Musculoskeletal Orofacial Pain and Other Signs and Symptoms of Temporomandibular Disorders During Pregnancy: A Prospective Study

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Aims: *To describe the course of reported musculoskeletal pain in the temporomandibular region and other signs and symptoms of temporomandibular disorders (TMD) as well as psychological distress over the course of pregnancy and 1 year postpartum.* ***Methods:*** *Women with musculoskeletal orofacial pain (n = 19) and pain-free comparison subjects (n = 16) in the first trimester of pregnancy were selected through records review from the population of a large health maintenance organization. Subjects completed a self-administered questionnaire assessing pain, depression, and somatic symptoms; provided a sample of whole unstimulated saliva; and underwent a standardized clinical examination during the third, sixth, and ninth months of pregnancy and 1 year postpartum.* ***Results:*** *At baseline (third month of pregnancy), 16 of the 19 patients with musculoskeletal orofacial pain met criteria for an RDC/TMD diagnosis. Reported musculoskeletal orofacial pain diminished significantly during the second or third trimester of pregnancy and increased again postpartum. Measures of mandibular opening increased over pregnancy in both cases and comparison subjects and remained high postpartum. Depression and somatic symptoms changed little over the course of pregnancy but were substantially lowered at 1 year postpartum for both groups. As expected, subjects with pain had higher levels of palpation pain, diminished mandibular range of motion, and higher levels of psychological distress compared to subjects without orofacial pain.* ***Conclusion:*** *Musculoskeletal orofacial pain and related symptoms appear to improve over the course of pregnancy. This improvement occurs in the presence of increased joint laxity and is not paralleled by improvements in psychological distress. Thus, it was concluded that the improvement in pain is most likely associated with the dramatic hormonal changes occurring during pregnancy.* J OROFAC PAIN 2005;19:193–201

Key words: hormones, pain, pregnancy, psychological distress, temporomandibular disorders

Musculoskeletal orofacial pain is a prominent feature of temporomandibular disorders (TMD) and the primary reason persons with TMD seek care. It is well known that painful TMD are more common in women than in men and that women of reproductive age are the demographic group at highest risk for experiencing TMD pain.[1–3] Several theories involving both biological and psychosocial factors have been proposed to explain this gender difference.[4] Although the evidence is somewhat contradictory,[5–9] a number of studies suggest that the use of exogenous hormones—oral contraceptives and hormone replacement therapy (HRT)—may be associated with increased risk of

TMD. In a large case-control study of postmenopausal women,[5] those receiving HRT were found to be at higher risk for TMD than those not receiving HRT. Specifically, risk of TMD was related to use of estrogen; a clear dose-response relationship was observed between amount of estrogen prescribed in the previous year and risk of TMD. Postmenopausal women on HRT have also been found to be at increased risk for back pain.[10]

It has recently been reported[11] that the intensity of TMD pain varies systematically across the menstrual cycle, with the highest pain levels occurring at times of low or rapidly fluctuating estrogen. Specifically, mean facial pain intensity levels in normally cycling women not using oral contraceptives were found to rise toward the end of the menstrual cycle, when estrogen levels are rapidly falling, and pain peaked during the first 3 days of menstruation, when estrogen levels are low. Normally cycling women with TMD experienced a secondary pain peak around the time of ovulation, a time of rapid estrogen fluctuation. In a parallel manner, women with TMD who used oral contraceptives experienced rising facial pain intensity levels toward the end of the cycle when placebo pills were substituted for active medication (ie, when exogenous estrogen was withdrawn for days 21 to 28), and pain intensity peaked during the first days of menstruation. However, no secondary pain peak was observed in women using oral contraceptives, who rarely ovulate. These findings of highest TMD pain at times of low or rapidly fluctuating estrogen suggest that estrogen may serve as a pain modulator in humans, as appears to be the case in rodents.[12–14]

