

การประเมินความเสี่ยงและผลของการให้ความรู้ในการเกิดโรคหัวใจและหลอดเลือด ในหญิงที่ใช้ยาเม็ดคุมกำเนิดชนิดฮอร์โมนรวม

The Risk Assessment and Effects of Education for Cardiovascular Disease in Women Using Combined Oral Contraceptive Pills

นิพนธ์ฉบับ

Original Article

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วารสารไทยเภสัชศาสตร์และวิทยาการสุขภาพ 2563;15(4):244-250.

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บทคัดย่อ

Abstract

วัตถุประสงค์: เพื่อประเมินความเสี่ยงของการเกิดโรคหัวใจและหลอดเลือดและเปรียบเทียบคะแนนความรู้ก่อนและหลังการให้ความรู้ในหญิงที่ใช้ยาเม็ดคุมกำเนิดชนิดฮอร์โมนรวม **วิธีการศึกษา:** เป็นการศึกษาแบบกึ่งทดลอง ศึกษาในหญิงที่ใช้ยาเม็ดคุมกำเนิดชนิดฮอร์โมนรวมที่มารับบริการในร้านยาเขตจังหวัดมหาสารคาม จำนวน 3 ร้าน ระหว่างมีนาคม ถึงเมษายน พ.ศ. 2562 การศึกษาส่วนแรกเป็นการประเมินความเสี่ยงในการเกิดโรคหัวใจและหลอดเลือดโดยใช้แบบประเมินที่จัดทำขึ้นอ้างอิงตามคำแนะนำของ U.S. Medical Eligibility criteria 2016 ร่วมกับติดตามผลการปรับพฤติกรรมเสี่ยง และผลการส่งต่อในผู้ที่มีข้อห้ามใช้ ส่วนที่สองคือประเมินผลการให้ความรู้เกี่ยวกับวิธีการใช้และอาการข้างเคียงของยาเม็ดคุมกำเนิดชนิดฮอร์โมนรวม โดยใช้แบบทดสอบที่จัดทำขึ้นเพื่อเปรียบเทียบคะแนนความรู้ระหว่างก่อนและหลังการให้ความรู้ที่ 2 สัปดาห์ **ผลการศึกษา:** มีผู้เข้าร่วมการศึกษาทั้งหมด 50 คน มีอายุเฉลี่ย 26.84 ปี มีสถานภาพโสด (ร้อยละ 70.0) ยาคุมกำเนิดที่ใช้ส่วนมากคือ cyproterone acetate 2 mg ร่วมกับ ethinyl estradiol 35 µg (ร้อยละ 42.0) และมีวัตถุประสงค์ในการใช้เพื่อคุมกำเนิด (ร้อยละ 54.0) หลังจากประเมินพบผู้ที่มีข้อห้ามใช้คือปวดศีรษะไมเกรนชนิดที่มีอาการนำ 1 คน (ร้อยละ 2.0) จึงส่งต่อไปยังสถานพยาบาล และพบผู้ที่มีความเสี่ยงในการเกิดโรคหัวใจและหลอดเลือด คือมีความดันโลหิตสูง 1 คน (ร้อยละ 2.0) และได้รับคำแนะนำให้ปรับพฤติกรรม ผลของการให้ความรู้พบว่าคะแนนเฉลี่ยหลังการเรียนรู้เพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติ (P -value < 0.001) สรุป: เภสัชกรมีส่วนช่วยเพิ่มความปลอดภัยในการใช้ยาคุมกำเนิดโดยการให้คำแนะนำปรับเปลี่ยนพฤติกรรมหรือการส่งต่อ การให้ความรู้ทำให้มีความเข้าใจเกี่ยวกับวิธีการใช้และอาการข้างเคียงของยาเม็ดคุมกำเนิดชนิดฮอร์โมนรวมเพิ่มขึ้น

คำสำคัญ: ยาเม็ดคุมกำเนิดชนิดฮอร์โมนรวม, การประเมินความเสี่ยงในการเกิดโรคหัวใจและหลอดเลือด, การให้ความรู้

