21 (42%) subjective baseline characteristics were reported during the study. Prior to the study, these characteristics were reported and included eight (16%)

Table 1. Semi-quantitative analysis of acne vulgaris in women using Oilezz , all $p < 0.05$ compared with baseline (Wilcoxon matched pairs test)

Facial -Acne	Beginning	1st month	3rd month	6th month
No acne N (%)	0	8 (16%)	20 (40%)	40 (80%)
Mild	33 (66%)	30 (60%)	25 (50%)	10 (20%)
Moderate	17 (34%)	12 (24%)	5 (10%)	0

Table 2. Facial seborrhea grades by Sebutape assessments

Sebutape	Baseline	1st month	3rd month	6th month
1+	6 (12%)	10 (20%)	22 (44%)	46 (92%)
2+	10 (20%)	18 (36%)	16 (32%)	4 (8%)
3+	27 (54%)	16 (32%)	9 (18%)	0
4+	7 (14%)	6 (12%)	3 (6%)	0

subjects with breast tenderness, five (10%) subjects with dysmenorrhea and four (8%) subjects with headache. The symptoms that were present after the first cycle were eight (16%) subjects with breast tenderness, five (10%) subjects with dysmenorrhea, four (8%) subjects with headache and one (2%) subject with bleeding irregularity. In the third cycle there were two (4%) subjects with breast tenderness and only one (2%) subject with headache. All symptoms disappeared by the six cycles. No body weight increase, mood change, migraine, rash, abdominal discomfort, malaise, nausea and decrease in libido were demonstrated in this study.

Discussion

Desogestrel is a progestational agent with a high degree of clinical contraceptive efficacy[11]. It has fewer metabolic side effects compared with older progestational compounds. Major advantages seem to include its effect on level of SHBG and testosterone and the improved acne and hirsutism. Volpe et al[14]. 1994 study of a biphasic oral contraceptive containing ethinylestradiol and desogestrel, showed that cycle control was satisfied and fibrinopeptide-A remained stable with increased SHBG concentrations, significant reduction of total and free testosterone levels.

Sebutape method is an established technique for determining sebum excretion on the skin surface[19,20]. The sebum output collected using Sebutape can be estimated by visual inspection and comparison with reference patterns. Prilepskaya, et al[21] showed that skin and greasy hair of women were significantly improved, after one, three and six cycles of DSG-OC, by 69%, 93%, and 98% respectively. Visual Analogue Scale (VAS) scores in response to questions dealing with self-esteem and self-confidence were significantly improved after three cycles and in some cases after just one cycle. These findings were similar to the present study.

The open questionnaire results confirm the importance of skin condition to women. They rated their satisfaction level at 100% based on the decrease in their greasiness of their skin and lower acne. The results were similar with Winkle UH, et al[22] that at 6 cycles for Profile of Mood States(POMS) scales and derived POMS T scores, the mean change from baseline was greater in the 20EE/DSG group compare with 20EE/LNG group. However, acne is a skin disease caused by multifactorial factors, but it respond to the treatment with OCs that decreased the circulating testosterone[6-8].

Only one subject had early withdrawal bleeding during the first cycle, which was due to the irregular intake of the pills. Changes in body weight, blood pressure, nausea, headache, dysmenorrhea and breast tenderness, were noted but not statistical significant.

In conclusion, facial seborrhea, acne and fertility control were obtained with satisfactory result with Oilezz .

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การศึกษาประสิทธิภาพในการลดสิว ผิวมัน และควบคุมรอบประจำเดือนของยาเม็ดคุมกำเนิดชนิดรับประทาน Oilezz

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วัตถุประสงค์: *เพื่อศึกษาประสิทธิภาพของยาเม็ดคุมกำเนิดชนิดรับประทาน Oilezz ในการลดสิว, ผิวมัน*

วัสดุและวิธีการ: *การวิจัยเชิงพรรณนา(Descriptive study)แบบไปข้างหน้า ศึกษาในสตรีอาสาสมัครที่มีอายุ 18-30 ปี 50 คน ที่มารับบริการคุมกำเนิดโดยใช้ยาเม็ดรับประทานชนิดฮอร์โมนรวม ที่หน่วยวางแผนครอบครัว โรงพยาบาลจุฬาลงกรณ์ คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ตั้งแต่วันที่ 1 มิถุนายน พ.ศ. 2548 ถึงวันที่ 30 พฤศจิกายน พ.ศ. 2548 เข้าร่วมโครงการโดยใช้ยาเม็ดคุมกำเนิด Oilezz เริ่มภายใน 5 วันหลังมีประจำเดือนวันแรก จากนั้นจะได้รับการตรวจติดตามผลโดยการสัมภาษณ์ ตรวจร่างกาย ตรวจภายใน ตรวจลักษณะสิว และความมันบนใบหน้าโดยใช้ SEBUTAPE และบันทึกข้อมูลลงในแบบสอบถามในเวลา 1 เดือน, 3 เดือน และ 6 เดือน หลังใช้ยาเม็ดคุมกำเนิด Oilezz*

ผลการศึกษา: *ประเมินระดับความรุนแรงของสิวลดน้อยลงอย่างมีนัยสำคัญเมื่อเทียบกับสภาวะเริ่มต้นซึ่งมีสิวเล็กน้อย 66%, ปานกลาง 34%, ในเดือนที่ 1 ไม่มีสิว 16%, สิวเล็กน้อย 60%, ปานกลาง 24%, เดือนที่ 2 ไม่มีสิว 40%, สิวเล็กน้อย 50%, ปานกลาง 10%, และไม่มีสิว 80% สิวเล็กน้อย 20%, ปานกลาง 0% ในเดือนที่6 จำนวนผู้ไม่มีสิวเพิ่มขึ้น และจากการประเมินโดยใช้ SEBUTAPE ระดับความมันบนใบหน้าลดน้อยลงอย่างมีนัยสำคัญโดยไม่ก่อให้เกิดอาการข้างเคียงที่รุนแรงตลอดการศึกษาและลดอาการก่อนมีประจำเดือน เช่น อาการปวดศีรษะ 8%, คัดตึงเต้านม 16%, ปวดประจำเดือน 10%, มีประจำเดือนก่อนกำหนด 1% และจะลดลงในเดือนที่ 3 จนกระทั่งใน เดือนที่ 6 ไม่พบอาการใด ๆ จากคำถามปลายเปิดพบว่าได้รับการตอบรับที่ดีเมื่อสิ้นสุดการศึกษาทั้งในแง่ของการลดสิว ผิวมัน และการควบคุมรอบประจำเดือน*

สรุป: *การศึกษาในสตรีอาสาสมัคร 50 คนที่มารับบริการคุมกำเนิดโดยใช้ยาเม็ดรับประทานชนิดฮอร์โมนรวม Oilezz พบว่าสามารถลดสิว ผิวมันและควบคุมรอบประจำเดือนได้อย่างประสิทธิภาพ*