Pregnancy produces dramatic changes in levels of estrogens and progesterone. Both estrogen and progesterone levels rise throughout pregnancy, with the steepest rate of increase beginning in the second trimester for both hormones. Plasma estradiol levels during the normal menstrual cycle range from 0.1 ng/mL during menses to about 0.4 ng/mL at ovulation. Around the 12th week of pregnancy, these levels begin to rise steeply, reaching about 15 ng/mL just prior to delivery.[15,16] High levels of other forms of estrogen (estriol and estrone) also are found during the second and third trimesters of pregnancy. Progesterone peaks at around 10 ng/mL in the menstrual cycle but reaches 120 to 150 ng/mL during the ninth month of pregnancy.[15,16] If levels of estrogen and progesterone influence the experience of musculoskeletal orofacial pain, substantial changes in pain report might be expected throughout the course of pregnancy.

Although responses to experimental pain have been studied in pregnant women,[17] and animal research indicates that the high levels of estrogen and progesterone characteristic of pregnancy activate antinociceptive responses,[18] little is known about the course of pre-existing clinical pain conditions, other than rheumatic conditions, during pregnancy. A Medline search from 1980 to present revealed no studies describing the prevalence, incidence, or course of TMD during pregnancy. There is, however, a clinical impression that TMD pain improves, at least somewhat, during pregnancy (Truelove E, Goulet J-P, Stohler C, Sommers E, Greene C, personal communications, 1997). The purpose of this longitudinal study was to describe the course of reported musculoskeletal pain in the temporomandibular region and other signs and symptoms of TMD, as well as psychological distress, over the course of pregnancy and at a follow-up 1 year postpartum. Thus, the primary analyses of interest are within-subject analyses, wherein the subject serves as her own control at various stages of pregnancy and at 1 year postpartum (when not pregnant).

A comparison group of women without orofacial pain was also included in order to ascertain whether the hormone levels of these women during pregnancy and postpartum differed from those of the pain cases. In addition, patterns of change in psychological distress in this nonpain group and in the musculoskeletal orofacial pain cases were compared across the study period to determine whether changes in levels of psychological distress observed in the women with pain were normal pregnancy-related changes or could be attributable to changes in pain.

Materials and Methods

Subject Selection

Subjects were identified using the databases of Group Health Cooperative, a large health maintenance organization (HMO) in Washington State. Group Health refers TMD patients to several outside providers, and these referrals are recorded in a referral database. Databases are also maintained for laboratory tests conducted in Group Health facilities. On a monthly basis, Group Health's automated laboratory test database was used to identify current Group Health enrollees who had had a positive pregnancy test in the prior month. To identify potential pain cases, the list of women with positive pregnancy tests was matched with

the referral database to identify those who had received a referral to an outside provider for TMD treatment in the last year.

Diagnosis and procedure codes from the automated outpatient visit file were used to eliminate women with spontaneous or induced abortions shortly after their positive pregnancy test. After identifying potential cases through automated data, the paper medical record of each potential case was examined to further verify that the woman was in the first trimester of pregnancy and planned to carry the pregnancy to term. Potential eligible cases living in the Puget Sound area then received a mailing from Group Health that included a letter with information about the study and a form to return giving or denying Group Health permission to release her name and contact information to researchers at the University of Washington. If the potential case did not return the form within 10 days, a staff member from the Group Health Center for Health Studies telephoned her to request her permission to release her name.

Age-matched pregnant women without pain in the temporomandibular region were identified for the comparison group through a similar process. The laboratory test database was used to identify women in the Puget Sound area who had had a positive pregnancy test, and the Group Health referral and enrollment databases were checked for any outside referral for TMD treatment since 1989 (when records became available). Using the resulting pool of women confirmed to be in their first trimester of pregnancy and expected to carry the pregnancy to term, comparison subjects were matched to relevant cases by birth year, plus or minus 1 year. If multiple age-matched women were identified, the list of all eligible women was sorted in random order and further procedures (review of the paper medical records and consent procedures identical to those for the pain cases) took place. Because a lower acceptance rate was anticipated among comparison subjects than among pain cases, the first 2 eligible comparison subjects (first according to randomly assigned numbers) received invitation letters. If these 2 letters did not yield a subject, the process was repeated every month until a comparison subject was successfully identified.

