A Quantitative Analysis of Pressure Pain Threshold and Pain Tolerance In Different Trimesters of Pregnancy and Relation with Ovarian Sex Hormones

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OBJECTIVE: To define the Pressure Pain Threshold (PPT) and pain tolerance (PT) at different trigger points in different trimesters of healthy pregnant and non-pregnant women.

STUDY DESIGN: A prospective, controlled study of ten women in the first, 16 women in the second and 16 women in the third trimester of pregnancy, and 10 non-pregnant women were enrolled as four groups. Pain assessment was done using the dolorimeter over eight points on the body. Serum estradiol and progesterone levels were determined.

RESULTS: PPT at the sternum was significantly lower in the third trimester pregnant group and PT at the sacrum was significantly higher in the non-pregnant group compared to the other groups. Maternal estradiol and progesterone levels were not correlated with PPT and PT at any point in four groups.

CONCLUSION: Estradiol and progesterone may not affect pain sensitivity in pregnancy. The causative effects of the decline in PT at the sacrum in the first trimester of pregnancy, needs to be studied further.

Key Words: Pain, Pregnancy

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Introduction

Pregnancy is considered to be a complex process continuing for an average of 40 weeks divided into three trimesters and including mechanical and hormonal changes. Even in pregnancies not complicated due to obstetrical reasons, pain can occur in the different trimesters, localized especially in the pelvis and lower back.1 This pain can have an adverse impact on the mother’s quality of life and can result in work absenteeism for those who are affected.2

In the literature, the involvement of sex hormones in many chronic pain syndromes has been demonstrated.3-5 Moreover, studies on pain perception across the menstrual cycle have shown that estradiol and progesterone affect pain sensitivity.6,7 Although an involvement of sex hormones in pain seems certain, their interactions with the pain pathways are not yet clear.

Material and Method

In this prospective, controlled study, the protocol was approved by the Ethics Committee for Clinical Research of Gaziantep University, and subjects were selected from among women attending the Obstetrics and Gynecology Department of Gaziantep University. Fifty-two women were enrolled in this study in four groups. All of the subjects were healthy non-smokers with no history of drug use. Of these, 10 women were
in the first trimester, 16 in the second trimester and 16 in the third trimester of pregnancy. The remaining 10 women were non-pregnant healthy women who served as controls. Eligible cases were between 19-40 years of age with singleton pregnancies. Women in labor, with ruptured membranes, multiple pregnancy, or any concurrent medical complications before or developing during pregnancy, such as preeclampsia, diabetes mellitus, hyperthyroidism, intrauterine growth retardation, or inflammatory diseases were not included in the study.

Data were obtained regarding obstetric history, current pregnancy characteristics, medical history and State-Trait Anxiety Inventory (STAI). The purpose of the study and evaluation method were explained to all subjects included in the trial, and their informed consents were obtained.

Pain assessment was done using the dolorimeter (Chatillon DFE-100, Digital force Gauge/AMETEK) in the Algology Department of Gaziantep University.

Before evaluation of PPT and PT, systolic and diastolic blood pressure was measured in all subjects. Pressure was forced over eight points on the body: the deltoid, sternum, forearm, sacrum, and thigh at 10-minute (min) intervals. Deltoid, forearm and thigh points were assessed bilaterally and the score was presented as an average of the two sides.

The dolorimeter has a maximal scale of 11 kg, with a neoprene stopper footplate of 1 cm² contact area. The pressure was steadily increased at a rate of approximately 1 kg per 1 second (s). When the subjects described the sensation as painful, the amount of pressure was recorded as libre (Lb) and regarded as the PPT for the specific tender point. When the subjects experienced the most intense pain sensation tolerable, the amount of pressure was recorded and the difference between these data and the PPT was regarded as the PT. All examinations were performed by a single investigator.

Serum estradiol and progesterone levels were measured in venous blood samples from all subjects and were determined with Chemiluminescent Microparticle Immunoassays on an Architect i2000 SR analyzer (Architect Estradiol and Progesterone assays, Abbott Diagnostics, Longford, Ireland). Samples with higher estradiol and progesterone levels than the reportable limits of the assays (1000 pg/mL and 40 ng/mL, respectively) were reanalyzed after appropriate dilution (100- and 50-fold, respectively). Internal controls were included in each analytical run. Intraassay and interassay precision performances of the assays were determined on 10 replicates in a single run and in 20 different runs, respectively, from the quality control data of the laboratory-yielded coefficients of variation (CVs) within 3.5-8.6% range.

