

Oral Contraceptive Use and Smoking Habits in Young Israeli Women: A Cross-Sectional Study

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Key words: oral contraceptives, smoking, cardiovascular risk, women's health, obesity

Abstract

Background: Oral contraceptive users are at increased risk for both arterial and venous thrombosis, some of which can be fatal. Studies are consistent with the existence of a synergism between cigarette smoking and OC use in the pathogenesis of myocardial infarction in young women.

Objectives: To study the relationship between OC use, cigarette smoking and other cardiovascular risk factors among young women.

Methods: A systematic sample of military personnel, upon discharge from service in the Israel Defense Forces, was asked to complete a research questionnaire. Body weight and height were measured and body mass index computed.

Results: Overall, 16,258 questionnaires were collected and analyzed during this 20 year study. There was a gradual, significant increase in OC use until the mid-1980s, from approximately 45% to 60% ($P < 0.001$), followed by steady rates of 58–64% since then. In contrast, the rates of smoking decreased significantly in the mid-1980s, from approximately 42% to a nadir of 22% in 1991. Since then, the rate of smoking has increased slowly but steadily to reach a level of 35% in 1999. The OC users were more often of western (Ashkenazi) origin and came from families with more education and fewer siblings. They were more often smokers than non-OC users, and started smoking at a younger age. They had significantly lower BMI than non-users. OC use was nearly identical in groups with or without multiple cardiovascular risk factors (smoking, obesity, family history).

Conclusions: Smoking and OC use are strongly associated. Other cardiovascular risk factors (smoking, obesity, family history) do not prevent OC users from smoking or smokers to use OC. We suggest that primary care physicians discourage smoking among adolescent females who wish to start using OC. A thorough medical history should be obtained in order to recognize all risk factors for cardiovascular disease and to provide for appropriate contraception counseling.

IMAJ 2004;6:546–549

The use of oral contraceptives is known to increase the risk of cardiovascular disease [1,2]. The WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception provided information on the risks of idiopathic venous thromboembolism, ischemic and hemorrhagic stroke, and acute myocardial infarction associated with the use of combined OC [3–5]. Furthermore, OC users with one or more risk factors for cardiovascular disease, especially smoking, were shown to be at a significantly higher risk of MI [6]. Additional studies are consistent

with the existence of a synergism between cigarette smoking and OCs in the pathogenesis of MI in young women [7].

In Israel, there is mandatory military conscription of females at the age of 18 years for a period of 22 months. Using a systematic sampling process at the time of completion of their military service, conscripts are asked to voluntarily complete (after obtaining a signed informed consent) a research questionnaire on their medical history and several health-related topics, such as oral contraceptive use, smoking, etc. We took advantage of these questionnaires to study the epidemiology of OC usage in relation to smoking and other selected cardiovascular risk factors in Israeli female conscripts. Specifically, we tested the post-hoc hypotheses that: a) lower socioeconomic class (as measured by number of children in the family, combined number of years of school education of the conscript's parents, and the years of the conscript's school education) is a predictor of both OC use and tobacco smoking; b) OC use is associated with a higher incidence of smoking; and c) known associated cardiovascular risks do not prevent adolescent smokers from using OC, or physicians from prescribing them.

Subjects and Methods

This cross-sectional study was based on the prospectively established database of the Israel Defense Forces Medical Corps during the years 1980–1999.

Subjects

Our study sample was drawn from an ongoing survey designed by the IDF Medical Corps to provide population-based data and prevalence estimates of health-relevant measures, including health behaviors and attitudes and anthropometric data. The survey was conducted for a representative sample of IDF personnel upon discharge from compulsory service, usually at the age of 20–21 (women) or 21–22 (men). The sampling process is systematic, based on a predetermined combination of digits of the subjects' serial number, as previously described [8]. Of those approached to participate in the study, 91% agreed and provided signed informed consent. The IDF Medical Corps Review Board approved the study as well as the manner in which informed consent was obtained from subjects.