Procedures

Potential subjects who agreed to be contacted were telephoned by a registered dental hygienist. The hygienist explained the study in further detail, and if the subject expressed interest in participating, an appointment was scheduled at the subject's home. At this initial appointment, which took place during the third month (around week 12) of pregnancy, the subject gave her written informed consent, completed a self-administered questionnaire, provided a sample of whole unstimulated saliva, and underwent a standardized clinical examination conducted by the hygienist using the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD).[19] Similar data were collected during the sixth and ninth months of pregnancy (around weeks 24 and 37, respectively) and 1 year postpartum (18 months after baseline). Women were paid $50 US upon completion of the study.

Measures

Demographic information (age, race, education, employment, income, marital status) was collected at baseline. The following measures were assessed at each visit:

Pain Measures. The Graded Chronic Pain Scale[20] was used to assess pain severity. This scale includes a measure of characteristic pain intensity (mean of ratings of worst pain in the past 3 months, average pain in the past 3 months, and "pain right now," scored on a scale from 0 to 10).

Psychological Distress. Depression, somatic symptoms, and somatic symptoms excluding items related to pain were assessed with SCL-90 items[21] as described in the RDC/TMD.[19] Subjects were asked how often they had been distressed by each item (symptom) in the past month. Each item was rated on a 5-point scale from 0 (not at all) to 4 (extremely). Mean item scores are reported for each scale.

Clinical Findings. Clinical TMD findings were assessed using the standardized RDC/TMD clinical examination, and Axis I diagnoses were generated according to RDC/TMD criteria. An extraoral muscle palpation pain severity score was calculated by summing the subject's ratings of pain on palpation of 16 muscle sites (bilateral palpation of the posterior, middle, and anterior temporalis; superior, middle, and inferior masseter; posterior mandibular region; and submandibular region). Ratings for each site can range from 0 (no pain) to 3 (severe pain), so the severity score can range from 0 to 48. Measures of pain-free unassisted mandibular opening and maximum assisted mandibular opening (in millimeters) were also collected.

Salivary Hormone Measures. At each session, subjects collected whole unstimulated saliva, and

saliva samples were assayed for levels of estradiol and progesterone. The assessment of these hormones in saliva is a reliable and valid reflection of the level of unbound (bioactive) fraction of the hormone in blood.[22,23] Salivary concentrations of these hormones are independent of salivary flow rate and do not exhibit strong diurnal variability.[24–27] The subject was asked to spit unstimulated saliva into a 50-mL polypropylene centrifuge tube until a 2.5-mL sample was collected. Immediately after the saliva was collected, the hygienist stored it on ice. The sample was either returned to the university directly after the session or stored in the hygienist's home freezer until it could be brought to the university. At the university, the volume of the sample was determined by gravimetry, and samples were stored at –20°C until analysis. Saliva Testing and Research Laboratory, Seattle, WA, used enzyme immunoassay with commercial kits (Pantex) to assess salivary progesterone and estradiol concentrations. Samples were analyzed in duplicate, and analyses were repeated if the intra-assay variation was ≥ 20%.

Data Analysis

Initially, descriptive analyses were conducted and frequency distributions, means, standard deviations (SDs), and medians were examined. Differences between the case and comparison groups were assessed using *t* tests for continuous variables and Fisher's exact test for dichotomous variables. These analyses were followed by multivariate analysis of variance (MANOVA) to examine between-subject differences by group (pain versus nonpain), as well as differences within subjects over time (pregnancy months 3, 6, and 9 and 1 year postpartum). Time-by-group interactions were also examined to determine whether there were different patterns over time for the women with pain and the comparison (pain-free) group.

