Risk Factors of Venous Thromboembolism (VTE) in Thai Reproductive Aged Female: King Chulalongkorn Memorial Hospital Experience

Chatchadaporn Worralurt MD*,
Surasak Taneepanichskul MD*

** Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University*

Objective: *To estimate the risk factors of VTE focusing on oral pill use, alcohol intake and smoking among women who attended at King Chulalongkorn Memorial Hospital between 1 January 1995 and 31 December 2004.*

Material and Method: *The study design was case-control study. A Case was defined as the female inpatient who was diagnosed with VTE and a control was defined as the healthy female patient who attended gynecological clinic for annual check up. The questionnaires were developed to interview both cases and controls. The ratio of case per control was 1:2. The data was analyzed with SPSS/PC$^+$ version 12.0. The statistic uses were mean, standard deviation, t-test, Odds ratio and 95%confidence interval.*

Results: *Seventy of cases and one hundred and forty of controls were recruited into the study. The mean +/- SD of age of case was 37.2 +/- 9.3 years and the control was 35.6 +/- 9.9 years. There were no significant difference in term of age, parity, weight, height and BMI between cases and controls. The Odds ratio of oral contraceptive pill use, smoking and alcohol consumption were 0.94, 4.28, and 2.62, respectively. However, no statistical significance difference of Odds ratio in oral contraceptive pill use, and alcohol consumption were demonstrated.*

Conclusion: *Smoking and alcohol consumption increased risk of VTE in this study. Oral contraceptive pill use did not demonstrate increasing risk. However, there was no statistical significance of odds ratio in alcohol consumption. This result may be due to the small sample of cases. The further study should be recruited with more cases in order to demonstrated the risk factors of these female patients.*

Keywords: *Risk factors, Venous thromboembolism*

J Med Assoc Thai 2005; 88 (11): 1502-5
Full text. e-Journal: *http://www.medassocthai.org/journal*

Venous thromboembolism (VTE), consisting of deep vein thrombosis and pulmonary embolism, is the most common vascular disease in women of childbearing age[1]. It is a multifactor disease resulting from the interaction between genetic and environmental risk factors[1]. The former includes abnormalities causing inherited thrombophilia, such as deficiencies of the naturally occurring anticoagulants antithrombin, protein C, protein S, and the gain-of-function mutations in genes encoding coagulation factor V (factor V Leiden) and prothrombin. The environmental, transient risk factors associated with an increased risk of VTE are cancer, recent surgery, pregnancy and puerperium, use of oral contraceptives, and prolonged immobilization[2-5]. The increased risk of idiopathic VTE in users of oral contraception (OC), and smoking is well documented in numerous studies[3-5]. However, most of these studies were limited to European and American women. Alcohol consumption is a controversy in risk factor of VTE[6]. Nevertheless, there are few studies of these points in Thai women. The objective of this study was to evaluate the risk factors of VTE in Thai women focusing on oral pill use, smoking, and alcohol consumption.

Correspondance to : Taneepanichskul S, Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

Material and Method

Women aged 15-49 years old who were diagnosed with deep vein thrombosis and/or pulmonary embolism in King Chulalongkorn Memorial Hospital between January 1, 1995, and December 31, 2004 were included in the study. Deep vein thrombosis was objectively diagnosed and documented by Doppler ultrasound examination or venography and pulmonary embolism by perfusion or ventilation-perfusion lung scan, computed tomography, or angiography. The patients were contacted by mail or telephone for interview appointment. The questionnaire was developed and verified by the experts. It included demographic data, history of medical illness, oral pill use, alcohol intake, and smoking. All subjects were interviewed by investigators. Seventy eligible cases of deep vein thrombosis and pulmonary embolism were able to be contacted and recruited in the study. Control subjects were recruited from women who attended the gynecological check up clinic and volunteered to be included in the study. Two controls were matched to each patient for age ($\pm$ 5 years), and education level. The study protocol is approved by Ethicals Committee of Faculty of Medicine, Chulalongkorn University following with the principle of the Declaration of Helsinki. The statistical package SPSS/PC version 12.0 was used to analyze the data. Student's t-test, Chi-square, odd ratio and 95 % confidence interval were used.