**Statistical analysis**

Sample size was estimated using a power calculation based on 50% reduction in sacrum PT in the third trimester pregnancy group. It was estimated that at least 10 patients would be required to detect a significant difference between non-pregnancy and third trimester pregnancy groups at 80% power level and an alpha error of 5%. ANOVA test was performed to compare groups according to continuous variables, and the differences between subgroups were detected by LSD post-hoc test. Pearson Correlation Coefficient was calculated to evaluate the correlation between continuous variables. Mean ± standard deviations (SD) and frequencies were given as descriptive statistics. A value of p≤0.05 was accepted as significant. Analysis was performed by SPSS for Windows version 11.5.

**Results**

The demographic characteristics of the subjects are shown in table 1. There was no difference in mean age, gravidity, parity, and systolic and diastolic blood pressure between the subjects. Serum estradiol and progesterone levels were significantly different between groups, as expected.

PPTs in the deltoid, forearm, sacrum, and thigh were not significantly different between the first, second and third

**Table 1. Clinical characteristics of subjects in the four groups**

<table>
<thead>
<tr>
<th></th>
<th>1st Trimester</th>
<th>2nd Trimester</th>
<th>3rd Trimester</th>
<th>Non pregnant</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>25.4±6.2</td>
<td>28.6±6.6</td>
<td>30.1±5.6</td>
<td>26.9±8.5</td>
<td>0.242</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>9.5±2.7</td>
<td>21.6±3.7</td>
<td>33.9±2.7</td>
<td>0.001*</td>
<td></td>
</tr>
<tr>
<td>Parity</td>
<td>0.8±0.8</td>
<td>1.2±1.5</td>
<td>1.4±1.0</td>
<td>0.7±1.2</td>
<td>0.310</td>
</tr>
<tr>
<td>Gravidity</td>
<td>2.3±1.2</td>
<td>2.4±1.4</td>
<td>3.1±1.9</td>
<td>1.6±1.8</td>
<td>0.114</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.08±3.13</td>
<td>27.36±3.41</td>
<td>28.33±1.76</td>
<td>24.28±3.50</td>
<td>0.001*</td>
</tr>
<tr>
<td>Blood Pressure (mmHg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>120.8±12.5</td>
<td>119.6±11.0</td>
<td>121.8±15.3</td>
<td>131.5±10.63</td>
<td>0.089</td>
</tr>
<tr>
<td>Diastolic</td>
<td>74.3±7.6</td>
<td>69.0±6.9</td>
<td>76.6±23.7</td>
<td>84.33±9.745</td>
<td>0.095</td>
</tr>
<tr>
<td>Estradiol (pg/mL)</td>
<td>2124±1808</td>
<td>7032±4060</td>
<td>21937±7188</td>
<td>128±157</td>
<td>0.001*</td>
</tr>
<tr>
<td>Progesterone (ng/mL)</td>
<td>22.30±8.06</td>
<td>40.56±25.11</td>
<td>120.17±56.19</td>
<td>3.74±4.9</td>
<td>0.001*</td>
</tr>
</tbody>
</table>

*BMI: Body mass index.*
trimester pregnant and non-pregnant groups (Table 2). Only PPT at the sternum was significantly lower in the third trimester pregnant group compared to the other groups.

PTs at the sternum, deltoid and forearm were not significantly different between the four groups. Although PT at the sacrum was not significantly different between the first, second and third trimester pregnant groups, it was significantly higher in the non-pregnant group than the pregnant groups (Table 3).

STAI results were not significantly different between the four groups.

When the correlation analysis was performed both in the entire study group (Table 4) and in split file, maternal estradiol and progesterone levels were not correlated with PPT and PT at any point. In the entire study population, although PTT at the sternum was not correlated with PPT at other points, positive correlations were determined between PPT at the deltoid, forearm, sacrum, and thigh (Table 5). When the correlation analysis was performed in split file, no correlation was observed between maternal age, gravidity or parity and PPT or PT. Gestational age was significantly correlated with PTT (p: 0.026; r: -0.555) and marginally correlated with PPT (p: 0.064; r: -0.474) only in the second trimester at the sternum. In other groups and at other points, no correlation was observed between gestational age and PT or PPT.

