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Oral contraceptive use and risk of vulvodynia: a population-based longitudinal study

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Abstract

Objective—To assess whether the risk of vulvodynia is associated with previous use of oral contraceptives (OCs).

Design—Longitudinal population-based study.

Setting—Four counties in south-east Michigan, USA.

Population—A population-based sample of women, aged 18 years and older, enrolled using random-digit dialling.

Methods—Enrolled women completed surveys that included information on demographic characteristics, health status, current symptoms, past and present OC use, and a validated screen for vulvodynia. The temporal relationship between OC use and subsequent symptoms of vulvodynia was assessed using Cox regression, with OC exposure modelled as a time-varying covariate.

Main outcome measure—Vulvodynia, as determined by validated screen.

Results—Women aged <50 years who provided data on OC use, completed all questions required for the vulvodynia screen, and had first sexual intercourse prior to the onset of vulvodynia symptoms were eligible ($n = 906$). Of these, 71.2% ($n = 645$) had used OCs. The vulvodynia screen was positive in 8.2% ($n = 74$) for current vulvodynia and in 20.8% ($n = 188$) for past vulvodynia. Although crude cross-tabulation suggested that women with current or past vulvodynia were less likely to have been exposed to OCs prior to the onset of pain (60.7%), compared with those without this disorder (69.3%), the Cox regression analysis identified no

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Disclosure of interests

The authors report no conflict of interest.

Contribution to authorship

All authors have contributed to the study and approved the final version of this article: BDR, SDH, AS, research design; BDR, SDH, BWG, AS, MEH, data analysis; BDR, SDH, LJJ, MEH, HKH, BWG, AS, writing/editing of the article; BDR, SDH, LJJ, MEH, HKH, BWG, AS, conducting research; BDR and AS have access to all study data.

Details of ethics approval

This study was approved by the University of Michigan Medical Institutional Review Board on 17 January 2008 (HUM00017098).

association between vulvodynia and previous OC use (HR 1.08, 95% CI 0.81–1.43, $P = 0.60$). This null finding persisted after controlling for ethnicity, marital status, educational level, duration of use, and age at first OC use.

Conclusion—For women aged <50 years of age, OC use did not increase the risk of subsequent vulvodynia.

Keywords

chronic pain; oral contraceptives; population-based; risk factors; vulvodynia

Introduction

Although vulvodynia is now known to be common,^{1–4} and occurs at any age,^{1,5} little is known about risk factors for this disorder. Oral contraceptives are commonly used by women for reliable contraception as well as for urogenital and menstrual symptom management. Yet, controversy continues regarding the possible role of oral contraceptive (OC) use in the risk for vulvodynia, with some studies suggesting an increased risk in general,⁶ or related to age of first use,^{6–8} duration,⁹ or strength of hormonal composition,⁶ whereas other studies report no association between OC use and vulvodynia.^{10–12} These studies impact provider recommendations to patients regarding the benefits versus risks of starting or continuing the use of oral contraceptives, and hence sound data on this topic is crucial. However, past studies have been limited by patient selection from clinical populations, and by the lack of adequate data to establish whether OC use actually preceded the onset of pain.^{10–12}

We assessed the relationship between current or past vulvodynia (based on validated screening criteria),¹³ and the history and timing of OC use among a population-based sample of women participants in the Woman to Woman Health Study in south-east Michigan. These data allowed the assessment of vulvodynia risk associated with prior OC use using a survival analysis that included OC use as a time-varying covariate, incorporating information on the age of first intercourse, age of first OC exposure, and duration of OC exposure.

Methods

This study was approved by the University of Michigan Medical Institutional Review Board on 17 January 2008 (HUM00017098). Between September 2008 and November 2009, a population-based sample of 2542 women, aged 18 years and over, were recruited from a four-county area in south-east Michigan, and were enrolled in the Woman to Woman Health Study. Details of the sample were reported previously.¹ In brief, recruitment was conducted using random-digit dialling. A woman aged 18 years or older was randomly selected from each household contacted, and was invited to participate in this study on women's health. Participants completed a brief telephone interview, followed by an online or written 26-page survey, which assessed demographic characteristics, contraceptive and medical history, and current and past gynaecological symptoms. Dates of initial vulvar pain, of onset and final use of OCs, of reason for initial use, and for discontinuation of OCs, and estimated duration of use were assessed. Consent was implied by survey completion after reading the cover letter detailing human subjects issues. Previously validated survey-based criteria for predicting vulvodynia case status were used to identify current cases, past cases, and non-cases (control women).¹³ This validation study had indicated that predicting the case status based on symptoms and duration has very good consistency, compared with that based on a clinical examination. Based on these criteria, cases were defined as those with pain at the opening to the vagina (either provokable or non-provokable/spontaneous) that had been

present for 3 months or longer. Past cases met the same criteria, but reported that the pain had resolved. Non-cases were women denying a history of vulvar pain that had lasted 3 months or longer.

