

Use of Combined Oral Contraceptives and Headaches

Diana Šimonienė¹, Virginija Vanagienė¹, Birutė Žilaitienė², Tadas Vanagas¹

¹Medical Academy, Lithuanian University of Health Sciences,

²Institute of Endocrinology, Medical Academy, Lithuanian University of Health Sciences, Lithuania

Key words: combined oral contraceptives; headaches; Migraine Disability Assessment Scale.

Summary. *Objective.* The study was designed to examine the certain patterns of combined oral contraceptive use in women of childbearing potential and evaluate the relationship between the use of combined oral contraceptives and headaches, bad habits, type of work, and concomitant diseases.

Material and Methods. In total, 194 randomly selected women aged 18 to 40 years who visited a gynecologist for preventive gynecological examination were surveyed. Respondents were categorized as combined oral contraceptive users ($n=116$; study group) and nonusers ($n=78$; control group). An anonymous questionnaire developed by the authors of this study and a standardized scale called the Migraine Disability Assessment Scale (MIDAS) were used for the survey.

Results. A multivariate logistic regression analysis demonstrated a significantly higher prevalence of combined oral contraceptive use in women older than 20 years (odds ratio, 6.0; 95% CI, 2.6–14), better educated women (odds ratio, 5.7; 95% CI, 2.1–15.2), and women reporting a steady sexual partner (odds ratio, 4.0; 95% CI, 1.5–11.0). Relationship between headaches and use of combined oral contraceptives as well as other factors were analyzed in a group of 178 respondents; the rest 16 respondents reported not having headaches at all. The prevalence of reported minimal-to-mild and moderate-to-severe impact of headaches on daily activities did not differ significantly between the study and control groups, women with and without bad habits, and white-collar and blue-collar groups ($P>0.05$). However, women with concomitant diseases significantly more often reported moderate-to-severe impact on daily activities due to headaches ($P<0.01$). Differences in impact of headaches on daily activities between women using combined oral contraceptives containing 20 or less μg of ethinylestradiol and 30 or more μg of ethinylestradiol did not differ significantly.

Conclusions. The prevalence of combined oral contraceptive use was higher in women older than 20 years, better educated women, and women reporting a steady sexual partner. The impact of headaches on daily activities did not differ significantly between the combined oral contraceptive users and nonusers.

Introduction

Combined oral contraceptives (COCs) were first approved more than four decades ago. Due to effectiveness and comfort of use, they made a breakthrough in the field of family planning (1). Currently, more than 8 million women use COCs worldwide (2). Though COCs are safe and highly effective in preventing unwanted pregnancy, headaches are among the most common adverse effects of COC use, which quite often lead to discontinuation of use by women (3–5). Many previous studies, which assessed the impact of COC use on the development of migraine headaches, were performed in the 1970s when COCs contained higher levels of estrogen (from 50 to 100 μg of ethinylestradiol). Clinical studies on COCs containing high levels of estrogens demonstrated a general tendency toward the development of more severe headaches in COC

users (5). Data on the impact of modern COCs containing low levels of estrogens (15–35 μg) on headaches are limited and rather controversial.

This study was designed to examine certain patterns of COC use in the group of surveyed women and the relationship between COC use and headaches as well as other factors (bad habits, type of work, and concomitant diseases) that can have an impact on the prevalence and manifestation of headaches.

Material and Methods

Randomly selected respondents of childbearing potential (aged 18 to 40) who visited Šančiai, Šilainiai, and Dainava Maternity Centers for preventive gynecological examination were asked to complete an anonymous questionnaire. The study took 23 months from April 2008 through Decem-

Correspondence to B. Žilaitienė, Institute of Endocrinology, Medical Academy, Lithuanian University of Health Sciences, Eivenių 2, 50028 Kaunas, Lithuania. E-mail: zilaitiene@gmail.com

Adresas susirašinėti: B. Žilaitienė, LSMU MA Endokrinologijos institutas, Eivenių 2, 50028 Kaunas
El. paštas: zilaitiene@gmail.com

ber 2009. Questionnaires were given to 198 women; completed questionnaires were returned by 194 respondents (response rate, 97.9%). Of these women, 116 used contraceptive pills (study group), and 78 were nonusers (control group). Exclusion criteria were as follows: 1) women younger than 18 and older than 40 years; 2) women suffering from migraine; 3) women who did not consent to take part in the study. The study was approved by Kaunas Regional Ethics Committee for Biomedical Research (approval No. BC-MF-32). All women gave a written consent to participate in the study.

