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Responses to mechanical and electrical stimuli are not attenuated by late pregnancy

C. STAIKOU (*), I. SIAFAKA (**), G. PETROPOULOS (***), A. KATAFIGIOTI (****) and A. FASSOULAKI (*****)

Abstract : Pregnancy has been associated with increased pain threshold. This study investigates the responses to mechanical and electrical stimuli in pregnant and non-pregnant women. Thirty pregnant women were subjected before and four days after elective caesarean section under regional anaesthesia to mechanical and electrical stimuli on both forearms. Thirty nonpregnant women were subjected to the same stimuli at the same time points. The responses to mechanical stimuli were expressed in mm of the Visual Analogue Scale (VAS) and averaged for both forearms. The VAS scores obtained after the electrical stimuli were divided by the mA recorded when the stimulus was applied, expressed in mm/mA and averaged. The responses to mechanical stimuli recorded before and four days after application did not differ between the two groups ($F = 0.884$, $df = 3,116$, $P = 0.452$). In the pregnant group the VAS values before and four days after the caesarean section were 16.4 ± 14.4 mm and 12.8 ± 12.5 mm respectively. In the nonpregnant group the VAS values recorded four days apart were 17.5 ± 14.3 mm and 13.4 ± 11.9 mm respectively. The responses to electrical stimuli applied four days apart also did not differ between the two groups ($F = 2.433$, $df = 3,116$, $P = 0.069$). The VAS values obtained after the first and second application of the electrical stimulus were 0.914 ± 0.606 mm/mA versus 0.586 ± 0.410 mm/mA in the pregnant and 0.853 ± 0.538 mm/mA versus 0.725 ± 0.467 mm/mA in the nonpregnant group. These results, under the study conditions, do not support the hypothesis that late pregnancy is associated with increased antinociception in humans.

Key words : Pregnancy ; antinociception ; mechanical stimulation ; electrical stimulation ; caesarean section.

INTRODUCTION

Increased pain thresholds, wider dermatomal spread of local anaesthetics under subarachnoid and epidural anaesthesia and reduced anaesthetic requirements, all have been associated with pregnancy (8, 9, 13, 16). In pregnant subjects requirements for inhaled anaesthetic agents are decreased, and chronically administered progesterone decreases halothane requirements in rabbits (13, 16).

Higher plasma and CSF progesterone concentrations detected during pregnancy could contribute to the changes in pain perception and decreased anaesthetic/analgesic requirements (1). On the other hand, in pregnant animals intrathecal application of a κ-opioid receptor selective antagonist and a δ-opioid receptor antagonist diminished the pregnancy related increase in pain threshold (2, 3). Circulating oestrogens and progesterone activate the κ- and δ- endogenous opioid antinociceptive systems but the mechanism is unknown (4, 10).

This prospective, open, controlled study was designed to test the hypothesis that pain response to stimuli during pregnancy is decreased. For this reason, the response to a mechanical and an electrical stimulus in pregnant women before and four days after elective caesarean section was investigated. The same stimuli were also applied to female, age-matched, non-pregnant volunteers.

C. STAIKOU, M.D., D.E.A.A. ; I. SIAFAKA, M.D. ; G. PETROPOULOS, M.D. ; A. KATAFIGIOTI, M.D. ; A. FASSOULAKI, M.D., Ph.D., D.E.A.A.
Department of Anaesthesia, Aretaieion Hospital, Medical School, University of Athens, 75, Vassilissis Sofias Avenue, Athens 11528, Greece.
(*) Instructor, Department of Anaesthesia, Aretaieion Hospital, Medical School, University of Athens.
(**) Assistant Professor, Department of Anaesthesia, Aretaieion Hospital, Medical School, University of Athens.
(***) Instructor, Department of Anaesthesia, Aretaieion Hospital, Medical School, University of Athens.
(****) Resident in Anaesthesia, Department of Anaesthesia, Aretaieion Hospital.
(*****) Professor and Chairperson, Department of Anaesthesia, Aretaieion Hospital, Medical School, University of Athens.
Correspondence address : A. Fassoulaki, 57-59 Raftopoulou Street, Athens 11744, Greece. Tel./fax : 30210 9024530.
Tel. : 30210 7286334 and 30210 7286323.
E-mail : afassou1@otenet.gr.
E-mail : fassoula@aretaieio.uoa.gr.

