Nocebo-Induced Hyperalgesia During Local Anesthetic Injection

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Common practice during local anesthetic injection is to warn the patient using words such as: “You will feel a big bee sting; this is the worst part.” Our hypothesis was that using gentler words for administration of the local anesthetic improves pain perception and patient comfort. One hundred forty healthy women at term gestation requesting neuraxial analgesia were randomized to either a “placebo” (“We are going to give you a local anesthetic that will numb the area and you will be comfortable during the procedure”) or “nocebo” (“You are going to feel a big bee sting; this is the worst part of the procedure”) group. Pain was assessed immediately after the local anesthetic skin injection using verbal analog scale scores of 0 to 10. Median verbal analog scale pain scores were lower when reassuring words were used compared with the harsher nocebo words (3 [2–4] vs 5 [3–6]; P < 0.001). Our data suggest that using gentler, more reassuring words improves the subjective experience during invasive procedures. (Anesth Analg 2010;110:868–70)

METHODS

Healthy parturients at term requesting labor epidural analgesia or nonlaboring parturients presenting for elective cesarean delivery under spinal anesthesia were included in this study. Exclusion criteria included administration of opioids in the 4 hours before study enrollment, IV magnesium sulfate within the last 24 hours, diabetes mellitus (Type I and II), >1 attempt at IV cannulation during the current admission, neurocardiogenic signs or symptoms (e.g., dizziness, lightheadedness, bradycardia, and syncope) during IV cannulation, and cervical dilation <2 or >6 cm (if in labor).

Patients were randomized to 1 of 2 different choices of words used during the administration of the local anesthetic. In the nocebo group, patients were told: “You are going to feel a big sting and burn in your back now, like a big bee sting; this is the worst part of the procedure.” In the placebo group, the words used were “We are going to inject the local anesthetic that will numb the area where we are going to do the epidural/spinal anesthesia and you will be comfortable during the procedure.” Three milliliters of lidocaine 10 mg/mL was injected intradermally and subcutaneously over 3 seconds through a 25-gauge needle to create a skin wheal during an interval between contractions. During the local anesthetic injection, only the anesthesiologist gave verbal instructions to the patients; the nurse was requested to remain silent throughout this portion of the procedure. Immediately after the local anesthetic injection, a blinded observer was called into the room to assess the patient’s pain on an 11-point verbal analog scale (VAS) from 0 (no pain) to 10 (worst imaginable pain). After collection of the VAS score, the study was considered complete and the remainder of the anesthetic was performed as per usual clinical routine.

The protocol was approved by our IRB, with allowance for waiver of informed consent. Waiver of informed consent may be requested and is allowed when the following criteria are met: (a) the research involves no additional risk to the patient over what is already involved in the provision of standard clinical care, (b) the waiver will not adversely affect the rights and welfare of the subjects, (c) the research could not practicably be performed without the waiver, because a description of the choice of words and goals of the study would almost certainly influence the responses of the patients, and (d) additional information about the study is provided, when appropriate, to the patients after completion of the data collection.

The primary outcome was VAS pain scores. To detect a minimal difference of 30% in VAS pain scores as the smallest meaningful reduction in pain5 between nocebo and placebo groups, with a power β = 0.8 and α = 0.05, a sample size of at least 59 patients in each group is required. One hundred forty patients were randomized using a


**DISCUSSION**

The principal finding of this investigation is that the words used during local anesthetic skin wheal administration have a significant influence on the subjective experience of pain as reported by our patients. Physicians and nurses often use relatively harsh words to describe invasive procedures in an attempt to prepare, and possibly calm and reassure, the patient in advance of what may be an uncomfortable procedure. Our results indicate that this approach may be wrong. The use of harsher words actually increased the subjective experience of pain, whereas the use of more calming and reassuring words resulted in lower pain scores.