Objective: To evaluate cardiovascular (CVD) risk and compare score of knowledge about the use of combined hormone oral contraceptive pills (OCPs) before and after the education session. **Methods:** In this quasi-experimental study, women used combined oral OCPs were recruited at 3 drug stores in Mahasarakham province during March to April 2019. The study first part was cardiovascular risk assessment according to the U.S. Medical Eligibility criteria 2016 followed by monitoring of risk behavior modification and referral for participant who had contraindication. The second part was knowledge assessment on the use and adverse effects of combined hormone OCPs before and 2 weeks after the education session. **Results:** Of the total of 50 participants, their average age was 26.84 years. The majority were single (70.0%), and used the regimen of cyproterone acetate 2 mg and ethinyl estradiol 35 µg (42.0%). The objective of use was birth control (54.0%). After assessment, a person who had contraindications (migraine with aura) (2.0%) was referred to the hospital and the other one with CVD risk (high blood pressure) (2.0%) was advised for behavioral modification. Mean knowledge score increased significantly 2 weeks after the education session (P -value < 0.001). **Conclusion:** Pharmacist could increase the safety of combined hormone OCPs via counseling for behavioral modification and referral. Education could improve knowledge about OCP use and safety.

Keywords: combined hormone oral contraceptive pill, risk assessment of cardiovascular disease, education

Editorial note

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Introduction

Unplanned pregnancy has been a major problem in Thailand. The problem is prevalent among in teenagers or adolescents with an increasing number of labor up to the highest of 53.4 per 1,000 populations of women aged 15 – 19 years old in 2012.¹ Unplanned pregnancy leads to other public health problems such as unsafe pregnancy termination, low birth weight newborns, sexually transmitted diseases, and

divorce and disrupted education in teenagers which could further negatively affect the quality of population in the future.

With a concern on the severity of the problem, public sectors have put more effort to tackle the problem intensively. As a result, rate of labor among teenagers has been decreasing to 42.5 per 1,000 populations of women aged 15 – 19 years old in 2016. One of the promising tools to alleviate this problem was the Prevention and Solution of the

Adolescents Pregnancy Problem Act, B.E. 2559 (2016) which was published in the Royal Gazette on March 31, 2016 and enforced on July 29, 2016.² Based on the Act, in addition to the provision of knowledge and counseling on proper pregnancy protection, contraception with various methods is also encouraged. Based on data from the World Health Organization (WHO)'s Thailand and Family Planning project, statistics of contraception methods in 2009 suggested that among all contraceptive methods used, 35% of them were oral contraceptive pills (OCPs); while emergency contraceptive pills were used the least (0.3%).³ Even though it has been widely used, OCPs offer both advantages and disadvantages. OCP users should be advised by physicians or pharmacists. Inappropriate use of OCPs could pose the risk on health.

One of the risks of combined hormones OCPs is cardiovascular disease such as venous thromboembolism, stroke and myocardial infarction with coagulation accelerated by estrogen hormone. A meta-analysis on more than 24 studies revealed that combined hormones OCPs increases the risk of stroke and myocardial infarction by 1.6 times compared with no use.⁴

With such adverse effects of combined hormone OCPs, WHO Medical Eligibility Criteria defined the contraindication for combined hormone OCPs as relative contraindication (Category 3) which means they have some risks of CVD and OCPs should not be used, and absolute contraindication (Category 4) which means OCPs must not be used because of the high risk of CVD. A previous study reported that in 2006 – 2008 there were significantly more women who bought OCPs from drugstores with Category 3 (relative contraindication) than those receiving OCPs from clinic (13% and 9%, respectively, $P = 0.006$).⁵ This finding offers an alarming sign of safety issue in women using OCPs. However, such study has not been conducted among Thai women using combined hormone OCPs.

A study in Thai women on behavior and knowledge about OCPs revealed that 29.8% of women receiving OCPs from drugstores had less confidence in information provided by the personnel of the drugstore than those at the hospital.⁶ Knowledge about what to do when for⁶ A qualitative study in the US also revealed that women were confidence in information provided by the pharmacist and they want to have the pharmacist's advice OCP use.⁷ Pharmacists at community pharmacy or community pharmacists have been considered a provider of health and drug use information for their

community. They take a major role in evaluating appropriate combined hormone OCP use at the community pharmacy. They also provide counseling on the use of combined hormone OCPs and relevant health behavior change.

A study by Gardner and colleagues in 2003 showed that community pharmacist's service on advising and selecting OCPs effective and safe for given women with a 12-month follow-up made the customers satisfied and allowed them to use OCPs safely.⁸ However, studies on effects of pharmaceutical care on knowledge and cardiovascular risk assessment relating to combined hormone OCPs have been limited.