To assess the relationship between hormone levels and pain over time within subjects, the Spearman rank correlation coefficient between hormone levels and pain was computed for each individual, and the statistical significance of the median correlation coefficient across all subjects was tested using the Wilcoxon signed rank test.

Results

Thirty-three eligible pain cases were contacted, and 21 (64%) agreed to participate in the study. After consenting, 2 subjects missed 1 or more data collection sessions, leaving 19 women with pain who provided questionnaire data at all 4 data collection points. For 2 of these 19 women, one of the in-person sessions could not be scheduled within its necessary time window, so questionnaires were completed and returned by mail. Thus, examination data are available at all data collection points for 17 of the 19 women with pain in the temporomandibular region.

Fifty-three eligible pregnant women without a history of treatment for TMD were contacted in order to find 21 age-matched comparison subjects (40% acceptance rate). After completing the baseline (3-month) data collection session, 5 of the comparison subjects missed one or more follow-up sessions, and 1 completed only the self-report measures at one data collection point. Thus, complete questionnaire data were available for 16 women in the comparison group, and complete examination data were available for 15 of these 16.

Table 1 displays the demographic data for the 19 pain cases and 16 pain-free comparison subjects who provided data at all 4 collection points. The women with pain and those in the comparison group did not differ significantly in age, employment, or marital status. However, the comparison subjects who agreed to participate in the study were, on average, more highly educated than the cases and had higher household income. A higher percentage of the cases were nonwhite. The proportion of women for whom this was the first pregnancy was similar for both groups. As might be expected with any population of cases seeking treatment for pain, women with musculoskeletal pain in the temporomandibular region also had, on average, more pain conditions elsewhere in the body (back pain, headache, and chest, stomach, and joint pain) than did the comparison group.

At baseline (third month of pregnancy), 84% (16/19) of the women with musculoskeletal orofacial pain received an RDC/TMD Axis I diagnosis. These RDC/TMD diagnoses were distributed as follows: 4 subjects had myofascial pain only (Group I); 5 subjects had both a myofascial pain diagnosis and a disc-displacement diagnosis (Groups I and II); 5 subjects had myofascial pain along with arthralgia or arthritis (Groups I and IIIa or IIIb); and 2 subjects had myofascial pain, disc displacement, and arthralgia (Groups I, II, and IIIa). Three subjects (16%) with substantial musculoskeletal pain in the masticatory system (characteristic pain intensities of 4.7, 5.7, and 6.0 and pain on mandibular function) did not meet RDC/TMD criteria for any diagnosis, although they clearly met the criteria for clinical manage-

ment of TMD pain used in the TMD and Orofacial Pain Clinic at the University of Washington. By contrast, none of the women in the comparison group either reported pain in the temporomandibular region or met the criteria for an RDC/TMD pain diagnosis (Groups I, IIIa, or IIIb).

At baseline, 1 subject did not complete the pain-related interference and disability days items needed to calculate Graded Chronic Pain. Of the remaining 18 women, 50% of the women in the pain group had a Graded Chronic Pain score of 1 (low-intensity characteristic pain, defined as > 0 and < 5 on a 0-to-10 scale, and low pain-related disability), 44% had grade 2 pain (high-intensity characteristic pain, ie, pain intensity > 5 on a 0-to-10 scale and low pain-related disability), and 6% (1 subject) had a Graded Chronic Pain score of 4 (severely disabling pain); characteristic pain intensity for this subject was 5.7.