Results

A total of 75 cases were recruited in the study. There were 44 cases of deep vein thrombosis, 16 cases of pulmonary embolism and 15 cases of combine deep vein thrombosis and pulmonary embolism. Interviews were not completed for 5 cases due to loss of contact and were excluded from the study. All cases are still alive. 140 healthy women were recruited as control group. The characteristics study population is shown in Table 1. The mean age +/- SD of case was 37.2 $\pm$ 4.3 year and the control was 35.6 $\pm$ 9.9 year. There were no statistical difference in term of age, parity, weight, height and BMI between 2 groups. The risk factors of VTE are shown in Table 2.The Odds ratio of oral contraceptive pill use, smoking and alcohol consumption were 0.94, 4.28 and 2.62, respectively. No statistical significant difference of odds ratio in oral contraceptive pill use, and alcohol consumption were demonstrated. However, smoking was shown to be statistical by significant risk factor of VTE.

Discussion

The subjects of case and control groups in this study did not demonstrated significant difference in term of age, parity, weight, height, and BMI. The

Table 1. Characteristics of study population

Variable	Case (n = 70)	Control (n = 140)	95%CI	p value
Age (years)	37.2 $\pm$ 9.3	35.6 $\pm$ 9.9	-1.20, 4.4	ns
Parity	1.2 $\pm$ 1.2	1.1 $\pm$ 1.1	-0.23, 0.43	ns
Weight (Kgs)	54.1 $\pm$ 12.6	55.4 $\pm$ 11.2	-4.67, 2.07	ns
Height (cm)	157.9 $\pm$ 4.6	157.9 $\pm$ 4.9	-1.39, 1.39	ns
BMI (Kg/m^2)	21.7 $\pm$ 4.8	24.0 $\pm$ 15.9	-6.17, 1.57	ns

Table 2. Risk Factors of VTE

Factor	Case (n = 70)	Control (n = 140)	OR	95%CI
OC use				
Ever/present	33	68	0.90	0.53, 1.65
Never	37	72		
Smoking				
Ever/present	6	3	4.28	1.04, 17.7*
Never	64	137		
Alcohol				
Ever/present	5	4	2.62	0.65, 10.1
Never	65	136		

* Statistical significance

concerned risk factors were oral combined pill use, smoking, and alcohol consumption. Oral combined pill did not show any increasing risk of VTE in this study. This finding was quite different from the previous studies[3,7-10]. The recognition of an increased risk of VTE associated with the OC pill has resulted in many studies. Third generation OC users are more likely to develop VTE rather than second generation OC users[7-10]. In this study, OC use did not show any increase risk for VTE. This finding is different from other previous studies. Factor V Leiden mutation is responsible for increase risk of VTE in OC users[7-10]. This factor is more common in caucasian women rather than Asian women particularly, Thai women[11]. The less prevalence of factor V Leiden mutation in OC users among Asian women may be the reason to explain this finding[11]. However, the result may be underestimated due to the number and characteristics of the base population selected for study.

Smoking was demonstrated as the risk factor of VTE in this study. Both clinical and basic research has linked smoking and COPD to abnormalities of coagulation and fibrinolysis and to VTE[5]. Several potential mechanisms involving inflammation, fibrinogen synthesis, clotting factors, and impaired fibrinolysis are suggested as possible links[5-6]. Alcohol consumption was also found to have increased the risk of VTE in this study. However, the odd ratio was not shown to be statistically significant. The association of alcohol consumption and VTE is not well documented[1,2,6]. Some studies demonstrated the association while some did not elaborate in relationship with VTE[1,2,6]. Alcohol consumption and VTE should be investigated further in order to establish this association.

In conclusion, this study had some results different from the recent studies. It was shown that oral contraceptive pill use was not the risk factor of VTE in Thai women. Smoking and alcohol consumption increased the risk of VTE. However, only smoking was demonstrated to be statistically significant. Further study should be conducted using a bigger sample in order to evaluate these risk factors.