### Table 2: Comparison of pressure pain threshold (PTT) between the four groups

<table>
<thead>
<tr>
<th></th>
<th>1st Trimester</th>
<th>2nd Trimester</th>
<th>3rd Trimester</th>
<th>Non pregnant</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sternum</td>
<td>3150±1105</td>
<td>3044±1109</td>
<td>2180±1249</td>
<td>3925±1136</td>
<td>0.001*</td>
</tr>
<tr>
<td>Deltoid</td>
<td>3150±1036</td>
<td>3447±1130</td>
<td>2849±1680</td>
<td>3963±1196</td>
<td>0.152</td>
</tr>
<tr>
<td>Forearm</td>
<td>3730±842</td>
<td>3719±1131</td>
<td>3219±1629</td>
<td>4183±846</td>
<td>0.205</td>
</tr>
<tr>
<td>Sacrum</td>
<td>3870±1286</td>
<td>4460±1456</td>
<td>3853±1853</td>
<td>4671±1608</td>
<td>0.049</td>
</tr>
<tr>
<td>Thigh</td>
<td>4680±1995</td>
<td>5491±1919</td>
<td>4733±2411</td>
<td>5979±1551</td>
<td>0.030</td>
</tr>
</tbody>
</table>

### Table 3: Comparison of Pain Tolerance (PT) between the four groups

<table>
<thead>
<tr>
<th></th>
<th>1st Trimester</th>
<th>2nd Trimester</th>
<th>3rd Trimester</th>
<th>Non pregnant</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sternum</td>
<td>1270±631</td>
<td>1197±612</td>
<td>1230±838</td>
<td>1824±947</td>
<td>0.139</td>
</tr>
<tr>
<td>Deltoid</td>
<td>3150±1036</td>
<td>3447±1130</td>
<td>2849±1680</td>
<td>3963±1196</td>
<td>0.152</td>
</tr>
<tr>
<td>Forearm</td>
<td>2080±1445</td>
<td>2381±1026</td>
<td>1743±900</td>
<td>2433±1128</td>
<td>0.228</td>
</tr>
<tr>
<td>Sacrum</td>
<td>2260±847</td>
<td>2022±852</td>
<td>1922±914</td>
<td>3550±1656</td>
<td>0.001*</td>
</tr>
<tr>
<td>Thigh</td>
<td>2380±1358</td>
<td>2441±1339</td>
<td>1605±972</td>
<td>2478±718</td>
<td>0.066</td>
</tr>
</tbody>
</table>

### Table 4: Correlation of Pain Tolerance (PT) between estradiol and progesterone levels in pregnancy

<table>
<thead>
<tr>
<th></th>
<th>Deltoid</th>
<th>Forearm</th>
<th>Sacrum</th>
<th>Thigh</th>
<th>Sternum</th>
<th>Progesterone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol</td>
<td>r</td>
<td>-0.09</td>
<td>-0.046</td>
<td>0.075</td>
<td>0.016</td>
<td>0.428</td>
</tr>
<tr>
<td></td>
<td>p</td>
<td>0.663</td>
<td>0.954</td>
<td>0.759</td>
<td>0.619</td>
<td>0.914</td>
</tr>
<tr>
<td>Progesterone</td>
<td>r</td>
<td>-0.157</td>
<td>-0.120</td>
<td>-0.053</td>
<td>-0.100</td>
<td>-0.214</td>
</tr>
<tr>
<td></td>
<td>p</td>
<td>0.293</td>
<td>0.424</td>
<td>0.721</td>
<td>0.502</td>
<td>0.149</td>
</tr>
</tbody>
</table>

### Discussion

Even in pregnancies not complicated by obstetrical problems or systemic disease, pain can be observed in different trimesters, especially localized at the pelvis and lower back. These complaints are generally dismissed as the normal aches and pains of pregnancy; however, this pain can have an adverse impact on the mother’s quality of life and can result in work absenteeism for those who are affected.²,¹⁴

Although mechanical,¹⁵ hormonal ¹⁶ and metabolic ¹⁷ factors can be the cause of pelvic and low back pain in pregnancy, the pathophysiological mechanism of this pain is unclear. Quantitatively determining pain sensitivity and clarifying the
effective factors on pain sensitivity in a healthy pregnancy is essential for proper management of pain in pregnancy. In the literature, studies have been conducted to qualify and quantify pain during pregnancy. However, a limited number of these studies were focused on labor and the third trimester.

This is the first study to evaluate any correlation between PPT and PT at different trigger points and ovarian sex steroid levels in different trimesters in healthy pregnant and non-pregnant groups.

Ohel et al. evaluated changes in PPT before, during and after active labor at specific pressure points using a dolorimeter, and they demonstrated, similar to our study, no significant differences between the three groups at the deltoid and paraspinus 2-4 cm, trapezius, and teres minor points.