As is typical for hormonal measures, values for levels of salivary estradiol and progesterone were highly variable across subjects (eg, 3-month estradiol ranged from 6 pmol/L to 72 pmol/L; 3-month progesterone from 201 pmol/L to 1,812 pmol/L). However, as expected for normal pregnancies, levels of estradiol and progesterone rose steeply over the course of pregnancy, with estradiol levels increasing more than 6-fold between the 3-month and 9-month visits, from a mean of 21 pmol/L to a mean of 134 pmol/L, and progesterone levels more than tripling in the same time period, from a mean of 535 pmol/L to a mean of 1,826 pmol/L. The levels of both hormones at 1 year postpartum dropped to within the normal range of variability for these hormones in saliva across the menstrual cycle, ie, means of 1.8 pmol/L for estradiol and 67 pmol/L for progesterone. Although the data reveal the expected pattern of significant changes over time ($P < .001$), the average levels of estradiol and progesterone did not differ between women with pain and comparison subjects ($P > .13$ for both), and the pattern of changes over time was similar in both groups.

Among the women with musculoskeletal pain in the temporomandibular region, there were significant changes over time in both characteristic pain intensity and worst pain intensity (Fig 1). Reported pain decreased from the first to the second trimester of pregnancy and remained low at 9 months. Both characteristic pain intensity and worst pain intensity rose again 1 year postpartum, almost reaching baseline levels.

The median (within-subject) correlation of characteristic pain intensity with estradiol level was –0.40, $P = .038$ (ie, higher pain was associated with lower estradiol levels). A similar negative association (rank $r = –0.40$, $P = .022$) was observed for worst pain and estradiol. Negative associations were also observed between progesterone levels and both pain measures. The correlation between progesterone level and characteristic pain intensity was –0.32 ($P = .10$); the correlation between progesterone and worst pain was also –0.32 ($P = .021$).

Table 1 Demographic Data on Pain Cases (n = 19) and Comparison Subjects (n = 16)

	Pain cases	Nonpain comparison group	*P**
Mean (SD) age (y)	28.5 (4.9)	28.4 (4.1)	.88
Race (% white)	73.7	100	.049
Education (high school or less) (%)	42.1	0	.004
Employed (%)	84.2	86.7	> .99
Married (%)	100	93.3	.45
Yearly household income ≥ $50,000 (%)	52.6	86.7	.064
No prior children (%)	42.1	43.7	> .99
Mean (SD) no. of non-TMD pain conditions (0–5)	2.8 (1.1)	1.0 (0.9)	< .001

* *t* tests for continuous variables; Fisher exact test for dichotomous variables.

Table 2 shows findings from the clinical examinations over time in cases and comparison subjects. Overall, cases showed substantially higher palpation pain ($P = .002$) and reduced pain-free unassisted opening ($P = .002$) as compared to the comparison group, but the differences for maximum assisted opening were not as large ($P = .17$).

Extraoral palpation pain severity did not change significantly over time ($P = .28$), although, for the pain cases, this variable followed a pattern identical to the pattern for pain report shown in Fig 1. Unassisted pain-free opening also did not change significantly over time ($P = .39$). However, there was a marginally statistically significant effect of time on maximum assisted opening ($P = .064$), with both cases and comparison subjects showing increased measurements over the course of the pregnancy and further increases postpartum. For the pain cases, extraoral palpation pain severity followed a pattern identical to the pattern for pain report shown in Fig 1, but the difference in palpation pain severity over time was not statistically significant.

Consistent with other studies,[11,28] levels of depression, somatization, and somatization excluding pain were higher for pain cases than for