References

1. Heit JA, Silverstein MD, Mohr DN. The epidemiology of venous thromboembolism in the community. Thromb Haemost 2001; 86: 452-63.
2. Rodger L, Bick MD. Cancer-associated thrombosis. N Engl J Med 2003; 349: 109-11.
3. Vandenbrouke JP, Rosing J, Bloemenkamp KWM, Helmerhorst FM, Bouma B, Rosendaal FR. Oral contraceptives and the risk of venous thrombosis. N Engl J Med 2001; 344: 1527-35.
4. Hansson PO, Eriksson H, Welin L, Svardsudd K, Wilhelmsen L. Smoking and abdominal obesity: risk factors for venous thromboembolism among middle-aged men: the Study of Men Born in 1913. Arch Intern Med 1999; 159: 1886-90.
5. Tuut M, Hense HW. Smoking, other risk factors and fibrinogen levels: evidence of effect modification. Ann Epidemiol 2001; 11: 232-8.
6. Nightingale AL, Farmer RD. Ischemic stroke in young women. Stroke 2004; 35: 1574-8.
7. World Health Organisation. World Health Organisation Collaborative Study of cardiovascular disease and steroid hormone contraception. Venous thromboembolic disease and combined oral contraceptive: results of international multicentre case control study. Lancet 1995; 364: 1575-82.
8. Jick H, Jick SS, Gurewich V, Myers MW, Vasilakis C. Risk of idiopathic cardiovascular death and nonfatal venous thromboembolism in women using oral contraceptives with differing progestagen components. Lancet 1995; 346: 1589-93.
9. Jick H, Kaye JA, Vasilakis-Scaramozza C, Jick S. Risk of venous thromboembolism among users of third generation oral contraceptives compared with users of oral contraceptives with levonorgestrel before and after 1995: cohort and case control analysis. Br Med J 2000; 321: 1190-5.
10. Heinemann LAJ, Lewis MA, Spitzer WO, Thorogood M, Guggenmoos-Holzman I, Bruppacher R. The Transnational Research Group on Oral Contraceptives and the Health of Young Women. Thromboembolic stroke in young women. A European case-control study on oral contraceptives. Contraception 1998; 57: 29-37.
11. Chuansumrit A, Jarutwachirakul W, Sasanakul W, Rurgkhum S, Kadegasem P, Kitpoka P, et al. Absence of factor V Arg306 - The and low factor V Arg306 - Gly mutation prevalence in Thai blood donors. Southeast Asian J Trop Med Public Health 2004; 35: 450-2.

ปัจจัยเสี่ยงของการเกิดภาวะลิ่มเลือดอุดตันในหลอดเลือดดำของสตรีไทยในวัยเจริญพันธุ์: ประสบการณ์ของโรงพยาบาลจุฬาลงกรณ์

ชัชฎาภรณ์ วรเลิศ, สุรศักดิ์ ฐานีพานิชสกุล

การศึกษาปัจจัยเสี่ยงของการเกิดภาวะลิ่มเลือดอุดตันในหลอดเลือดดำของสตรีไทย ได้ทำการศึกษาที่โรงพยาบาลจุฬาลงกรณ์ โดยรวบรวมประวัติของสตรีที่เป็นภาวะลิ่มเลือดอุดตันในหลอดเลือดดำ ที่รักษาในโรงพยาบาลจุฬาลงกรณ์ ตั้งแต่วันที่ 1 มกราคม พ.ศ. 2538 ถึง วันที่ 31 ธันวาคม พ.ศ. 2547 ทุกรายยังมีชีวิตอยู่ จำนวน 70 ราย โดยสัมภาษณ์ถึงปัจจัยเสี่ยงต่าง ๆ ที่ทำการศึกษาคือ การรับประทานยาเม็ดคุมกำเนิด การสูบบุหรี่ และการดื่มสุรา เปรียบเทียบกับสตรีที่มีสุขภาพสมบูรณ์แข็งแรงทั่วไปจำนวน 140 ราย จากการศึกษาพบว่า สตรีทั้ง 2 กลุ่ม ไม่มีความแตกต่างในเรื่องของอายุ จำนวนบุตร น้ำหนัก ส่วนสูงและค่าดัชนีมวลกาย การรับประทานยาเม็ดคุมกำเนิด ไม่เป็นปัจจัยเสี่ยงสำหรับภาวะลิ่มเลือดอุดตันในหลอดเลือดดำ ส่วนการสูบบุหรี่และการดื่มสุราเพิ่มความเสี่ยงต่อการเกิดภาวะลิ่มเลือดอุดตันในหลอดเลือดดำ แต่มีเพียงการสูบบุหรี่ที่เป็นปัจจัยเสี่ยงต่อการเกิดภาวะลิ่มเลือดอุดตันในหลอดเลือดดำ อย่างมีนัยสำคัญทางสถิติ