For this report, participants included only those aged <50 years, a criterion adopted to minimise both recall bias and the likelihood of exposure to postmenopausal hormone therapy. We further limited analysis to those who provided all data needed to assess vulvodynia case status, and who provided information on OC use or non-use. We excluded women who reported vulvodynia prior to the age of 15 years, on the premise that they were reporting symptoms reflective of childhood onset of vulvodynia, and prior to the time they might be expected to take OCs. We also excluded women whose age at first intercourse and symptoms of vulvodynia occurred in the same year, unless they reported having had no pain at first intercourse, as we could not otherwise determine whether or not the OC use preceded the vulvodynia. Women who had never had intercourse were excluded because intercourse is the activity that will most consistently demonstrate the sensitivity to women (and hence those not having intercourse may be unaware of vulvar sensitivity).

Frequency distributions of each variable were calculated. Non-parametric estimates of the distributions of OC starting age and of vulvodynia onset were obtained by the Kaplan–Meier method. Cross-tabulation between prior OC use and subsequent vulvodynia status, and chi-square statistics, were calculated. A crude assessment of the relationship between OC use and subsequent vulvodynia is misleading, as it does not adequately control for the number of years a woman was at risk for starting OCs and for presenting with vulvodynia (duration from first intercourse to onset of vulvodynia or to current age). We used a Cox regression model with age of onset of vulvodynia as the outcome, and OC use modelled as a time-varying covariate, allowing for a more accurate and comprehensive assessment of risk. The participant was considered to be taking OCs from the age at first use to the age of last reported use. This analysis properly accounts for OC use by allowing a subject to be in the exposed risk set for developing vulvodynia only during the period that she was an OC user. The age range ran from the age of first intercourse to either the age at the onset of vulvodynia (event) or the age at which the last survey was completed without vulvodynia occurring (censoring). We also assessed the model with 1 year added to the age of first intercourse to minimise the possibility of incorrectly detecting an association, because of the relationship between starting intercourse and starting OCs. To allow for the possibility of OC use affecting the risk of vulvodynia only after a sustained duration of use, alternative definitions of the OC time-dependent covariate set the variable as positive only after 1, 2, 5, or 10 years had passed following first OC use. As it was unknown whether past OC exposure might impact future risk, we also tested a time-dependent covariate that started OC exposure at the reported start year, but continued OC exposure until the age at interview, regardless of stopping OC use.

We tested for a changing risk of OCs with increasing age by including an age*OC interaction in the model. The assessment of risk at various ages of first OC use was further demonstrated using analyses of subsets of women who started OCs at various ages, compared with those not using OCs. Covariates added to all models included ethnicity, education, and marital status. Statistical analyses were carried out in PASW STATISTICS 18.0 (SPSS, Chicago, IL, USA) and SAS 9.3 (SAS/STAT® 9.3 User's Guide; SAS Institute, Cary, NC, USA).

Results

Of the 1083 women aged 18–49 years in the Woman to Woman Health Study who completed the initial survey, 1076 (99.4%) completed the question on their use of OCs. Of

these, 1032 (95.9%) completed the questions needed to predict the presence of vulvodynia. We excluded 17 women who reported symptoms of vulvodynia prior to the age of 15 years, 44 women who reported identical ages at first intercourse and the onset of vulvodynia symptoms, and who had not had pain-free intercourse preceding the onset of vulvodynia symptoms, 18 women who reported vulvodynia symptoms that started prior to first intercourse, 37 women who had not had intercourse, and ten women who did not give an age of first intercourse. Thus, a total of 906 of the 1083 women (83.7%) were eligible for this analysis.