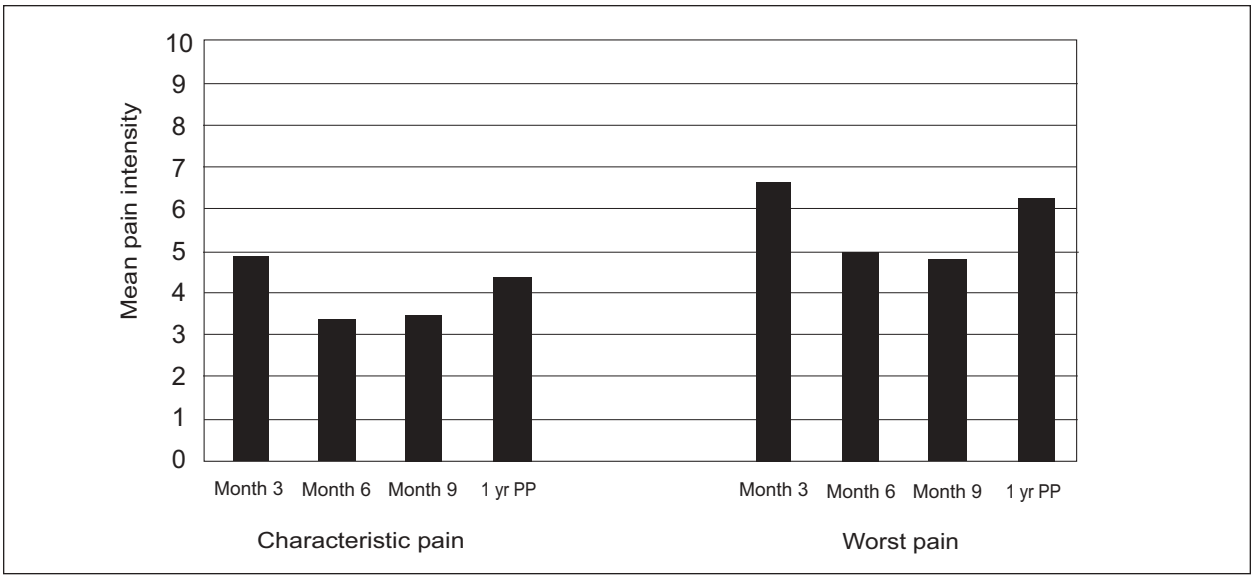

Fig 1 Mean characteristic pain intensity (0-to-10 scale) and mean intensity of worst pain in the last 3 months (0-to-10 scale) at 3, 6, and 9 months of pregnancy and 1 year postpartum (PP) for 19 women with musculoskeletal pain in the temporomandibular region. F test (MANOVA) for time effect: characteristic pain intensity, $P = .014$; worst pain intensity, $P = .010$.

Table 2 Clinical Examination Findings Over Time: Pain Cases (n = 17) and Comparison Subjects (n = 15)

	Extraoral palpation pain severity Mean (SD)	Unassisted pain-free opening Mean (SD)	Maximum assisted opening * Mean (SD)
Cases			
Pregnancy month 3	8.3 (7.6)	39.1 (10.5)	51.9 (8.9)
Pregnancy month 6	7.8 (8.0)	39.0 (11.3)	52.1 (6.6)
Pregnancy month 9	6.9 (7.4)	40.9 (10.9)	53.8 (6.8)
1 year postpartum	9.5 (10.2)	41.4 (10.0)	54.6 (6.1)
Comparison subjects			
Pregnancy month 3	0.5 (1.5)	48.5 (5.5)	55.6 (6.2)
Pregnancy month 6	0.9 (2.2)	48.7 (6.1)	55.6 (6.2)
Pregnancy month 9	1.1 (2.5)	49.7 (6.1)	56.9 (6.5)
1 year postpartum	1.5 (3.1)	50.5 (6.6)	57.3 (6.6)

*Complete data were available for 16 cases and 14 comparison subjects for this measure.

Table 3 Depression and Somatic Symptoms Over Time: Pain Cases (n = 19) and Comparison Subjects (n = 16)

	Depression Mean (SD)	Somatization Mean (SD)	Somatization (without pain items) Mean (SD)
Cases			
Pregnancy month 3	1.0 (0.7)	1.3 (0.7)	0.8 (0.8)
Pregnancy month 6	1.0 (0.7)	1.3 (0.8)	1.1 (0.9)
Pregnancy month 9	1.2 (0.7)	1.5 (0.7)	1.3 (0.7)
1 year postpartum	0.7 (0.7)	0.8 (0.7)	0.5 (0.7)
Comparison subjects			
Pregnancy month 3	0.6 (0.4)	0.7 (0.5)	0.5 (0.5)
Pregnancy month 6	0.6 (0.4)	0.6 (0.4)	0.4 (0.3)
Pregnancy month 9	0.6 (0.4)	0.7 (0.5)	0.5 (0.5)
1 year postpartum	0.4 (0.5)	0.4 (0.3)	0.1 (0.2)