A two-part questionnaire was used for the survey. It included a 16-item questionnaire developed by the authors and a standardized questionnaire called the Migraine Disability Assessment Scale (MIDAS). The questionnaire developed by the authors contained questions related to sociodemographic characteristics, COC use, bad habits, and diseases suffered by respondents that can have an impact on headaches.

The MIDAS questionnaire contains 5 questions describing the most common types of daily activities for a respondent aged 18 to 40. The patient reports the number of days in the last 3 months he/she missed from work or school (first question), did not do household work (third question), and missed leisure activities (fifth question) because of headaches. The other two questions assess a severe reduction in productivity. The total score is obtained by summing the scores for all five questions on the impact of headaches on daily activities: Grade I (score 0–5, minimal or no impact on activities); Grade II (score 6–10, mild impact on activities); Grade III (score 11–20, moderate impact on activities); and Grade IV (score 21+, severe impact on activities) (6–8). For analysis purposes, the impact of headaches on daily activities was grouped into two categories of minimal-to-mild (Grades I and II) and moderate-to-severe (Grades III and IV) impact.

For statistical data analysis purposes, the statistical software package SPSS 17.0 for Windows was used. A statistical relationship between qualitative variables was assessed using the Pearson χ^2 test or exact Kruskal-Wallis test (for three and more independent samples) and the Mann-Whitney U test (for two independent samples). Differences in data were considered statistically significant when $P < 0.05$. A multivariate backward stepwise logistic regression method was used to predict the use of combined oral contraceptives. Age, level of education, and marital status were included as independent factors into the logistic regression model.

Results

The mean age of respondents in this study was 23.6 years (SD, 5.2). The mean age of COC users

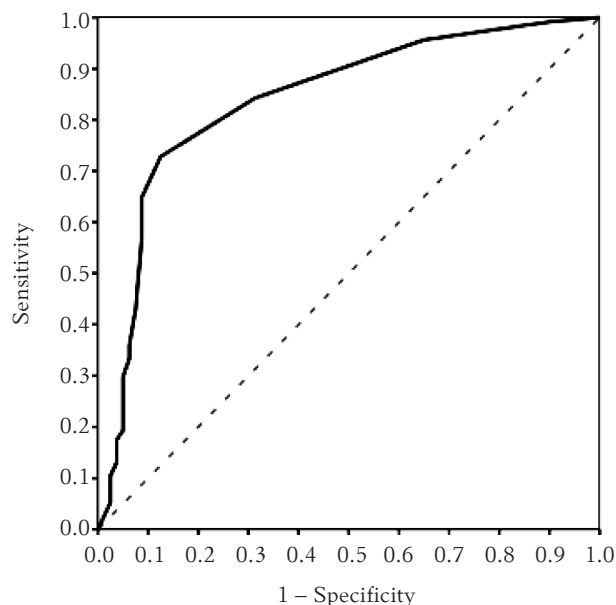


Fig. 1. The receiver operating characteristic curve of cutoff value for women's age according to combined oral contraceptive use (area under the curve, 83.9%)

and nonusers was 25.6 years (SD, 5.2) and 20.5 years (SD, 3.4), respectively. The receiver operating characteristic (ROC) curve analysis was performed to select an optimal cutoff point for assessing COC use. In our study, the cutoff point was 20 years of age (AUC 83.9%, $P < 0.001$) with a sensitivity of 0.9 and a specificity of 0.7 (Fig. 1).

For further analysis, women were assigned to two groups according to their age: women aged 20 and younger and women older than 20 years. It appeared that significantly more respondents in the study group (COC users) were older than 20 years of age (81.8%) as compared with the control group (i.e., nonusers), which contained significantly more women aged 20 and younger (76.7%) ($P < 0.001$).

The data analysis of the level of education and marital status also revealed significant differences between the COC user and nonuser groups. COC users significantly more often had better education and lived with a steady sexual partner ($P < 0.001$).

A binary multivariate backward stepwise logistic regression method was used to determine the odds ratios for individual characteristics of the COC users and select optimal combinations (Table 1).

Based on the available data, higher prevalence of COC use in women older than 20 years (odds ratio, 6.0; 95% CI, 2.6–14), better educated women (odds ratio, 5.7; 95% CI, 2.1–15.2), and women reporting a steady sexual partner (odds ratio, 4.0; 95% CI, 1.5–11.0) can be predicted. The classification table of the logistic regression analysis shows that 83.2% of predictions were correctly classified. A rather high coefficient of determination ($r^2 = 0.4$) shows that the model was selected correctly.