With a concern on the limited understanding on cardiovascular risk among women using combined hormone OCPs, this study aimed to evaluate the cardiovascular risk in women using combined hormone OCPs by community pharmacists, to compare scores of knowledge about OCPs before and after the educational session.

Methods

In this pretest-posttest quasi-experimental study, women acquiring combined hormone OCPs at the three community pharmacies in Mahasarakham province during March to April 2019 were recruited. The study was divided into two phases. Phase 1 involved assessment cardiovascular risk in women using combined hormone OCPs, monitoring follow-up on modifiable risk factors in those with the risk, and referral of women with the risk to the hospital. In phase 2, knowledge of the participants was assessed before and after the provision of information about appropriate OCP use, its adverse effects and its cardiovascular risk with how to modify the risk factors.

To be eligible for the study, participants had to be women aged 15 – 50 years asking for OCPs for contraception and/or acne treatment and hormone adjustment. They were willing to participate and be followed up. However, those using combined hormone OCPs as hormone replacement therapy for post-menopausal women were excluded.

Sample size was estimated based on the finding from the work of Kanjanasilp and colleagues where scores of knowledge about OCPs were 3.2 (SD = 1.61) points before the educational session with electronic applications at drugstores, and 3.7 (SD = 1.42) points after the session.⁹ Based on the comparison of two dependent means with a type I error of 5%, a sample size of 82 participants.

Research instruments

Two instruments were used in this study, namely data collection form and experiment tool. In the data collection form, we collected the participant's general information and medical history and assessed risk of cardiovascular disease. The tool to assess CVD risk was guided by the United States Medical Eligibility Criteria for Contraceptive Use (U.S. MEC) (2016) and consisted of the following questions: OCP brand the participant was using, history of CVD, smoking history, history of migraine with aura, history of breast cancer, history of vascular or pulmonary embolism, history of operation with subsequent prolonged immobility, and breast feeding of less than 21 weeks post delivery as shown in Table 1.¹⁰

Table 1 Questions to assess risk of cardiovascular (CVD) in women using combined hormone oral contraceptive pills (OCPs).

Criteria for the use of combined hormone OCPs of the U.S. Medical Eligibility	Questions to assess CVD risk
High risk, the use of combined hormone OCPs is contraindicated (Category 4)	
Breast feeding of less than 21 weeks post delivery	Are you breast feeding? If so, please give the delivery date.
Smoker aged ≥ 35 yrs, ≥ 15 cigarette/day	Are you smoking? If so, how many cigarette you are smoking per day?
Systolic blood pressure (BP) of ≥ 160 mmHg or diastolic BP of ≥ 100 mmHg	Does your systolic blood pressure (BP) read ≥ 160 mmHg or diastolic BP read ≥ 100 mmHg?
History of vascular or pulmonary embolism	Have you had bloodclot (embolism) in lung or leg?
History of operation with subsequent prolonged immobility?	Have you had an operation with subsequent prolonged immobility?
Stroke	Do you have stroke?
History of breast cancer	Do you have breast cancer?
Migraine with aura	Do you have migraine? If so, once it happens, do you have any of these signs? - seeing flash light - seeing zigzag line - seeing distorted picture - having blindspot
Having theoretical risk, or risk outweighs benefits of combined OCPs (Category 3)	
Post delivery woman with no breast feeding for 21 – 42 weeks in the group with the risk of vein embolism	Are you breast feeding? If so, please give the delivery date.
Post delivery woman with breast feeding for 30 – 42 weeks in the group with the risk of vein embolism	
Smoker aged ≥ 35 yrs, < 15 cigarette/day	Are you smoking? If so, how many cigarette you are smoking per day?
Hypertensive patient with blood pressure well controlled	Is your blood pressure $< 140/90$ mmHg? Are you taking any medications for high blood pressure?
Hypertensive patient with blood pressure well controlled who has systolic blood pressure of 140 - 159 mmHg or diastolic blood pressure of 90 - 99 mmHg	Is your blood pressures within 140 – 159 / 90 - 99 mmHg?
Gallbladder related diseases or taking medications for such disease	Do you any gallbladder related diseases?
Diabetes patients for more than 20 years or diseases with vascular disorder	Are you diabetic? If so, do you have any complications in the kidney, eyes or neurologic system?
Migraine without aura with age of ≥ 35 years	Do you have migraine? If so, once it happens, do you have any of these signs? - seeing flash light - seeing zigzag line - seeing distorted picture - having blindspot

