Emergency Contraception with Mifepristone 10 mg in Thai Women

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Objective: *Evaluate the use of low dose mifepristone 10 mg in term for efficacy, bleeding patterns, side effects, and satisfaction of Thai acceptors.*
Material and Method: *One hundred twenty women participated in the study. Their mean age was 33.4 ± 7.1 years. All of them were Buddhists and most of them finished secondary school or higher, 31.7% of the women had not been pregnant, 63.7% had had a live birth, and 20% had history of abortion. Most women had used oral pill in the past (58.3%).*
Results: *No pregnancies were occurred among clients. The pregnancy rate was 0%. Few had some side effects. There were statistically difference in interval and duration between previous and treatment cycle. The treatment cycle was longer than previous cycle in term of interval and duration.*
Conclusion: *The use of low dose mifepristone was effective, safe, and had few side effects.*

Keywords: *Mifepristone, Low-dose oral contraceptives, Emergency contraception*

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Emergency contraception (EC) can prevent unwanted pregnancies, unsafe abortions, and maternal deaths[1]. Bygdeman and Gemzell-Danielson et al have demonstrated that mifepristone also was very effective for EC[1]. Following administration of doses of 600, 50 and 10 mg after unprotected intercourse, pregnancy was observed in only 1.3%, 1.1%, and 1.2% of the cases, respectively[2]. Mifepristone is an anti-progesterone that, among other effects, arrests or delays ovulation[1]. The studies assessing the effectiveness of mifepristone 10 mg taken within 5 days after unprotected sex have shown it to be as successful as levonorgestrel (LNG), with similar rates of side effects[1,3]. Xiao et al, in a randomized clinical trial, demonstrated the equivalence of doses of 10 and 25 mg in terms of efficacy when it administered for EC[4]. The previous study in Thai women also demonstrated good efficacy and few side effects of EC with low dose mifepristone[5]. Although there are many contraceptive methods for Thai women, emergency contraception with very low dose mifepristone is not available in the family planning program. The objectives of the present study were to evaluate efficacy, bleeding patterns, side effects, and satisfaction of Thai women treated with the single dose of 10 mg mifepristone. The outcome of the present study would provide useful information for clients, providers, and policy makers in a family planning program in considering options for emergency contraception.

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Material and Method

Women who requested EC were recruited in the present study. The eligible criteria for subjects were required to be in good general health, unprotected intercourse between the 10th and 20th day of the current cycle within 120 hours, willing to abstain from further acts of intercourse or use a condom during that cycle, able to follow-up, willing to give informed consent and intending to continue pregnancy in case of treatment failure.

Women were excluded if they were currently pregnant, had a suspected pregnancy, or did not have

a pregnancy test done; used hormonal methods of contraception during the current cycle, or had a contraindication to the use of mifepristone. The institutional review board of the Chulalongkorn University Health Sciences Group approved the study protocol and informed consent documents.

At admission, the authors collected information on personal history, menstrual cycle, date of onset of last menstrual bleeding, and expected date of onset of next menstrual bleeding, date and time of unprotected coitus, use of contraception during the current cycle and reason for requesting EC. Physical examination, pelvic examination, Pap smear, and pelvic ultra-sonography were performed. Height and weight were measured and a urine pregnancy test was performed. A 10-mg mifepristone tablet was swallowed in the presence of a member of the study team and the date and time when it was taken were recorded.

Women were given a diary chart to record vaginal spotting and bleeding, possible side effects and further acts of intercourse, if any, and contraceptive methods used. A follow-up appointment was arranged about 7-10 days after the expected onset of the next menstruation. If no bleeding had occurred by that time, a urinary pregnancy test (hCG sensitivity 25 IU/L) was carried out. If the hCG assay was negative, a further follow-up visit 1 week later was arranged. If the hCG assay was positive, an ultrasound examination was carried out to estimate the duration of gestation. Participants were generally followed-up until the occurrence of menses. However, the follow-up of participant could also be discontinued from the study if no bleeding had occurred 14-17 days after the expected onset of menstruation and the pregnancy test was negative.