Data collection

Trained nurses from the IDF Health Surveillance Section interviewed participants on demographic data (subjects' country of birth

IDF = Israel Defense Forces

OC = oral contraceptives
BMI = body mass index
MI = myocardial infarction

and extent of formal education, paternal country of birth and level of education, and number of siblings); health behaviors (smoking, alcohol intake, level of recreational exercise); OC use (type of pill and age of onset); parental coronary heart disease morbidity data (defined as "angina pectoris," "chest angina," "heart attack," or "myocardial infarction") and the cause of death of deceased parents selected from the following: injury, cancer, stroke, MI, sudden death of unknown cause, and other causes of death. Weight and height, without outer garments and shoes, were measured using a weight and standing height scale (Sunbeam, Bridgeview, IL, USA).

Data analysis

For the purpose of analysis the following definitions were used: BMI was calculated as weight (in kilograms) divided by height squared (in meters) (kg/m^2). Paternal and maternal CHD history were defined as positive when the subject reported premature CHD morbidity of the father (under age 55) or mother (under age 65) and/or death due to CHD. Origin was defined according to the birthplace of the subject's father or paternal grandfather if the father was Israeli-born. Origin was classified as: Western (Ashkenazi) – including Europe (excluding Turkey), the Americas, Australia or South Africa; Oriental (Sephardic) origin – Asia, Turkey, North Africa or Ethiopia; and Israeli origin – subjects whose father and paternal grandfather were born in Israel. Both OC use and smoking referred to current habitus.

Statistical analysis

We used the Statistical Analysis System (SAS Institute Inc, Cary, NC, USA) to analyze the data. Data were tested for normality, and means and proportions were compared between women who smoked and those who did not by means of univariate analysis using Student *t*-tests or chi-square tests, as needed. Backward stepwise logistic regression analysis was used to study the independent effect of the variables on OC use that were found by univariate analysis to be significant. Results were expressed as mean \pm SD, or n (%). A *P* value of <0.05 was considered significant.

Results

Overall, 16,258 young females were included in this study. Figure 1 shows the rates of OC use and of smoking for the 22 years of the study. There was a gradual, significant increase in OC use until the mid-1980s, from approximately 45% to approximately 60% ($P < 0.001$), followed by steady rates of 58 to 64%. In contrast, the rates of smoking decreased significantly in the mid-1980s, from approximately 42% to a nadir of 22% in 1991. Since then, the rate of smoking has increased slowly but steadily, reaching a level of 35% in 1999.

Average age at discharge was 20.1 ± 0.7 years. Overall, 56.2% reported using OC regularly while 31.2% reported smoking at the time of the survey. Mean BMI was $22.4 \pm 3.4 \text{ kg}/\text{m}^2$. The OC group started using OC at an average age of 18.3 ± 1.3 years. Demographic data of the participants are presented in Table I, according to OC use. The OC users were more often of western (Ashkenazi) origin and came from families with more years of education and fewer siblings. They had on average a lower weight and a lower BMI. The OC users were more

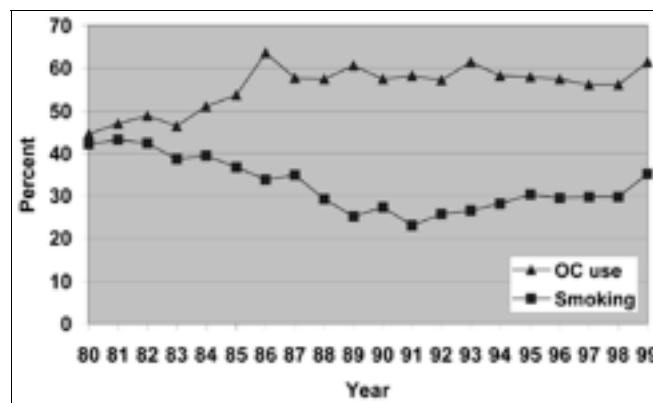


Figure 1. Rates of OC use and of smoking during the 20 years of the study

Table I. Demographic data according to OC use (mean \pm SD, or %)

	OC use		P value
	No	Yes	
BMI (kg/m)	3.7 \pm 22.7	22.2 \pm 3.1	>0.001
Smoking	26	36	>0.001
Family origin			
Israel	4.95	5.83	>0.001
Ashkenazi	35.18	51.19	>0.001
Sephardic	59.86	42.97	>0.001
Parent history of ischemic vascular disease (non-fatal)	12.59	11.73	>0.182
Either parent died from ischemic vascular disease	2	1.57	>0.049
Years of education	11.8 \pm 1.0	11.9 \pm 0.8	>0.001
Father's academic education	23.02	30.47	>0.001
No. of children in family	4.1 \pm 2.1	3.5 \pm 1.6	>0.001