women without pain (Table 3). For the 2 measures of somatization, MANOVA revealed a significant group effect ($P = .0023$ for somatization and $P = .0039$ for somatization excluding pain). For depression, the group effect was also statistically significant ($P = .033$). Both women with musculoskeletal orofacial pain and pain-free comparison subjects showed similar changes over time (group × time, $P > .05$ for all 3 measures), with substantially lower levels of depression and bothersome somatic symptoms 1 year postpartum than during pregnancy (time effect, $P < .001$ for all 3 measures).

Discussion

The findings indicate that the level of reported musculoskeletal orofacial pain intensity decreased over the course of pregnancy. Because mean pain levels rose again at the 1-year postpartum follow-up, it is likely that this change does not simply reflect the effect of time. Pain on palpation in the pain cases showed a pattern similar to the pattern for pain report, but the change in palpation pain over time did not achieve statistical significance in the present sample.

Measures of pain-free opening and maximum assisted opening tended to increase over the course of the study for both cases and comparison subjects, although the differences were not statistically significant. During pregnancy, the ligaments of the pubic symphysis and sacroiliac joints loosen, possibly because of the effects of the hormone relaxin.[29] This increased joint laxity extends to peripheral joints,[30] and the findings of the present study suggest increased laxity in the temporomandibular joint during pregnancy, as well. In the present subjects, mandibular opening measures remained high at the postpartum follow-up. Although the evidence is somewhat contradictory,[31] it has been suggested that once the ligaments have loosened during pregnancy, joints remain lax postpartum.[30,32] The findings of the present study are in keeping with this suggestion. Westling[33] has postulated that TMD are associated with joint laxity. However, in the current study, the increased joint laxity that occurred over the course of pregnancy was accompanied by decreased rather than increased pain levels.

Cases consistently reported higher levels of distressing depressive and somatic symptoms than did comparison subjects. However, levels of depressive and somatic symptoms did not change dramatically over the course of pregnancy for either group. This suggests that the substantial improvements in pain report across pregnancy are probably not attributable to changes in mood and overall symptom perception. Levels of depression and somatic symptoms were substantially lower 1 year after delivery than at any time during pregnancy. However, reported pain was higher for pain cases at this time than it was during the latter stages of pregnancy. Again, changes in pain did not parallel changes in psychological distress.

Pregnancy has been reported to bring about changes in other symptomatic clinical conditions with predominantly female prevalence. A retrospective study of women with fibromyalgia found that symptoms appeared to worsen during pregnancy.[34] Pregnancy also appears to exacerbate symptoms of systemic lupus erythematosus (SLE),[35] but pregnancy generally has a beneficial effect on rheumatoid arthritis (RA).[36] It has been postulated that this difference can be explained by the fact that during pregnancy cell-mediated immune function (which exacerbates RA) is suppressed, whereas humoral immunity (which exacerbates SLE) is enhanced.[35] Clinical diagnoses of rheumatological conditions were not available for the present study sample. However, none of the women in either group reported a history of RA or SLE. Although it is possible that some of the women in the pain group had fibromyalgia or chronic widespread pain, it is unlikely that the presence of fibromyalgia could have been responsible for the pattern of results observed, since the available evidence[34] indicates that fibromyalgia worsens, rather than improves, during pregnancy.

It is also possible that the improvements in musculoskeletal orofacial pain were associated with improvements in headache. The presence of "severe headache or migraine" was assessed over the past 3 months with a single item at each follow-up. It does appear that headache disappeared for some women during pregnancy; 15 of 19 cases (79%) reported headache at baseline (3 months), 12 at 6 months, and 10 at 9 months. Thirteen of the 19 cases reported headache at the 1-year follow-up. Whether these changes represent parallel effects of hormonal changes on headache and pain in the temporomandibular region, or reflect the potential confounding of these conditions, remains an issue for further investigation.