The data were analyzed by using statistical package SPSS/PC version 16. The study's primary outcome measure was the effectiveness of treatment in preventing pregnancy. Women lost to follow-up were excluded from the analysis. Efficacy was measured by calculating crude failure rates, percentage of pregnant women. Descriptive data were expressed in term of percent, mean, and standard deviation. The analytical statistic use was student's t-test with $p < 0.05$ for statistical significance. Numbers and percentages of subjects with side effects were calculated, along with their 95% confidence interval.

Results

One hundred twenty women were recruited for the present study between June and October 2008 at the sex counseling clinic, College of Public Health Sciences and the reproductive health clinic, Chulalongkorn Hospital. The mean age of subject was 33.4 $\pm$ 7.1 years. The minimum and maximum age was 20 and 44 years respectively. All were Buddhists and most of them finished secondary school or higher. 31.7% of the women had not been pregnant, 63.7% had a live birth, and 20% had a history of abortion. The characteristics of women who requested EC are shown in Table 1.

Most women had used oral contraceptives in the past (58.3%). The previous contraceptive methods are shown in Table 2. No pregnancies were reported among the participants.

Side effects within the first week after treatment were mild and observed in a very small proportion of women. The most common symptom was irregular bleeding which was reported in eight cases. Nausea and vomiting occurred in two cases.

Table 1. The characteristics of subjects (n = 120)

Characteristics	Mean $\pm$ SD
Age (year)	33.4 $\pm$ 7.1
Weight (kg)	56.1 $\pm$ 7.5
Height (cm)	158.8 $\pm$ 5.1
Blood pressure	
Systolic (mmHg)	114.3 $\pm$ 5.9
Diastolic (mmHg)	72.3 $\pm$ 6.4
Previous live birth (n = 120)	76 (63.3%)
Previous abortion (n = 120)	24 (20%)
Religious	
Buddhists	120 (100%)
Education	
Primary School (n = 120)	14 (11.7%)
Secondary School (n = 120)	46 (38.3%)
Vocational College (n = 120)	24 (20%)
University (n = 120)	36 (30%)
Gravida	
0 (n = 120)	38 (31.7%)
1 (n = 120)	48 (40%)
2 (n = 120)	18 (15%)
More than 2 (n = 120)	16 (13.3%)
Abortion	
0 (n = 120)	96 (80%)
1 (n = 120)	22 (18.3%)
More than 1 (n = 120)	2 (1.7%)
Parity	
0 (n = 120)	44 (36.7%)
1 (n = 120)	52 (43.3%)
2 (n = 120)	18 (15%)
More than 2 (n = 120)	6 (5%)

Headache also occurred in two cases. Side effects were summarized in Table 3.

Data on the timing of the next menstrual period suggest a slight delay in onset. The mean duration of interval in the previous cycle was 28.2 $\pm$ 3.4 days and the mean duration of bleeding days in the previous cycle was 4.2 $\pm$ 1.2 days. However, the mean duration of interval in treatment cycle was 29.8 $\pm$ 4.2 days and the mean duration of bleeding day was 5.2 $\pm$ 3.8 days. There was statistical difference in interval and duration of menstruation between previous and treatment cycle. 95% CI of mean duration of interval and bleeding days were -2.57, -0.63 and -1.72, -0.28 respectively. Details regarding cycle duration and bleeding duration are demonstrated in Table 4.

Considering the participant satisfaction and usage of low dose mifepristone, subjects expressed satisfaction with this method and were willing to use it if it was marketed in Thailand. All of them would also recommend it to others, and desired that it be sold over the counter.

Table 2. Previous contraceptive uses

Contraceptive method	Number	Percent
Oral pill	70	58.3
Implant	2	1.7
Intrauterine device	2	1.7
None	46	38.3
Total	120	100.0

Table 3. The side effects of mifepristone use

Side effect	Number (n = 120)	Percent
Nausea and vomiting	2	1.7
Headache	2	1.7
Irregular bleeding	8	6.7

Table 4. Mean interval and duration of menstruation

Interval and duration	Previous cycle (mean $\pm$ SD)	Treatment cycle (mean $\pm$ SD)	95% CI
Interval (days)	28.2 $\pm$ 3.4	29.8 $\pm$ 4.2	-2.57, -0.63
Duration (days)	4.2 $\pm$ 1.2	5.2 $\pm$ 3.8	-1.72, -0.28

Discussion

There are many regimens of emergency contraception, including Yuzpe, levonorgestrel, high dose and low dose mifepristone and intrauterine devices[6]. However, low dose of mifepristone is the most recently reported type of emergency contraception, particularly 10 mg[1-6]. Many studies of low dose mifepristone have demonstrated high effectiveness, safety, and low side effects[1-6]. Nevertheless, to date there is only one study in Thai women. The objective of the present study was to evaluate the effectiveness, safety, side effects, and satisfaction of 10 mg mifepristone used for EC in Thai women. The results of the present study would benefit Thai women and provide information for policy makers to consider this regimen to use as EC in a family planning program.