Table 2. Results of the logistic regression

Variable	Odds ratio	95% confidence interval
Year of study	0.99	0.98–1.003
Smoking	1.80	1.65–1.97
Either parent died from ischemic vascular disease	1.25	0.93–1.69
Ethnic origin		
Ashkenazi vs. Israeli	0.83	0.69–0.97
Oriental vs. Israeli	0.52	0.48–0.56
BMI	0.94	0.93–0.95

often smokers as compared to non-OC users, and started smoking at a younger average age [Table I]. Non-users of OC more often had a parent who died from ischemic vascular disease than did OC users ($P < 0.05$) [Table I].

In logistic regression analysis taking into account OC use as the dependent variable and the year of study (entered as stochastic), smoking, the death of a parent from ischemic vascular disease, ethnic origin and BMI as the independent variables, only the number of years of study ($P < 0.0001$), smoking ($P < 0.0001$), ethnic origin ($P < 0.0001$) and BMI ($P < 0.0001$) remained significantly associated with OC use [Table 2].

Table 3. Rates of various combinations of cardiovascular risk factors (smoking, increased BMI, and positive family history) in OC and non-OC users (%)

Risk Factors	OC use	Non-OC use	P value
Smoker and one parent with IHD (n=396)	66.9	33.1	>0.001
Smoker and one parent with IHD and BMI > 27 (kg/m ²) (n=49)	49.0	51.0	0.19
Smoker with one parent who died of IHD (n=103)	62.1	37.9	0.22

IHD = ischemic heart disease

Table 3 compares the rates of various combinations of cardiovascular risks (smoking, increased BMI, and positive family history combined) in OC and non-OC users: there were significantly more OC users among smokers who had one parent with ischemic heart disease (66.9% versus 33.1%, $P < 0.001$). OC use was nearly identical in groups with or without the risk factors of BMI >25 and/or death of a parent from ischemic heart disease. Of the 29 smokers with a high BMI and a parent who died from ischemic heart disease, 51.7% used OC.

Discussion

Our data show that the rates of OC use among Israeli teenagers increased gradually over the past 20 years. The rate of 56% is significantly higher than that reported in other countries such as The Netherlands (35–45%) [9]; however, the 56% rate observed in our study was not based on a national representative sample and might represent an overestimation.

Despite the decrease in smoking rates in the mid-1980s, it appears that over the past 10 years the rates are once again increasing, slowly but steadily. Moreover, in this large study of more than 16,000 young women discharged from the IDF, we found a strong association between OC use and smoking. Sixty-four percent of smokers used OC, compared with 53% of non-smokers. This happened despite various public campaigns against the untoward effects of tobacco smoke and despite recent legislation against smoking in public places.

The recently increasing rates of smoking among teenagers are not unique to the IDF or the State of Israel. Adolescents start smoking in response to social influences, emulating the behavior of friends and family members, and are influenced by the media [10]. This was observed in the United States [11], where consumer organizations have accused tobacco companies of selectively focusing their ad campaigns on females, teenagers, and minorities – all potential “new customers” [12,13]. Nevertheless, although legislation placing limitations on tobacco ads exists also in Israel, the young women in our study were not immune to the social and/or advertising pressures that led them to start smoking, even in the military setting that provides free detoxication programs and whose official policy disapproves of tobacco smoking. Tobacco smoking is tremendously addictive and the long-term success of various methods of smoking cessation is not very impressive, due to high relapse rates, particularly in adolescents [14]. Therefore, the probable best strategy against tobacco addiction is prevention, which should be developed at or before the age children start

smoking, i.e., during their early adolescence.

Although OC may be associated with many significant health benefits, such as preventing unwanted pregnancies, lowering the need and associated risks of abortions, etc., the fact that many smokers used OC, or conversely, that many OC users smoked tobacco, was a worrisome finding of our study. The link between the two conditions was expected. It may be suggested that adolescents who smoke are more likely to be of lower socioeconomic status (a condition that may be linked to early sexual initiation) [15]. Surprisingly, markers of low socioeconomic class specific to Israel – such as large number of siblings, oriental (Sephardic) origin, or fewer years of parental education – were in fact linked to a lower incidence of smoking and of OC use. This may partly be due to the fact that, in Israel, these markers are also markers of social-religious behaviour (religious families, which disapprove of premarital sex, have more children and fewer years of parental higher education) [16,17].