Findings from studies of experimental pain suggest that the high levels of estrogen and progesterone characteristic of the later stages of pregnancy have antinociceptive properties.[17,18] In the present study, the report of clinical pain in the temporomandibular region was lowest in the latter stages of pregnancy, and pain report was nega-

tively correlated with levels of these hormones. Whether these effects are associated with estrogens or progesterone[37] or both remains to be determined. The findings of this study parallel the findings of a prior study by the authors showing highest TMD pain at phases of the menstrual cycle when estrogen levels are low or rapidly falling and lower pain when estrogen levels are relatively high.[11] The suggestion that high levels of estrogen could have an antinociceptive or pain modulatory effect may appear inconsistent with earlier findings that estrogen replacement therapy is a risk factor for TMD pain.[5] However, a common protocol for use of exogenous hormones (both HRT and oral contraceptives) involves the withdrawal of estrogen for 1 week each month. It is possible that it is not the presence, but rather the withdrawal, of estrogen that puts women at risk of experiencing pain. It is also possible that the changes in clinical pain observed in this study of pregnant women are attributable not to changes in estrogen, but to changes in progesterone (or to changes in both estrogen and progesterone), since levels of both hormones change in a similar way over the course of pregnancy.

This study has a number of methodological limitations. Additional data on the pattern of pain over a comparable (18-month) period in female TMD cases who were not pregnant could also have been useful for illuminating the effects of pregnancy on pain in the temporomandibular region. However, data from existing longitudinal studies[38] indicate that the pattern of pain in treated TMD cases over a 1- to 2-year period is quite variable. In addition, because this was 1 of the first studies of the course of musculoskeletal orofacial pain during pregnancy, the researchers did not know whether to expect pain changes during early pregnancy. Thus, the pain group was chosen based on a history of seeking care for TMD pain, rather than on the presence of a clinical or an RDC/TMD diagnosis at the initial assessment, which took place during the third month of pregnancy. In fact, the case group included a few women who, although they had substantial pain, did not meet criteria for an RDC/TMD diagnosis at this initial assessment. The proportion of women in the pain group not meeting RDC/TMD criteria for an Axis I diagnosis (16%) is similar to that reported previously for a TMD clinic population[39] and somewhat lower than that reported for a population of patients diagnosed with acute TMD pain.[40] Repetition of all analyses with these women eliminated resulted in findings very similar to those reported here.

This study is also limited by the relatively small sample size of both the case and the comparison groups. In addition, the 2 groups, although selected in a similar manner from the same population, differed in socioeconomic status. The authors speculate that this difference is most likely attributable to a high refusal rate among potential comparison subjects of lower socioeconomic status. Nevertheless, the differences in pain, clinical findings, and psychological distress measures between the pain cases and women without orofacial pain are most logically attributed to differences in pain state, rather than to differences in socioeconomic status. Also, despite the rather small sample size, substantial within-subject differences were found over time for pain report and clinical findings.

To the authors' knowledge, this is the first prospective study of orofacial pain during pregnancy, and 1 of only a few prospective studies of any clinical pain condition during pregnancy. The findings of the present study suggest that the clinical impression that musculoskeletal pain in TMD patients improves during pregnancy is probably correct. Additional research is needed to investigate the causes of this clinical improvement.

Acknowledgments

This work was supported by grant no. R01 DE 012470 from the U.S. National Institute of Dental and Craniofacial Research. The authors wish to thank Melinda Lane, Perdis Jacobsen, Barbara Omalev, and Nancy Alleman for conducting the data collection sessions; Beatrice Gandara for supervising the processing of saliva and providing expert advice concerning the salivary measures; and Julie Sage and Glenn Unruh for help with data management.

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