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METHODS

Participants

The study was approved by the Local Ethics Committee and written informed consent was obtained from all subjects. Thirty pregnant women scheduled for elective caesarean section were recruited in this prospective, open study, which was conducted in the Aretaieion Hospital. We studied concurrently a control group of 30 nonpregnant women, to assess the impact of learning (previous exposure to the stimulus) on the reporting of VAS scores. Exclusion criteria for participants of both groups were smoking, history of drug use, neurologic, metabolic and endocrinological diseases, concurrent pain conditions and use of analgesics. Women with complications of pregnancy were also excluded from the study.

All measurements of responses to stimuli in the pregnant and nonpregnant group were carried out by the same investigator (last author) and during morning hours, between 8 and 11 a.m. The subjects during test application were in a quiet environment in a sitting position. The assessment of pain response to a mechanical and an electrical stimulus was explained to all women. The investigator was exposed to both stimuli before applying the tests to each subject for first time. The visual analogue scale (VAS) was also explained. Each subject was given a sliding ruler and was asked to move it along a distance of 100 mm, according to the degree of pain after each stimulus, the 0 mm representing no pain and the 100 mm the worst, unbearable pain. The divisions were marked on the reverse side of the ruler.

For caesarean section pregnant women received spinally 1.7 to 1.8 ml of 0.5% levobupivacaine at the L3-L4 intervertebral space with a 27 gauge spinal needle through a Tuohy epidural needle. The spinal needle was withdrawn, and an epidural catheter was threaded in, via the Tuohy needle. Postoperative analgesia consisted of 10 ml of 0.2% ropivacaine every 6 hours for the following 72 hours. Women requiring other analgesics given systematically should be excluded from the study.

Mechanical and electrical stimuli

A pressure palpator was firmly applied to the medial volar surface of each forearm for 3 sec. The pressure palpator, used also in previous studies (5, 6), exerts a standardized mechanical painful stimulus of 650 gr (Pressure Feeler 650 gr Sedatelec® ; Chemin des Muriers, Irigny, France). A 2 Hz, 0.25 msec square wave electrical impulse was applied in the same sequence (right or left forearm first) but approximately 5 to 6 cm peripherally to the mechanical stimulus, to avoid possible short lasting hyperalgesia, caused by sensitization from the prior 3 sec mechanical stimulation. The electrical stimulus was applied three times (3 twitches delivered). A peripheral nerve stimulator (Organon®) was used. The current of the electrical stimulus was set at 60 mA. The delivered current (mA) and the VAS score obtained after each stimulus application were recorded.

The order of testing (right versus left forearm) was random, by tossing a coin, heads for right forearm to be tested first, and tails for the left. Four days after the caesarean section all parturients were tested for response to the same mechanical and electrical stimuli, reversing the order of previously tested forearms. Otherwise tests were performed similarly as before delivery. The non-pregnant women received similar stimuli also four days apart.

The VAS values obtained after electrical stimulus were normalized for the current by dividing the VAS (mm) by the mA passing through the skin when the stimulus was applied. For this reason the response to the stimulus is expressed as mm/mA. For each type of stimulus the VAS scores obtained from the right and left forearm were averaged. We compared the averaged VAS values recorded after the mechanical stimulus between the two groups four days apart as well as the averaged VAS values after the electrical stimulus at the same time points.