For the experimental tool, a questionnaire to test knowledge of the participants, educational leaflet and referral form were developed. The 10 questions covered 3 components of OCPs, specifically, general knowledge of OCP use (2 questions), how to use OCPs (4 questions), and adverse effects of OCPs (4 questions). The response format was correct and incorrect. The educational leaflet contained provided information about rare but severe adverse effects of combined hormone OCPs. The referral form was for referring participants with the need for medical attention was also developed. The knowledge questionnaire was examined for content validity according to the study objectives by three experts. The content validity was found to be high with an average Item Objective Congruence Index (IOC) of 0.89. When tested in 25 individuals comparable to the prospective participants, the knowledge questionnaire had an acceptable internal consistency reliability with a KR-20 coefficient of 0.701.

Data collection procedure

Customers receiving service at the community pharmacy who passed inclusion and exclusion criteria were included in the study. They were provided with the study objectives and conducts. Once they provided the voluntary written informed consent, these participants were interviewed and tested as follows. Participants were assessed for risk of CVD associated with the use of combined hormone OCPs which took about 10 minutes per participant. The assessment was to identify if the participant had any of the risks of CVD as guided by the U.S. MEC (Table 1) which meant the participant had a risk of CVD from combined hormone OCPs (Category 3) or were contraindicated for the use of OCPs (Category 4).

The participants were tested on knowledge about OCPs before educational session (pre-test) which took about 10 minutes per participant. Participants were then educated about OCP's use and adverse effects relating to CVD caused by OCPs. Participants were appointed for telephone follow-up two weeks later.

Participants with modifiable risk of CVD were advised individually. For smoking, they were advised to seek and join smoking cessation program. For those with high bloodpressure, they were advised to avoid alcohol intake, engage more exercise of at least 30 minutes per day, at least 5 days per week, and follow DASH diet (Dietary Approaches to Stop Hypertension).

For participants with contraindication for the use of OCPs, referral to the hospital for medical attention was made with the filled referral form.

Human right protection

This study was approved by the Ethics Committee on Human Study, Faculty of Pharmacy, Mahasarakham University (Approval number: 011/2561).

Data analysis

Demographic and general clinical data of the patients were presented with descriptive statistics including mean with standard deviation and frequency with percentage. Pretest and posttest knowledge scores were compared using Wilcoxon signed rank test since they were not normally distributed. Proportions of participants with correct answer for each question before and after the educational session were tested using McNemar test. Statistical significance for all tests was set at a type I error of 5% (P -value < 0.05). All statistical analyses were carried out using statistical software SPSS version 22.0.

Results

There were 50 participants eligible for the study. Their average age was 26.84 years. The majority were single (35 participants or 70.0%). Only three of them had underlying diseases (6.0%) with two with allergy and one with asthma. Only one participant smoked (2.0%). Five of them (10.0%) had a history of alcohol abuse. Combined hormone OCPs with the most used was cyproterone acetate 2 mg + ethinyl estradiol 0.035 mg (42.0%). Average number of years of OCP use was 1.12 years. Slightly more than half of them used OCPs for contraception (27 participants or 54.0%) (Table 2).

Based on the CVD risk assessment, U.S. MEC category 4 (absolute contraindication) as found with one participant with migraine with aura (2.0%), and U.S. MEC category 3 or risk of CVD was found in one participant with hypertension which was a modifiable factor (2.0%).

In terms of knowledge, mean score of knowledge increased from 5.86 ± 5.86 out of 10 points before educational session to 8.90 ± 0.96 points after the session with statistical significance (P -value < 0.001) (Table 3). Before the educational session, no individual questions were correctly answered by all participants. The most correctly answered

Table 2 General information of the participants (N = 50).

