Comparison of Cycle Control and Side Effects between Transdermal Contraceptive Patch and an Oral Contraceptive in Women Older than 35 Years

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Objective: *To compare menstrual patterns and side effects between transdermal contraceptive patch and oral contraceptive use in Thai women over 35 years old.*
Design: *Open labeled randomized control trial.*
Setting: *Family Planning Clinic, King Chulalongkorn Memorial Hospital, Bangkok, Thailand.*
Material and Method: *Ninety-six women above the age of 35 years old were randomized to receive either transdermal contraceptive patch (n = 48) or oral contraceptive (n = 48). The patch regimen was three consecutive 7-day patches (21 days) followed by 1 patch-free week per cycle; the oral contraceptive contained with ethinyl estradiol (EE) 30 µg and levonorgestrel 150 µg.*
Results: *There were no statistically significant differences between the two groups in terms of cycle length. The mean duration in the transdermal contraceptive group was longer than the COC group with statistically significant difference. More patients in the COC group experienced spotting than the transdermal contraceptive group. Neither amenorrhea nor pregnancies occurred in both groups.*
Conclusion: *Transdermal contraceptive patch provides reliable contraceptive efficacy. It also provides good cycle control equal to COC in Thai women aged above 35 years old. However, a higher incidence of minor adverse effects such as breast tenderness and nausea were demonstrated when compared to oral contraceptive containing with ethinyl estradiol (EE) 30 µg and levonorgestrel 150 µg.*

Keywords: *Transdermal contraceptive patch, Cycle control*

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The contraceptive methods available for women above 35 years of age warrant special consideration. During this period, fertility decreased because of a decrease in sexual activity, number of ovulatory cycles, increase in abortion, side effects of contraceptive method, and bleeding of vagina[1]. Pregnancy above the age of 35 years involves an increased risk to both mother and fetus[1]. Vaginal bleeding in women more than 35 years old needs an invasive procedure to diagnosis. Therefore, women of this age need absolutely efficacious contraceptives with fewer side effects.

The United States Food and Drug Administration (FDA) approved the transdermal combination hormonal contraceptive in November 2001, expanding the current options already available to women seeking effective birth control[2]. The contraceptive patch contains the progestin norelgestromin (NGMN), the primary active metabolite of norgestimate, and the familiar estrogen estradiol (EE). A single 20-cm^2 patch delivers esthynyl estradiol 20 µg and norelgestomine 150 µg which sufficient hormone to last the scheduled 7 days, and actually provides enough hormone to sustain the inhibition of ovulation for 9 days[2-4]. In addition to excellent rates of adhesion, clinical trials showed that this unique system has been found to facilitate an enhanced compliance profile[2-4]. However, most of the contraceptive patch studies have been done in women of young reproductive age[5,6]. The objectives of the present study were to compare menstrual patterns and

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side-effects between transdermal contraceptive patch and oral contraceptive use in Thai women aged over 35 years old during a 3-month follow-up period.

Material and Method

This 3-month open-label randomized controlled trial was conducted at the Family Planning Unit, Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok, beginning in December 2005 to December 2006. Ninety-six women aged between 35 and 48 years were enrolled in the present study. The inclusion criteria for the present study were multiparity, age 35 years or above, normal medication history, no contraindication for hormonal contraceptive use, normal physical and pelvic examination, no prior use of oral contraceptive or implanted contraceptive within 3 months, and no prior use of DMPA within 1 year. The exclusion criteria were breastfeeding, postpartum period, pregnancy, and unable to follow up for 3 months. All participants were randomized to use transdermal contraceptive patch or oral contraceptive pill. Randomization of treatment was done in simple random technique. All participants had physical and pelvic examination, including body weight, height, and blood pressure measurements. Follow-up visits were scheduled for every month after being enrolled in the present study.

At each follow-up visit, they were given a repeat physical examination, including weight, and blood pressure. The menstrual bleeding patterns were recorded in a menstrual diary card, and subjective complaints as well as side effects were recorded on questionnaire forms. The period of follow-up was 3 months. Telephone calls and letters were used in cases of missed appointments.

Statistical analysis

Socio-demographic characteristics were elaborated by descriptive statistics (mean, standard deviation, minimum, maximum). Mean age, body mass index data, cycle length, and duration of withdrawal bleeding were compared by Student's t-test. Adverse events reported during treatment were reported in number and percent. All data were coded and analyzed by using statistical package, SPSS12.0 for window. The significance level was considered at p-value < 0.05.