Statistical analysis

Initial sample size estimation showed that approximately 30 subjects should be included in each group in order to ensure a power of 0.80 for detecting a meaningful difference by one third (33%) in VAS after noxious mechanical stimulation between the two measurement times. The standard deviation of VAS scores after mechanical noxious stimulation, estimated from initial pilot observations, was 13 (in mm), and alpha error was assumed to be 0.05. The normality of distributions was tested using Kolmogorov-Smirnov tests, and the equality of variances between compared variables with Levene's tests. All variables followed normal distribution. Demographics between the two groups and current amplitudes before and after electrical stimulation within each group were compared using independent Student's t-tests. We used multifactorial ANOVA to analyze a) the VAS scores (mm)

Table I

Demographic data

	Pregnant group	Nonpregnant group	
Age (years)	31 ± 5.0	32 ± 3.6	P = 0.305
Body Weight (kg)	83 ± 11.2	61 ± 9.7	P < 0.001
Height (cm)	165 ± 6.2	164 ± 4.4	P = 0.429

obtained four days apart after mechanical stimuli in both groups and b) the VAS scores obtained after electrical stimuli (mm/mA) in both groups at the same time points. Values of $P < 0.05$ were considered statistically significant. Statistical analysis was performed using the Microsoft, Excel X for Mac, GB-Stat PPC 6.5.4, and SPSS 11.0.2 for Mac OS X statistical software.

Table II

The VAS scores after application of the mechanical (mm) and the electrical (mm/mA) stimuli in each group four days apart

VAS mechanical (mm)	Pregnant group	Nonpregnant group
First application		
Mean	16.4 ± 14.4	17.5 ± 14.3
CI	5.1	5.1
Second application		
Mean	12.8 ± 12.5	13.4 ± 11.9
CI	4.5	4.2
VAS electrical (mm/mA)		
First application		
Mean	0.914 ± 0.606	0.853 ± 0.538
CI	0.22	0.19
Second application		
Mean	0.586 ± 0.410	0.725 ± 0.467
CI	0.15	0.17

Values are mean ± SD. No significant difference between the groups.

Results

Demographics of the pregnant and nonpregnant participants are shown in Table I. The two groups did not differ except for the body weight, pregnant participants being heavier.

With regard to the mechanical stimulus, the VAS scores obtained from the pregnant group before and after cesarean section and from the nonpregnant group at the same time points did not differ between the two groups ($F = 0.884$, df = 3,116, $P = 0.452$). Similarly, the responses to electrical stimulus did not differ between the pregnant and nonpregnant groups before and after the application of the stimulus ($F = 2.433$, df = 3,116, $P = 0.069$). The VAS values before and after mechanical and electrical stimuli in each group are shown in Table II and figures 1 and 2.

The intensity of the current passing the skin was lower during the first application of the stimulus when compared with the current intensity four days later. Thus we recorded 41.6 ± 8.4 mA versus 48.8 ± 5.4 mA, ($P < 0.001$) in the pregnant participants and 38.9 ± 6.9 versus 41.8 ± 4.54 mA ($P = 0.018$) in the non-pregnant participants.

Discussion

Our results failed to show a change in the response to a mechanical or electrical stimulus in parturients four days after an elective caesarean section as well as in the nonpregnant group.

In rats pregnancy has been associated with a profound antinociception. Extradural administration

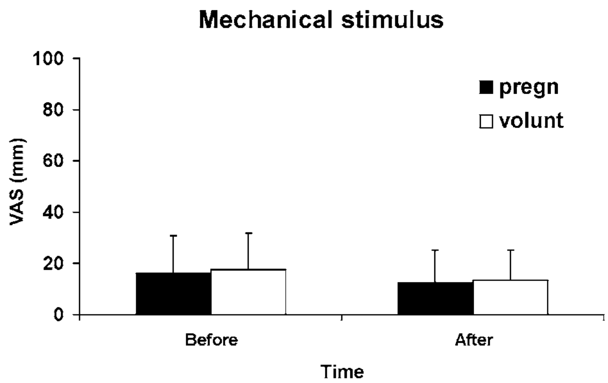

Fig. 1. — Mean ± SD values of VAS obtained four days apart in the pregnant and in the volunteer groups after application of a mechanical stimulus.