Characteristics	N	%
Age, mean \pm SD	26.84 \pm 8.19	
History of alcohol intake	5	10.0
History of smoking	1	2.0
Occupation		
Students	26	52.0
Government employee	4	8.0
Business owner	4	8.0
Labor	4	8.0
Housewife	2	4.0
Small business	2	4.0
No job/others	8	16.0
Marital status		
Single	35	70.0
Married	15	30.0
Education level		
Bachelor's degree	35	70.0
High school	6	12.0
Senior vocational school diploma / associate degree	3	6.0
Higher than Bachelor's degree	3	6.0
Junior vocational school diploma	2	4.0
Primary school	1	2.0
Regimen of combined hormone OCPs		
Cyproterone acetate 2 mg + ethinyl estradiol 0.035 mg	21	42.0
Levonorgestrel 0.15 mg + ethinyl estradiol 0.03 mg	6	12.0
Chlormadinone acetate 2 mg + ethinyl estradiol 0.03 mg	5	10.0
Drospirenone 3 mg + ethinyl estradiol 0.03 mg	4	8.0
Desogestrel 0.15 mg + ethinyl estradiol 0.02 mg	4	8.0
Drospirenone 3 mg + ethinyl estradiol 0.02 mg	3	6.0
Desogestrel 0.15 mg + ethinyl estradiol 0.03 mg	2	4.0
Desogestrel 0.025 mg + ethinyl estradiol 0.04 mg μ re: Desogestrel 0.125 mg + ethinyl estradiol 0.03 mg (2 levels)	2	4.0
Gestodene 0.075 mg + ethinyl estradiol 0.02 mg	1	2.0
Gestodene 0.06 mg + ethinyl estradiol 0.015 mg	1	2.0
Norgestrel 0.15 mg + ethinyl estradiol 0.03 mg	1	2.0
Objectives of OCP use		
Contraception	27	34.0
Acne treatment	7	14.0
Hormone adjustment	5	10.0
Multi-purpose	9	18.0
Others (ovarian cyst), contraception after abortion	2	4.0

was question 4 (by 45 participants or 90.0%). This means that most participants knew that 21-tablet package needs 7-day off period before stating the new package, while 27-tablet package needs no such step. Question with the least correct answer was question 8 (7 participants or 14.0%). This suggests that most participants did not only certain, not all, OCPs could cause edema relating to water retention. After educational session, all 10 questions had higher proportion of participants who answered correctly. However, once compared with such proportions before educational session, but statistical significance was found in 7 of them. The three questions with no statistical significance were question 2 (correct and regular use of OCPs could effectively prevent pregnancy), question 4 (21-tablet package needs 7-day off period before stating the new package, while 27-tablet package needs no such step), and question 5 (OCPs could be taken at any time on different days).

Table 3 Knowledge assessments on combined hormone oral contraceptive pills (OCPs) (N = 50).

Questions	Number of participants with correct answer, N (%)		
	Before educational session	After educational session	P-value ^a
1. Use of combined hormone OCPs could prevent sexually transmitted disease.	36 (72)	48 (96)	< 0.001
2. Correct and regular use of OCPs could effectively prevent pregnancy	44 (88)	47 (94)	0.375
3. Start to take OCPs on days 1 – 5 of the menstruation cycle.	37 (74)	50 (100)	< 0.001
4. 21-tablet package needs 7-day off period before starting the new package, while 27 - tablet package needs no such step	45 (90)	50 (100)	0.062
5. OCPs could be taken at any time on different days.	31 (62)	36 (72)	0.125
6. If miss 1 tablet of OCP, take the last pill you missed now, even if this means taking 2 pills in 1 day and carry on taking the rest of the pack as normal.	40 (80)	49 (98)	0.004
7. Nausea, vomiting or blood spotting, if occurs, usually could get better over the use of 2 - 3 package of OCPs.	32 (64)	47 (94)	< 0.001
8. All OCPs can cause edema from water retention.	7 (14)	28 (56)	< 0.001
9. All OCPs can cause severe adverse effect which is blood clot in blood vessel.	13 (26)	44 (88)	< 0.001
10. Women with migraine with aura (seeing flash light, zigzag line, distorted picture, blindspot) should not use combined hormone OCPs.	8 (16)	45 (90)	< 0.001
Mean total score (out of 10 points)	5.86 ± 1.78 (median = 6)	8.90 ± 0.96 (median = 9)	< 0.001 ^b

^a Comparison of proportions of participants with correct answer before and after educational session using McNemar's test.

^b Comparison of mean total score before and after educational session using Wilcoxon signed rank test.