Table 1. Binary Multivariate Logistic Regression Analysis of the Study Group According to Age, Level of Education, and Marital Status of the Subjects

Characteristic Analyzed	OR (95% CI)
Age (in years)	
20 and <	1
>20	6.0 (2.6–14.0)*
Education	
secondary	1
higher	5.7 (2.1–15.2)*
Marital status	
no steady sexual partner	1
a steady sexual partner	4.0 (1.5–11.0)*
Constant	–1.615*

CI, confidence interval; OR, odds ratio. * $P < 0.001$.

The majority of women, i.e., 91.8% ($n = 178$), in both groups reported having experienced headaches at some point in their life; 8.2% ($n = 16$) of respondents reported that they had never had headaches. The distribution of answers to this question did not differ significantly between the study and control groups.

All 178 women who reported having experienced headaches at some point in their life also completed the MIDAS questionnaire.

Furthermore, 78.4% of COC users reported minimal-to-mild impact of headaches on their daily activities, while 21.6% of COC users assessed the impact of headaches on their daily activities as moderate-to-severe (Fig. 2). The nonusers less frequently reported moderate-to-severe impact of headaches on daily activities, but the difference was not significant (Table 2).

Other factors that can be related to headaches, such as the level of ethinylestradiol in the COC pills used, smoking, alcohol consumption, and concomitant diseases, were also assessed in the study and control groups.

Fifteen women (13.6%) using COC containing 30 μg of ethinylestradiol reported a minimal-to-mild impact of headaches on daily activities, while 5 women (4.5%) in this group rated the impact as moderate-to-severe. The impact of headaches on daily activities in the users of COCs containing 20 μg of ethinylestradiol was minimal-to-mild in 34 cases (30.9%) and moderate-to-severe in 8 cases (7.3%). The impact of headaches on daily activities of COC users who used formulations with 20 and 30 μg of ethinylestradiol did not differ significantly.

The impact of headaches on daily activities did not differ significantly between smokers and non-smokers as well as between moderate alcohol users and nonusers ($P > 0.05$ in both cases). The prevalence of moderate-to-major impact of headaches on daily activities was not significantly higher in COC users with bad habits ($P > 0.05$) as compared with nonusers with bad habits.

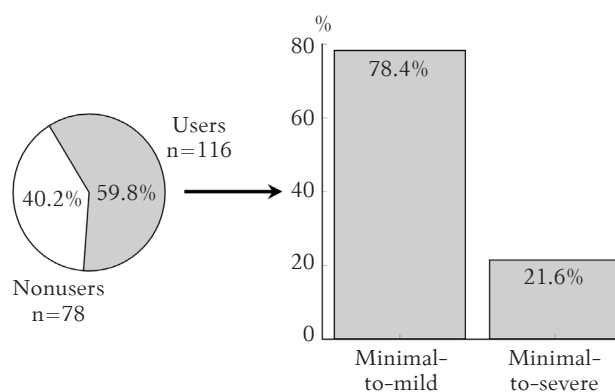


Fig. 2. Impact of headaches on daily activities of combined oral contraceptive (COC) users (the MIDAS questionnaire)

Table 2. Relationship Between the Impact of Headaches on Daily Activities and Combined Oral Contraceptive (COC) Use, Bad Habits, Type of Work, and Concomitant Diseases

Factor	Minimal-to-Mild Impact n=140	Moderate-to-Severe Impact n=38	P
COC use	78 (57)	23 (60.5)	>0.05
Smoking	32 (22.9)	12 (31.6)	>0.05
Alcohol consumption	96 (68.6)	23 (60.5)	>0.05
White-collar workers	113 (84.3)	32 (84.2)	>0.05
Concomitant diseases	14 (10)	10 (26.3)	<0.01

Values are number (percentage).

Women with concomitant diseases (renal diseases, hypertension, diabetes mellitus, etc.) significantly more often reported a moderate-to-severe impact on daily activities due to headaches as compared with women having no concomitant diseases ($P < 0.05$). A univariate regression method used for data evaluation allowed for prediction that women with concomitant diseases had a 2.7-fold (95% CI, 1.1–6.6) higher risk of headaches with a moderate-to-severe impact on their daily activities as compared with healthy women.

Discussion

Irrespective of efforts by family planning centers and education of society, effective contraceptives still gain limited popularity in certain countries, especially in Eastern Europe and Baltic countries (9). Lithuania is also out of step with many other developed European countries according to effective modern contraceptive use (10–12). Our study revealed that COCs were more often used by slightly older, better educated women reporting a steady sexual partner. Consequently, organizations engaged in educational work and health care providers (family doctors and obstetricians-gynecologists) should take into account that young, unmarried, and less educated women rarely use effective contraception, which results in very high risks of unwanted pregnancy.