The combination of tobacco smoking and OC use has significant health risks. It has been estimated that approximately 1.2 of 10,000 OC users aged 20 who smoke will experience MI, hemorrhagic stroke, ischemic stroke, or venous thromboembolism per year [18]. The risk of one of the abovementioned life-threatening events increases further, exponentially, with increasing age [18]. Even the newer, lower dose OCs were recently shown to increase the risk of MI in smokers to a level about 30 times that in non-smokers who do not use OC [19]. The mechanisms by which OC users who smoke are at increased cardiovascular risks are complex: smoking favors thrombogenesis in OC users probably through various mechanisms, as it inhibits prostacyclin formation [20], increases thromboxane A2 formation [21], and decreases antithrombin III activity [7]. Low dose OCs may not significantly worsen lipid profile but still decrease the blood HDL_{2a} concentrations. Young women who smoke have significantly lower levels of high density lipoprotein-cholesterol and of its HDL_{2a} subfractions when compared to even older non-smoking controls [22]. In addition, reduced physical activity in smokers may increase the risk of CHD.

The use of OC significantly increases the risk of venous thrombosis in a woman with inherited thrombophilia. Studies have shown that the frequency of inherited thrombophilia among healthy subjects is around 5–10% among white women [23]. Factor V Leiden and the G20210A mutation in the prothrombin gene, which are common among healthy Caucasians, account for most of these thrombophilias. In a study of women using OC, the risk of venous thrombosis was increased by a factor of 3.8 in normal women and by 34.7 in women who were heterozygous for factor V Leiden [24]. With the use of third-generation OCs the risk is twice that of second-generation OCs [25]. These studies conclude that women with inherited thrombophilia should avoid using OC, particularly if they have a personal or family history of venous thrombosis. Since screening healthy women for thrombophilias is not recommended, screening should be confined to women with a personal or family history of venous thrombosis, requiring the physician to take a thorough medical history.

In our study, the presence of various risk factors did not appear to be a powerful motivating agent for OC users to quit

smoking, or for smokers to not use OC. It is extraordinary that more than 60% of females who smoked and who have lost a parent due to ischemic heart disease (who, due to the young age of our participants were probably in their forties or fifties) still used OC. It is likely that these young women represent the group at the highest risk and we would like to be certain that they were fully informed of the risk when they chose to use OC. Even in an era when low dose OCs are being used, we suggest that primary care physicians who prescribe OC to young women screen them for conventional vascular risk factors (both arterial and venous), and explain the risks involved. For women with multiple risk factors and seeking birth control, clinicians should discuss other contraceptive devices and let the patients make an informed decision. If the patient is a smoker she should be informed of the specific risks and advised to quit smoking; and if she does not smoke regularly she should be informed of the risks and encouraged to quit completely. This is also true for women who use OC for regulation of their menstrual period or for the treatment of dysmenorrhea.

There are several limitations in our study. We did not record the number of cigarettes per day for smokers and therefore were not able to distinguish between light and heavy smokers. Also, there might have been a recall bias when asking the participants about their parental medical history. Moreover, this post-hoc analysis could not take into account the possible relationship between habits and clinical outcomes. The cross-sectional approach did not allow us to consider the possible impact of military service upon OC use. Also, since 9% of potential participants did not respond to the questionnaire, this may have introduced a slight bias as there might have been a higher rate of refusal among smokers. Lastly, the results of this study are not applicable to the general population, which also includes specific groups that do not customarily join the army and may significantly differ in terms of habitus, such as Israeli Arabs or ultra-Orthodox Jews.

In conclusion, we found a worrisome link between OC use and smoking. We suggest that an attempt be made to discourage smoking among young women who wish to start using OC. We also recommend that the physician take a careful medical history in order to recognize all risk factors for cardiovascular disease and provide for appropriate contraception counseling.

