



OPPERA Study Identifies an Association Between the Use of Hormonal Contraceptives and Orofacial Pain and Headaches

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Introduction

- Hormone therapy has been described as a risk factor for chronic pain conditions such as low back pain and temporomandibular disorders (TMD)^{1,2}
- Hormonal contraception (HC) may affect pain by altering the function of the endogenous opioid system³ and augmenting serotonin metabolism⁴
- HC has been shown to increase experimental heat and ischemic pain sensitivity in women with TMD and migraine headaches⁵
- Women using HC also demonstrate decreased pressure pain and tactile thresholds of the temporalis and masseter muscles compared to healthy women not using HC^{6,7}
- An association between the use of HC and painful conditions such as migraine headaches and TMD^{2,5} has been described in previous studies although the nature of this association remains unclear
- This analysis sought to determine the relationship between HC use and painful symptoms (particularly headaches and orofacial pain)

Methods

- OPFERA (Orofacial Pain: Prospective Evaluation and Risk Assessment) is a prospective cohort study designed to identify risk factors for the onset of TMD
- 1,863 women who did not have TMD when examined at enrollment were recruited at 4 U.S. study sites from 2006-2008
- Follow-up for up to five years was conducted using questionnaires completed every three months to evaluate the frequency and severity of the painful symptoms in the orofacial region
- Follow-up questionnaires also asked about pain in other bodily regions and use of medications, including HC
- Mixed effects regression models were used to evaluate the association between HC use and presence of orofacial pain symptoms in each three-month follow-up period

- Each three-month period had three outcome variables: 1) presence of orofacial pain and headache, 2) number of months with orofacial pain during the three-monthly period, and 3) aches and pains lasting a day or longer in each of 12 different bodily regions
- HC use was modeled as a fixed effect, along with dummy variables for each study site, and a separate random effect was fitted for each participant
- Standard linear mixed effects models were used for continuous outcome variables, and logistic generalized linear mixed models were used for binary outcome variables
- Since HC can be used to treat menstrual pain and other types of pain, the analysis was repeated excluding women with pre-existing orofacial pain or severe menstrual pain and women who previously used HC to treat pain

Results

Table 1. Association of HC use and pain complaints of various bodily regions

Pain Region	Event	Total	Odds Ratio	95% Confidence Interval	P-value
Orofacial (Any)	6367	16088	1.51	[1.33, 1.72]	<0.0001
Headache	9553	15897	1.70	[1.47, 1.97]	<0.0001
Body Aches (Any)	6101	15803	1.11	[0.97, 1.27]	0.107
Head	1563	15803	1.34	[1.11, 1.62]	0.002
Face	585	15803	1.36	[1.0, 1.84]	0.045
Neck	1469	15803	1.16	[0.95, 1.43]	0.139
Hips	548	15803	0.81	[0.54, 1.22]	0.301
Hands	292	15803	1.20	[0.72, 1.98]	0.475
Abdomen	1024	15803	0.93	[0.73, 1.18]	0.522
Chest	264	15803	0.88	[0.51, 1.52]	0.639
Legs	1411	15803	1.04	[0.84, 1.28]	0.724
Back	2751	15803	1.02	[0.87, 1.20]	0.822
Shoulders	1452	15803	0.98	[0.79, 1.2]	0.839
Feet	627	15803	1.02	[0.75, 1.37]	0.922
Arms	627	15803	0.99	[0.72, 1.37]	0.973

- There was a significant association between HC use and the presence of cheek and jaw pain (OR=1.5, 95% CI=1.3,1.7) and headaches (OR=1.7, 95% CI=1.5,2.0)
- When participants were asked to rate the intensity of their orofacial pain on a scale from 0 to 10, HC users reported greater pain intensity (mean difference=0.25, 95% CI=0.15,0.35)
- There was also a statistically significant difference between HC users and non-users in the number of months with 5 or more days with orofacial pain (mean difference=0.03, 95% CI=0.01,0.04)
- HC use was significantly associated with aches and pains lasting a day or longer in the face (OR=1.4, 95% CI=1.0,1.8) and head (OR=1.3, 95% CI=1.1,1.6)
- There was no significant association (at the p<0.05 level) between HC use and aches and pains in other regions of the body
- The results remained essentially unchanged after excluding women with pre-existing orofacial pain or severe menstrual pain or past HC use to treat pain

Table 2. Association of HC use and pain complaints of various body regions excluding women with pre-existing orofacial pain, severe menstrual pain, and past HC use to

Pain Region	Event	Total	Odds Ratio	95% Confidence Interval	P-value
Orofacial (Any)	3256	9151	1.56	[1.32, 1.85]	<0.0001
Headache	4975	9034	1.73	[1.44, 2.09]	<0.0001
Body Aches (Any)	3012	8984	1.22	[1.03, 1.45]	0.020
Head	738	8928	1.45	[1.11, 1.90]	0.006
Face	288	8928	1.81	[1.16, 2.82]	0.008
Neck	686	8928	1.23	[0.92, 1.64]	0.153
Abdomen	419	8928	0.82	[0.58, 1.15]	0.238
Hips	237	8928	0.74	[0.42, 1.31]	0.295
Hands	147	8928	1.44	[0.68, 3.03]	0.335
Arms	290	8928	1.17	[0.80, 1.73]	0.410
Back	1308	8928	1.08	[0.86, 1.34]	0.512
Shoulders	665	8928	1.08	[0.81, 1.44]	0.593
Chest	127	8928	1.17	[0.55, 2.49]	0.680
Feet	285	8928	1.09	[0.72, 1.66]	0.680
Legs	640	8928	1.04	[0.78, 1.39]	0.773

Conclusions

- HC use was associated with the presence, severity, and duration of orofacial pain
- No association was observed between HC use and pain in other bodily regions
- After excluding women with pre-existing orofacial pain and severe menstrual pain, the association between HC use and orofacial pain remained, so it is unlikely that the association between HC use and orofacial pain can be explained by the likely use of HC by some women to treat dysmenorrhea and other painful conditions
- The complex nature of the relationship between HC use and orofacial pain is a subject for future research

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