PREGNANCY AT TERM DOES NOT ALTER THE RESPONSES TO A MECHANICAL AND AN ELECTRICAL STIMULUS AFTER SKIN EMLA APPLICATION

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Abstract

Background: Pregnancy is associated with reduced local anesthetic requirements and increased pain thresholds, possibly due to hormonal changes and activation of endogenous opioids.

Methods: We compared the responses to a mechanical and an electrical stimulus in 30 pregnant women (pregnant group) scheduled for cesarean section and 30 healthy female volunteers (control group) matched for age. Pain was assessed by Visual Analogue Scale (VAS) on two different days after skin application of EMLA or placebo cream on the forearms. EMLA and placebo cream were randomly applied on the medial surface of both forearms for 30 min in a blind cross over manner and the subjects received a mechanical stimulus generated through a pressor palpator followed by an electrical stimulus generated through a nerve stimulator.

Results: Average VAS values from both trials did not differ between pregnant and control group exposed to the mechanical or electrical stimulus after EMLA application or after mechanical or electrical stimulus after placebo cream application.

Conclusions: Late pregnancy is not associated with increased sensitivity to local anesthetics (EMLA) applied to the skin, under our study conditions.

Key words: pregnancy, pain perception, mechanical stimulus, electrical stimulus, local anesthesia; EMLA.

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Introduction

Decreased local anesthetic requirements during regional analgesia, increased sensitivity to local anesthetics and increased pain thresholds have all been reported during pregnancy. Mechanical factors such as increased lumbar lordosis and/or distension of the epidural veins, or hormonal alterations, such as increased progesterone and estrogen levels, have been implicated to explain the above changes.

The present study was designed to investigate in pregnant women of 38 weeks of gestation the response to a mechanical and an electrical stimulus after skin application of Eutectic Mixture of Local Anesthetics (EMLA). These responses were compared to the responses obtained from nonpregnant young women treated similarly.

Materials and Methods

Study population

After Institutional Review Board approval and patient written informed consent, 30 parturients ASA I-II with singleton pregnancy (24 primiparas and 6 multiparas) of completed 38 weeks of gestation scheduled for elective cesarean section, and 30 healthy female volunteers matched for age range, were enrolled in this prospective study. Exclusion criteria consisted of body weight more than 20% of the ideal body weight for volunteers and more than 20 Kg weight gain during pregnancy for parturients, complicated pregnancy, thyroid gland disease, central or peripheral nerve disease, diabetes mellitus, hypertension, analgesic consumption or illegal drug abuse, alcoholism and non-Greek speaking language.

Study protocol

The mechanical and electrical stimuli were demonstrated to all participants and the Visual Analogue Scale (VAS) was explained the day before. Tests were performed by the same investigator (A.K) on two consecutive days in both the parturients and the controls. All subjects were tested in the sitting position in a quiet room during the morning hours.

Day 1: An independent anesthesiologist filled syringes of 2 ml with EMLA, or placebo creams, and applied these on the medial surface of the forearm in the middle of the distance between the wrist and the elbow. Both creams were covered with Tegaderm™ tape. The forearm right versus left to receive EMLA cream was determined by tossing a coin, heads indicating EMLA application on the right and tails on the left forearm. Thirty minutes later the creams were removed and the responses to a mechanical and electrical stimulus were assessed by Visual Analogue Scale (VAS).

Day 2: Both parturients and control subjects were exposed to the same tests on the following day but in a reverse order regarding EMLA and placebo application on the right versus the left forearm.

Unless contraindicated, epidural analgesia was the technique of choice. Mechanical and Electrical Stimuli.

Mechanical stimulus was applied for 3 sec by a pressure palpator (Pressure Feeler 650 gr Sedatelec®; Chemin des Muriers, Irigny, France) exerting a standard force on its end of 650 gr. This was followed by an electrical stimulus consisted of a 2Hz, 0.25 msec square wave electrical impulse, generated by a peripheral nerve stimulator (Organon®).

The primary endpoint of our study was the VAS scores obtained in pregnant and nonpregnant women after applying a mechanical and an electrical stimulus on the skin exposed to EMLA and to placebo cream.

Statistical Analysis

Statistical analysis was conducted using the SPSS version 13.0 (SPSS Inc., Chicago IL). Patient characteristics between the two groups were compared with Student’s t-test and smoking habit was analyzed with X² test.

VAS scores obtained after EMLA application on the right and left forearm of the same subject were averaged. Similarly were treated VAS scores after placebo cream.