One of the common reasons for reluctance to use hormonal contraceptives or discontinuation immediately after starting the use is the fear of side effects or actual side effects. Headaches are a common complaint in women of different ages undoubtedly related to hormonal swings in the woman's body (13). Even in our small-scale study, 21.4% of all surveyed women reported a moderate-to-severe impact of headaches on daily activities. Limited data are available in the world's literature on the relationship between COC use and prevalence of headaches. To the knowledge of the authors, no such studies have been performed in Lithuania at all.

The MIDAS questionnaire was chosen for this study. Pain is a rather subjective feeling, and what is of utmost importance is the level to which daily activities are disturbed by pain. A variety of questionnaires are used for evaluation of headaches, such as the Head-HUNT Questionnaire, the Headache Impact Questionnaire (HimQ), etc. All these questionnaires are precise, but rather long, and it is difficult to interpret the results obtained. In 1997, American neurologists developed the MIDAS questionnaire to assess the impact of migraine and headaches on the quality of life in general (8). This short self-administered questionnaire was translated into Lithuanian and validated in Lithuania (14). The Head-HUNT questionnaire is often used in the studies to assess the impact of COC use on headaches. Only one study was found in this field to use the MIDAS questionnaire and assess the impact of headaches on daily activities of COC users (15).

The data obtained in our study show that the impact of headaches on daily activities does not differ between COC users and nonusers. Most of the studies performed by other authors also did not confirm the relationship between COC use and headaches. In 2005, van Vliet et al. conducted a study in women suffering from cluster headache attacks in order to assess the impact of hormonal products on such attacks (16). In this study, 224 women were surveyed. A screening questionnaire based on the International Headache Society (IHS) criteria for cluster headache was used. Of the 169 women who had ever used COCs and suffered cluster headache attacks, 20 (12%) reported an increase in headaches after starting COC use. Seven women (4%) reported an improvement. According to the authors, the study revealed an insignificant impact of oral contraceptive use on cluster headache attacks in general population. Loder et al. examined if the prevalence of headaches (not migraine) was higher in those taking monophasic contraceptive pills as compared with the placebo group (17). They found no significant difference in the prevalence of headaches between women using placebo and monophasic contraceptives; however, women with a history of migraine or other head-related problems may be at

the increased risks of developing more severe headaches in the background of COCs. In 2007, Westhoff et al. performed a large-scale study ($n=1716$). The purpose of this study was to find out the impact of side effects of contraceptives, especially headaches, on discontinuation of COC use in a group of women younger than 25 years (18). Nearly 60% of subjects discontinued COC use by 6 months; however, most subjects reported no increase in headaches. Women complaining about the increased headache were more likely to early discontinue COC use. Nonetheless, the discontinuation of COC use is not related to the side effects of contraceptive pills, especially headaches. In the same year, American scientists conducted a research to assess the severity of headaches in COC users: a standard 28-day combined oral contraceptive cycle consisting of 21 hormone-containing pills (estrogen + progestin) and 7 placebo pills was converted to a 168-day (24 continuous weeks) extended placebo-free COC regimen (15). The study assessed headaches on a severity scale of 0 to 10 (daily) along with the results according to the MIDAS questionnaire (weekly). During the first 24 days, the results did not differ in both study groups ($P>0.05$). A significant difference was detected on days 25 through 28 ($P<0.0001$), which demonstrated that the elimination of a 7-day placebo period from the standard COC regimen led to a decrease in headache severity based on the daily assessments according to the pain scale. Comparison of the MIDAS score in women using the 21/7 COC regimen and the extended placebo-free regimen revealed that women using placebo-free COC regimen had a decrease in the impact of headaches on daily activities ($P<0.05$) and the duration of headache ($P=0.003$). Thus, as compared with a standard COC (21/7-day) regimen, a 168-day extended placebo-free COC regimen led to a decrease in headache severity along with an improvement in the productivity related to daily activities. Finally, the results of recent studies performed in 2009 demonstrated no relationship between headache and the composition of COCs (both in the type and amount of hormones), but headaches were more manifested in COC users suffering from menstruation-related migraine (19).