The 906 women included in the analysis had a mean age of 36.9 ± 8.6 years: 71.8% were white, 18.5% were black, and 3.9% were Hispanic; 55.0% had completed college; 69.7% were married or cohabiting; 56.9% had a household income $\leq \$60\,000$; and 44.9% found it difficult to pay for basics (food, shelter, heat, and health care). Compared with the 177 women (of the original 1083) who were ineligible for this analysis, no differences were found in ethnicity or educational level; however, compared with those who were ineligible, eligible women were more likely to be older (mean = 36.9 versus 32.4 years old, $P < 0.001$), have a household income of $\leq \$60\,000$ (56.9 versus 43.4%, $P = 0.002$), be married (69.7 versus 41.0%, $P < 0.001$), and have ever taken OCs (71.2 versus 50.6%, $P < 0.001$). These differences are in part an artifact of the inclusion criterion that required the women to have had intercourse at some time: a characteristic associated in our data with older age, being married, being a college graduate, being white, and having ever taken OCs. When only those women who had ever had intercourse were compared with those in the included and excluded groups, the only statistically significant differences found were the greater likelihood among those included of being married (69.7 versus 58.9%, $P = 0.005$), and of having a household income of $\leq \$60\,000$ (56.9 versus 43.8%, $P = 0.01$).

Vulvodynia screening of the 906 women identified 74 women positive for vulvodynia (with a prevalence of 8.2%, 95% CI 6.4–10.0%), and an additional 188 women screened positive for past vulvodynia (20.8%, 95% CI 18.2–23.4%). The age of the reported onset of vulvar pain ranged from 15 (lower limit eligible for this analysis) to 48 years of age (median 25.0 years, 95% CI 23.4–26.6; Figure 1a, Kaplan–Meier estimate). The estimated duration of pain from onset to resolution ranged from less than a year to 29 years (Figure 1b). Only one of the 74 (1.4%) women screening positive for vulvodynia, and five of the 188 (2.7%) with past vulvodynia, reported having been given a diagnosis of vulvodynia previously, decreasing the likelihood of bias related to previously suggested risk factors. Women with current or past vulvodynia, when compared with controls, were similar in age (36.8 ± 8.2 versus 37.0 ± 8.8 years, $P = 0.71$), high school graduation rates (97.3 versus 97.2%, $P = 0.43$), ethnicity (75.2 versus 70.5% white, $P = 0.15$), being married or cohabiting (70.8 versus 69.3%, $P = 0.66$), and ability to pay for basics (42.0 versus 45.7%, $P = 0.44$).

Oral contraceptive use at some point in their lifetime was reported by 71.2% ($n = 645$) of the participants, with first use of OCs occurring at 12–39 years of age (Figure 2a), with a median age of first use of 19.0 years. Current OC use was reported by 15.0% ($n = 136$). The duration of use (estimated from ages of first and last use, and censored at the time of the survey for current users) ranged from less than a year to 35 years (Figure 2b), with a median duration of use of 10.0 years. The number of brands used and the reasons for starting and stopping OCs are shown in Table 1. Women who met criteria for case and/or past case status did not differ from the non-cases in whether they were currently taking OCs, age at first use of OCs, number of brands used, duration of use, or years since last use of OCs. Reasons for initiating and discontinuing OC use were similar also. Comparable results were obtained when assessing the characteristics of those with current vulvodynia only, compared with non-cases (data not shown).

The timing of OC use compared with the onset of vulvodynia was also assessed (Figure 3). Women considered 'exposed' to OCs ($n = 605$, 66.8%) were those who started using OCs who had never previously developed symptoms of vulvodynia. Those who had either not taken OCs to date ($n = 261$, 28.8%) or started taking OCs at or after the age of onset of vulvar pain, consistent with vulvodynia ($n = 40$, 4.4%), were considered unexposed.

The demographic characteristics of women who were categorised as exposed and unexposed to OCs were assessed. Compared with those not exposed, women who had been exposed to OCs were more likely to be older (37.9 ± 8.2 versus 35.0 ± 9.1 years, $P < 0.0001$), be white [78.6% (473) versus 58.1% (175), $P < 0.0001$], have started intercourse at a younger age (17.4 ± 3.0 versus 18.0 ± 3.9 years, $P = 0.02$), be married [74.5% (448) versus 60.3% (179), $P < 0.0001$], and have a higher income [65.0% (346) versus 40.5% (106) with a household income of \$60 000, $P < 0.0001$].

