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Chronic frequent headache in the general population

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Chapter 5

Oral contraceptive use and headache frequency - a cross-sectional study -

Submitted

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Abstract

Oral contraceptive (OC) use is associated with an increase of headache prevalence. It is not known whether use of OCs can increase headache frequency. We studied the association of oestrogen containing oral contraceptive (OC) use with chronic frequent headache in the general population. A general health survey was held in sixteen general practices in the Netherlands amongst all registered patients, aged 25-55 years, by sending a questionnaire. Respondents were allocated into groups according to headache frequency: Chronic Frequent Headache (CFH: > 14 days/month), Very Frequent Headache (8-14 days/month), Infrequent Headache (1-4 days/month) and No Headache (< 1 day/month), and received a second questionnaire. Several factors possibly associated with chronic frequent headache were studied, including oral contraceptive use. In the headache groups 136 (29%) of 465 women used OCs, compared to 71 (21%) of 340 in the No Headache group, adjusted OR 1.4 (95% CI 1.0 to 2.1). In the CFH group 8% (95% CI -18 to 0) fewer women used OCs than the Infrequent Headache group. Odds ratio for the association between OC use and CFH was 0.7 (95% CI 0.4 to 1.1), and after adjusting for age and educational level 0.6 (95% CI 0.4 to 1.1). OC use in the VFH group was similar to the Infrequent Headache group, 32% vs. 33% respectively, a difference of 1% (95% CI -1 to 1). We conclude that there is no association between oestrogen containing OC use and CFH.

Introduction

Headache is more prevalent in women and menstruation is often reported to be a precipitating factor, suggesting that female hormones play a role in the aetiology of headache.¹ Many headache patients wonder whether they should start or discontinue OC use to improve headache. A recent review of studies on the effect of OC use on headache shows inconsistent results, some women improve, and others worsen.² In a large population-based study in Norway an increased prevalence of headache among users of oestrogen containing OCs was found.³ The association was found for both migraine (OR 1.4, 95% CI 1.2 to 1.7) and for non-migraine headache (OR 1.2, 95% CI 1.0 to 1.4). There was no dose-response relationship between oestrogen content and headache prevalence, nor was there an association with OCs containing progestagen only.

One in 25 people suffers from chronic frequent headache (CFH), defined as headaches on more than 14 days per month, for at least 3 months.⁴⁻⁶ Usually their headaches start as an episodic migraine or tension-type headache, which gradually increases in frequency until headaches occur almost daily. The cause of this chronification process is not known, but several risk factors have been associated with CFH.⁶⁻⁹ It is not known whether use of OCs can increase headache frequency.

In our population-based study on the prevalence and associated factors of CFH,⁶ participants recorded all medication use, including oral contraceptives. Here we report whether oestrogen containing OC use was associated with CFH in the Netherlands.

Methods

The study design and methodology have been described in detail previously.⁶ Briefly, we conducted a general health survey (Q1) in the general population (aged 25-55) in the Netherlands, which contained a question on headache frequency in the past three months. In total 21,440 subjects received Q1, and 16,232 (76%) completed Q1. Respondents were allocated into groups according to headache frequency: Chronic Frequent Headache (CFH: headache on > 14 days/month), Very Frequent Headache (VFH: headache on 8-14 days/month), Frequent Headache (FH: 5-7 days/month), Infrequent Headache (IH: 1-4 days/month) and No Headache (NH: headache on < 1 day/month). All CFH and VFH subjects

and a random sample of the subjects with Infrequent Headache and No Headache received a second, more detailed, questionnaire (Q2) containing questions on headache characteristics and medication use. To identify factors associated with chronification of headache, we compared subjects with CFH to subjects with Infrequent Headache (1-4 days/month). To discern chronification factors from factors associated with headache in general we also compared the headache groups to the No Headache group (< 1 day/month). The Very Frequent Headache group was added because these subjects have a high headache frequency and may be in the process of developing daily headache.¹⁰ The Frequent Headache group was not further analyzed.

Q2 was sent to 654 CFH subjects and completed by 273 (42%) subjects. The non-respondent analysis showed that non-responders were slightly younger and were more often male than the respondents. In the VFH, IH and NH groups the response percentages were similar; 42%, 32% and 43% respectively. Re-assessment of headache frequency in Q2 (time between questionnaires was five months) showed that headache frequency had changed in many subjects. We first analyzed all subjects who completed Q2, and then repeated analysis in a subset of subjects in whom the reported headache frequency had not changed between the two surveys (i.e. the stable frequency group).