From the present study, it was found that this contraceptive method was effective, safe, and free of side effects. These findings were similar to those of previous studies[1-6]. The studies of Cheng et al and Xiao, et al also demonstrated the effectiveness and safety of low dose mifepristone[4,7]. The WHO study demonstrated that low dose mifepristone had the same effectiveness as levonorgestrel[6]. These studies elaborated the effectiveness of low dose mifepristone the same as high dose regimen in emergency contraception but it had fewer side effects[1-6]. However, the women who were treated with low dose mifepristone had delayed menstruation[1-6]. The present study also demonstrated the delay of menstruation. The mean cycle interval and duration of menstruation between the previous and the treatment cycle were significantly different. The mean interval and duration of the treatment cycle was longer than the previous cycle. This is probably attributable to the effect of mifepristone use in treatment cycle. These findings corresponded with the studies of Xiao and others[4,7,8].

In consideration of side effect, it was found that there were few side effects in using low dose mifepristone. Most of the side effects were nausea and vomiting followed by irregular bleeding and headache. These side effects were the same as the studies from WHO, Hamoda and Xiao[2-4]. However, these side effects were mild and did not disrupt the use of emergency contraception. No adverse events or serious side effects were reported. Previous research reported the satisfaction with mifepristone in Thai acceptors[5]. The present study also demonstrated the clients' satisfaction with low dose mifepristone. All were satisfied and willing to use this regimen for EC.

Moreover, they would advise others to use it. They also preferred over the counter selling rather than prescription. These findings demonstrated the need of emergency contraception in Thai women. This contraceptive method would be the alternative choice of Thai women who need contraception.

In summary, low dose mifepristone was effective, safe and had few side effects EC as well as preferable choice of Thai women. The present study also further confirms that 10 mg mifepristone for EC is sufficient to prevent unwanted pregnancies among eligible clients and is a safe medication for EC in Thai women.

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การคุมกำเนิดแบบฉุกเฉินด้วยยา mifepristone 10 มิลลิกรัมในสตรีไทย

สุรศักดิ์ ฐานีพานิชสกุล

การศึกษาสตรีไทยที่ใช้ mifepristone ขนาดต่ำ 10 มิลลิกรัม ในการคุมกำเนิดแบบฉุกเฉิน โดยมีวัตถุประสงค์เพื่อประเมินถึงประสิทธิภาพ ลักษณะระดู ผลข้างเคียง และความพึงพอใจในการใช้ยาดังกล่าวเพื่อคุมกำเนิดแบบฉุกเฉิน สตรีจำนวน 120 คน อายุเฉลี่ย 33.4 $\pm$ 7.1 ปี ทั้งหมดนับถือศาสนาพุทธ 31.7% ยังไม่เคยตั้งครรภ์ 58.3% เคยใช้ยาเม็ดคุมกำเนิด จากการศึกษาไม่พบว่ามีการตั้งครรภ์ มีผลข้างเคียงต่ำ แต่ระยะเวลาของรอบระดู และระยะเวลาของการมีระดูแตกต่างกันในรอบเดือนก่อน และรอบเดือนที่ใช้ยา mifepristone โดยในรอบเดือนที่ใช้ mifepristone จะมีระยะเวลาของรอบระดู และระยะเวลาของการมีระดูนานกว่า อย่างมีนัยสำคัญทางสถิติ การศึกษานี้สรุปได้ว่าการใช้ยา mifepristone ขนาดต่ำ 10 มิลลิกรัม เพื่อการคุมกำเนิดแบบฉุกเฉินมีประสิทธิภาพสูง ปลอดภัย และผลข้างเคียงต่ำในสตรีไทย