Among those with current or past vulvodynia ($n = 262$), only 60.7% ($n = 159$) reported the use of OCs anytime prior to the onset of the symptoms, compared with 69.3% ($n = 446$) of those who screened negative for current or past vulvodynia ($P = 0.013$, RR 0.69, 95% CI 0.51–0.92), suggesting a protective role of OC use. As described in the Methods, this crude analysis gives misleading results because of the variable number of years each participant was at risk for taking OCs and for presenting with symptoms of vulvodynia, and the variable number of years she took OCs. Hence, Cox regression on the age of onset of vulvodynia, with time-dependent OC covariates, was used to assess the hazard ratio for OC use. The hazard ratio for time-dependent OC use (versus non-use) was 1.08 (95% CI 0.81–1.43), with a non-significant $P = 0.60$ (controlled for ethnicity, marital status, and educational attainment; Table 2). Hence, the rate of vulvodynia onset did not differ significantly among those who had used OCs compared with those who had not, when accounting for the specific years each woman took OCs. We further assessed whether having *ever* used OCs altered the risk of developing vulvodynia, i.e. by modelling risk if OCs were started, but not considering the time of discontinuation. No increased risk for vulvodynia if the woman had *ever* taken OCs was noted (Table 2). When the start time of OC use was shifted by 1, 2, 5, or 10 years (testing whether a duration of 1, 2, 5, or 10 years might impact risk, when undifferentiated current use did not), no significant OC effect was found (Table 2). Furthermore, testing for a change in OC risk for subsequent vulvodynia by age at first use did not reveal a significant effect (Table 2). To further show this lack of an OC effect across four age (of first use) groups, a separate model for each age group was run (OCs started at 16, 17–18, 19–20, and >20 years of age), each selecting participants who started OCs in the given age interval, compared with those never exposed to OCs. This analysis indicated no association between age at first use compared with those not exposed at all ($P = 0.17$ –0.70 in the four analyses).

Discussion

Main findings

In this population-based sample of women, we found no increased risk of vulvodynia following OC use. The evaluation of subgroups that might demonstrate an increased risk, including those with a younger age at first OC use, or those with a longer duration of OC use, indicated that the risk of developing vulvodynia was not increased by OC use in any of these specific subgroups, although we did observe a non-significant trend towards a decreased risk with longer durations of OC use. These data provide evidence against the clinical belief that OC use is associated with risk of vulvodynia.

The evidence for and against an association between OC use and vulvodynia has been controversial. Some studies were limited by study-design issues, including failure to assess

whether OC use preceded the vulvar pain, with most studies targeting a clinic-based population that may not be representative of the community at large. Two studies targeting women seen in vulvar specialty clinics,^{6,7} and one using a combination of a population-based cohort as well as a clinic-based cohort,⁸ found younger age at OC onset was associated with increased risk. It is possible that these results may reflect a longer time between initial exposure and years observed (to their present age) in which they may develop vulvodynia. We did not find an increased risk among those starting OCs at a younger age. Other published reports suggesting a relationship between duration of OC use and vulvodynia in young women have had small samples and minimal information about OC use, thereby limiting the quality of their evidence.^{9,14} Other studies that have similarly shown no association or a decreased risk of vulvodynia with OC use did not assess the timing of OC use compared with the onset of vulvar pain, thereby limiting their findings,^{10–12,15,16} or had a small sample size.²

In a case–control study of 138 women with secondary vestibulodynia and 309 controls (with a mean age of 22 years),⁶ Bouchard and colleagues additionally reported an increased risk of vulvodynia among those using ‘high-risk’ oral contraceptives, which they defined as high progestational, high androgenic, and low estrogenic compounds; however, because of the low numbers of women who had taken only high-risk OCs (<2% of participants), the confidence limit was quite wide. In the current study, women across the reproductive age range were included, and hence we reported on a longer period of time in which they may have taken OCs. The validity of reporting accurate brands and durations of individual oral contraceptives over that time frame is limited, and hence no stratification on hormonal content was attempted. We anticipate the proportion of women who had only taken high-risk oral contraceptives, as defined by Bouchard et al., would be similarly small, and hence would not have altered the findings.⁶

The data on OC use and genital pain in general are similarly inconsistent, with some studies reporting increased dysmenorrhea with OCs, but most studies reporting less.¹⁷ The clinical data on dyspareunia after OC use is also conflicting. Caruso noted decreased sexual activity and desire among young women starting 15 µg ethinyl estradiol OCs, but no significant change in reported dyspareunia,¹⁸ but later suggested a lessening of dyspareunia following 3 and 6 months of Yasminelle and Yaz use.¹⁹

