Obstetrics; *Maternal-Fetal Medicine and Perinatology*

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

Ebru ÖZTÜRK[1], Lutfiye PİRBUDAK COCEL[12], Mete Gürol UĞUR[1], Seval KUL[3], Ayse BERBAĞCI[4], Pınar ERDALOĞLU[2], Sevgi SARI DEMİR[1], Özcan BALAT[1]

Gaziantep, Turkey

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

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 effect 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

Gynecol Obstet Reprod Med 2011;17:137-141

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.

[1]Department of Obstetrics and Gynecology, [2]Department of Algology, [3]Department of Biostatistics and [4]Department of Biochemistry Gaziantep University Faculty of Medicine, Gaziantep

Address of Correspondence: *Mete Gürol Uğur*
Gaziantep Üniversitesi, Tıp Fakultesi
Kadın Hastalıkları ve Doğum Polikliniği,
Şahinbey, Gaziantep
metegurolugur@hotmail.com

Submitted for Publication: *25. 10. 2011*
Accepted for Publication: *26. 10. 2011*

Pain is a subjective feeling, and studies have been undertaken to qualify and quantify pain during pregnancy.[8,9] However, a limited number of these studies were focused on labor and the third trimester.[10,11]

Because of the inaccuracies in evaluating pain, a few methods have been developed to try and quantify the degree of pain by using an objective means, such as pressure pain threshold (PPT) and pain tolerance (PT) by dolorimeter.[12]

It was demonstrated that quantitative sensory tests are quite sensitive for evaluating nociception.[13] The algometer is a quantitative sensory test to measure pain threshold.

The present study was aimed to define the PPT and PT at different trigger points in different trimesters of healthy pregnant and non-pregnant groups using dolorimeter and to demonstrate any correlation between the PPT and PT and ovarian sex steroids in pregnancy.

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 nonsmokers 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 cm^2 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 (Architech 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 $p \leq 0.05$ 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

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

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 PT (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 5: Correlation of pressure pain threshold (PTT) between the five trigger points in pregnancy

		Sternum	Thigh	Sacrum	Forearm	Deltoid
Deltoid	r	0.314	0.766	0.826	0,799	
	p	0.377	0.010	0.003	0,006	
Forearm	r	0.372	0.711	0.856		
	p	0.290	0.021	0.002		
Sacrum	r	0.498	0.476			
	p	0.143	0.165			
Thigh	r	0.377				
	p	0.283				

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

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

	1st Trimester	2nd Trimester	3rd Trimester	Non pregnant	p
Sternum	3150±1105	3044±1109	2180±1249	3925±1136	0.001*
Deltoid	3150±1036	3447±1130	2849±1680	3963±1196	0.152
Forearm	3730±842	3719±1131	3219±1629	4183±846	0.205
Sacrum	3870±1286	4460±1456	3853±1853	4671±1608	0.429
Thigh	4680±1995	5491±1919	4733±2411	5979±1551	0.302

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

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

Table 4. Correlation of Pain Tolerance (PT) between estrodiol and pregesteron levels in pregnancy

		Deltoid	Forearm	Sacrum	Thigh	Sternum	Progesterone
Estradiol	r	0.071	-0.009	-0.046	0.075	0.016	0.428
	p	0.663	0.954	0.759	0.619	0.914	0.003*
Progesterone	r	-0.157	-0.120	-0.053	-0.100	-0.214	
	p	0.293	0.424	0.721	0.502	0.149	

effective factors on pain sensitivity in a heathy pregnancy is essential for proper management of pain in pregnancy. In the literature, studies have been conducted to qualify and quantify pain during pregnancy.[8,9,18] However, a limited number of these studies were focused on labor and the third trimester.[10,11]

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.[8] 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 paraspinal 2-4 cm, trapezius, and teres minor points.

Bajaj et al.[18] performed a study to evaluate PPT, heat pain threshold and tactile threshold in different trimesters of pregnants 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 PT (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.[19]

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 [20] and humans[10,11,21] 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 pregnants and 25% of all postpartum women[1] 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.[22] 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".[23] Although there is a gradual increase in the levels of plasma progesterone as well as those of estradiol and estriol in normal human pregnancy,[24] the effect of estradiol and progesterone levels on pain sensitivity during pregnancy has not been clearly elucidated.

In the literature, Watanabe et al.[25] 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 17 β-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 17 β-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.[19] 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 pregnants within trimesters and non–pregnants, 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 significant decline in PT in pregnants as compared to non-pregnants. 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 Ağrı Eşiği ile Ağrı Toleransının Kantitatif Analizi ve Ovaryan Seks Hormonları ile İlişkisi

AMAÇ: Farklı trimesterlerdeki gebeler ve gebe olmayan kadınlarda basınç ağrı eşiği (BAE) ile ağrı toleransının (AT) farklı tetik noktalarda tanımlanması

GEREÇ VE YÖNTEM: Prospektif-kontrollü olarak ilk trimesterdeki 10, ikincideki 16 ve üçüncüdeki 16 gebe ile 10 gebe olmayan kadın 4 gruba ayrıldı. Ağrının değerlendirilmesi vücuttaki 8 noktadan dolorimetre ile uygulandı. Serum östradiol ve progesteron seviyeleri ölçüldü.