Bajaj et al. performed a study to evaluate PPT, heat pain threshold and tactile threshold in different trimesters of pregnant with and without pelvic pain. In their study, although the PPT was higher in trimester 3 as compared to trimesters 1 and 2 in the pain group, there was no significant difference in PPT within trimesters in the non-pain group. Similar with the non-pain group in that study, we also found no significant difference in PPT at the deltoid, forearm and thigh within different trimester healthy pregnant and non-pregnant groups.

In contrast to the results of Bajaj et al. and Ohel et al., we observed PPT in the third trimester group at the sternum to be significantly low compared to the other three groups. This difference could be the result of enlargement of the uterus, which caused an increase in pressure at that point and increased the anteroposterior diameter of the chest. Supporting this result, we demonstrated that gestational age was significantly correlated with PPT (p: 0.026; r: -0.555) and marginally correlated with PPT (p: 0.064; r: -0.474) at the sternum only in the second trimester of pregnancy, in which uterine enlargement was observed gradually. In fact, between 20 and 31 weeks, the height of the uterine fundus correlates closely with gestational age in weeks.

Although we did not observe a significant difference in PPT at the sacrum between the four groups, PT at the sacrum was shown to be significantly high in the non-pregnant group compared to the pregnant group.

During the late stage of pregnancy, pain thresholds or sensory thresholds have been reported to be increased in both rats and human in response to noxious stimuli, including electric, heat and pressure stimuli. However, these studies were focused on late pregnancy and active labor. Our study is the first in the literature to demonstrate the decline in PPT at the sternum and PT at the sacrum in human pregnancy.

In fact, pelvic and low back pain is a very common complaint in pregnancy, affecting approximately 45% of all pregnant and 25% of all postpartum women. Although peak intensity of pelvic and low back pain in pregnancy is between the 24th and 36th weeks of pregnancy, this pain can also start in the first trimester or continue 3 weeks after delivery. The cause of so common an observation of pelvic and low back pain in pregnancy may be the result of the decline in PT in pregnancy.

It is now generally accepted that sex steroids such as estradiol and progesterone affect brain function by modulating neurotransmission and act as “neuroactive steroids”. Although there is a gradual increase in the levels of plasma progesterone as well as those of estradiol and estriol in normal human pregnancy, the effect of estradiol and progesterone levels on pain sensitivity during pregnancy has not been clearly elucidated.

In the literature, Watanabe et al. evaluated the relationship between current perception threshold (CPT), estimated from the dominant ankle section (lumbar/sacral sites) and ovarian sex steroids in third trimester pregnant and non-pregnant women. They demonstrated that while there was also no significant correlation between CPT and estradiol and progesterone, there was a significant correlation between CPT and the ratio of 17β-estradiol/progesterone. In our study, when the correlation analysis was performed in the entire study group and in the first, second and third trimester pregnant and non-pregnant groups, there was no correlation between maternal estradiol and progesterone levels or the ratio of 17β-estradiol/progesterone and PPT or PT at any point.

In contrast to other studies, a non-pregnant group was evaluated in this study, and PPT of non-pregnant women was observed to be similar to that of pregnant women.

Psychologic factors, such as fear, apprehension and anxiety, also influence the degree of pain and suffering during childbirth. In this study, STAI results were not significantly different between the four groups, and no correlation was observed between STAI results and PPT or PT at any of the trigger points.

In conclusion, using dolorimeter, our results supported that there were no significant differences in PPT except at the sternum between healthy pregnant and non-pregnant women in different trimesters, and there was no significant correlation between PPT, PT and estradiol and progesterone levels. While there was no significant difference in PT in pregnancy within trimesters, there was a significant difference in PT in pregnant as compared to non-pregnant women. This topic, particularly the causative effects of the decline in PT at the sacrum in the first trimester of pregnancy, needs to be studied further for proper management of pain in pregnancy.
Farklı Trimesterlerdeki Gebelerde Basınç Ağrısı ile Ağrı Toleransının Quantitative Analizi ve Ovaryan Seks Hormonları ile İlişkisi

AMAC: Farklı trimesterlerdeki gebeler ve gebe olmayan kadınlarda basınç ağrı eşiği (BAE) ile ağrı toleransının (AT) farklı trimesterde tanımlanması


SONUÇLAR: Östradiol ve progesteron gebelikte ağrıya hassasiyeti metkilemeyebilir. İlk trimesterde sakrumdaki AT azalması konusunda neden olan etkinin ileri araştırma ile açıklanmasına ihtiyaç vardır.

Anahtar Kelimeler: Ağrı, Gebelik

References

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