Results

Ninety-six patients were randomized into two treatment groups. The demographic characteristics of the two groups are summarized in Table 1. Demographic and baseline characteristics were similar between the treatment groups. The length of the menstrual cycle and the menstrual flow were normal at screening in all cases. Previously, 75% and 35.4% of the participants in each group had used a contraceptive method. Over the 3 months of treatment, the maximum weight gain from baseline was 1.5 kg in the transdermal contraceptive group and 5 kg in the COC group. During the present study, the mean length of menstrual cycles did not significantly change, whereas the mean length of menstrual flow showed a statistically significant decrease among COC users in comparison with transdermal contraceptive group (Table 2 and 3). No amenorrhea or unintended pregnancy was recorded throughout the investigation. Considering the cycle control, spotting bleeding occurred more frequently in COC users than the transdermal contraceptive group. Three participants in the COC group and no participant in the transdermal contraceptive group experienced spotting. The participants in transdermal contraceptive group experienced nausea, breast tenderness more frequently than those in the COC group. In the transdermal contraceptive group, seven and ten participants experienced nausea and breast tenderness respectively. While in the COC group, the participants experienced nausea only in three

Table 1. Demographic and baseline characteristics data

Characteristic	Transdermal patch (n = 48)	30 µg EE/150 µg LNG (n = 48)	p-value
Mean age $\pm$ SD (years)	38.79 $\pm$ 3.75	37.69 $\pm$ 2.59	NS
Mean height $\pm$ SD (cm)	156.37 $\pm$ 4.67	155.52 $\pm$ 5.45	NS
Mean weight $\pm$ SD (kg)	54.76 $\pm$ 7.53	56.85 $\pm$ 6.75	NS
Mean body mass index $\pm$ SD (kg/m^2)	22.65 $\pm$ 3.08	23.07 $\pm$ 2.79	NS
Length of cycle (day)	28.50 $\pm$ 1.64	28.89 $\pm$ 1.25	NS
Length of withdrawal bleeding (day)	4.20 $\pm$ 1.09	4.04 $\pm$ 1.28	NS

NS: not significance

Table 2. Mean ± SD cycle length (day)

Cycle	Mean duration ± SD (day)		p-value
	Transdermal patch (n = 48)	30 µg EE/150 µg LNG (n = 48)	
1	26.98 ± 0.83	26.90 ± 1.49	NS
2	28.04 ± 0.74	27.79 ± 0.72	NS
3	27.09 ± 0.69	28.19 ± 0.86	NS

NS: not significance

Table 3. Mean ± SD duration of withdrawal bleeding (day)

Cycle	Transdermal patch (n = 48)	30 µg EE/150 µg LNG (n = 48)	p-value
1	4.48 ± 1.01	3.75 ± 1.32	0.003*
2	4.35 ± 0.97	3.69 ± 1.05	0.002*
3	4.10 ± 0.80	3.79 ± 0.98	>0.05

* Statistical significant $p < 0.05$

cases and no breast tenderness was found. Evidence of improvement, however, was reported after 2 months. In the transdermal contraceptive group, the most common adverse event was application site reaction and found in about 43% of the users. The rate of patch detachment was 18% and only partial patch detachment was reported. No treatment-related serious side-effect occurred during the present study.

Discussion

The number of perimenopausal women who give birth has doubled since 1970[7]. The increasing number of births in these women is due to the larger population of women aged 35-45 years and a real increase in birth rate after age 35 years[7]. Pregnancy among these women carries a special risk and certain social and psychological implication[1]. The use of contraception by these women implies special risks and benefit[1]. Transdermal systems for the delivery of estrogens and estrogen-progestin combination have been developed for hormone replacement therapy[8]. Until recently, the transdermal delivery of sufficient amounts of progestin and estrogen for effective contraception had not been possible. A new transdermal contraceptive patch has been developed that offers potential advantages over oral contraceptives, including greater convenience and better user[5]. Nevertheless, no study on transdermal contraceptive patch use in older women has been reported in Thailand. Previous studies have shown transdermal contraceptive patch to be a safe and effective method for contraception[5,6,9,10]. However, most studies evaluating the use of transdermal contraceptive patch have been conducted in younger women.