BULGULAR: BAE üçüncü trimester grubunda sternumda anlamlı olarak düşüktü. Sakrumda AT gebe olmayan grupta diğer gruplara oranla daha yüksekti. Maternal östradiol ve progesteron seviyeleri hiçbir grupta BAE ve At ile korelasyon göstermedi.

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

1. Wu WH, Meijer OG, Uegaki K et al. Pregnancy-related pelvic girdle pain (PPP), I: Terminology, clinical presentation, and prevalence. Eur Spine J 2004;13:575-89.
2. Sydsjo A, Sydsjo G, Alexanderson K. Influence of pregnancy-related diagnoses on sick-leave data in women aged 16-44. J Womens Health Gend Based Med 2001;10:707-14.
3. Aloisi, A.M., Bonifazi, M. Sex hormones, central nervous system and pain. Horm Behav 2006;50:1-7.
4. Marcus DA. Interrelationships of neurochemicals, estrogen, and recurring headache. Pain 1995;62:129-39.
5. Dao, TT., LeResche, L. Gender differences in pain. J Orofac Pain 2000; 14:169-84.
6. Riley JL 3rd, Robinson ME, Wise EA, Price DD. A meta-analytic review of pain perception across the menstrual cycle. Pain 1999;81:225-35.
7. Fillingim RB, Maixner W, Girdler S, et al. Ischemic but not thermal pain sensitivity varies across the menstrual cycle,. Psychosom Med 1997; 59:512-20.
8. Ohel I, Walfisch A, Shitenberg D, et al. A rise in pain threshold during labor: a prospective clinical trial. Pain 2007;132 (Suppl 1):104-8.
9. Dunbar AH, Price DD, Newton RA. An assessment of pain responses to thermal stimuli during stages of pregnancy. Pain 1988;35:265-9.
10. Cogan R, Spinatto JA. Pain and discomfort thresholds in late pregnancy. Pain 1986;27:63-8.
11. Whipple B, Josimovich JB, Komisaruk BR. Sensory thresholds during the antepartum, intrapartum, and postpartum periods. Int J Nursing Stud 1990;27:213-21.
12. Amodei N, Nelson-Gray RO. Reactions of dysmenorrheic and nondysmenorrheic women to experimentally induced pain throughout the menstrual cycle. J Behav Med 1989; 12:373-85.
13. Rolke R, Baron R, Maier C, et al. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): standardized protocol and reference values. Pain 2006;123:231-43.
14. Vermani E, Mittal R, Weeks A. Pelvic girdle pain and low back pain in pregnancy: a review. Pain Pract 2010;10:60-71.
15. Ostgaard HC, Andersson GB, Schultz AB, Miller JA. Influence of some biomechanical factors on low-back pain in pregnancy. Spine 1993;18:61-5.
16. MacLennan AH, Nicolson R, Green RC, Bath M. Serum relaxin and pelvic pain of pregnancy. Lancet 1986;2 (8501):243-5.
17. Björklund K, Naessén T, Nordström ML, Bergström S. Pregnancy-related back and pelvic pain and changes in bone density. Acta Obstet Gynecol Scand 1999;78:681-5.
18. Bajaj P, Bajaj P, Madsen H, Møller M, Arendt-Nielsen L. Antenatal women with or without pelvic pain can be characterized by generalized or segmental hypoalgesia in late pregnancy. J Pain 2002;3:451-60.
19. Jimenez JM, Tyson JE, Reisch JS. Clinical measures of gestational age in normal pregnancies. Obstet Gynecol 1983;61:438-43.
20. Wong, C.A. Obstetric pain. In: Fishman, S.M., Ballantyne, J.C., Rathmell, J.P. (eds.) Bonica's Management of Pain, 4th edn. Lippincott Williams&Wilkins, Philadelphia, pp. 2010;786-91.
21. Oshima M, Ogawa R, Londyn D. Current perception threshold increases during pregnancy but does not change across menstrual cycle. J Nippon Med Sch 2002;69:19-23.
22. Gutke A, Ostgaard HC, Oberg B.Pelvic girdle pain and lumbar pain in pregnancy: a cohort study of the consequences in terms of health and functioning. Spine 2006; 31:E149-155.
23. Foster TC. Interaction of rapid signal transduction cascades and geneexpression in mediating estrogen effects on memory over the life span. Front Neuroendocrinol 2005; 26:51-64.
24. Cunningham, FG, MacDonald PC, Gant NF, Leveno KJ, Gilstrap LC, Hankins GD, Clark SL (eds.) Williams Obstetrics. Appleton&Lange, NewYork, pp. 1997;144-5.
25. Watanabe S, Otsubo Y, Araki T.The current perception thresholds in normal pregnancy. J Nippon Med Sch 2002; 69:342-6.