VAS scores obtained after mechanical and electrical stimuli following EMLA application as well as VAS scores obtained after mechanical stimulus following placebo cream application did not follow a normal distribution (Kolmogorov-Smirnov test) and were compared between the groups with Mann-Whitney test. VAS scores after electrical stimulus following placebo cream followed normal distribution.
Animal studies have shown that pregnancy results in a progressive increase of pain thresholds possibly due to activation of endogenous opioid system and to steroid hormone elevation. Nevertheless these results have not been reproduced in human studies in the same consistent manner. Staikou et al., in a similar setting as in our study, found no difference between pregnant and control subjects regarding pain responses to mechanical and electrical stimuli. Also Dunbar et al., reported no differences in VAS scores after nociceptive thermal stimuli before or after pregnancy, although no control group was investigated. Coolkasian et al., found that pregnant women are more willing to report pain than non pregnant subjects. Saisto et al., reported reduced pain tolerance and increased VAS scores after cold pressor test in pregnant women fearing labor pain than pregnant women not fearing labor pain. All subjects reported increased VAS scores before than after delivery but no change in pain endurance.

In contrast Cogan et al., reported increased pain thresholds, after a pressure stimulus, before delivery than after delivery and increased discomfort thresholds between pregnant and controlled subjects.

Also electrical stimuli of 5, 250 and 2000 Hz have resulted in increased pain thresholds during pregnancy with greatest reduction observed at 5Hz stimulation. Nevertheless no control group was included in this study and the study population was small. Carvalho et al., in a recent controlled study found increased heat pain tolerance in pregnant women a finding not reproduced by cold pressor stimulus.

The controversial results in humans might be attributed to lack of control group in most studies, to different stimuli used to access the pain perception, to different time points of testing, but also to interindividual variability.

Enhancement of local anesthetic effects has been also documented during pregnancy, and although the reason is not clear, hormonal and mechanical factors have been investigated. Datta et al, found decreased latency of conduction block of nerve fibers from pregnant rabbits to bupivacaine, suggesting either increased sensitivity or enhanced diffusion to receptor site due to increased progesterone levels during pregnancy. Flanagan et al in two studies showed that chronic exposure of rabbit nerve fibers to progesterone

<table>
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<th>Stimulus</th>
<th>Pregnant</th>
<th>Controls</th>
<th>p</th>
<th>Z</th>
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</thead>
<tbody>
<tr>
<td>Mechanical</td>
<td>EMLA</td>
<td>20(18)</td>
<td>19(10.8)</td>
<td>0.58</td>
<td>-0.54</td>
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<tr>
<td></td>
<td>Placebo</td>
<td>20(14.5)</td>
<td>19(11.8)</td>
<td>0.883</td>
<td>-0.14</td>
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<tr>
<td>Electrical</td>
<td>EMLA</td>
<td>26(22)</td>
<td>24(16.6)</td>
<td>0.853</td>
<td>-0.18</td>
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<tr>
<td></td>
<td>Placebo</td>
<td>21.4(15)</td>
<td>17(10.1)</td>
<td>0.21</td>
<td>1.24</td>
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</table>
Long term exposure to progesterone might play
the key role as Bader et al, could not find an effect of
acute progesterone treatment in conduction blockade
of isolated rabbit vagus nerve24. Hirabayashi et al.,
found that pregnancy at second, third trimester and at
term, enhances the spread of hyperbaric amethocaine
compared to nonpregnant or to first trimester
pregnant women, which again supports the role of
progesterone rather than mechanical factors producing
these changes3. Progesterone alterations have also
been proposed to explain the decrease halothane25,
enflurane26 thiopental requirements during pregnancy27
although the mechanism remains unknown.

Nevertheless, mechanical factors cannot be
excluded to explain subarachnoid block alterations
during pregnancy. James et al., in a non blinded
study, have shown increased anesthetic requirements
in preterm women (28-35 weeks of gestation) than at
term women (38-42 weeks of gestation) presenting for
cesarean section28. They also found a strong correlation
between fundal height taken from the symphysis pubis
to the fundus and the block height achieved. Fassoulaki
et al, found higher level of subarachnoid sensory block
with hyperbaric lidocaine in pregnant compared to non
pregnant women2.

Our results are in contrast to the results of
Butterworth et al., who found increased susceptibility
of the median nerve to 5 ml of 1% lidocaine HCL in
pregnant women29. We chose EMLA cream which
penetrates the intact skin and successfully obliterates
pain during pinprick30, so the local anesthetics used
in Butterworth and in our study are not comparable.
Eogan et al., found prolonged median nerve latencies
in pregnant compared to non pregnant subjects which
might be the underlying reason of the results of
Butterworth31.

A limitation of our study is the short time of
EMLA application (30 min), as it has been shown that
increased time of application or increased time between
removal of the EMLA and stimulus application results
in more effective blockage of nociceptive receptors as
assessed with laser stimulus32,33.

In conclusion, the response to a mechanical and
an electrical stimulus after EMLA or placebo cream
application to the skin, did not differ between pregnant
and non-pregnant women.
References