In the present study, the authors evaluated menstrual patterns, side-effects of transdermal contraceptive patch versus a standard oral contraceptive use in Thai women over 35 years old during a 3-month follow-up period and the results indicated that both contraceptive regimens provide a reliable form of contraception with good cycle control. There was no occurrence of pregnancies in either group. Transdermal contraceptive patch provides good cycle control equal to COC in Thai women aged above 35 years old. The mean cycle length of both groups showed no differences. The mean duration in the transdermal contraceptive group was longer than 30 µg EE/150 µg LNG group with statistically significant difference in first and second cycle, but not in the third cycle. There was no amenorrhea in the present study.

Considering the side effects of transdermal contraceptive patch in women above 35 years old, the most common adverse event was application site reaction but did not disturb the acceptors and none discontinued for this reason. The other adverse events were breast tenderness and nausea, similar to other

age groups[11]. No spotting was found in the transdermal contraceptive group. In the COC group, the adverse events were only spotting and nausea. The rate of patch detachment was 18%, similar to other age groups[11] and only partial patch detachment was reported. Side-effects of pill and patch in the present study i.e. bleeding, breast tenderness, nausea etc. might be due to hormonal absorption and level of hormone in the blood of both methods of contraception was different. It would be useful to do hormonal blood level during the use of both contraceptive methods. Due to the small number of side-effects, a future study should be conducted for a longer period and with a larger sample size to evaluate the side-effects.

In conclusion, from the present study, the authors found that transdermal contraceptive patch provided reliable contraceptive efficacy during the 3 months-follow up. It also provided good cycle control equal to COC in Thai women aged above 35 years old. However, more adverse effects such as breast tenderness and nausea were demonstrated when compared to the oral contraceptive.

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การศึกษาเปรียบเทียบลักษณะของประจำเดือนและผลข้างเคียงของการใช้แผ่นแปะคุมกำเนิด และยาเม็ดคุมกำเนิดในสตรีไทยที่มีอายุ 35 ปีขึ้นไป

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***วัตถุประสงค์**: เพื่อศึกษาเปรียบเทียบลักษณะของประจำเดือนและผลข้างเคียงของการใช้แผ่นแปะคุมกำเนิด และยาเม็ดคุมกำเนิดในสตรีไทยที่มีอายุ 35 ปีขึ้นไป*

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***วัสดุและวิธีการ**: สตรีไทยที่มีอายุ 35 ปีขึ้นที่ต้องการคุมกำเนิดไปทั้งหมด 96 คน แบ่งเป็น 2 กลุ่ม กลุ่มแรกได้รับการคุมกำเนิดโดยใช้แผ่นแปะคุมกำเนิด (จำนวน 48 คน) กลุ่มที่ 2 ได้รับการคุมกำเนิดโดยใช้ยาเม็ดคุมกำเนิด (จำนวน 48 คน)*

***ผลการศึกษา**: ผลการศึกษาพบว่าไม่มีความแตกต่างในความยาวของรอบระดูระหว่างทั้งสองกลุ่ม จำนวนวันที่มีประจำเดือนในกลุ่มที่ใช้แผ่นแปะคุมกำเนิดมากกว่าในกลุ่มที่ใช้ยาเม็ดคุมกำเนิดอย่างมีนัยสำคัญ ส่วนเลือดออกระหว่างรอบเดือนพบมากกว่าในกลุ่มที่ใช้ยาเม็ดคุมกำเนิด ไม่พบภาวะขาดประจำเดือนและการตั้งครรภ์ในทั้งสองกลุ่มที่ทำการศึกษาวิจัย*

***สรุป**: การใช้แผ่นแปะคุมกำเนิดในสตรีไทยที่มีอายุ 35 ปีขึ้นไปมีประสิทธิภาพดีและลักษณะของประจำเดือนในขณะใช้แผ่นแปะคุมกำเนิดใกล้เคียงกับการใช้ยาเม็ดคุมกำเนิด อย่างไรก็ตามพบว่าอุบัติการณ์ของผลข้างเคียงเช่น คัดตึงเต้านมและคลื่นไส้อาเจียนพบมากกว่าในสตรีที่ได้รับแผ่นแปะคุมกำเนิด*