Strengths and limitations

This study has several strengths, including the use of a validated screening instrument to predict the vulvodynia diagnosis,¹³ random population-based recruitment, and consideration of the timing of starting OC use compared with the onset of vulvodynia pain. We limited our analysis to those who were of an age in which exposure might occur (≥ 15 years) and who had had intercourse prior to the onset of symptoms of vulvodynia. Notably, when we repeated the Cox analysis without these age and intercourse restrictions, the results were similar (data not presented). However, limitations also exist. Despite the excellent validity of screening for vulvodynia on surveys,^{13,20} some of the women predicted to have vulvodynia may have other dermatological or infectious diagnoses; previous studies suggest that this proportion would be small. Similarly, residual confounding may remain if other factors impact OC use (side effects, need for contraception, or the use of other contraceptive modalities).

In addition, women may start and stop OCs several times over their reproductive years, and may take a number of OC formulations during that time, including those containing only progestogens (seen in 2.2% of current users in this population). This study did not have the data to assess the potential impact of these variations.

Conclusion

The use of OCs was not found to increase the risk of new-onset vulvodynia in this population-based sample of women aged <50 years, and trends suggested that a longer duration of OC use might decrease the risk of developing vulvodynia. Further work is needed to assess these findings in a prospective study, including subgroups that may differ in risk, and to assess the impact of potential OC use on the characteristics and duration of vulvodynia.

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Figure 1.

(a) Age of vulvodynia onset (Kaplan–Meier estimation); (b) duration of vulvodynia, among those who have current or past vulvodynia.

Figure 2.

(a) Ages at which OCs were first started among those who have used OCs; (b) duration of OC use among those who took or are taking OCs.

Figure 3.

Categories comprising the exposed and non-exposed subgroups, stratified by case or control status.

Table 1

Characteristics of oral contraceptive use (multiple options could be selected)

Oral contraceptive use	Prevalence
Number of different brands used	
Mean 2.6 ± 1.5 , range 1–12, median 2	
Reason for initial use (top five reasons only) *	
1 to prevent pregnancy	510 (79.9%)
2 to regulate periods	170 (26.2%)
3 to decrease dysmenorrhea	149 (23.4%)
4 to decrease heavy menstrual bleeding	102 (16.0%)
5 to decrease premenstrual symptoms	76 (11.9%)
Reason for discontinuation if no longer using (top five reasons only) **	
1 no longer needed	192 (38.6%)
2 concerned about possible risks	108 (21.7%)
3 had side effects	109 (21.9%)
4 desired other type of contraception	48 (9.7%)
5 too expensive	36 (7.2%)

* Other reasons included to treat acne (6.4%), or because her parents (8.6%), her partner (5.5%), or her physician (16.0%) recommended them.

** Other reasons included no partner (6.2%), had a hysterectomy (2.4%), reached menopause (1.6%), or doctor recommended discontinuation (6.8%).

Table 2Hazard ratios for the development of vulvodynia following oral contraceptive use ($n = 906$)*

	Hazard (95% CI)	P
Hazard ratio based on time-dependent OC use between the ages of start and stop of OCs	1.08 (0.81–1.43)	0.60
Hazard ratio based on time-dependent continuous OC use from age of starting OCs	1.02 (0.77–1.36)	0.89
Hazards for various minimal durations of OC use, assuming a latency period**		
Minimum 1-year OC use (OC age + 1)	1.00 (0.75–1.32)	0.97
Minimum 2-year OC use (OC age + 2)	0.98 (0.73–1.32)	0.89
Minimum 5-year OC use (OC age + 5)	1.08 (0.77–1.52)	0.65
Minimum 10-year OC use (OC age + 10)	0.68 (0.41–1.15)	0.15
Hazard ratio of the interaction term: age* OC use	0.97 (0.94–1.02)	0.29

* Using the duration from age of OC onset to discontinuation or age at survey completion (or other interval, as noted) to create the time-dependent covariate(s), with age at first intercourse and age at vulvodynia onset as the events. Controlled for marital status, education, and ethnicity (age is already the time axis of the model, and is therefore fully adjusted).

** In each case, the time-dependent OC use variable returned to zero at the cessation of OC use.