Therefore, it should be noted that a number of studies (different in methodology and samples used) performed to date did not prove that healthy COC users more often suffered from headaches or that headaches suffered by healthy COC users were more manifested as compared with nonusers; however, women suffering from migraine developed more severe headaches. As it was mentioned above, our study, in fact, confirmed no relationship between COC use and headaches. The study also assessed the impact of headaches on daily activities (the MIDAS questionnaire was used), which makes

our study different from others. A sample studied in our study was not very large but uniform in terms of selected population, which is an undoubted advantage of the study. All subjects were white Lithuanian women, and this eliminated potential racial or ethnic predispositions to headaches. According to literature, headaches are more common in white women as compared with general population (20). Moreover, contrary to other studies (15, 16, 19, 21), other factors that can have an impact on the development of headaches and their impact on daily activities were also taken into account.

Conclusions

In summary of the study results, an average com-

bined oral contraceptive user in the study group can be described. It is a woman older than 20 years, married or living with a steady sexual partner, and predominantly with higher education. An original methodology (the MIDAS questionnaire) was used to study the relationship between headaches and combined oral contraceptive use. No relationship between the impact of headaches on daily activities and combined oral contraceptive use was established. The final conclusion on the impact of combined oral contraceptives on headaches calls for a larger-scale and more detailed study.

Statement of Conflict of Interest

The authors state no conflict of interest.

Sudėtinių kontraceptinių tablečių vartojimas ir galvos skausmai

Diana Šimonienė¹, Virginija Vanagienė¹, Birutė Žilaitienė², Tadas Vanagas¹

¹Lietuvos sveikatos mokslų universiteto Medicinos akademija,

²Lietuvos sveikatos mokslų universiteto Medicinos akademijos Endokrinologijos institutas

Raktažodžiai: sudėtinės kontraceptinės tabletės, galvos skausmai, galvos skausmų sukeltos negalios vertinimo skalė

Santrauka. *Tyrimo tikslas.* Ištirti kai kuriuos sudėtinių kontraceptinių tablečių vartojamumo savitumus vaisingo amžiaus moterų grupėje ir įvertinti tablečių vartojimo sąsajas su galvos skausmais, žalingais įpročiais, darbo pobūdžiu, gretutinėmis ligomis.

Medžiaga ir metodai. Apklaustos atsitiktinės atrankos būdu atrinktos 194 18–40 metų moterys, atvykusios profilaktinės ginekologinės patikros. 116 tiriamosios grupės respondentės vartojo sudėtines kontraceptines tabletes, 78 kontrolinės grupės respondentės nevartojo. Naudotas autorių sudarytas anoniminis klausimynas ir standartizuotas galvos skausmų įtakos kasdieniui veiklai (MIDAS) klausimynas.

Rezultatai. Atlikus daugiaveiksnės logistinės regresijos analizę, nustatyta, jog reikšmingai dažniau sudėtinės kontraceptines tabletes vartoja vyresnės nei 20 metų moterys, šansų santykis – 6,0 (95 proc. PI 2,6–14), turinčios aukštąjį išsilavinimą, šansų santykis – 5,7 (95 proc. PI 2,1–15,2) ir turinčios pastovų partnerį, šansų santykis – 4,0 (95 proc. PI 1,5–11,0). Galvos skausmų sąsajos su sudėtinių kontraceptinių tablečių vartojimu ir kitais veiksniais analizuotos 178 respondentų grupėje, nes likusios 16 nurodė, jog niekada nėra jautusios galvos skausmų. Teiginių dažnis, jog galvos skausmai turi labai mažą arba mažą įtaką ir vidutinę arba didelę įtaką kasdieniui veiklai, reikšmingai nesiskyrė tiriamojoje ir kontrolinėje grupėse, turinčių ir neturinčių žalingų įpročių grupėse, dirbančių protinį ir dirbančių fizinį darbą grupėse ($p > 0,05$). Tačiau sergančioms gretutinėmis ligomis reikšmingai dažniau galvos skausmai turėjo vidutinę arba didelę įtaką kasdieniui veiklai ($p < 0,01$). Galvos skausmų įtakos kasdieniui veiklai skirtumai vartojančioms sudėtines kontraceptines tabletes 20 µg ir mažiau bei 30 µg ir daugiau etinilestradiolio respondentėms buvo nereikšmingi.

Išvados. Sudėtinės kontraceptines tabletes dažniau vartoja vyresnės nei 20 metų amžiaus moterys, turinčios aukštąjį išsilavinimą ir pastovų lytinį partnerį. Galvos skausmų įtaka kasdieniui veiklai reikšmingai nesiskyrė vartojančių ir nevartojančių sudėtines kontraceptines tabletes respondentų grupėse.

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Received 23 March 2010, accepted 16 May 2011

Straipsnis gautas 2010 03 23, priimtas 2011 05 16