References

- Mann JJ, Vessey MP, Thorogood M, Doll SR. Myocardial infarction in young women with special reference to oral contraceptive practice. *Br Med J* 1975;2:241-5.
- Jick H, Dinan B, Herman R, Rothman KJ. Myocardial infarction and other vascular disease in young women: role of estrogens and other factors. *JAMA* 1978;240:2548-52.
- World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Venous thromboembolic disease and combined oral contraceptives: Results of an international multicenter case-control study. *Lancet* 1995;346:1575-82.
- World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Haemorrhagic stroke, overall stroke risk, and combined oral contraceptives: results of an international multicenter case-control study. *Lancet* 1996;348:505-10.
- World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Acute myocardial infarction and combined oral contraceptives: results of an international multicenter case-control study. *Lancet* 1997;349:1202-9.
- Mann JJ, Inman WHW, Thorogood M. Oral contraceptive use in older women and fatal myocardial infarction. *Br Med J* 1976;2:445-7.
- Fruzzetti F, Ricci C, Fioretti P. Haemostasis profile in smoking and nonsmoking women taking low-dose oral contraceptives. *Contraception* 1994;49:579-89.
- Kark JD, Laor A. Cigarette smoking and educational level among young Israelis upon release from military service in 1988 - a public health challenge. *Isr J Med Sci* 1992;28:33-7.
- Centraal Bureau voor Statistiek. Statistisch jaarboek 1998. The Hague: SDU/Uitgeverij, 1998:491.
- Sargent JD, Beach ML, Dalton MA, et al. Effect of seeing tobacco use in films on trying smoking among adolescents: cross sectional study. *Br Med J* 2001;323:1-6.
- Wechsler H, Rigotti NA, Gledhill-Hoyt J, Lee H. Increased levels of cigarette use among college students: a cause for national concern. *JAMA* 1998;280:1673-8.
- Davis RM. Current trends in cigarette advertising and marketing. *N Engl J Med* 1987;316(12):725-32.
- Sepe E, Glantz SA. Bar and tobacco promotions in the alternative press: targeting young adults. *Am J Public Health* 2002;92:75-8.
- Aveyard P, Cheng KK, Almond J, et al. Cluster randomized clinical trial of expert system based on the transtheoretical ("stages of change") model for smoking prevention and cessation in schools. *Br Med J* 1999;319:948-53.
- Coker AL, Richter DL, Valois RF, McKeown RE, Garrison CZ, Vincent ML. Correlates and consequences of early initiation of sexual intercourse. *J Sch Health* 1994;64:372-7.
- Hogan RM. Influences of culture on sexuality. *Nurs Clin North Am* 1982;17:365-76.
- Schenker JG. Women's reproductive health: monotheistic religious perspectives. *Int J Gynaecol Obstet* 2000;70:77-86.
- Farley TMM, Meirik O, Poulter NR. Combined oral contraceptives, smoking, and cardiovascular risk. *J Epidemiol Community Health* 1998;52:775.
- Rosenberg L, Palmer JR, Rao RS, Shapiro S. Low-dose oral contraception use and the risk of myocardial infarction. *Arch Intern Med* 2001;161:1065-70.
- Mileikowsky GN, Nadler JL, Huey F, Francis R, Roy S. Evidence that smoking alters prostacyclin formation and platelet aggregation in women who use oral contraceptives. *Obstet Gynecol* 1988;159:1537-52.
- Rangemark C, Benthin G, Granstrom EF, Persson L, Winell S, Wennmalm A. Tobacco use and urinary excretion of thromboxane A2 and prostacyclin metabolites in women stratified by age. *Circulation* 1992;86:1495-500.
- Notelovitz M, Levenson I, McKenzie L, Khan FY. The effect of low-dose oral contraceptives on lipids and lipoproteins in two at-risk populations: young female smokers and older premenopausal women. *Contraception* 1991;44(5):505-16.
- Seligsohn U, Lubetsky A. Genetic susceptibility to venous thrombosis. *N Engl J Med* 2001;344(16):1222-31.
- Vandenbroucke JP, Koster T, Briet E, Reitsma PH, Bertina RM, Rosendaal FR. Increased risk of venous thrombosis in oral-contraceptive users who are carriers of factor V Leiden mutation. *Lancet* 1994;344:1453-7.
- Bloemenkamp KWM, Rosendaal FR, Helmerhorst FM, Buller HR, Vandenbroucke JP. Enhancement by factor V Leiden mutation of risk of deep-vein thrombosis associated with oral contraceptives containing a third-generation progestagen. *Lancet* 1995;346:1593-6.

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