Previous work in non-obstetric settings has found similar results. After abdominal hysterectomy, an increase in VAS scores, plasma cortisol levels (as an indirect stress marker), and postoperative morphine consumption administered via patient-controlled IV analgesia were noted when “negative” words were used compared with “positive” words. In an interventional radiology setting, warning patients before potentially painful procedures using descriptive words that conveyed painful or undesirable experiences increased the patients’ pain and anxiety. These authors concluded that neutral statements, positive suggestions, or providing distraction should be the focus of the communication. One study randomized patients to either harsh or gentler words during IV cannulation before elective surgery. Pain, as measured by spontaneous patient vocalization of discomfort and assessed by the anesthesiologist performing the IV insertion, was less when gentler words were used, and these authors concluded that warning patients of a “sting” before IV cannulation may not be helpful. However, the authors did acknowledge that the lack of blinding represents a limitation of their study and also that there are logistical problems with obtaining informed consent for randomized trials that involve behavioral interventions. Thus, even though our results are consistent with those of others, our current study improves on those previous investigations by using a blinded observer to assess pain scores, and intentional omission of informed consent.

Perioperative and intrapartum communication skills have long been recognized as integral to the care we provide. The American Board of Anesthesiology requires the anesthesiologist to “demonstrate effective interpersonal and communication skills that result in the effective exchange of information and collaboration with patients, their families and other healthcare professionals.” Using language with negative content during invasive procedures can increase patients’ anxiety and pain. Obstetric patients can place particular demands on the interpersonal skills of an anesthesiologist. Childbirth is an inherently stressful event, and sedatives are rarely, if ever, used during routine obstetric anesthetics. Hence, patients are wide awake and acutely aware of their surroundings during normal obstetric anesthesia procedures. Moreover, obstetric anesthesiologists often have little time to develop a relationship of trust and rapport with their patients. Thus, any tools, including verbal and other subtle communication methods (e.g., body language, tone of

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**Table 1. Anthropometric Data**

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Nocebo</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>33 ± 1</td>
<td>32 ± 1</td>
<td>0.29</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30 ± 1</td>
<td>29 ± 1</td>
<td>0.68</td>
</tr>
<tr>
<td>Gestational age (wk)</td>
<td>39 (38–40)</td>
<td>39 (38–40)</td>
<td>0.27</td>
</tr>
<tr>
<td>Gravity</td>
<td>2 (1–3)</td>
<td>2 (1–2)</td>
<td>0.07</td>
</tr>
<tr>
<td>Parity</td>
<td>1 (0–1)</td>
<td>1 (0–1)</td>
<td>0.34</td>
</tr>
<tr>
<td>Cervical dilation*</td>
<td>4 (2–6)</td>
<td>4 (2–6)</td>
<td>0.57</td>
</tr>
</tbody>
</table>

Data are presented as mean and standard deviation (mean ± sd) or median (interquartile range).

BMI = body mass index.

* Cervical dilation (median [min–max]) at initiation of analgesia is calculated for labor group only, because the cesarean delivery group consisted only of elective procedures in patients not in labor.

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**RESULTS**

Seventy patients were enrolled into the placebo and 70 in the nocebo group. Anthropometric data are presented in Table 1. The nocebo group reported a significantly higher score after injection of the local anesthetic compared with the placebo group (Fig. 1). Subgroup analysis of the VAS in the labor analgesia and the cesarean delivery groups still shows a marked increase in the pain scores of the nocebo compared with the placebo group (Fig. 2).
voice, and facial expressions) that can enhance our relationships with patients may be useful.

The growing popularity and efficacy of hypnotic techniques for use during invasive procedures or during labor attest to the importance of nonpharmacologic methods of pain control. Many nonpharmacologic methods of analgesia are entirely compatible with pharmacologic techniques. For example, the use of hypnotic procedures or a trained labor support personnel member such as a doula can be effective even in the presence of an epidural analgesic. Likewise, our findings suggest that the words used during local anesthetic skin wheal injection can complement the pharmacologic analgesia produced by the lidocaine injection.

Our findings are in contrast to popular belief and practice of both physicians and nurses. It is common practice to warn patients with harsh words such as “bee sting!,” “big ouch!,” “lots of burning!,” or “worst part!” before invasive procedures, even relatively simple procedures such as IV placement or local anesthetic skin wheal injection. Although these warnings are made with good intent to prepare the patient for what may be an uncomfortable event, in reality we may be inducing a “nocebo” effect and actually worsening the discomfort. Providers need to be cognizant of the implications of the words they use and other communication tactics that frame the patient’s perception of the actual experience.

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REFERENCES