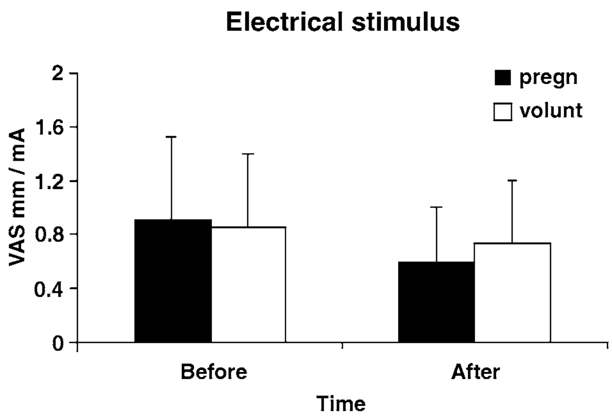

Fig. 2. — Mean ± SD values of VAS obtained four days apart in the pregnant and in the volunteer groups after application of an electrical stimulus.

of lidocaine in pregnant rats had a longer antinociceptive effect on visceral and somatic antinociception than in nonpregnant rats (12). Also, in pregnant rats the pain threshold as assessed by reflexive jumping elicited after electric shock was increased (11).

However, results from animal studies cannot be extrapolated to humans. In humans, changes in postpartum progesterone levels did not correlate with the postpartum reduction in current perception threshold (14). In another clinical study the current perception threshold was quantitatively evaluated in 10 full term gestation pregnant women and in 14 healthy, age-matched female volunteers (18). No difference was found between the two groups for the 5 and 250 Hz stimuli. The current perception threshold was increased in pregnant women only for the 2000 Hz stimulus (18).

In gravid women, increased values of current perception threshold in myelinated fibers (Aβ and Aδ for the 2000 and 250 Hz stimuli respectively) were found when compared to non-gravid women. The investigators used sinusoidal alternating currents at 2000, 250 and 5 Hz at intensities 0 to 10 mA, until a specific sensation was reported by the subject. The sensory current perception threshold was found less after parturition when compared with the values obtained before elective caesarean section, the 5 Hz stimulus exhibiting the most pronounced decrease (15).

Our results are not consistent with the results reported by OSHIMA *et al.* (14), though both studies compare sensory changes during and after pregnancy. Regarding the mechanical stimulus, this has not been tested in previous studies. The electrical stimulus we applied was 2 Hz and set to release a current of 60 mA, but the current released varied. For this reason we normalized the VAS values dividing them by the mA passing through the skin. The type of stimuli applied, mechanical versus electrical, the frequency (Hz) and the intensity (mA) of the electrical stimuli, the duration of application, and the site of application, may be some of the reasons for the different results. Regarding the site of application, our methodology is more accurate, since we obtained responses from both forearms, averaged them, and repeated the tests four days later.

Pain threshold and pain tolerance assessed in women in labour before and one hour after extradural analgesia were significantly decreased 24 hours later (post-delivery) (17). No control group was examined in this study. However, labor pain stimulates the release of β-endorphin and of cortisol in the maternal plasma. On the contrary, the pregnant women in our study were scheduled for elective caesarean section and did not experience any labor pain. In a previous study, parturients scheduled for caesarean section, consumed more morphine postoperatively using PCA (patient controlled analgesia) than patients having total abdominal hysterectomy, both groups operated under combined spinal-epidural anaesthesia (7).

Limitations of our study are the short period between the pre and postpartum tests and the relatively low intensity of the stimuli. We conducted the tests only four days after the caesarean section as parturients leave the hospital on the postoperative fourth day. Mothers were unwilling to come back to the Hospital to have these tests beyond the 4th day due to their family duties. Besides, SHAPIRA *et al.* found a difference in pain tolerance 24 hours after delivery, which is not consistent with our results obtained on the 4th postdelivery day (17). High intensity stimuli are not acceptable by many patients, and we believe these should be avoided in pregnant women for ethical reasons.

In contrast to the previous investigators, who studied changes in sensory current perception threshold after delivery, our study was conducted to detect changes in the perception of pain intensity from application of stimuli, both mechanical and electrical. An increased threshold to perceive a stimulus does not necessarily represent increased threshold to a noxious stimulus neither decreased perception of pain intensity.

In conclusion, under the present experimental design, our results suggest that the response to a mechanical and an electrical stimulus in full term pregnant women the day before elective caesarean section does not differ from the response to the same stimuli, applied four days after caesarean section. The nonpregnant group exhibited the same behavior to the same stimuli and for the same time points, and therefore the analgesic requirements in the parturients may be similar to the nonpregnant women.

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