In terms of adverse effects of OCPs, from monitoring follow-up, behavior modifications for modifiable risk factors, and the follow-up on referred participants to the hospital, there was one out of 50 participants who had breast engorgement associated with the first package of OCPs. The researcher explained the cause of such event. The participant was convinced by the researcher that the pain was mild and common and would disappear with 2 – 3 packages of OCPs. For the follow-up on modifiable risk factors in patients with CVD risks associated with combined hormone OCP use, the researcher measured the participant blood pressure. Based on the triplicate measures, the average blood pressure was 133/92 mmHg. After the advice, the participant had been modifying her behaviors but her blood pressure at 2 weeks after the advice session was still high with an average of 139/91 mmHg from triplicate. The researcher advised the

participant and allowed another 3-month behavior modification period. If blood pressure is high at the level that could be the risk for CVD in person using combined hormone OCPs (systolic BP of 140 - 159 mmHg or diastolic BP of 90 - 99 mmHg), the participant will be recommended to seek medical attention at the healthcare provider.

There was one participant with OCP contraindication because of migraine with aura. After the advice on contraceptions proper for the participant, the participant was referred to medical clinic nearby the participant's house. At the telephone follow-up 2 weeks later, physician at the clinic switched from OCPs to contraceptive injection and no adverse effect had not been found.

Discussions and Conclusion

The use of the U.S. Medical Eligibility (2016) allowed us to determine proportion of participants who had CVD risk relating to combined hormone OCP use (U.S. MEC category 3) (2.0%) and those with contraindication to use combined hormone OCPs (U.S. MEC category 4) (2.0%), which was a total of 4.0%. However, in the study of Lauring and colleagues, as high as 103 of 987 participants or 10.44%¹¹ were contraindicated for combined hormone OCPs which was much higher than 2.0% found in our study. This discrepancy could be due to a small sample size in our study. In addition, contraindication associated with migraine with aura which was 81% of all contraindicated cases in the study of Lauring and co-workers.¹¹ Like our study, they also advised the participants on contraceptive methods appropriate for individuals with migraine with aura which reflected a crucial role of healthcare providers in preventing CVD associated with combined hormone OCPs.¹¹ Our result was also consistent with that of Grossman and colleagues (2008) in Mexico.¹² They found that migraine with aura was the most found contraindication among women using combined hormone OCPs.¹²

We found that education session for individual participants on the use of OCPs and its adverse effects could improve their knowledge. This was in accordance with the study of Hall and co-workers the score of knowledge about OCPs increased after the education significantly ($P < 0.001$).¹³

Our leaflet, in addition to oral presentation in the educational session, could have helped remind the participant about adverse effect of combined hormone OCPs and risk factors of CVD relating to OCPs. The leaflet thus served well

as a reminder at the participant convenience. As a result, score of knowledge was improved significantly after the intervention. The study of Kanjanasilp and colleagues also showed similar result.⁹ Phone applications Mypill[®] and manual for OCP use were provided and the score of knowledge on OCP use increased from 3.4 ± 1.69 out of 10 points at pre-test to 6.2 ± 1.99 points at post-test with a statistical significance (P -value < 0.001).⁹

In monitoring behavior change to modify risk of CVD associated with OCPs, participants were followed up by telephone 2 weeks after the individual educational session. Participants changed their behavior partially but their blood pressure was still high so the risk still existed. This could be due to a relatively duration of follow-up which did not allow for a change. These behaviors usually need a relatively long period of time to change including daily activities, food consumption, and exercise.

These behavior modifications need continuous, regular practice in a long period to see the improvement. Thus no change in blood pressure was found. However, with more knowledge they received about modifying risks of CVD associated with OCP, they were expected to keep modifying their behavior to reduce their risk. There were also expected to use the acquired knowledge to prevent and alleviate adverse effects of OCPs.

Our study had certain limitations. A sample size smaller than the estimated one did not allow for identifying individuals with CVD risks or contraindication for OCP. This small sample size limited generalization to the actual population. Therefore, a larger sample size and a wide array of geographical areas are needed for future studies. Telephone follow-up could cause some confusion in communication regarding precision and understanding on questions and issues. A short duration of 4 weeks to monitor adverse effects and behavioral changes could not allow for substantial number of incidents and changes. A longer period of follow-up should be used in future studies.

Our present study demonstrated a role of community pharmacist in assessing CVD risk associated with combined hormone OCP use. Identified cases with the risk could be referred to medical service for appropriate contraceptive method. Educational session for individual customers could help improve knowledge and adverse effects of OCP and its CVD risk. These could further enforce desirable health behavior to modify risk factors of CVD. More safety benefit of

community pharmacy could be realized by society. This in turn could encourage community pharmacists to put more effort to take care of customers using combined hormone OCPs especially CVD risk assessment, and effective and safe OCP use. Ultimately, customers could be more confident in community pharmacy service.

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