First we compared all headache groups to no headache. Secondly, we compared CFH to infrequent headache to analyze the association between OC use and chronification of headache. And finally, we compared the VFH to the infrequent group because this group is at greatest risk of becoming CFH. Differences between groups are presented with 95% confidence intervals (95% CI). Odds ratios are calculated. We used logistic regression to adjust for confounders (age and educational level).

The Medical Ethics Committee of Leiden University Medical Centre approved this study.

Results

There were 465 women in the headache groups and 340 in the No Headache group. Differences in age and educational level per group are presented in table 1. More CFH subjects had a low level of education compared to the Infrequent Headache group (difference 17%, 95%CI 8 to 26).

Table 1 Age and educational level

	CFH	VFH	IH	NH
	N = 176	N = 146	N = 143	N = 340
Mean age, y (SD)	42 (8)	42 (9)	41 (8)	44 (9)
Educational level	n = 174	n = 145	n = 143	n = 340
Low, n (%)	53 (31)	31 (21)	19 (13)	48 (14)
Medium, n (%)	73 (42)	69 (47)	53 (37)	125 (37)
High, n (%)	48 (28)	45 (31)	71 (50)	167 (49)

CFH = chronic frequent headache (>14 d/m), VFH = very frequent headache (8-14 d/m), IH = infrequent headache (1-4 d/m), NH = no headache (< 1 d/m).

Overall, 136 (29%) women in the headache groups use oestrogen containing OCs, compared to 71 (21%) in the No Headache group, a difference of 8% (95% CI 2 to 14). Crude odds ratio for the association between OC use and headache was 1.6 (95% CI 1.1 to 2.2), and after adjustment for age and educational level 1.4 (95% CI 1.0 to 2.1).

OC use per headache group is presented in table 2. Results in the subgroups with a stable headache frequency were similar to the results of the whole group, so there was no need to study the stable frequency group separately.

In the CFH group 24% used oestrogen containing OCs, which is 8% (95% CI -18 to 0) less than the Infrequent Headache group, and 4% (95% CI -4 to 11) more than the No Headache group. Crude odds ratio for the association between OC use and CFH was 0.7 (95% CI 0.4 to 1.1), and after adjusting for age and educational level 0.6 (95% CI 0.4 to 1.1). Oestrogen containing OC use in the VFH group was similar to the Infrequent Headache group, 32% vs. 33% respectively, a difference of 1% (95% CI -1 to 1).

Table 2 Oestrogen containing oral contraceptive use per group

	CFH	VFH	IH	NH
All subjects	N = 176	N = 146	N = 143	N = 340
OC use, n (%)	43 (24)	46 (32)	47 (33)	71 (21)
Stable frequency	n = 125	n = 89	n = 97	n = 215
OC use, n (%)	30 (24)	28 (32)	29 (31)	46 (21)

CFH = chronic frequent headache (>14 d/m), VFH = very frequent headache (8-14 d/m), IH = infrequent headache (1-4 d/m), NH = no headache (< 1 d/m).

Discussion

We found no association between oestrogen containing OC use and CFH in the general population in the Netherlands. The percentage of women using OCs was even lower in the CFH group than in the Infrequent Headache group. We could argue that OC use protects against chronification of headache, however it is more likely that women with CFH had discontinued OC use because of their frequent headaches. As in the Norway study³ we found that headache is associated with OC use, but we did not find an association with increasing headache frequency and OC use. Even in the Very Frequent Headache group, which is a group at high risk of developing CFH,¹⁰ OC use was comparable to the Infrequent Headache group.

This is a cross-sectional study based on self-reported use of medication. We think our results are a reliable estimate of OC use in women aged 25-55 years, because the percentage is in accordance with earlier reports from the Netherlands.¹¹ Although the response to Q2 was low, it is unlikely that this may have caused a bias in the associations, because we have no reason to believe that OC use is dependent on response status. A limitation of our study is that we have no information on duration of OC use, or about previous use of OCs, and the effect on headache. In a cross-sectional study, questions on headache patterns and OC use in the past are unreliable due to recall bias. A cohort study would be needed to address important questions like the incidence of CFH in women starting to use OCs and the effect of stopping OCs on headache frequency.

To our knowledge, there are no studies examining the effect of OCs in patients with CFH. The increased prevalence of headache in OC users may reflect withdrawal headache as a side effect during the pill-free week. Sulak et al. demonstrated that compared to the traditional 21/7 OC/placebo regimen, an extended 168-day placebo-free OC regimen actually led to a reduction in daily headaches.¹² There is as yet no evidence that discontinuing or switching OCs will improve headache frequency in patients with CFH.

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